KAUNAS UNIVERSITY OF TECHNOLOGY

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SYNTHESIS AND CHARACTERIZATION OF NEW 1',3,3',4-TETRAHYDROSPIRO[CHROMENE-2,2'-INDOLE] DERIVATIVES

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SYMBOLS AND ABBREVIATIONS

δ - Chemical shift (NMR)
^{13}C NMR – Carbon ^{13}C isotope magnetic resonance
^{15}N NMR – Nitrogen ^{15}N isotope magnetic resonance
^{1}H NMR – Hydrogen ^{1}H magnetic resonance
BIPS – benzoindolinospiropyran
COSY – Correlation Spectroscopy (NMR)
DCC – N,N-dicyclohexylcarbodiimide
DEPT – Distortionless Enhancement by Polarization Transfer (NMR)
DMAP – dimethylaminopyridine
DMF – Dimethylformamide (solvent)
DMSO – Dimethyl Sulfoxide (solvent)
HSQC – heteronuclear single quantum coherence
Et_2O – Diethyl ether
equiv – equivalent
IR – infrared
mp – melting point
MS – mass spectrometry
NMR – nuclear magnetic resonance
NOESY - nuclear Overhauser effect spectroscopy
ppm – parts per million
R_f – retention factor
rt – room temperature
TEA – Triethylamine
TFA – Trifluoroacetic acid
THF – Tetrahydrofuran (solvent)
TLC – thin layer chromatography
UV – ultraviolet
Vis – visible
XRD – X-ray diffraction

1. INTRODUCTION

Relevance of the work. As material science developed, many new cost-efficient high-quality materials began to be exploited in various fields of engineering and environmental monitoring. During the last ten decades, the materials have become multifunctional and started requiring the optimization of different properties and characterizations for various applications including commercial, industrial, medical and research functions.

Molecular switches have the potential for use in a number of advanced technologies. The defining characteristic of these compounds is their ability to shift between different states when affected by various stimuli, such as light, temperature, electric current, or changes in pH [1]. Light-driven molecular switches are components of photochromic systems that undergo reversible changes in their ground state when irradiated with UV light and revert back to the original state when exposed to light of a different wavelength or via thermal routes [2]. As reversible structural changes occur at a single-molecule level, the phenomenon is potentially interesting for the miniaturization of optic devices down to the molecular level and for applications in molecular opto-electronics, especially for information storage, controlling of photochromic reactions and for the physico-chemical properties of materials.

The detection of anions is also a subject of major importance. Among them, cyanide (CN^-) is a highly hazardous chemical leading directly to the death of human beings, even at small concentrations [3]. Chemical substances containing cyanide occur naturally [4] and are prepared artificially for use in various areas of industry, including the extraction (cyanidation) of gold and silver from ores [5], base metal flotation [6], fumigation of ships, buildings, flour mills, fruits and seeds in vacuum chambers [7] as well as electroplating and case-hardening of metals [8]. Large quantities of sodium cyanide are used to introduce cyano groups into organic compounds [9], in particular through a reaction with organic halogen compounds to yield nitriles [10]. The wide use of cyanides has been creating a number of serious environmental problems due to their high toxicity which ultimately affects human health and wildlife [11] and leads to complicated waste water management [12]. In order to control the presence of cyanide in food, feedstock, drinking water and the environment, numerous studies have focused on the development of methods for its detection including the use of chemosensors in which a change in colour or fluorescence is monitored [13].

It was documented that spiropyran derivative 6-nitro BIPS, well known for its photochromic properties also behaves as a selective and sensitive cyanide anion receptor in aqueous media under UV irradiation[14]. This dye is converted to colored merocyanine form upon UV irradiation, and when cyanide anion is added, the compound-CN^- adduct is formed, which causes the rise of a new absorption band.

In this work, an attempt was made to synthesize a series of spiro[chromene-2,2'-indole] derivatives, to investigate their photochromic properties and to

determine whether they have a potential to be used for spectrophotometric or naked-eye visual cyanide ion detection.

Aim of the work was to synthesize new 1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] derivatives, to investigate their photochromic properties and the potential for cyanide ion detection.

The tasks proposed for the achievement of the above stated aim were as follows:

- Collect and analyze academic literature about the synthesis of indole moiety containing compounds characterized as photochroms and cyanide ion detectors.
- investigate *β*-C alkylation of 2-methylidene-2,3-dihydro-1*H*-indoles with 2-chloromethyl-4-nitrophenol and subsequent spirocyclization.
- investigate *β*-C alkylation of 2-methylidene-2,3-dihydro-1*H*-indoles with 2-chlormethyl-4-(4'-nitrophenylazo)phenol and 2-chlormethyl-4-(2'-chloro-4'-nitrophenylazo)phenol.
- determine photochromic properties of synthesized 1',3,3',4-tetrahydro-6-nitrospiro[chroman-2,2'-indole] derivatives.
- determine the highest potential of 1',3,3',4-tetrahydro-6-nitrospiro[chroman-2,2'-indole] derivatives to detect cyanide ion.

Scientific novelty. A new class of fast photochromic organic molecular switches was designed and synthesized. The reaction of Fisher's base and analogous compounds with 2-chloromethyl-4-nitrophenol resulted in the formation of 1-alkyl-[2-(2-hydroxy-5-nitrophenyl)ethyl-1]-3,3-dimethyl-3*H*-indolium chlorides, which underwent spirocyclization by treatment with a base to afford 1',3,3',4-tetrahydrospiro[chromene-2,2'-indoles] representing a new class of heterocyclic compounds notable for the single C_3-C_4 bond of their pyran ring. Irradiation of the 1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] solutions in acetonitrile with nanosecond laser pulses generated short-lived colored chromophores which thermally reverted back to the ground state over $10^1 – 10^2$ ns.

1',3,3',4-Tetrahydrospiro[chromene-2,2'-indole] derivatives undergo transformations to the colored ring-open form possessing the 4-nitrophenolate or 4-nitrophenylazophenolate chromophore when treated with cyanide in acetonitrile solution buffered with sodium phosphate. They consequently show a distinct color change. This change can be measured spectrometrically or detected by the naked eye. Furthermore, these compounds in particular exhibit high selectivity and are not affected by halide and other anions which are common interferents in the conventional sensing schemes for cyanide. This new chemosensor exhibits high sensitivity to low concentrations of cyanide and also demonstrates a very fast response up to tens of seconds.

Main statements presented for the defense:

1. When 2-methylene-1,3,3-dimethyl-2,3-dihydro-1*H*-indoles are alkylated with 2-chloromethyl-4-nitrophenol, it results in the formation of 1-alkyl-[2-(2-hydroxy-5-nitrophenyl)ethyl-1]-3,3-dimethyl-3*H*-indolium chlorides which undergo an intramolecular nucleophilic addition of the phenolic oxygen to the

α-carbon of the indole moiety by treatment with aqueous ammonia, to yield 1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] derivatives representing a new class of heterocyclic compounds.

2. When 2-methylene-1,3,3-dimethyl-2,3-dihydro-1*H*-indoles are alkylated with 2-chlormethyl-4-(4'-nitrophenylazo)phenol or 2-chlormethyl-4-(2'-chloro-4'-nitrophenylazo)phenol, they yield 1',3,3',4-tetrahydro-6-((4-nitrophenyl)diazenyl)spiro[chromene-2,2'-indole] derivatives.
3. Irradiation of 1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] derivatives (0.1 mM solutions in acetonitrile) with nanosecond laser pulses yields the cleavage of C-O bonds in the 3,4-dihydro-2*H*-pyran rings, forming short-lived colored species identified as *p*-nitrophenolate chromophores. These compounds subsequently revert back to the ground state thermally.
4. A new class of chemosensors based on the 1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] ring system detecting cyanide with high specificity is described. These chemosensors show a distinct color change when treated with cyanide in acetonitrile solution buffered with sodium phosphate due to covalent addition of cyanide anion. This procedure is fast and sensitive; it is not affected by the presence of other common anions.

2. LITERATURE REVIEW

The chemistry of indole had its beginnings in the dye industry and thus for a number of decades was mostly associated with the dye chemistry. The intensive and fertile research of this period produced a highly diverse group of indole moiety containing compounds. Today, the scope of indole chemistry is multiform, extending from the rather simple parent materials, through the condensed systems such as carbazole and its derivatives, the oxygenated indole derivatives, to the extremely complex materials which are synthesized in laboratories or occur naturally and have the potential for use in a number of advanced technologies.

2.1. Synthesis of novel indole moiety containing compounds possessing both photochromic and cyanide ion detection properties

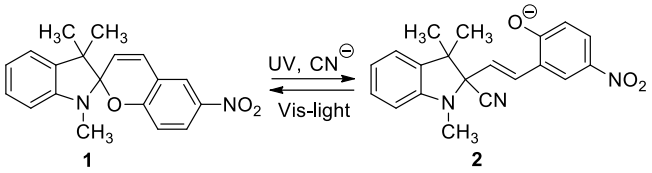
Photochromism is the reversible transformation of a chemical species between two forms by the absorption of electromagnetic radiation, where the two forms have different absorption spectra [15].

Photochromic materials are important for the design of molecular machines [16], chemical sensors [17], optical data storage units [18] and many other technically important devices.

Cyanide anion has been attracting scholarly attention for decades due to its important role in the modern industry, notably, plastics manufacturing, electroplating, gold and silver extraction, tanning, and metallurgy. The source of cyanide-containing chemicals is not only the vast industrial waste, air pollution and vehicle exhaust; such chemicals are also found in some natural biological processes by virtue of being metabolic products of bacteria, algae and fungi. They may also be ingested with food containing cyanogenic glycosides[19] or as a result of smoking [20]. The fatal toxicity of cyanides to organism by deactivation of the electron transport chain at cytochrome c oxidase with resultant inhibition of respiration urges extensive researches into simple but accurate methods for the detection of cyanide pollution.

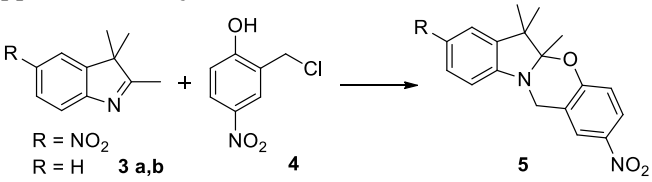
Many research groups are trying to create simple and inexpensive methods for cyanide detection, especially in aqueous environment. Chromogenic sensors tailored to change color when a molecule reacts with a specific analyte appear to be one of the most convenient solutions.

It has been recently found that spiropyran derivative 6-nitro BIPS **1** well known for his photochromic properties also behaves as a selective and sensitive cyanide anion receptor in aqueous media under UV irradiation [14]. This dye is converted to its colored merocyanine form upon UV irradiation and when cyanide anion is added, compound-CN^- adduct **2** is formed causing the rise of a new absorption band (*scheme 2.1*).



Scheme 2.1

Since the cyanide ion has strong nucleophilic properties, reaction-based optical detection mostly relies on nucleophilic addition. Recently Ren et al. [21] discovered that [1,3]oxazine **5** obtained by the reaction of 3*H*-indoles **3** with 2-chloromethyl-4-nitrophenol (**4**) (*scheme 2.2*), which is also known for its photochromic properties[22], selectively upon treatment with cyanide undergoes C-O bond cleavage in its oxazine ring, which is accompanied by the formation of 4-nitrophenolate chromophore and appearance of a yellowish color. This suggests a potential for the application for cyanide detection.

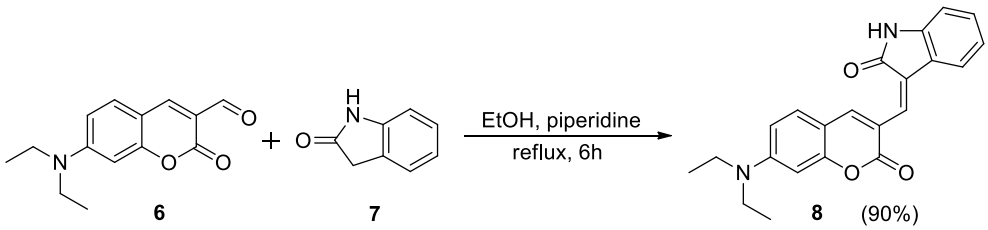


Scheme 2.2

Generally, many different types of chemosensors for the detection of cyanide have been reported. However, considering the exceptionaly high nucleophilicity and weak H-bonding of cyanide compared to other anions, CN^- chemodosimeters have flourished more recently. Based on the type of the functional group undergoing a reaction with cyanide, these chemodosimeters have been classified as cyanide addition to carbon–carbon double bond (Michael type addition), cyanide addition to carbon–heteroatom double bond and cyanide addition to heterocyclium derivatives.

2.2. Indole based cyanide chemosensors

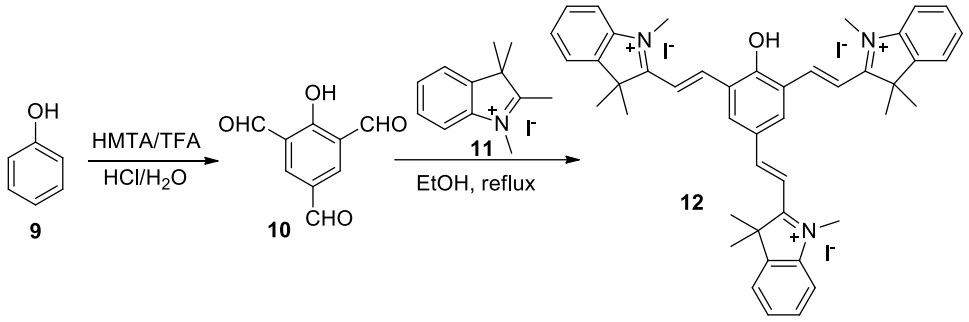
Y. Xu presented cyanide colorimetric and fluorescent chemosensor **8** prepared via a condensation reaction in high yield from 3-acetyl-7-(diethylamino)-2*H*-chromen-2-one (**6**) and indolin-2-one (**7**) (*scheme 2.3*) [23].



Scheme 2.3

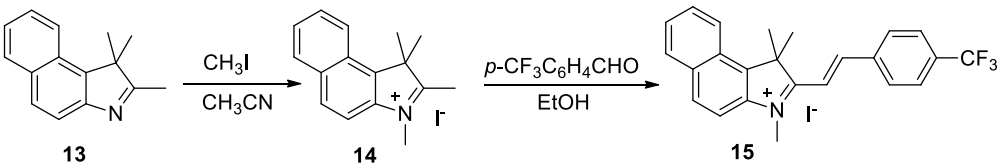
The detection mechanism was proved to be related with the Michael addition reaction induced by cyanide ions, which blocked the intramolecular charge transfer of the probe.

Another new highly selective and turn-on fluorescence probe **12** for the detection of cyanide was conveniently synthesized via the condensation of 2-hydroxy-1,3,5-benzenetricarbaldehyde (**10**) with 1,2,3,3-tetramethyl-3*H*-indolium (**11**) in ethanol (*scheme 2.4*). After the addition of all kinds of anions, only CN^- can induce a turn-on fluorescence accompanying a bluish-green fluorescence color. The mechanism is based on the nucleophilic addition reaction of cyanide anion with the polarized C-N bond of the indolium group blocking the π-conjugation between indolium and 2-hydroxy-1,3,5-benzenetricarbaldehyde [24].



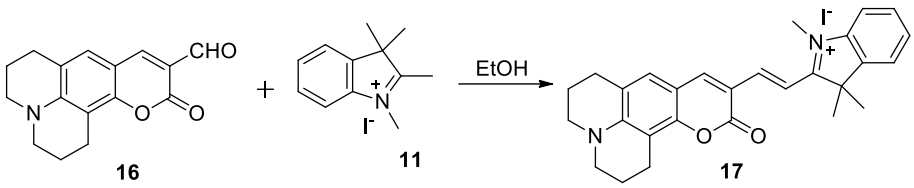
Scheme 2.4

Sun at al. [25] developed a new ratiometric fluorescent cyanide probe **15** bearing a benzo[*e*]indolium moiety as a fluorophore and a binding site. It was synthesized as shown in *scheme 2.5*. The detection of cyanide was performed via the nucleophilic attack of cyanide toward the benz[*e*]indolium group of the probe resulting in a notable fluorescence ratiometric change and a color change.



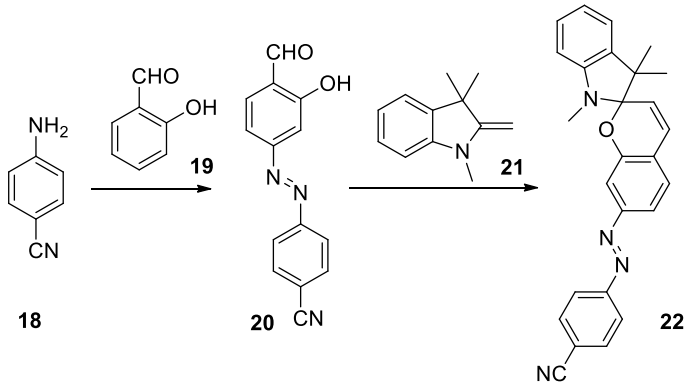
Scheme 2.5

One more colorimetric and 'turn-on' fluorescent chemosensor **17** based on a 4 hybrid coumarin-hemicyanine dye for cyanide was synthesized by K. Xiong et al. [26] via the condensation of coumarinaldehyde (**16**) and 1-methyl-2,3,3-trimethyl-3*H*-indolium iodide (**11**) in ethanol (*scheme 2.6*). The detection of cyanide was performed via the nucleophilic attack toward the polarized C=N bond of the probe.



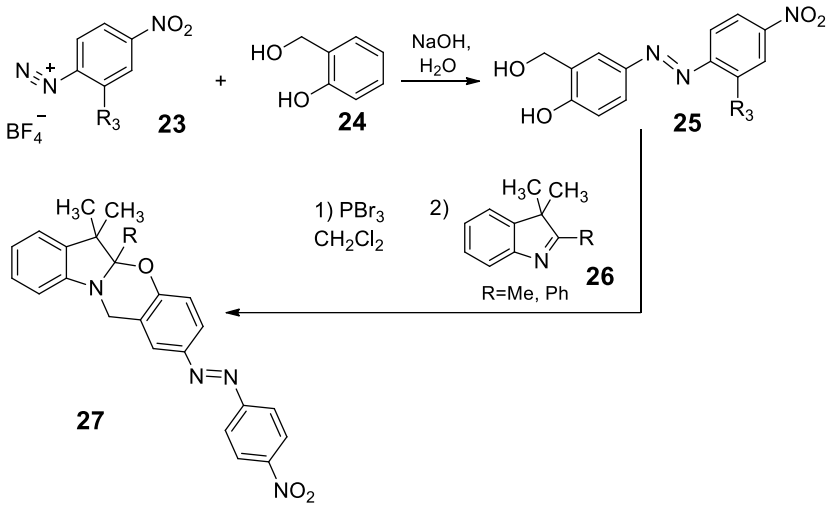
Scheme 2.6

Wang and Kim reported a colorimetric chemodosimeter **22** based on a spiropyrane-azosalicylal conjugated structure (the synthetic route is shown in *scheme 2.7*); the process takes more than 10 minutes for the cyanide ion nucleophilic addition reaction at room temperature and less time when it is under the condition of high temperature [27].



Scheme 2.7

Raymo et al. [28] showed that [1,3]oxazine **27** with the extended structure, having 4-nitrophenylazo moiety (*scheme 2.8*) and forming 4-nitrophenylazophenyl chromophore, when treated with cyanide ion gives an absorption band at 575 nm and is also a potential chemosensor for the cyanide detection. In this case if no phase transfer catalysis is used, the acetonitrile solution of the compound responds to the aqueous solutions of cyanide with a detectable absorbance change only if the cyanide concentration is greater than 0.1 mM. The detection of cyanide is also based on the nucleophilic addition.

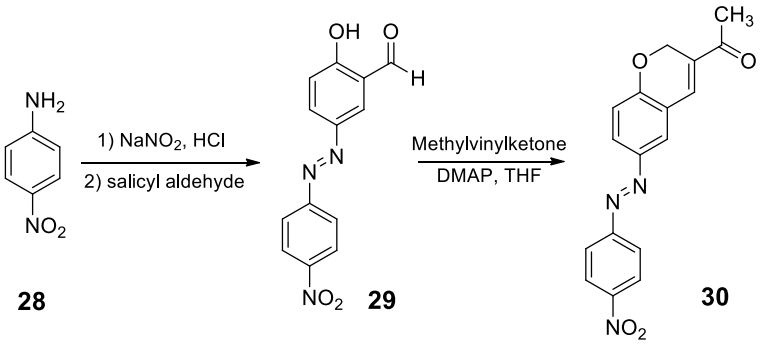


Scheme 2.8

2.3. Azo dye based cyanide chemosensors

Generally, the design of colorimetric receptors is based on the receptor-chromophore conjugate, which involves the binding of a specific analyte with the receptor site and a chromophore responsible for translating the binding of receptor–analyte into an optical signal. Azo dyes are known for their chromophoric strength, ease of preparation and economy and the coverage of the full range of shades of colors. The presence of the azo group improves the chromogenic ability of the chemosensors and thus serves as one of common chromophores for the target chemosensors [29].

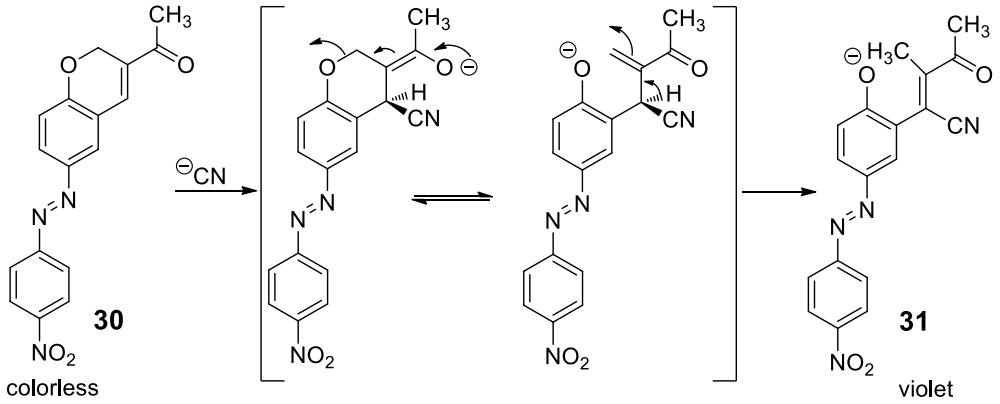
S. Park et al. reported a novel colorimetric probe for cyanide. Probe **30** was synthesized from 4-nitroaniline (**28**) as shown in *scheme 2.9*.



Scheme 2.9

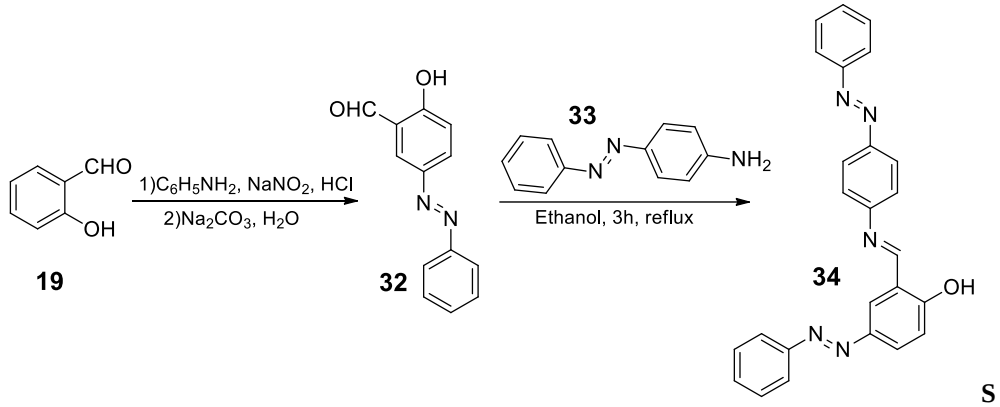
This probe possesses a masked phenol in the para position of the azo dye group. When treated with cyanide, probe **30** undergoes a ring opening reaction through the Michael addition of a cyanide ion and a subsequent [1,3]-sigmatropic rearrangement reaction, which gives rise to a stable free phenol whose signal is

transduced to the azo dye unit producing a significant color change (*scheme 2.10*) [30].



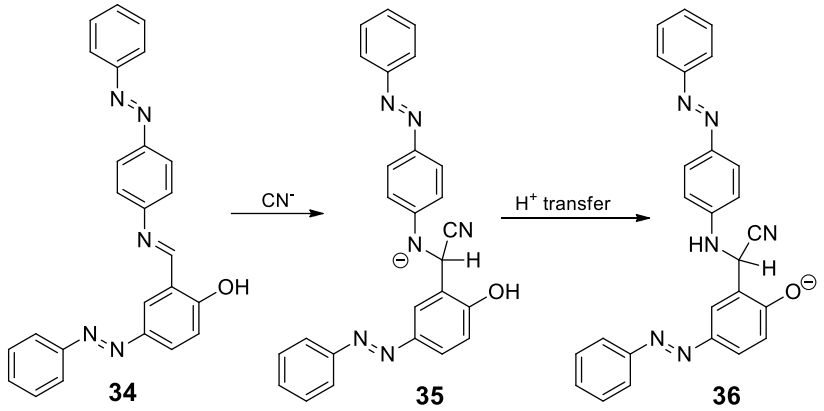
Scheme 2.10

A chemosensor **34** based on azo-linked Schiff base was presented by D. Udhayakumari et al. [31]. The synthetic route is shown in *scheme 2.11*.



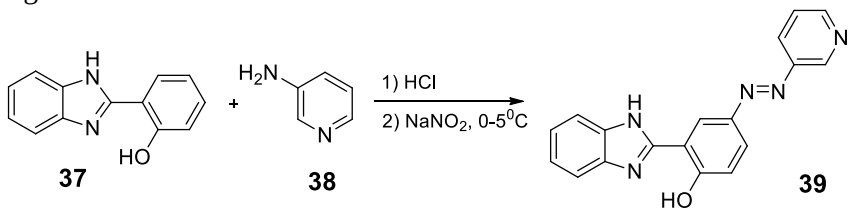
cheme 2.11

Receptor **34** showed selective detection of cyanide ion in 90% aqueous medium based on a nucleophilic addition followed by the intra molecular proton exchange process as demonstrated in *sheme 2.12*.



Scheme 2.12

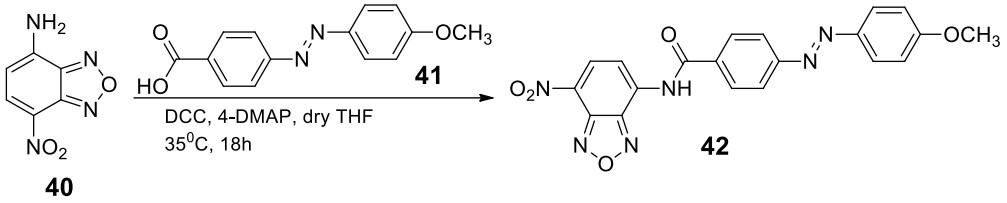
N. Kaur et al. demonstrated receptor **39** based on azo dye featuring a benzimidazole unit [32]. The preparation of the receptor was carried out by a diazo-coupling reaction as shown in *scheme 2.13*.



Scheme 2.13

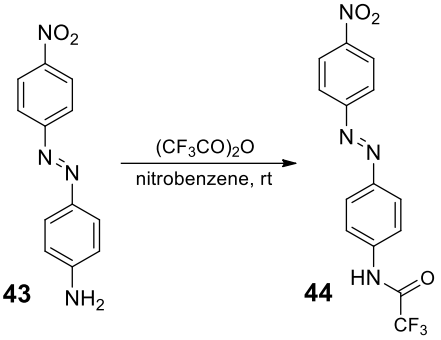
According to the authors, the cyanide ion sensing mechanism of receptor **39** may be attributed to the possible hydrogen bonding interaction and/or the deprotonation of the –OH and imidazole-NH groups.

Y.K. Tsui et al. designed cyanide receptor **42** based on 4-((4-methoxyphenyl)diazenyl)benzoic acid (chromophore) and 4-amino-7-nitro-2,1,3-benzoxadiazole (NBD) fluorophore which were connected by an amide functionality (*scheme 2.14*). Cyanide is detectable by a nucleophilic attack towards the amide carbonyl function followed by the fast proton transfer of the acidic amide hydrogen to the developing alkoxide anion of this compound. This proton transfer triggers the latent chromogenic nitro group of NBD into an active state (its anionic state) thus resulting in the enhancement of the push-pull character of the intramolecular charge transfer and photoinduced electron transfer transitions. It is reflected in the new absorption and fluorescence enhancement [33].



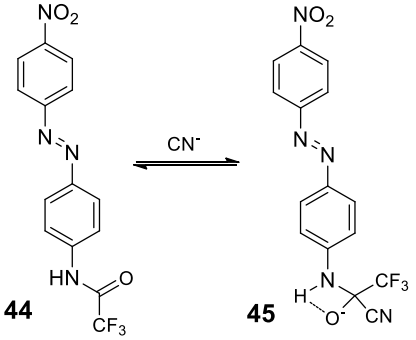
Scheme 2.14

Chemosensor **44** based on (4-(4-nitrophenylazo)aniline) was reported by H.T. Niu et al. [34]. It was synthesized in a single step starting from its commercially available precursor 4-(4-nitrophenylazo)aniline (**43**) and trifluoroacetic anhydride (*scheme 2.15*). These compounds were stirred in nitrobenzene overnight. Then the mixture was filtered, and the solid residue was crystallized from acetonitrile to obtain target compound **44**.



Scheme 2.15

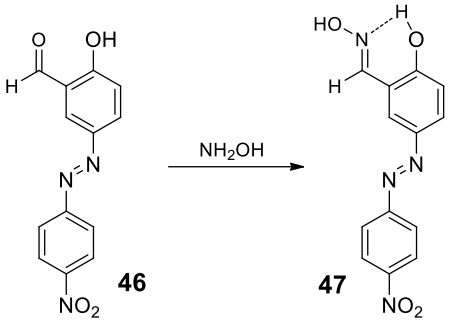
The proposed mechanism upon the addition of cyanide is shown in *scheme 2.16*. ^{1}H NMR titration experiments were carried out by the addition of Bu_4CN to the acetonitrile-d_3 solution of **44**. With the increasing addition of cyanide, all the aromatic protons exhibited an upfield shift to a different extent, which is compatible with the proposed switching mechanism.



Scheme 2.16

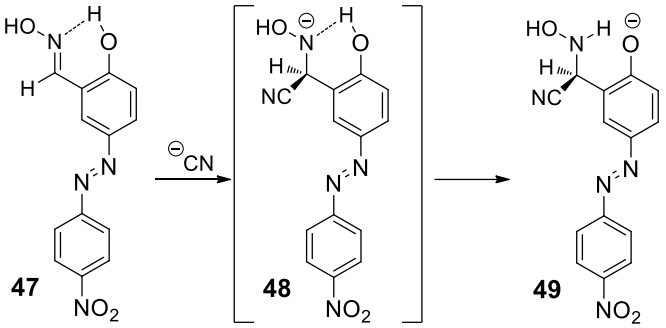
S.-Y. Na and H.-J. Kim recently developed an azo dye-based chemodosimeter possessing oxime functionality as a reaction unit with cyanides in the aqueous

environment [35]. The oxime functional group of **47** was introduced as a result of treatment of **46** with hydroxylamine (*scheme 2.17*).



Scheme 2.17

The detection mechanism is based on the nucleophilic addition of cyanide anions to the activated imine carbon and a subsequent proton transfer from phenol to amine (*scheme 2.18*).



Scheme 2.18

Despite remarkable achievements in cyanide anion detection, a high percentage of examples presented in the academic literature still exhibit major disadvantages, for example, poor sensitivity, interferences of other anions or low solubility in water. The already known methods often require preoptimized conditions, such as preconcentration, phase-transfer reagents, high temperatures, UV light or some special equipment.

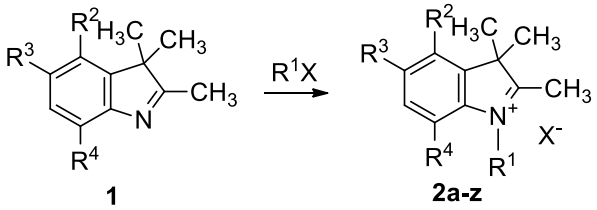
Consequently, there is still a need to develop sensitive and selective receptors capable to determine cyanide anion in aqueous media at a low cost and without the involvement of special equipment.

3. RESULTS AND DISCUSSION

3.1. Synthesis and *N*-alkylation of 3*H*-indole derivatives

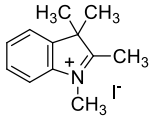
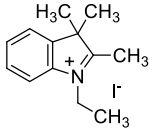
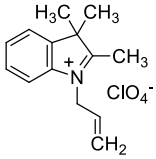
The indole moiety is probably one of the most common heterocyclic scaffolds present in many natural and unnatural compounds with significant biological activities [36]. Consequently, the synthesis of polyfunctional indole derivatives is an important area of research. Among the available methods, the Fischer indole reaction has remained very useful and important method for the synthesis of a variety of indole intermediates. Due to its simplicity, Fischer indolization of phenylhydrazines, first reported over 120 years ago, remains one of the most widely used procedures [37] which was also used in this work to synthesize various substituted 2,3,3-trimethyl-3*H*-indoles. The indolization reaction was carried out by heating ketone 3-methyl-2-butanone and the corresponding arylhydrazine with the appropriate acid, and in most cases converting the resultant indole to a hydrochloride by employing standard and well-known procedures.

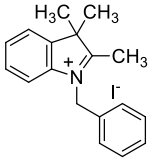
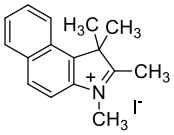
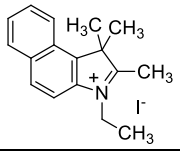
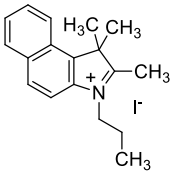
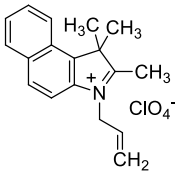
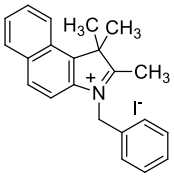
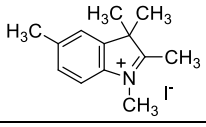
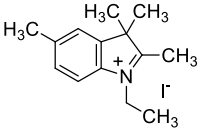
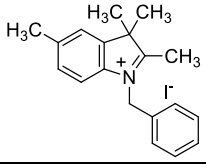
Indolium salts **2**·X^- (X = I, Br, ClO_4) were prepared as a result of the conventional reactions of the corresponding 2,3,3-trimethyl-3*H*-indole derivatives with alkyl iodides and bromides followed by anion exchange in the cases of perchlorates as shown in *scheme 3.1.1* and *table 3.1*.

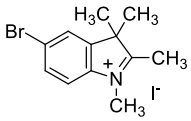
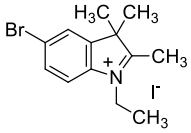
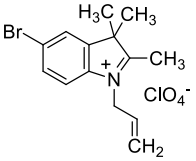
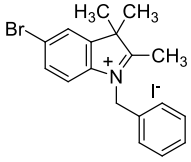
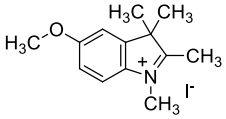
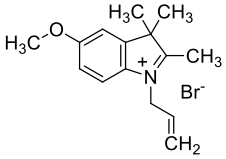
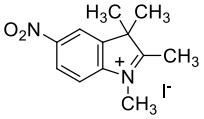
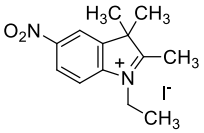
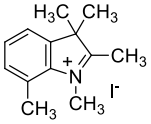
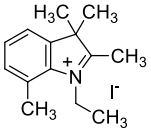


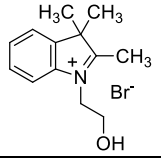
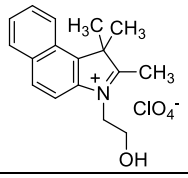
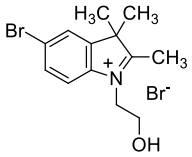
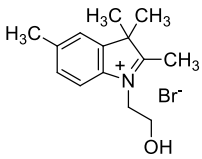
Scheme 3.1.1

Table 3.1. Synthesis of 3*H*- indolium salts

3*H*-indolium salt	R, X	Formula	Synthesis
2a	$R^1 = CH_3$; R^2, R^3, R^4 = H; X = I;		Following a procedure described in literature [38]. Yield 72%
2b	$R^1 = C_2H_5$; R^2, R^3, R^4= H; X = I;		Following a procedure described in literature [39]. Yield 45%
2c	$R^1 = -CH_2-CH=CH_2$; R^2, R^3,R^4 = H; X = ClO_4;		1) Allylbromide, acetone, reflux, 5h; 2) EtOH, $HClO_4$ [40]. Yield 51%

2d	R^1 = -CH_2-Ph; R^2, R^3,R^4 = H; X = I;		Benzyl iodide, CH_3CN, reflux 24h [41]. Yield 52%
2e	R^1 = CH_3, R^2, R^3 = CH=CH-CH=CH, R^4 = H; X = I;		Following a procedure described in literature [42]. Yield 90%
2f	R^1 = C_2H_5, R^2, R^3 = CH=CH-CH=CH, R^4 = H; X = I;		Following a procedure described in literature [43]. Yield 94%
2g	R^1 = C_3H_7, R^2, R^3 = CH=CH-CH=CH, R^4 = H; X = I;		Following a procedure described in literature [44]. Yield 41%
2h	R^1 = -CH_2-CH=CH_2, R^2, R^3 = CH=CH-CH=CH, R^4 = H; X = ClO_4;		1) Allylbromide, CH_3CN, reflux, 5h; 2) EtOH, $HClO_4$. Yield 25%
2i	R^1 = -CH_2-Ph, R^2, R^3 = CH=CH-CH=CH, R^4 = H; X = I;		Benzyl iodide, CH_3CN, reflux, 24h [41]. Yield 60%
2j	R^1, R^3 = CH_3; R^2, R^4 = H; X = I;		Following a procedure described in literature [45]. Yield 88%
2k	R^1 = C_2H_5; R^3 = CH_3, R^2, R^4 = H; X = I;		Ethyl iodide, reflux, 6h. Yield 84%
2l	R^1 = -CH_2-Ph; R^3 = CH_3; R^2, R^4 = H; X = I;		Benzyl iodide, CH_3CN, reflux, 24h. Yield 42%

2m	$R^1 = CH_3$, R^3 = Br, R^2, R^4 = H; X = I;		Following a procedure described in literature [46]. Yield 94%
2n	$R^1 = C_2H_5$; R^3 = Br, R^2, R^4 = H; X = I;		Following a procedure described in literature [47]. Yield 50%
2o	R^1 = -CH_2-CH=CH_2; R^3 = Br; R^2, R^4 = H; X = ClO_4;		Following a procedure described in literature [40]. Yield 25%
2p	R^1 = -CH_2-Ph; R^3 = Br, R^2, R^4 = H; X = I;		Benzyl iodide, CH_3CN, reflux, 24h. Yield 33%
2q	$R^1 = CH_3$, $R^3 = OCH_3$, R^2, R^4 = H; X = I;		Methyl iodide, CH_3CN, reflux, 12h. Yield 75%
2r	R^1 = -CH_2-CH=CH_2; R^3 = OCH_3; R^2, R^4 = H; X = Br;		Allylbromide, CH_3CN, reflux, 15h. Yield 30%
2s	$R^1 = CH_3$, $R^3 = NO_2$, R^2, R^4 = H; X = I;		Following a procedure described in literature [48]. Yield 74%
2t	$R^1 = C_2H_5$; $R^3 = NO_2$, R^2, R^4 = H; X = I;		Ethyl iodide, CH_3CN, reflux, 24h. Yield 53%
2u	R^1, $R^4 = CH_3$; R^2, R^3 = H; X = I;		Methyl iodide, reflux, 24h. Yield 67%
2v	$R^1 = C_2H_5$; R^2, R^3 = H; $R^4 = CH_3$; X = I;		Ethyl iodide, reflux, 24h. Yield 39%

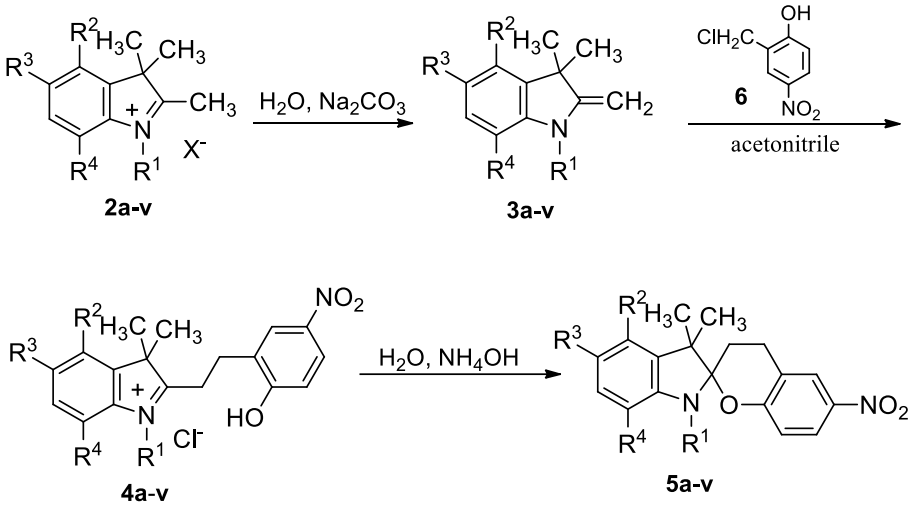
2w	R^1 = -CH_2-CH_2-OH; R^2, R^3, = H; X = Br;		Following a procedure described in literature [49]. Yield 71%
2x	R^1 = -CH_2-CH_2-OH, R^2, R^3 = CH=CH-CH=CH; X = ClO_4;		1) 2-bromoethanol, acetone, reflux, 15h; 2) EtOH, $HClO_4$. Yield 50%
2y	R^1 = -CH_2-CH_2-OH; R^3 = Br, R^2 = H; X = Br;		2-bromoethanol, microwave, according to a procedure described in literature [49]. Yield 95%
2z	R^1 = -CH_2-CH_2-OH; R^3 = CH_3, R^2, = H; X = Br;		2-bromoethanol, microwave, according to a procedure described in literature [49]. Yield 47%

3.2. Synthesis of 1',3',3'-trimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indoles]

The synthesis strategy for the target 1',3,3',4-tetrahydrospiro[chromene-2,2'-indoles] **5a-v** is outlined in *scheme 3.2.1*. The corresponding 2-methylidene-2,3-dihydro-1*H*-indoles **3a-v** were obtained from salts **2a-v** as a result of their treatment with a saturated aqueous sodium carbonate solution; they were used in the reactions without further purification.

It is known that the methylation of 1-alkyl-2-methylene-3,3-dimethyl-2,3-dihydro-1*H*-indole **3** (Fisher's base) takes place at the *β*-carbon atom of the enamine moiety to afford 2-ethylidene side-chain products [50].

In this work, the reactions of Fisher's bases **3** with 2-chloromethyl-4-nitrophenol were carried out in acetonitrile at room temperature or at reflux.



5 a: $R^1 = CH_3$; R^2, R^3, R^4 = H; (74%);
5 b: $R^1 = C_2H_5$; R^2, R^3, R^4= H; (30%);
5 c: $R^1 = -CH_2-CH=CH_2$; R^2, R^3,R^4 = H; (28%);
5 d: $R^1 = -CH_2-Ph$; R^2, R^3,R^4 = H; (29%);
5 e: $R^1 = CH_3$, R^2, R^3 = CH=CH-CH=CH, R^4 = H; (67%);
5 f: $R^1 = C_2H_5$, R^2, R^3 = CH=CH-CH=CH, R^4 = H; (56%);
5 g: $R^1 = C_3H_7$, R^2, R^3 = CH=CH-CH=CH, R^4 = H; (44%);
5 h: $R^1 = -CH_2-CH=CH_2$, R^2, R^3 = CH=CH-CH=CH, R^4 = H; (26%);
5 i: $R^1 = -CH_2-Ph$, R^2, R^3 = CH=CH-CH=CH, R^4 = H; (36%);
5 j: R^1, $R^3 = CH_3$; R^2, R^4 = H; (80%);
5 k: $R^1 = C_2H_5$; $R^3 = CH_3$, R^2, R^4 = H; (85%);
5 l: $R^1 = -CH_2-Ph$; $R^3 = CH_3$; R^2, R^4 = H; (20%);
5 m: $R^1 = CH_3$, R^3 = Br, R^2, R^4 = H; (87%);
5 n: $R^1 = C_2H_5$; R^3 = Br, R^2, R^4 = H; (67%);
5 o: $R^1 = -CH_2-CH=CH_2$; R^3 = Br; R^2, R^4 = H; (26%);
5 p: $R^1 = -CH_2-Ph$; R^3 = Br, R^2, R^4 = H; (33%);
5 q: $R^1 = CH_3$, $R^3 = OCH_3$, R^2, R^4 = H; (21%);
5 r: $R^1 = -CH_2-CH=CH_2$; $R^3 = OCH_3$; R^2, R^4 = H; (34%);
5 s: $R^1 = CH_3$, $R^3 = NO_2$, R^2, R^4 = H; (40%);
5 t: $R^1 = C_2H_5$; $R^3 = NO_2$, R^2, R^4 = H; (52%);
5 u: $R^1 = CH_3$; R^2, R^3 = H, $R^4 = CH_3$; (51%);
5 v: $R^1 = C_2H_5$; R^2, R^3 = H, $R^4 = CH_3$; (25%);

Scheme 3.2.1

In cases **3a**,**b**,**e**,**j**,**k**,**m**,**u**, alkylation with 2-chloromethyl-4-nitrophenol resulted in crystalline precipitation of chlorides **4**; in the other cases, chlorides were not isolated from the mixture but instead used for the further reaction without any purification.

When 2-chloromethyl-4-nitrophenol was added to **3a** in acetonitrile, after 3 h at room temperature the obtained crystalline precipitate was filtered to afford the

chloride **4a**. The structure of **4a** was confirmed by the presence of the following characteristic signals in the ^{1}H NMR spectrum (DMSO-d_6): the singlet at 1.61 (chemically equivalent protons of the 3',3'-CH_3 groups) and multiplets in the area of 2.96-3.42 ppm (the CH_2CH_2 moiety protons). The appearance of a signal at 195.7 ppm in the ^{13}C NMR spectrum was indicative of an N^+=C carbon and characteristic of 3*H*-indolium salts [51]. The treatment with sodium carbonate or sodium hydroxide of **4a** yielded the formation of the open form possessing nitrofenolate moiety, and no ring closing was observed. When treated with aqueous ammonia, chloride **4a** underwent an intramolecular nucleophilic addition of the phenolic oxygen to the α-carbon of the indole moiety to yield 1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5a** which possesses the asymmetric spiro C-2' carbon.

The structure of **5a** was proven with spectral methods. The IR spectrum of **5a** contained characteristic absorption bands at 3068 (C-H arom.) and 1509 (NO_2 asymm.) cm^{-1}, whereas no absorption was possible to be assigned to the OH group in the area of 3400–3100 cm^{-1}. The ^{1}H NMR spectrum (chloroform-*d*) of **5a** revealed a broadened six-proton singlet indicative of the geminal 3,3'-CH_3 groups at 1.26 ppm, while the resonances of the CH_2CH_2 moiety appeared as broadened multiplets in the range of 2.25–3.20 ppm. In the ^{13}C NMR spectrum of **5a,** the geminal methyl groups at C-3' gave separate signals at 21.8 and 25.5 ppm, which were both significantly broadened. All of the other carbon signals of **5a** remained sharp, including the characteristic signal of the sp^3-hybridized C-2' carbon at 104.2 ppm, which was indicative of a covalent C-O bond.[52] It is known that the broadening of NMR spectral lines very often reflects dynamic structural or conformational transformations of molecules in a solution [53]. In this case, the observed broadness and coalescence of the proton resonance signals of the diastereotopic geminal methyl groups can be explained by the inversion of the chiral center at C-2' in the interconversion of the (*R*)- and (*S*)-enantiomers of **5a** (*Fig. 3.2.1, b*). A similar phenomenon has been observed in indoline spiropyrans [54] and indole benzoxazines [55]. At ambient temperature, the interconversion involving thermally induced $C_{(2)}$-O bond cleavage to form the ring-opened intermediate **5'a** and the subsequent closure via the attack on either face of the planar intermediate is relatively fast on the NMR timescale. We investigated this process at a variable temperature in ^{1}H NMR. When the ^{1}H NMR spectrum of **5a** was recorded at -50 °C, the geminal methyl groups revealed two well-defined singlets (frequency difference of 9.6 Hz) as a result of slowing down the interconversion between enantiomers (*Fig. 3.2.1, a*). The coalescence of the geminal methyl group signals was observed at 0 °C. The rate constant *k* for the inversion of the configuration at C-2, [56], calculated by the Gutowsky–Holm equation [57] was thus 21 sec^{-1} at 0 °C. It is of key importance to note that the signals corresponding to intermediate **5'a** were not observed by ^{1}H NMR as its concentration in the solution was too low to be detected.

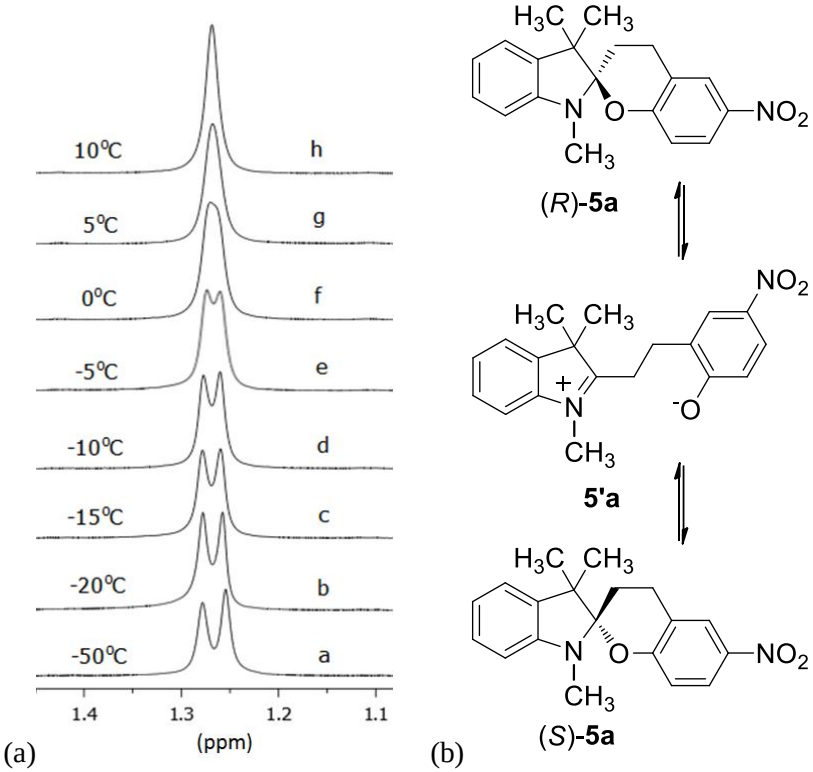


Fig. 3.2.1. (a) Partial ^{1}H NMR spectra (400 MHz, chloroform-*d*) of **5a** at variable temperatures; (b) interconversion of the (*R*)-**5a** and (*S*)-**5a** enantiomers *via* the ring-open form **5'a**.

The full assignment of chemical shifts obtained from the ^{1}H, ^{13}C and ^{15}N NMR spectra of compound **5a** (*Fig. 3.2.2*) was based on a combination of such standard NMR techniques as NOE-difference, NOESY, APT, DEPT, HSQC, HMBC and long-range INEPT spectra with selective excitation [58]. These NMR experiments were performed by Prof. dr. Wolfgang Holzer at University of Vienna. It is worth noting that the NOESY spectrum (*Fig. 3.2.2, a*) of **5a** revealed a cross-peak between the aromatic 8-H proton and the 1'-CH_3 group protons while the protons of the geminal 3',3'-CH_3 groups showed NOE's both with the aromatic 4'-H proton and the methylene protons at C-3 and C-4. These observations testify to the relatively stable nature of the ring-closed spiro system in the solution.

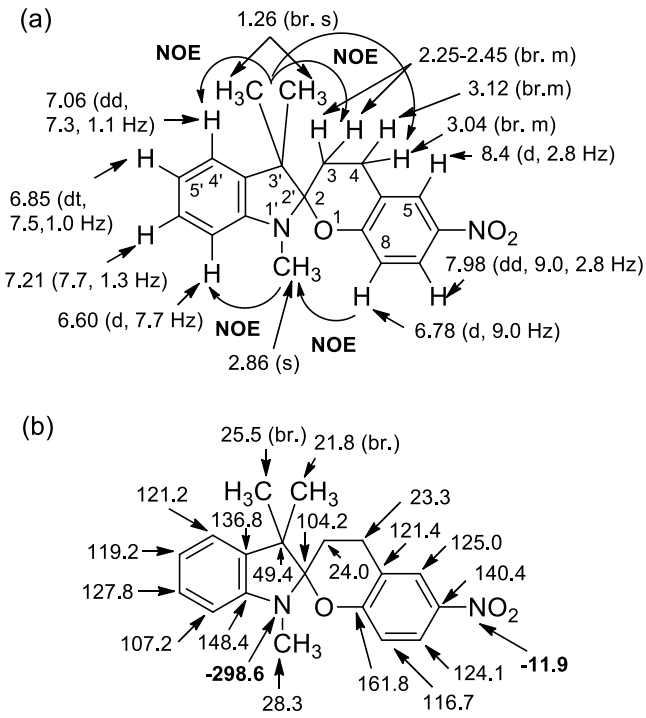


Fig. 3.2.2. (a) ^{1}H NMR (500 MHz, chloroform-*d*) chemical shifts (ppm; ref. TMS) and the relevant NOE correlations for **5a**; (b) ^{13}C and ^{15}N NMR (bold) chemical shifts [ppm; ref. TMS (^{13}C) and CH_3NO_2 (^{15}N)] for **5a**.

The ^{1}H NMR spectra (chloroform-*d*, ambient temperature) of compounds **5b-g**,**j**,**k**,**n**,**p**,**q**,**s**,**u-z** displayed the broadened singlet corresponding to the geminal 3',3'-CH_3 observed with **5a**. However, in the ^{1}H NMR spectrum of 5',6-dinitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5t,** the geminal 3',3'-CH_3 groups resonated as separate singlets at 1.28 and 1.29 ppm while the protons of the all three CH_2 groups revealed well-defined multiplets in the range of 2.24-3.52 ppm. Therefore, it could be concluded that the presence of the electron-withdrawing nitro substituent in the 5'-position of the indoline ring stabilizes the chiral spirocyclic system and slows the interconversion process of the corresponding enantiomers. However compounds **5h**,**i**,**l**,**m**,**o**,**r**,**t** also gave separate singlets for 3',3'-CH_3 groups (even though **5l** and **5r** have electron donating methyl and methoxy substituents in the 5'-position) suggesting that substituents at the nitrogen atom of the indole ring as well as other factors, such as steric, also influence the above described process of interconversion.

The structure of **5t** was investigated by single crystal X-ray analysis (*Fig. 3.2.3 a*). X-ray diffraction experiments here and later in this work were performed by Dr. S.V. Belyakov (Latvian Institute of Organic Synthesis). The compound consists of indole and benzopyran moieties connected through the spiro atom C(2). These moieties reside in nearly perpendicular planes where the indole-plane intersects the plane of the benzopyrane moiety at C(2) and cuts across the C(4')-C(10') bond. The C(3') atom sits outside the plane containing the remainder of the benzopyran moiety.

Substituents at C(2) and C(3') are in staggered conformation with a N(1)-C(2)-C(3')-C(4) dihedral angle of 171.28º. The sum of the bond angles at the indoline nitrogen is 357.5º, indicating sp^2 hybridization. The C(8)-N(1) bond length (1.378 Å) is similar to those of *N*,*N*-disubstituted aniline derivatives, [59], whereas the C(2)-O(1) bond length (1.483 Å) resembles those of 1',3'-dihydrospiro[chromene-2,2'-indoles] (1.48–1.50 Å) [60].

The single crystal of **5t** consisted of enantiomeric molecules in racemic columns (*Fig. 3.2.3 b*). These columns are held by extensive intermolecular hydrogen bonding utilizing both nitro groups of the molecules. The benzopyran-based nitro groups in both the *R*- and *S*-enantiomers form two pairs of hydrogen bonds apiece: H(10a)···O(12') (the bond length 2.567 Å) and H(3'a)···O(13') (2.498 Å). Similarly, three hydrogen bonds are formed with the nitro groups of indole moieties: H(13a)···O(16) (2.552 Å), H(11c)···O(15) (2.641 Å), H(11c)···N(14) (2.873 Å).

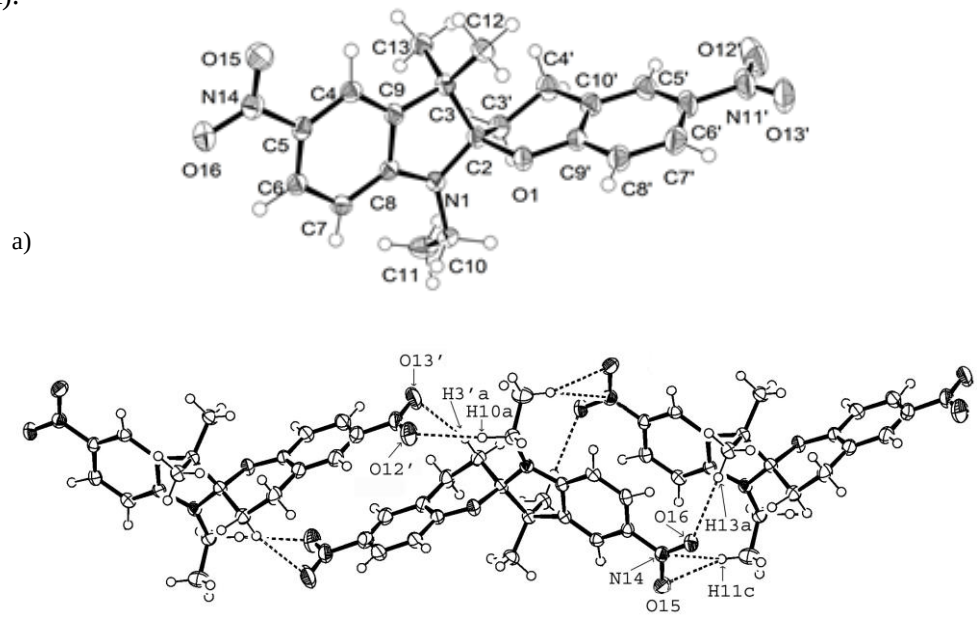


Fig. 3.2.3. a) ORTEP drawing of the (*R*)-enantiomer of compound **5t.** b) Hydrogen bonds in the racemic columns of the single crystal of **5t**.

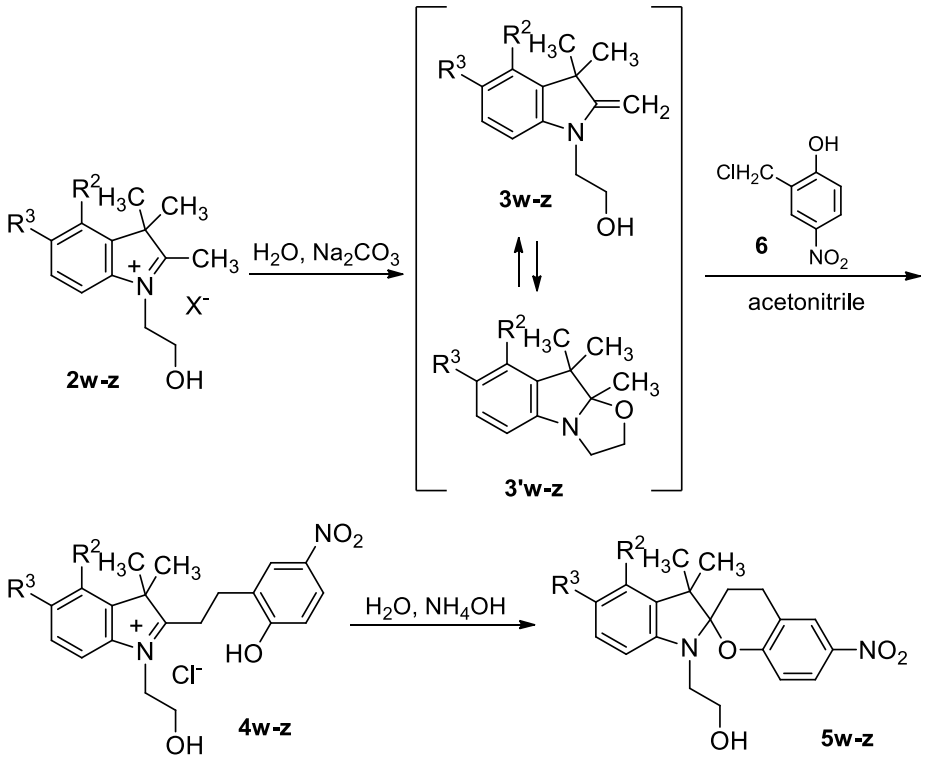
3.3. Synthesis of 3',3'-dimethyl-1'-(2-hydroxyethyl)-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indoles]

In order to expand the area of utilisation of tetrahydrospiro[chromene-2,2'-indoles] we considered the possibility to synthesize these compounds from the indoles possessing the hydroxyethyl group. It is known from academic literature that esterification and transesterification reactions on the hydroxyethyl group followed by polymerization enables the preparation of nanoparticles for fluorescence imaging [61] and photochromic polymer films [62].

N-Hydroxyethyl group is also significant in indole derivative based sensors capable of binding metal ions [63].

For this purpose, salts **2w-z** were treated with a saturated aqueous sodium carbonate solution expecting 2-methylidene-2,3-dihydro-1*H*-indoles thus undergoing the same process as **2a-v**. **2w** was treated with sodium carbonate and extracted with diethyl ether. Surprisingly, ^{1}H NMR spectra showed three singlets of methyl groups (at 1.17, 1.37 and 1.43 ppm), and ^{13}C NMR showed the characteristic signal of the sp^3-hybridized carbon at 108.8 ppm. This signal is indicative of covalent N-C-O bonds, as mentioned above. This data revealed that cyclic 9,9,9a-trimethyl-2,3,9,9a-tetrahydrooxazolo[3,2-*a*]indole was obtained.

Despite that, the reactions of compounds **3w-z** with 2-chloromethyl-4-nitrophenol (**6**) yielded the desired alkylation products **5w-z** suggesting that in the solution, the cyclic compounds **3'w-z** are in equilibrium with enamine **3w-z** (*scheme 3.3.1*) whose concentration in the solution is too low to be detected by NMR.



4w: R^2, R^3 = H; X = Br; (47%);
4x: R^2, R^3 = CH=CH-CH=CH; X = ClO_4; (43%);
4y: R^3 = Br, R^2 = H; X = Br; (37%);
4z: R^3 = CH_3, R^2 = H; X = Br; (52%);

5w: (33%);
5x: (51%);
5y: (57%);
5z: (18%);

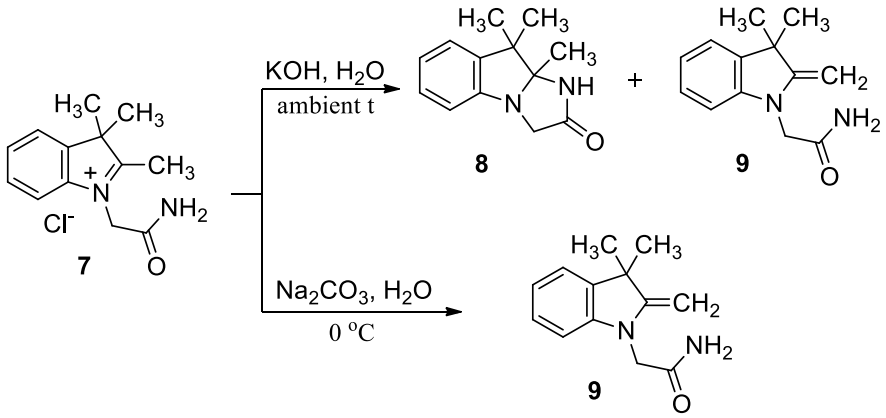
Scheme 3.3.1

3.4. Synthesis of 1'-carbamoylmethyl-3',3'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indoles]

In order to synthesize title compounds, the initial 1-carbamoylmethyl-3,3-dimethyl-3*H*-indolium chloride was obtained from 2,3,3-trimethyl-3*H*-indole and chloroacetamide following the procedure described in academic literature [64].

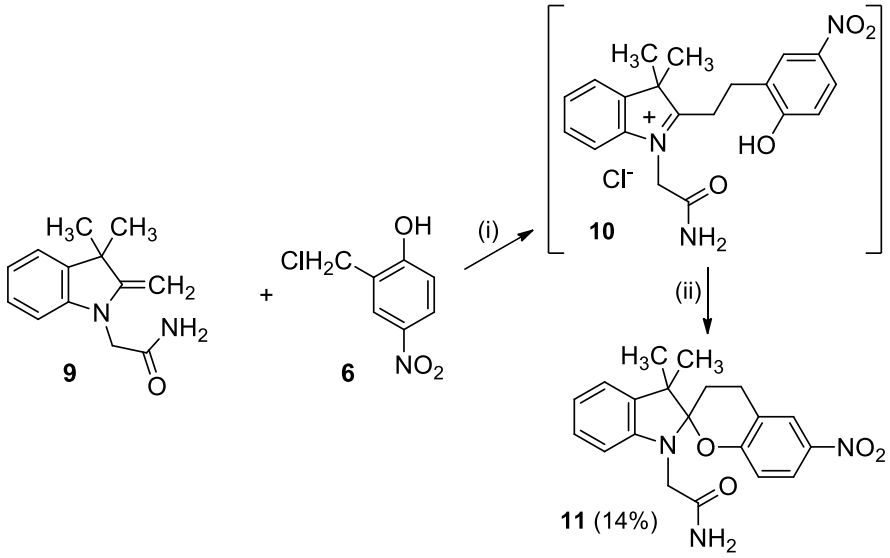
From the same scholarly source it is known that 1'-carbamoylmethyl-3',3'-dimethyl-3*H*-indolium chloride when treated with an alkali solution undergoes cyclisation to give product **8** or experiences deprotonation to yield product **9** (*scheme 3.4.1*). The latter was necesarry for a further reaction; so in order to improve its yield, 1'-carbamoylmethyl-3',3'-dimethyl-3*H*-indolium chloride was treated with sodium carbonate in aqueous solution at approximately 0ºC.

Upon TLC analysis of the reaction mixture, only traces of the side product was observed **8**.



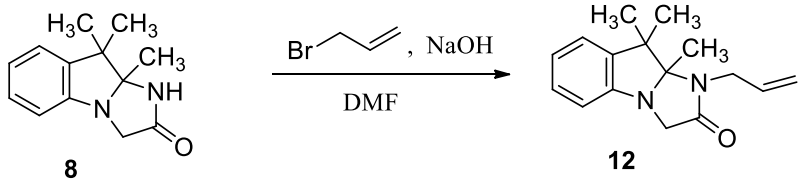
Scheme 3.4.1

When enamine **9** in acetonitrile was treated with 2-chloromethyl-4-nitrophenol, a crystalline precipitate was obtained in a few minutes, but ^{1}H and ^{13}C NMR spectra showed that it is a primary indolium salt **7**. A presumption was made that HCl (which is produced during the reaction) reacts with the enamine faster than the enamine reacts with 2- chloromethyl-4-nitrophenol. Sodium carbonate was used to eliminate hydrochloric acid, and anhydrous sodium sulphate was used to absorb water from the neutralization reaction. Then the desired product **11** was obtained (*scheme 3.4.2*).



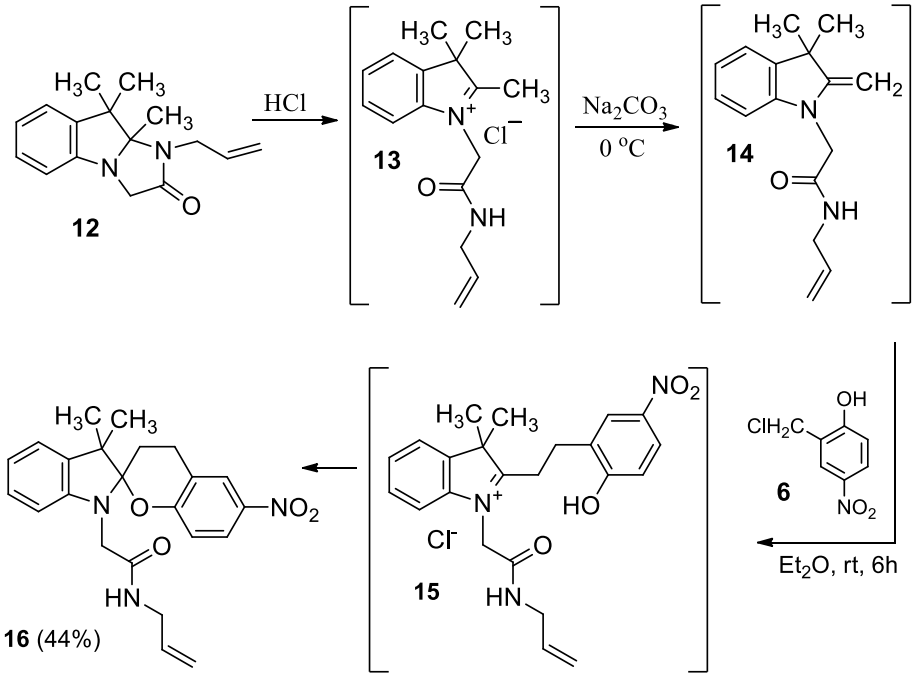
Scheme 3.4.2. *Reagents and conditions*: (i) Na_2CO_3, Na_2SO_4, acetonitrile, rt, 12 h; (ii) H_2O.

It has been described in academic literature that 1,2,3,9a-tetrahydroimidazo[1,2-*a*]indol-2(9*H*)-one can be alkylated with allylbromide [65] (*scheme 3.4.3*).



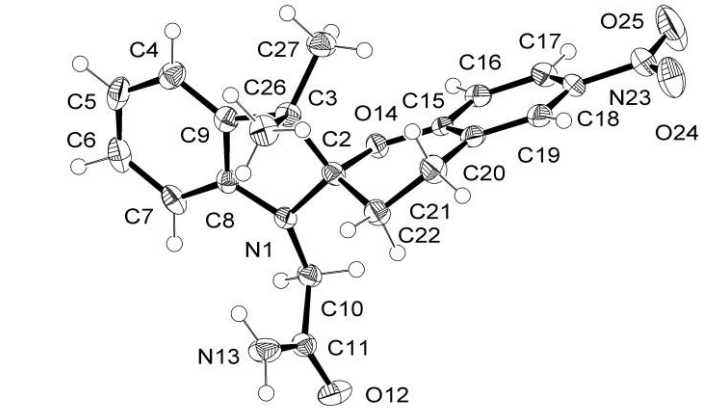
Scheme 3.4.3

When such product **12** was treated with hydrochloric acid and then with sodium carbonate at 0ºC, the intermediate enamine was obtained and alkylated with 2-chloromethyl-4-nitrophenol to yield product **16** (*scheme 3.4.4*).

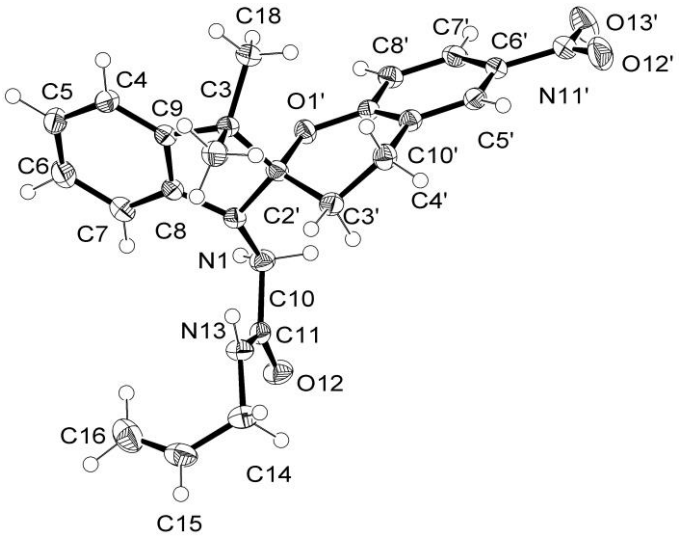


Scheme 3.4.4

The structures of **11** and **16** were investigated by single crystal X-ray analysis (*Fig. 3.4.1., Fig. 3.4.2., Fig. 3.4.3.*)



a)



b)

Fig. 3.4.1. ORTEP drawing of the (S)-enantiomers of compounds **11** (a) and **16** (b).

The asymmetric unit of both **11** and **16** consists of indole and benzopyran moieties, which reside in nearly perpendicular planes connected through the chiral spiro atom C(2') (*Fig. 3.4.1*). The indole moieties in both molecules are flat, and only spiroatom C(2') is inclined towards the plane of the pyran ring oxygen atom. Chroman ring skeletal atoms are situated in one plane with the exception of C(22) and C(3') respectively which are inclined towards the carboxamide group.

The sums of the bond angles at indoline nitrogen atom N(1) for structures **11** and **16** respectively are 352.53º and 347.42º. This indicates that the dominant hybridization of the outer layer electrons of nitrogen atom N(1) is sp^2 (76% and 60% respectively). The fact is also confirmed by C(8)-N(1) bond lengths of 1.394 Å and 1.405 Å, which are similar to those of *N*,*N*-disubstituted aniline derivatives as

mentioned above. Methylencarboxamide fragments of both molecules are directed to the opposite side from the indole plane than the chroman ring.

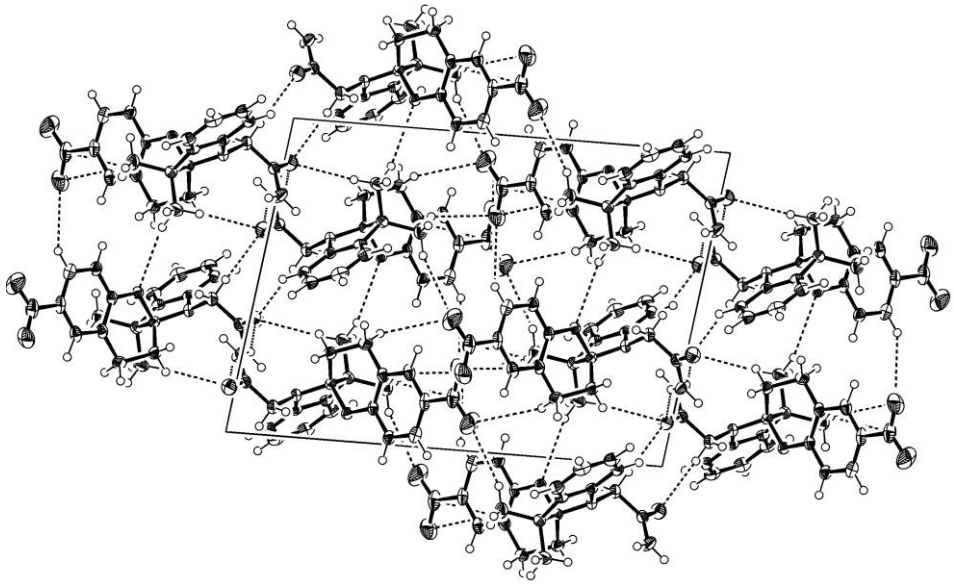


Fig. 3.4.2. Arrangement of the molecules and hydrogen bonds in the crystal lattice of **11** along the b axis

Crystal of compound **11** has monoclinic structure; the lattice parameters are: a = 12.4105 (3) Å; b = 8.5076 (3) Å, β = 97.7660 (11) °; 17.0049 (7) Å. The single crystal of **11** consists of enantiomeric molecules in racemic columns (*Fig. 3.4.2*). These columns are held by extensive intermolecular hydrogen bonding (*Table 3.2*).

Table 3.2. Hydrogen bonds in crystals of **11** and **16**

Crystal of compound **11**			Crystal of compound **16**		
Hydrogen bond	Bond length, Å	Angle C-H···O, º	Hydrogen bond	Bond length, Å	Angle C-H···O, º
C(10)-H(10b)···O(12)	2.674	135.33	C(3)-H(3b)···O(12)	2.145	150.34
C(17)-H(17)···O(24)	2.722	141.59	C(4')-H(4'a)···O(12)	2.945	130.17
C(26)-H(26b)···O(12)	2.573	172.50	C(5')-H(5')···O(12)	2.478	159.54
C(26)-H(26c)···O(14)	2.736	146.70	C(10)-H(10b)···O(12)	2.445	158.24
C(27)-H(27a)···O(25)	3.237	155.03			

The crystal of compound **16** exhibits the triclinic structure (a = 8.9254 (3) Å, α = 81.6879 °; b = 9.5278 (4) Å, β = 84.1266 (17) °; c = 12.2215 (7) Å, γ = 74.766 °).

The single crystal of **16** also consists of enantiomeric molecules in racemic columns (*Fig. 3.4.3*). These columns are held by extensive intermolecular hydrogen bonding between a carbonyl oxygen atom and a hydrogen atom from the phenolic moiety C(5')-H5'···O (12). There are also hydrogen bonds between the columns of different enantiomers which include the amide carbonyl group. These hydrogen bonds are center-symmetrical C(3)-H(3b)···O(12) and C(10)-H (10b)···O(12) with the same carbonyl oxygen atom between the enantiomers.

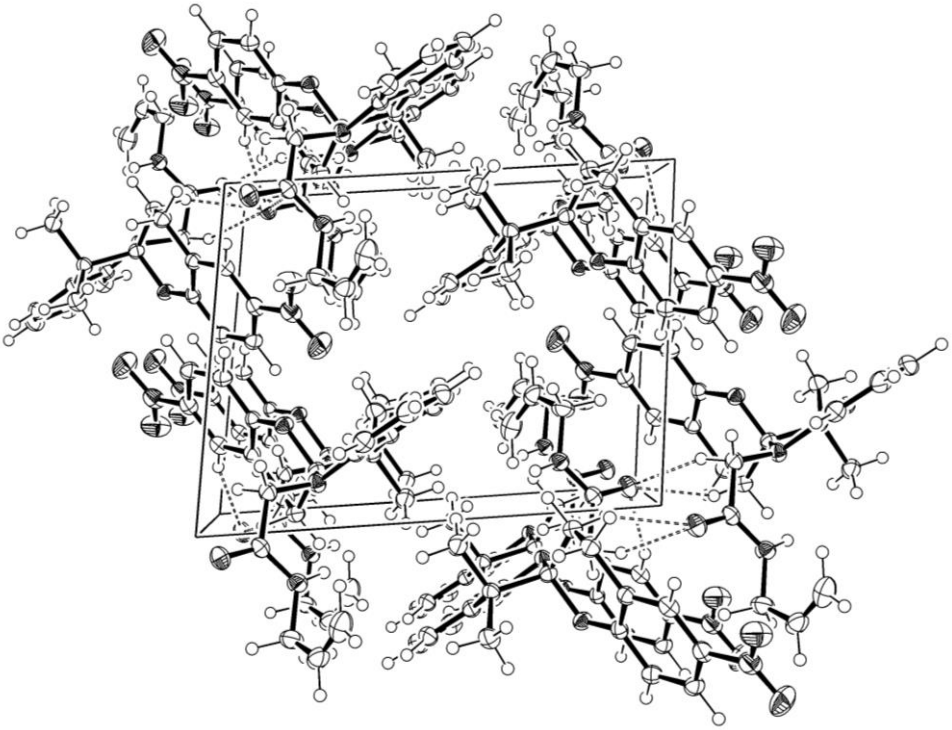
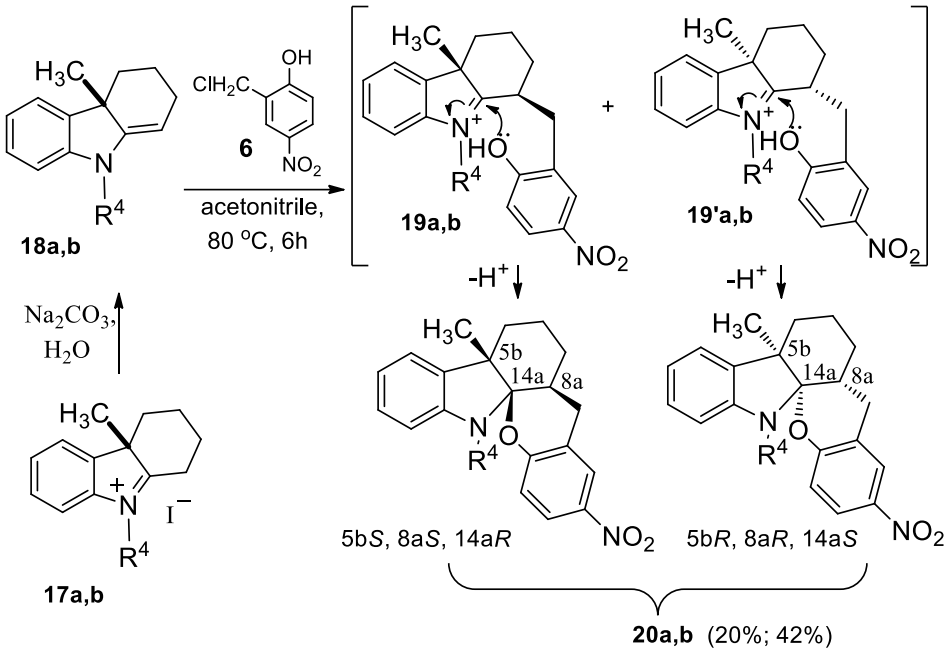


Fig. 3.4.3. Arrangement of the molecules and hydrogen bonds in the crystal lattice of **16** along the b axis.

3.5. Synthesis of (5b*R**, 8a*R**, 14a*S**)-5b-methyl-11-nitro-5b,6,7,8,8a,9-hexahydro-8*H*-indole[2,3-*c*]xantenes

4a-Methyl-2,3,4,4a-tetrahydro[4a*H*]carbazole can be viewed as cyclic analog of 2,3,3-trimethyl-3*H*-indole. Carbazole enamines were obtained from 4a,9-dimethyl-2,3,4,4a-tetrahydro-1*H*-carbazolium iodide (**17a**) and 9-ethyl-4a-methyl-2,3,4,4a-tetrahydro-1*H*-carbazolium iodide (**17b**) [66] by employing the same procedure as for **3a-v**. *β*-C Alkylation of **18** with 2-chloromethyl-4-nitrophenol in acetonitrile and the subsequent nucleophilic cyclization yielded the formation of one diastereomer **20** (*scheme 3.5.1*).



Scheme 3.5.1

13C NMR spectra of **20a** and **20b** contain 14a-C atom signal at 105.8 and 106.6 ppm respectively, similar to spiro[chromene-2,2'-indoles] **5** described above.

The structure of **20a** was investigated with single crystal X-ray analysis (*Fig. 3.5.1*). From *Fig. 3.5.1 (a)* it is evident that the cyclohexane ring has a chair conformation with carbon atoms C (2) and C (22) folding back from the ring plane to opposite directions. For the methyl group, the methylene group and the nitrogen atom of the indole are in axial positions. The pyrroline ring has an envelope conformation where C (2) atom is 0.463 Å folded back from the ring plane. The dihydropyrane ring also shows envelope conformation, wherein the C(3) is 0.722 Å folded from the ring plane. The length of the bond C(2)-O(1) is 1.49 Å, and it is very similar to the corresponding bond in indole spiropyrans, where it ranges from 1.452 Å to 1.5 Å (in two different forms of crystals) [67]. In the crystal lattice, enantiomers are located centrosymmetrically to each other and are held together by 4 hydrogen bonds: 2×($NCH_3\cdots O_2N$) and 2×(C(7)-H···O(1)) (*Fig.3.5.1 (b)*). Enantiomers form chiral columns with 8.058 Å distance between molecules. From the other side, the following two columns have additional hydrogen bonding with other pairs of columns that occur between the C (22) -H and the other oxygen atom of the nitro group. The acetonitrile molecule in the crystal is also involved in a number of hydrogen bonds.

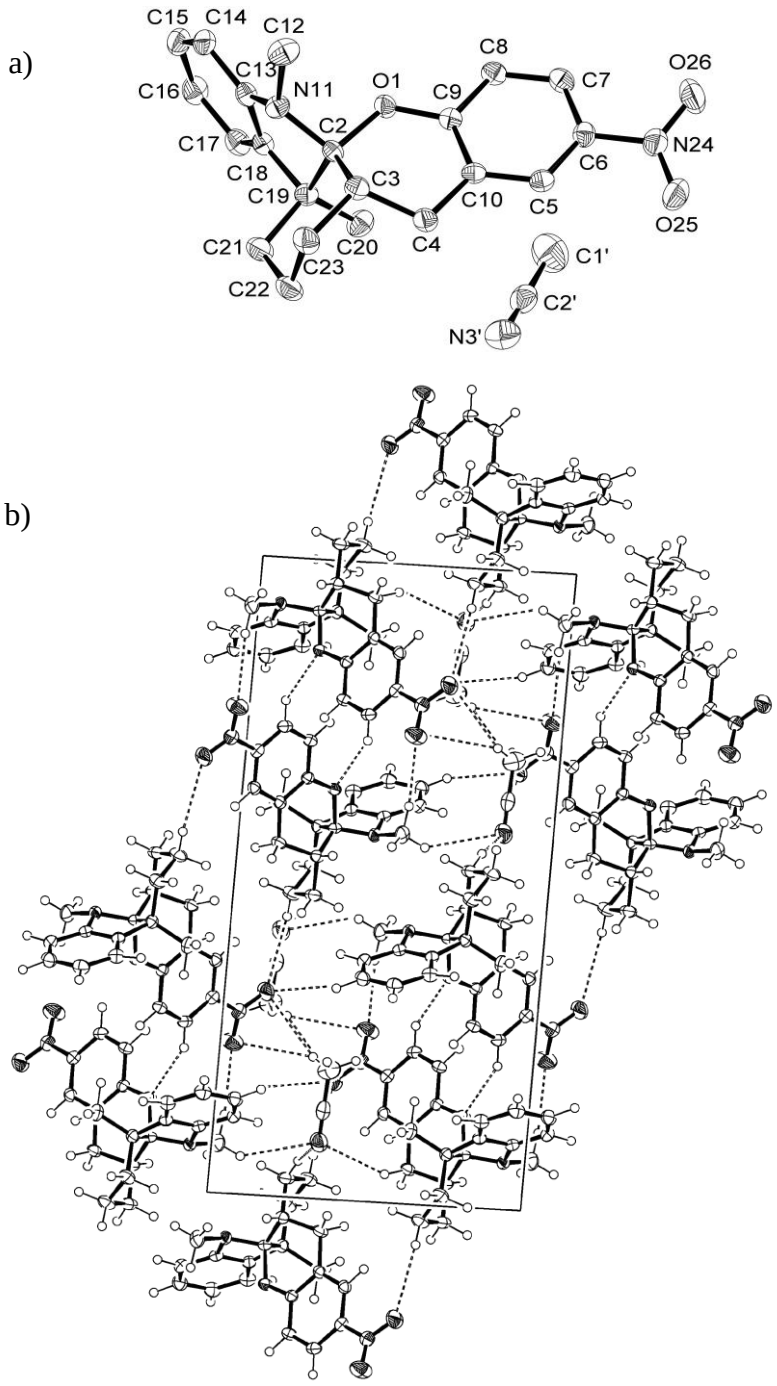
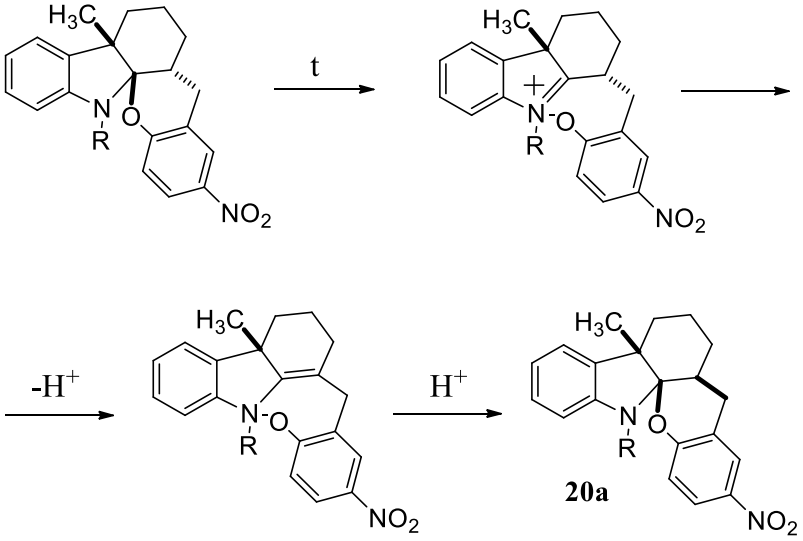


Fig. 3.5.1. a) ORTEP drawing of compound **20a** with the acetonitrile molecule. b) Hydrogen bonds in the crystal lattice of **20a**.

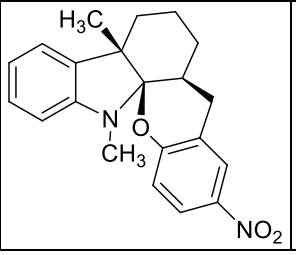
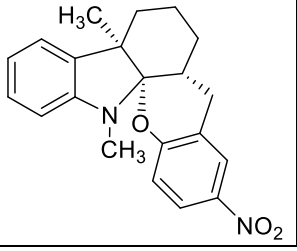
Although compound **20a** containing 3 asymmetric carbon atoms should theoretically have 8 possible stereostructures, yet in this case only one pair of enantiomers was observed. This can be rationalized by the steric action of 5a-methyl group. It was calculated[i] (Turbomole 7.0) that the energy of isolated diastereomer (5b*S**,8a*S**,14a*R**)-**20a** is the lowest if compared with the energy of the other possible diastereomers (Table 3.3.).

From the data presented in Table 3.3 it is evident that two diastereomers exhibit very similar energies (0 and 1.19 kcal/mol), and the formation of both diastereomers is possible. Nevertheless, only one diastereomer was isolated. This suggests that one diastereomer might be transformed to another, a more stable one, because of the proton transfer reaction during purification in the chromatography column or because of recrystalisation as shown in *scheme 3.5.2*.

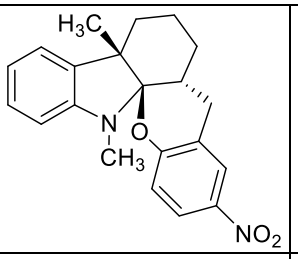
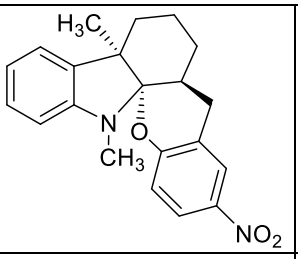
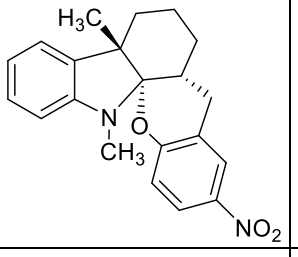
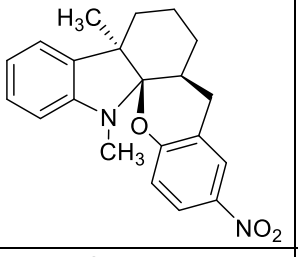
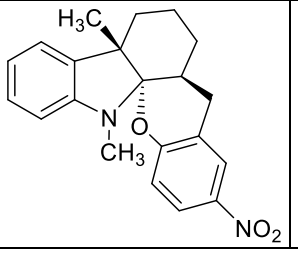
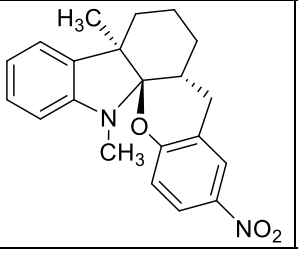


Scheme 3.5.2. Proton transfer reaction of **20a**

Table 3.3. Structures and energy (Trubomole 7.0, def2-SVP, B3-LYP, the lowest energy is set to zero) of all possible diastereomers of **20a**.

No.	Theoretically possible stereoisomers of **20a**		kcal/mol
1			0

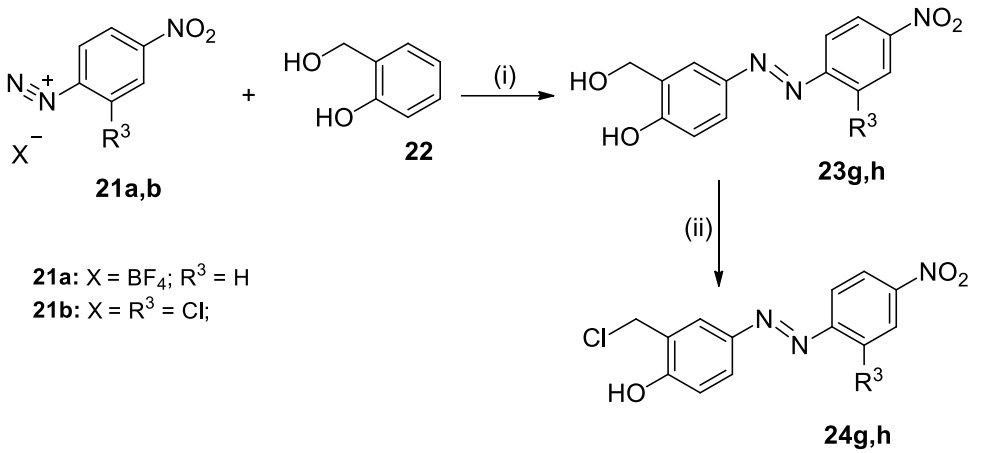
[i] Special thanks to Artiom Magomedov for the calculations.

2			+1.19
3			+10.977
4			+36.481

3.6. Indole and carbazole enamine alkylation with 2-chloromethyl-4-(4'-nitrophenylazo)phenols

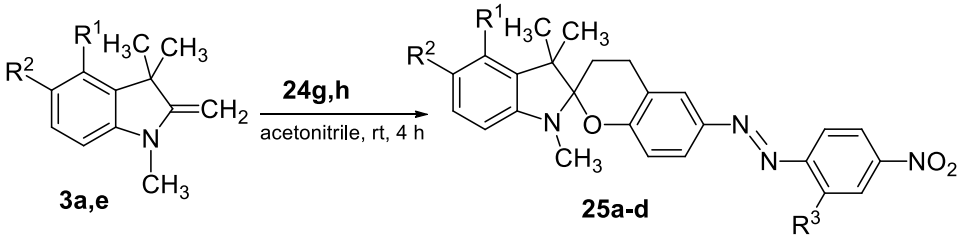
Azo dyes are known for their chromophoric strength, ease of preparation and economy as well as the coverage of the full range of shades of colors. Thus they serve as one of the more common chromophores for multipurpose organic synthesis [29].

The synthesis strategy for target compounds **25a-d** outlined in *scheme 3.6.2* is based on the reaction of enamine **3** with alkylating agents 2-chlormethyl-4-(4'-nitrophenylazo)phenol (**24g**) [68] or 2-chlormethyl-4-(2'-chloro-4'-nitrophenylazo)phenol (**24h**) (obtained by standard diazotation and azo coupling procedures as shown in *scheme 3.6.1*).



21a: X = BF_4; R^3 = H
21b: X = R^3 = Cl;

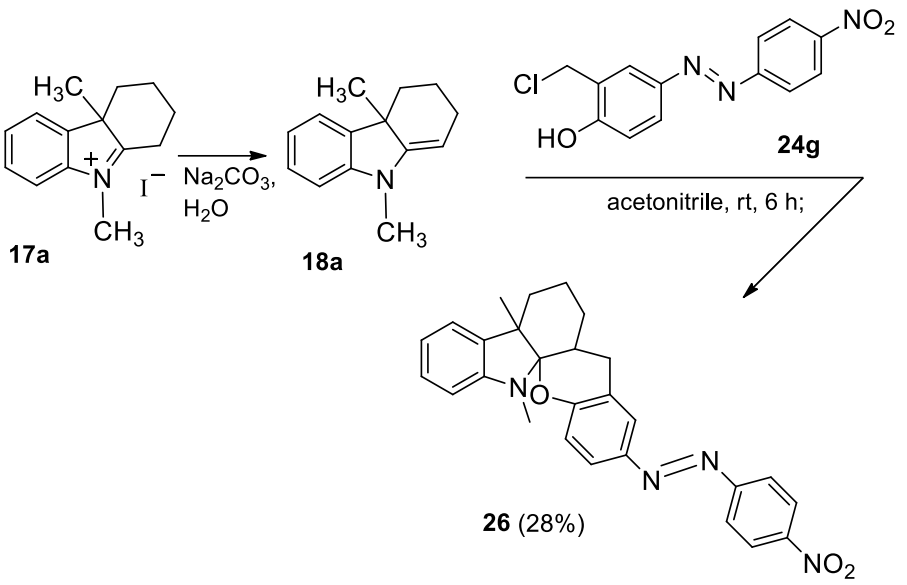
Scheme 3.6.1. *Reagents and conditions*: (i) NaOH, H_2O; (ii) HCl (35% solution), EtOAc, 70ºC, 4 h;



25a: R^1 = R^2 = R^3 = H; (47%)
25b: R^1 = R^2 = H; R^3 = Cl; (61%)
25c: R^1, R^2 = CH=CH-CH=CH; R^3 = H; (42%)
25d: R^1, R^2 = CH=CH-CH=CH; R^3 = Cl; (69%)

Scheme 3.6.2.

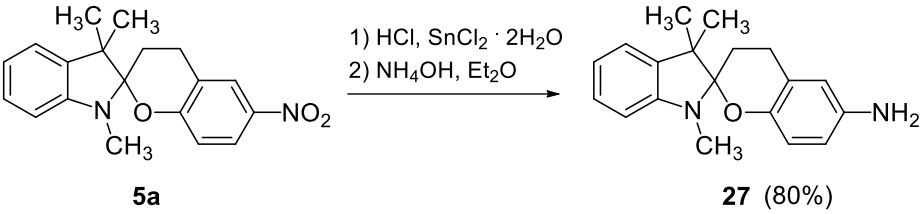
Carbazole enamine **18a**, obtained as described before, was treated with alkylating agent **24g** in order to obtain compound **26** (*scheme 3.6.3*).



Scheme 3.6.3. *Reagents and conditions*: (i) Na_2CO_3, H_2O; (ii) acetonitrile, rt, 6 h;

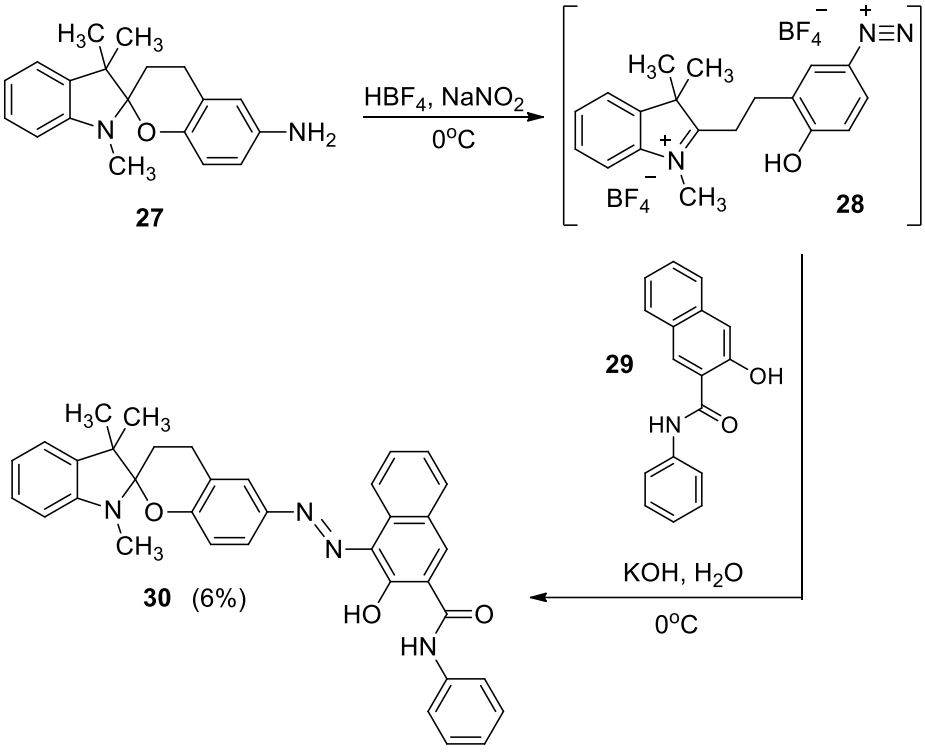
3.7. 1',3',3'-Trimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] nitro group reduction

When compound **5a** was treated with tin(II) chloride in hydrochloric acid HCl and than neutralized with aqueous ammonia solution, product **27** was extracted with diethyl ether (*scheme 3.7.1*).



Scheme 3.7.1

When 6-amino-1',3',3'-trimethyl-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **27** was synthesized, a possibility opened to convert it to diazonium salt and to perform the azo coupling reaction. Commercially available azotol A (**29**) was chosen as a coupling agent to obtain a product containing an even more extended chromophoric chain compared to compounds **25a-d**. The reaction was carried out as shown in *scheme 3.7.2*; it gave the desired product **30**, although with a yield of only 6%. The low yield might be a consequence of the incorrectly selected pH value for the azo coupling reaction even though several options were tested.



Scheme 3.7.2

In order to gain further insight into the structure of compound **30**, statistical thermodynamic calculation was performed by using *Spartan 08* software. Geometry optimizations were achieved as a result of using the semi-empirical AM1 molecular orbital for the density functional theory with a B3LYP/6-31G basis set. Calculation of energy due to solvation suggested that compound **30** features E configuration as shown in *scheme 3.7.2* since it possesses a lower energy value (-312.28 kJ/mol in comparison with -68.39 kJ/mol when calculated for Z isomer).

3.8. Photochromic behavior of 1',4',5',7'-substituted-3',3'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indoles]

One of the most studied classes of photoactive molecular switches is 1',3'-dihydrospiro[chromene-2,2'-indoles] also known in the academic literature as spiro[2*H*-1-benzopyran-2,2'-indolines] [69]. A typical representative of this class of photochromic compounds is 6-nitro-1',3'-dihydrospiro[chromene-2,2'-indole] **32** composed of indole and benzopyran moieties linked at an asymmetric spiro carbon atom [70]. After this chiral species is dissolved in an organic solvent it undergoes a thermally driven interconversion between the (*R*)-**32** and (*S*)-**32** enantiomers via a planar ring-opened form; it generally has a very low concentration in solution [71].

Under UV-irradiation, compound **32** undergoes fast (picosecond scale) C_{spiro}-O bond cleavage thus converting to the planar colored *trans*-merocyanine form **2** possessing the *p*-nitrophenolate moiety (*Fig.3.8.1*). However, the subsequent

thermal reversion of merocyanine **33** to **32** is relatively slow at room temperature due to the required structural changes such as *trans-cis* isomerization [72].

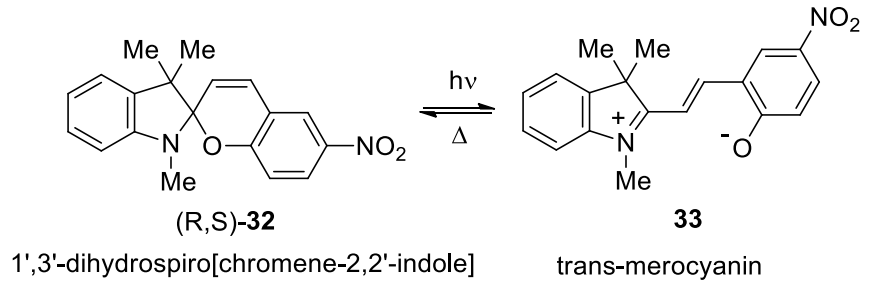


Fig. 3.8.1. Photochromism of 6-nitro-1',3'-dihydrospiro[chromene-2,2'-indole].

Recently, a new class of ultrafast organic optical switches based on the indolo[2,1-*b*][1,3]benzoxazine ring system has been developed (*Fig. 3.8.2*). These photochromes (**34**) obtained by the reaction of 3*H*-indoles with 2-chloromethyl-4-nitrophenol undergo C-O bond cleavage of the [1,3]benzoxazine ring upon UV excitation, which results in the formation of colored 4-nitrophenolate anions (**35**) within picoseconds and in the thermal reversion to the starting material within 10^2 nanoseconds after the excitation [73]. The high speed of photochrome's 'on-off' switching was explained by the lack of any significant structural transformation during the photoinduced reversible ring-opening process in contrast to indoline spirochromenes. These compounds also found application possibilities in the preparation of pH-sensitive luminescent quantum dots [74] and chemosensors [75].

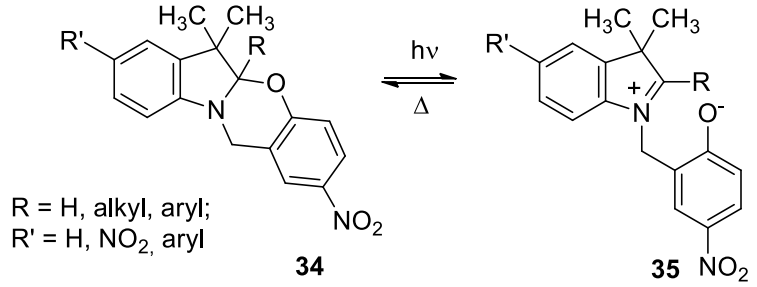


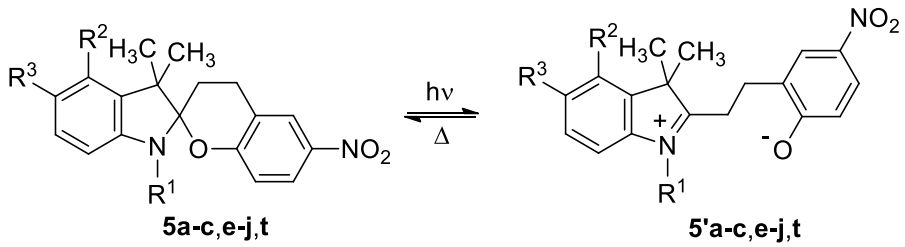
Fig. 3.8.2. Photochromism of 2-nitro-5a,6-dihydro-12*H*-indolo[2,1-*b*][1,3]benzoxazines.

Our study focused on the investigations of previously described 1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] ring system which is notable for the single C_3-C_4 bond of its pyran ring. This single bond eliminates the drawbacks associated with the relatively slow *cis–trans*- and *trans–cis*-isomerizations about the C_3=C_4 double bond in the ring opening-closing process of 1',3'-dihydrodrospiro[chromene-2,2'-indoles] thereby speeding up the reversible transformations of these light-driven molecular switches.

Compounds **5a-c,e-j,t** were chosen to test their photochromic behavior so that the influence of various substituents at the indole ring could be evaluated. What concerns compounds **5a-c,j,t**, measurements and calculations were performed at

Laser Research Center of Vilnius University by assoc. prof. dr. Mikas Vengris and Kipras Redeckas. Compounds **5e-i** were measured and relevant calculations were performed by the author of the present thesis at Depertment of Organic Chemistry of Kaunas University of Technology. Spectroscopic measurements of **5a-c,e-j,t** were carried out in acetonitrile; approximately 0.1mM solutions were used. Steady state absorbance spectra of all the compounds only revealed absorption in the UV-region of electronic spectra (Tables 3.4 and 3.5). Interestingly, a significant red shift was observed in the UV spectrum of **5t** when compared to those of the remaining compounds.

Flash-photolysis experiments were performed and transient absorption data in the nanosecond-to-microsecond time window were collected by using a flash-photolysis spectrometer (based on a Nd:YAG laser) as previously described [76]. Irradiation of **5a-c**,**e-j**,**t** (0.1 mM solutions in acetonitrile) with nanosecond laser pulses yielded cleavage of C-O bonds in the 3,4-dihydro-2*H*-pyran rings thus forming short-lived colored species identified as *p*-nitrophenolate chromophores **5'a-c**,**e-j**,**t** [77]. These compounds subsequently revert back to the ground state thermally (*scheme 3.8.3*).



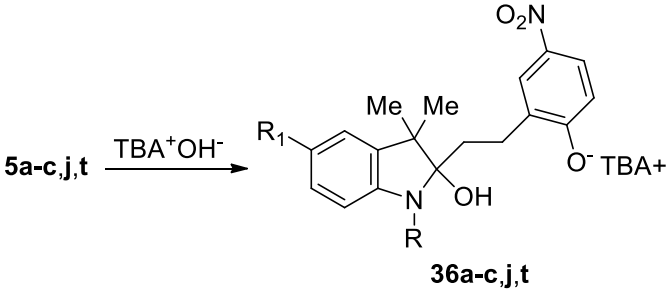
Scheme 3.8.3. Photochromism of 6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indoles]

All the tested compounds were shown to exhibit a photochromic response. The photochromic behavior of compounds **5a-c**,**j** is qualitatively similar; therefore the graphical data only for **5a** is presented.

As shown in *Fig. 3.8.1*, the electronic spectrum of compound **5a** measured 5 ns after excitation exhibits an absorption with a sharp maximum at 450 nm possibly originating from the *p*-nitrophenolate chromophore **5'a** formed upon excitation. This feature is accompanied by a broad plateau with an amplitude approximately five times less than the maximum. The photoinduced absorption spectra of **5b**,**c**,**j** were similar to that of **5a** and may be interpreted as evidence of the formation of the corresponding chromophores **5'b**,**c**,**j** (*Table 3.4*).

In contrast, the induced absorption spectrum of **5t** is dominated by a broad band covering the entire blue-green-yellow part of the visible spectrum with the red tail extending to 800 nm. Superimposed on the blue part of this band, a sharp feature peaking at 420 nm related to the *p*-nitrophenolate chromophore **5't** may be discerned; yet the amplitude of this peak is only 20% larger than that of the underlying band. It must be noted that the photoinduced spectra of **5a** and **5t** bear significant differences from the absorbance spectra of these compounds measured

after their treatment with tetrabutylammonium hydroxide (TBA^+OH^-), which suggests that the ring opening by a strong base results in a different molecular and conformational form, e.g., 2-hydroxyindoline derivatives **36a-c**,**j**,**t** (*Scheme 3.8.4*).



Scheme 3.8.4. The ring-opening reaction of **5a-c**,**j**,**t** induced by a strong base.

A study of the time dependence of interconversion (*Fig. 3.8.2, Table 3.4*) revealed that **5**'**a-c**,**j** reverted to their original ground states **5a-c**,**j** via thermal pathways over tens of nanoseconds. However, in the case of **5t**, the corresponding decay was substantially slower (484 ns), suggesting that the presence of the strong electron-withdrawing nitro group on the indole section of the molecule stabilizes the induced form (**5**'**t**) and inhibits the 3,4-dihydro-2*H*-pyran ring closure.

Quantum yields (Φ) of the photocoloration of **5a-c**,**j**,**t** were determined by applying the method described by Raymo et al. [78]. Benzophenone in acetonitrile was used as a reference. For **5a-c**,**j**,**t**, the observed Φ values ranged between 5.5% (**5a**) and 9.2% (**5t**) (*Table 3.4*).

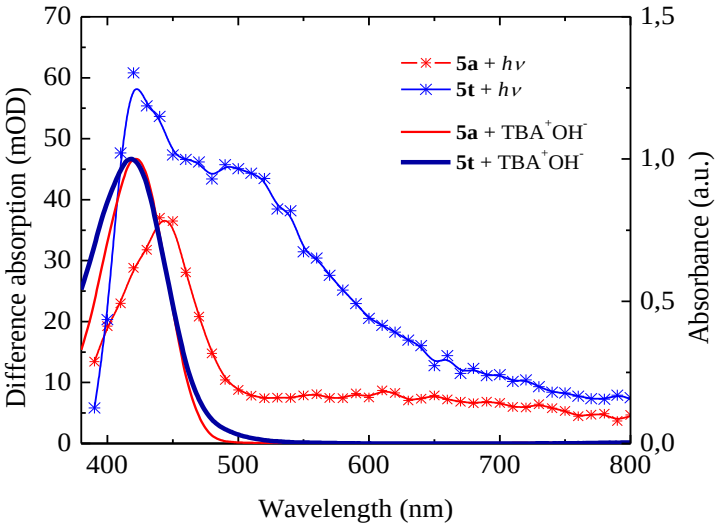


Fig. 3.8.1. Photo-induced absorption spectra of **5a** and **5t** measured at 5 ns after the excitation and normalized absorption spectra of **5**a and **5t** after treatment with TBA^+OH^-.

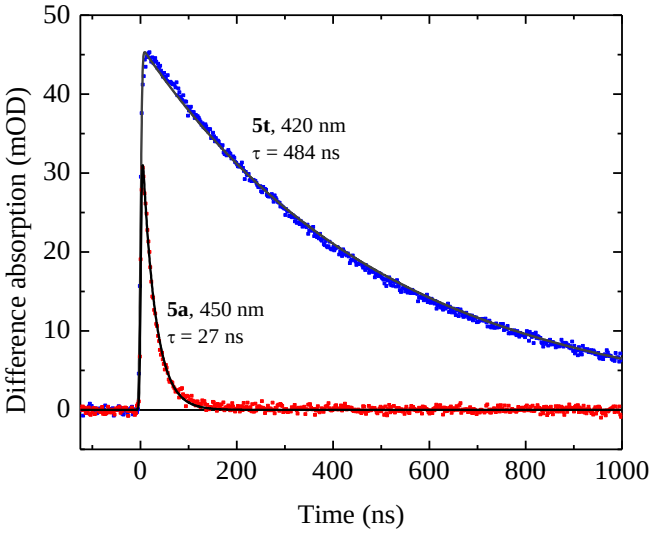


Fig. 3.8.2. Diff. absorption traces of **5'a** and **5't** for selected time delays.

During the collection of the flash-photolysis data, the photostability of the investigated compounds was also evaluated. Compound **5a** exhibited the highest photostability as it withstood 4000 pulses of approximately 3.5 mJ with negligible change in its steady-state and transient absorption spectra.

Benz[*e*]indole derivatives **5e-i** were also tested under the same conditions. Their photochromic behavior is qualitatively similar; therefore, only the graphic data of **5e** is presented. A study of the time dependence of interconversion (*Fig. 3.8.3, Table 3.5*) showed that **5'e** reverted to its original ground state **5e** via thermal pathways over 17 nanoseconds.

The electronic spectrum of compound **5e** measured 5 ns after excitation demonstrates an absorption with two maximums at 410 and 520 nm, possibly originating from the *p*-nitrophenolate chromophore **5'e** formed upon excitation and electronic system changes in benz[*e*]indole moiety (*Fig. 3.8.4, Table 3.5*).

Quantum yields (Φ) of the photocoloration of **5e-i**, ranged between 2.8% (**5g**) and 4.2% (**5i**) (*Table 3.5*).

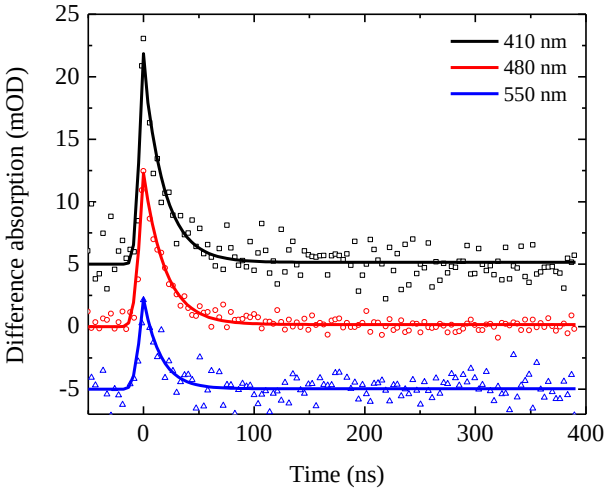


Fig. 3.8.3. Diff. absorption traces of **5e** for selected wavelengths

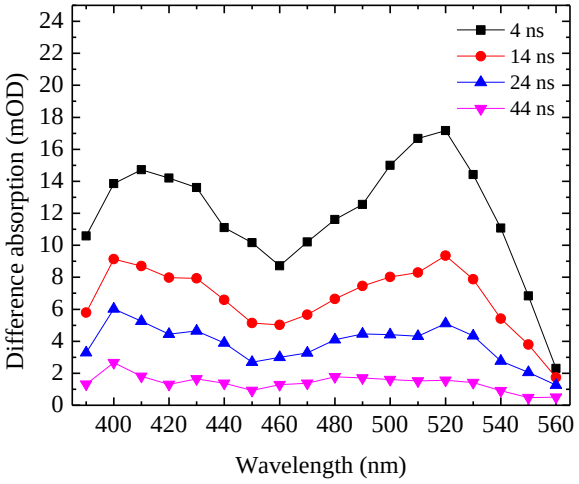


Fig. 3.8.4. Diff. absorption traces of **5e** for selected time delays

Photochromic properties of (5b*R**, 8a*R**, 14a*S**)-1,5b-dimethyl-11-nitro-5b,6,7,8,8a,9-hexahydro-8*H*-indole[2,3-*c*]xantene **20a** were tested under the same conditions (355 nm, 4 mJ excitation, acetonitrile solution, approximately 0.1mM). As shown in *Fig. 3.8.5*, the electronic spectrum of compound **20a** measuring 5 ns after excitation shows an absorption with a sharp maximum at 450 nm, possibly originating from the *p*-nitrophenolate chromophore as described above.

For the determination of the relaxation time, a two-component model was used in global analysis approximations, specifically, a double exponential decay with a time constant of 14 ns and 36 ns.

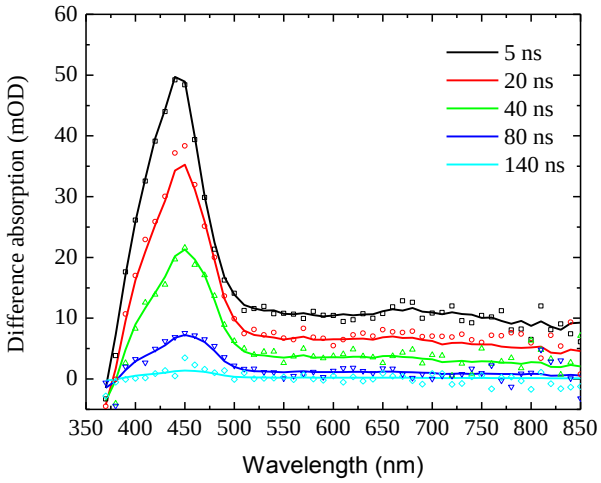


Fig. 3.8.5. Diff. absorption traces of **20a** for selected time delays

Azobenzene moiety containing compound **25a** was also tested as a potential photochrome under the same conditions (355 nm, 4 mJ excitation, acetonitrile solution, approximately 0.1mM). The experiment revealed that, under the above outlined conditions, **25a** as a photochrom is quite unstable nor does it show a considerable induced absorption. A long term (μs scale) emission signal was observed in the kinetic curves. The relaxation time of the weak signal of the induced absorption is approximately 130 ns (*Fig. 3.8.6*).

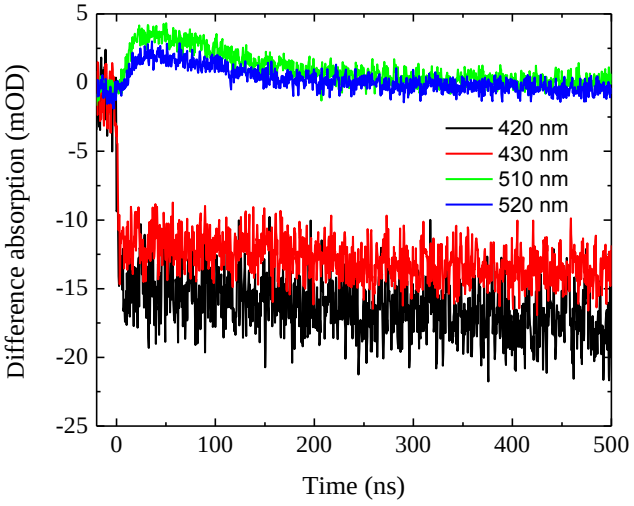
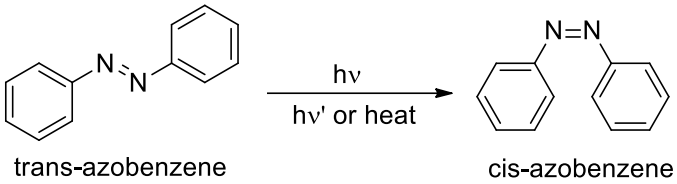


Fig. 3.8.6. Diff. absorption traces of **25a** for selected wavelengths

It is known that azobenzene in solutions undergoes photochemical cis-trans isomerization [79] as shown in *scheme 3.8.5.*



Scheme 3.8.5. Azobenzene photoisomerisation

The obtained data suggests that the energy of nanosecond laser pulses instead of cleaving C-O bonds in the 3,4-dihydro-2*H*-pyran ring might be causing azobenzene moiety isomerisation which was impossible to observe under the present research conditions since the process takes place in the femtosecond time scale.

Table 3.4. UV-VIS spectral and flash photolysis experiment data for the indoline derivatives **5a-c**,**j**,**t**

Entry	Compound	UV-VIS spectral data*		Flash photolysis experiment data*		
		λ_{max} of **5** (nm)	$\varepsilon \times 10^3$ (dm^3 mol^{-1} cm^{-1})	λ_{max} of the photoinduced form **5'** (nm)	Relaxation time, τ (ns)	Quantum yield, Φ (%)
1	**5a**	205 243 326	51.44 16.32 14.61	450	27	5.5
2	**5b**	205 246 326	42.29 14.41 12.48	450	36	5.8
3	**5c**	205 244 313	46.09 16.68 12.37	450	37	5.7
4	**5j**	206 245 313	46.30 15.74 13.57	450	22	5.6
5	**5t**	230 (shoulder) 330 (shoulder) 380	14.13 14.61 22.14	420	484	9.2

***** Measurements and calculations were performed at Laser Research Center of Vilnius University by assoc. prof. dr.Mikas Vengris and Kipras Redeckas.

Table 3.5. UV-VIS spectral and flash photolysis experiment data for the benz[*e*]indoline derivatives **5e-i**

Entry	Compound	UV-VIS spectral data**				Flash photolysis experiment data**		
		λ_{max} of **5** (nm)	$\varepsilon \times 10^3$ (dm^3 mol^{-1} cm^{-1})	λ_{max} of the chemically induced form **36**(with TBAOH) (nm)	$\varepsilon \times 10^3$ (dm^3 mol^{-1} cm^{-1})	λ_{max} of the photoinduced form **5'** (nm)	Relaxation time, τ (ns)	Quantum yield, Φ (%)
1	**5e**	293 304 326	12.6 14.9 13.8	297 310 321 **440**	10.5 13.0 12.1 24.2	410 520	17	3.5
2	**5f**	294 304 326	13.0 15.5 13.5	311 322 **438**	14.4 15.0 23.5	420 530	22	3.3
4	**5g**	295 305 326	14.4 17.0 15.0	312 322 **440**	16.0 17.5 23.7	410 520	24	2.8
3	**5h**	292 304 326	13.8 16.0 14.6	297 309 320 **439**	11.8 14.3 13.3 23.8	420 530	25	3.5
5	**5i**	293 304 324	14.1 16.4 14.6	296 308 320 **439**	12.7 14.8 12.7 23.3	420 530	31	4.2

****** The measurements and calculations were performed by the author of the thesis at the Department of Organic Chemistry of Kaunas University of Technology.

3.9. Cyanide dedection using 1',3,3',4-tetrahydrospiro[chromene-2,2'-indoles]

Common methods for the determination of cyanides involve optical (naked eye detection [80] and spectrophotometry [81]), electrochemical (potentiometry [82] and amperometry [83]) methods, mass spectrometry [84] and gas chromatography [85]. Many variations of these methods are known and have already been thoroughly described [86]. Although the listed techniques satisfy common legal requirements, usually they are still complex and time-consuming; they also suffer from numerous interferences and often require significant preconcentration. Many research groups made efforts to create simple and inexpensive but rapid, sensitive and selective methods for cyanide detection, especially in aqueous environment. Optical sensors for cyanide, in which a change in color and/or fluorescence intensity (or emission wavelength) is monitored, appeared to be one of the most convenient options and have been actively researched during the last decade [87].

In this paper it was determined that spiro[chromene-2,2'-indole] derivatives have a potential to be used for spectrophotometric or naked-eye visual cyanide ion detection.

The steady state absorbance spectra of compounds **5a-j**,**q**,**s-u** measured for solutions in the CH_3CN/phosphate buffer revealed absorption in the UV-region of electronic spectra (*Table 3.6*). However, when a NaCN solution buffered with sodium phosphate (pH 7.6) was added to the aforementioned solutions of compounds **5a-j**,**q**,**s-u** (0.1 mM of **5a-j**,**q**,**s-u**; 1 mM NaCN in the cell), a new absorption band was observed in the visible area of approximately 420 nm (*Table 3.6*, *Fig. 3.9.1*).

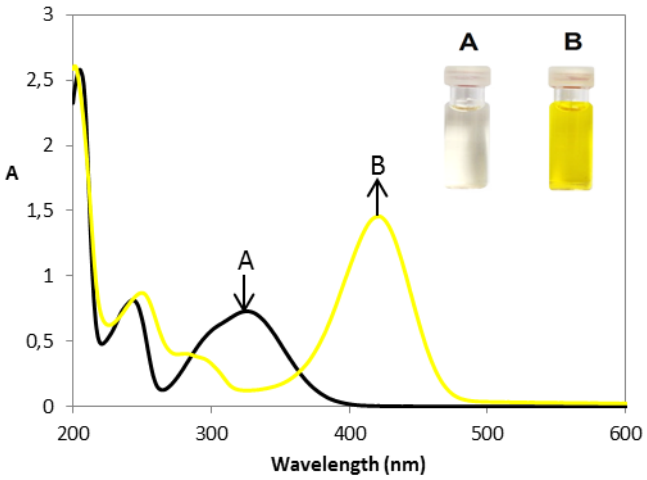
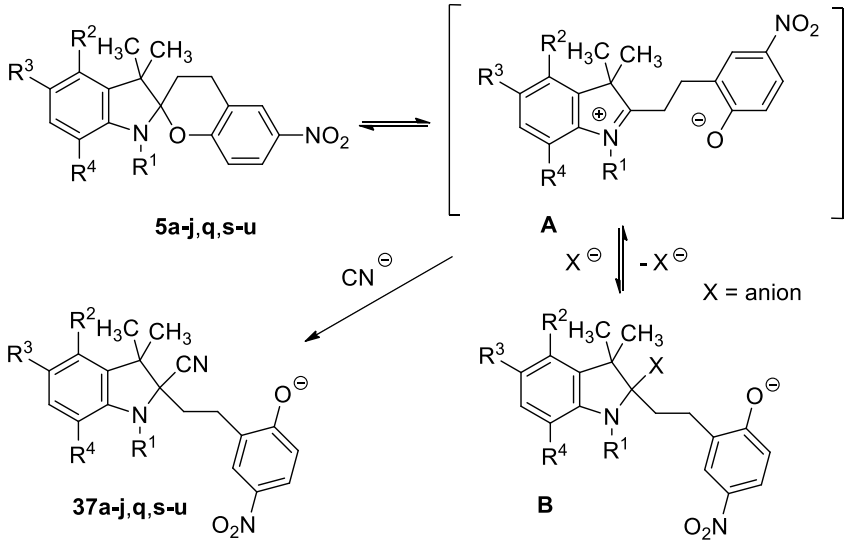


Figure 3.9.1. Absorption spectra of **5a** (0.1 mM, 298 K) in a mixture of CH_3CN/phosphate buffer (Na_2HPO_4/NaH_2PO_4, 7.5 mM, pH 7.6) (19:1, v/v) without NaCN (spectrum A) and with NaCN (10 equiv, spectrum B)

Table 3.6. UV-vis spectral data

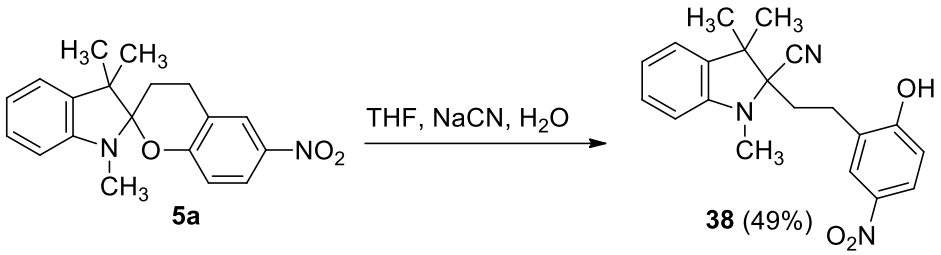
Compound	λ_{max} of **5** (nm)	$\varepsilon \times 10^3$ ($dm^3mol^{-1}cm^{-1}$)	λ_{max} of **37** (nm)	$\varepsilon \times 10^3$ ($dm^3mol^{-1}cm^{-1}$)
5a	205	51.4	250	17.2
	243	16.3	282	7.7
	326	14.6	**422**	29.0
5b	205	42.3	253	12.2
	246	14.4	286	9.1
	326	12.5	**420**	20.7
5c	205	46.1	254	42.3
	244	16.7	298	23.4
	313	12.4	**419**	23.4
5d	205	54.3	252	31.3
	242	17.9	298	17.2
	312	12.9	**418**	17.6
5e	213	51.8	214	55.6
	247	71.6	250	72.24
	324	21.0	422	37.1
5f	213	36.2	216	36.6
	250	57.5	254	53.3
	323	15.5	422	25.6
5g	213	33.4	215	34.1
	249	54.3	254	50.4
	325	14.4	422	23.3
5h	214	34.6	215	35.2
	248	56.9	252	52.0
	325	14.6	422	23.7
5i	212	43.3	215	41.7
	248	60.4	251	51.1
	324	15.2	422	22.0
5j	206	46.3	255	41.9
	245	15.7	300	23.3
	313	13.6	**422**	24.8
5q	238	21.0	246	19.3
	317	21.6	304	6.8
			422	34.6
5s	229	11.8	254	13.8
	321	12.7	**422**	30.0
	375	19.0		
5t	230	14.1	257	14.5
	330	14.6	**424**	32.3
	380	22.1		
5u	210	37.2	253	10.4
	246	10.7	293	4.2
	326	11.2	**422**	21.8

The appearance of this band in the visible region can be rationalised by the spirochromene ring-opening and the formation of 4-nitrophenolate chromophores **37a-j**,**q**,**s-u** due to the nucleophilic substitution of the phenolic oxygen by a cyanide group. In this case, the limiting step of the reaction is the $C_{(spiro)}$-O covalent bond cleavage and the formation of the intermediates **B** which are in an equilibrated mixture with the starting 1',3,3',4-tetrahydrospiro [chromene-2,2'-indoles] **5a-j**,**q**,**s-u**. However, the intermediates **A** are quickly consumed as the nucleophilic addition of the cyanide anion to the C-2 carbon tends to form stable nitriles **37a-j**,**q**,**s-u**. In such a scenario, the ring-opening reaction of **5a-j**,**q**,**s-u** becomes irreversible (*scheme 3.9.1*).



Scheme 3.9.1. Formation of 4-nitrophenolate chromophore **37**.

When compound **5a** was treated with sodium cyanide in THF containing a small amount of water, the reaction afforded the indole-2-carbonitrile **38** (*Scheme 3.9.2*) whose structure was confirmed by spectroscopic research methods and elemental analysis. The IR spectrum of **38** showed an absorption band at 2222 cm^{-1}, which is characteristic for nitriles [88]. The heteronuclear multiple bond coherence (HMBC) spectrum revealed three bonds range coupling between methylidene protons at 2.15 and 2.30 ppm and the nitrile carbon at 118.49 ppm [89]. These protons also interacted with the quaternary carbon at 76.75 ppm separated by two bonds and with the quaternary carbons at 46.76 and 128.16 ppm separated by three bonds. The full assignments presented in *Fig. 3.9.2* were based on the combined application of such standard NMR techniques as COSY, NOESY, ROESY, APT, DEPT, HSQC and HMBC spectra.



Scheme 3.9.2. Formation of 1*H*-indole-2-carbonitrile **38**.

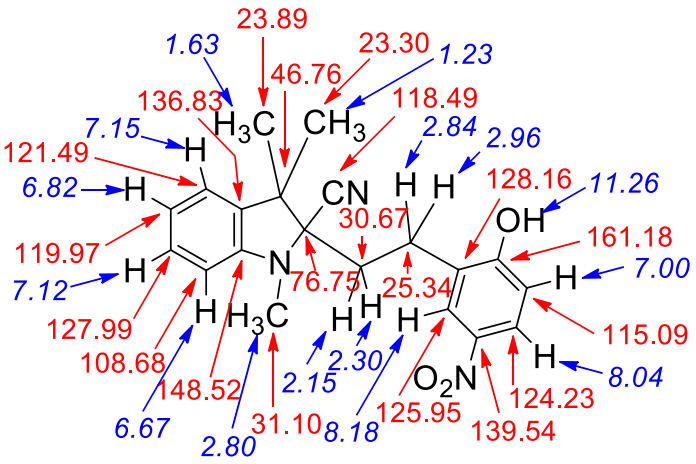


Fig. 3.9.2. ^{1}H (italics, in blue) and ^{13}C (in red) chemical shifts [ppm] for **38** in DMSO-d_6.

6-((4-Nitrophenyl)diazenyl)spiro[chroman-2,2'-indole] derivatives **25a-d** were also investigated as potential chemosensors for cyanide detection. Since these compounds have a more extended chromophoric system, they showed a substantial color change from orange to magenta (in cases of **25a,c**) and from orange to blue (**25b,d**) when treated with cyanide ions in CH_3CN solution buffered with sodium phosphate (*Fig. 3.9.3)*. The mechanism for detection is analogous to the one described above: the nucleophilic substitution of the phenolic oxygen atom at the indoline C-2 atom by the cyanide anion forms a stable indolylnitrile adduct and generates the colored 4-nitrophenylazophenolate chromophore as shown in *scheme 3.9.3*.

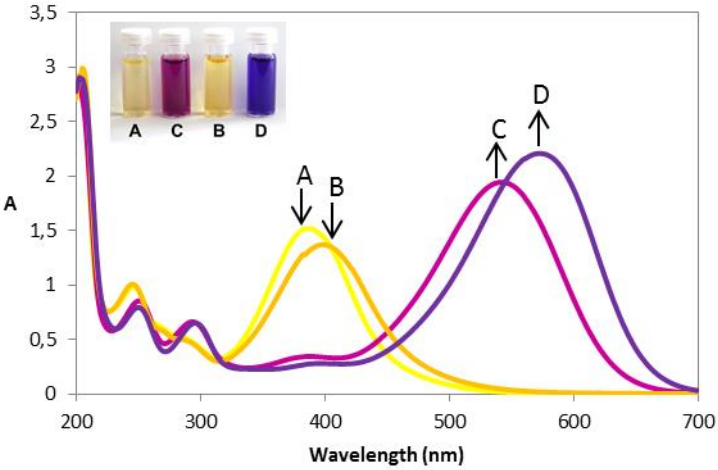
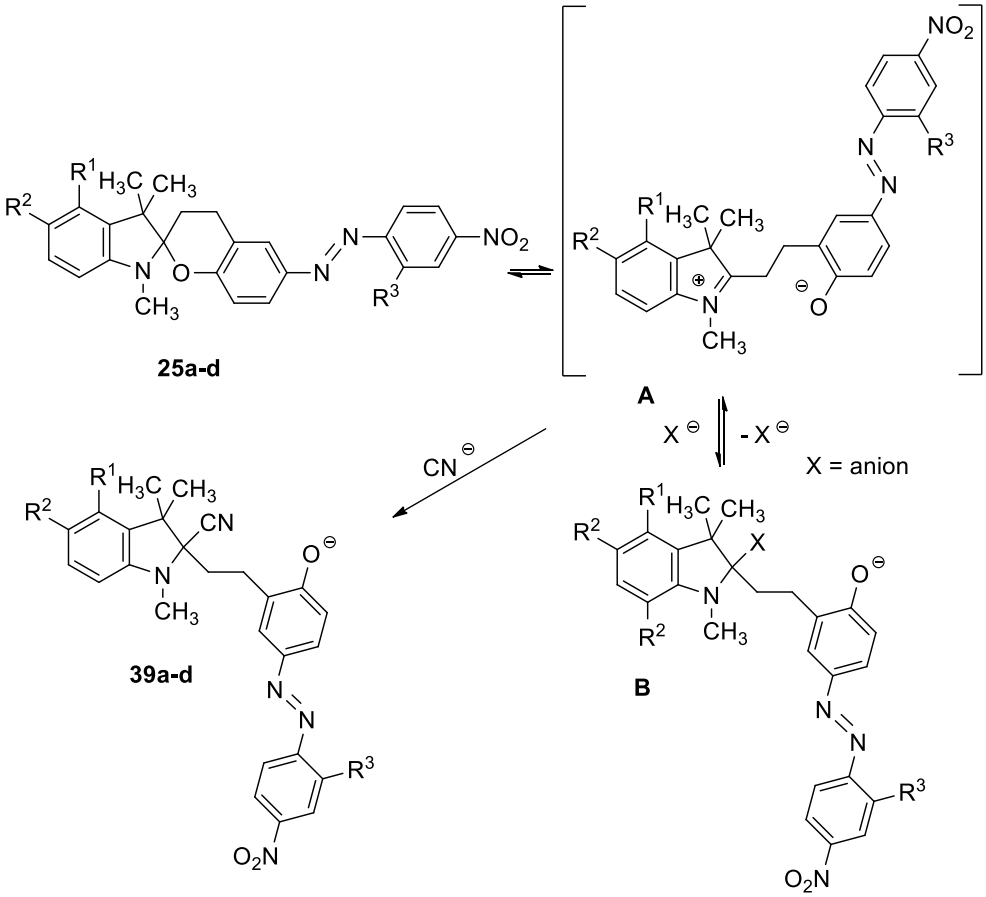


Fig. 3.9.3. Absorption spectra of **25a** and **25b** (0.1 mM, 298 K) in a mixture of CH_3CN/phosphate buffer (Na_2HPO_4/NaH_2PO_4, 7.5 mM, pH 7.6) (19:1, v/v) without NaCN (**25a** – spectrum A, **25b** – spectrum B) and with NaCN (10 equiv, **39a** – spectrum C, **39b** – spectrum D).



Scheme 3.9.3. Formation of 4-nitrophenylazophenolate chromophore

It was observed that the chloride atom in the (4-Nitrophenyl)diazenyl part of the molecule causes a batochromic shift in the absorption spectra: from 388 nm to 398 nm between **25a** and **25b**, and from 544 nm to 574 nm between **39a** and **39b**. Analogous shifts were also observed for **25c** and **25d** as well as for **39c** and **39d**.

3.9.1. Response time

For various types of chemosensors, the response time is very important for the practical detection of analytes. In this paper it was observed that the response time depends on the structure of the compound. After the addition of sodium cyanide to the solutions of compounds **5a**,**b**,**e**,**f**,**j**,**q**,**u**, a strong new absorption band at 422 nm appeared within 1 to 3 minutes (*Fig. 3.9.4*) while for compounds **5c**,**d**,**g-i**,**s**,**t** this process took 20 minutes to 1.5 h (*Fig. 3.9.5*). We concluded that the presence of a nitro group at C-5 of the indole nucleus at **5s**,**t** stabilizes the closed-form of the molecule and slows down the formation of the final adduct **37s**,**t**. Both electronic and steric effects may be considered for explaining the influence of the propyl, allyl and benzyl groups at the indole nitrogen atom on the formation of adducts **37c**,**d**,**g-i**

after the addition of sodium cyanide to a solution of compounds **5c**,**d**,**g-i** respectively.

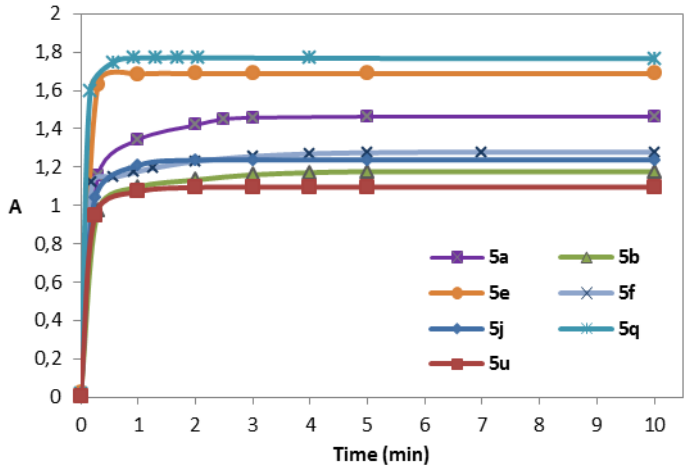


Fig. 3.9.4. Absorbance changes at 422 nm for **5a**,**b**,**e**,**f**,**j**,**q**,**u** (0.1 mM, 298 K) in a mixture of CH_3CN/phosphate buffer (Na_2HPO_4/NaH_2PO_4, 7.5 mM, pH 7.6) (19:1, v/v) after the addition of NaCN (10 equiv).

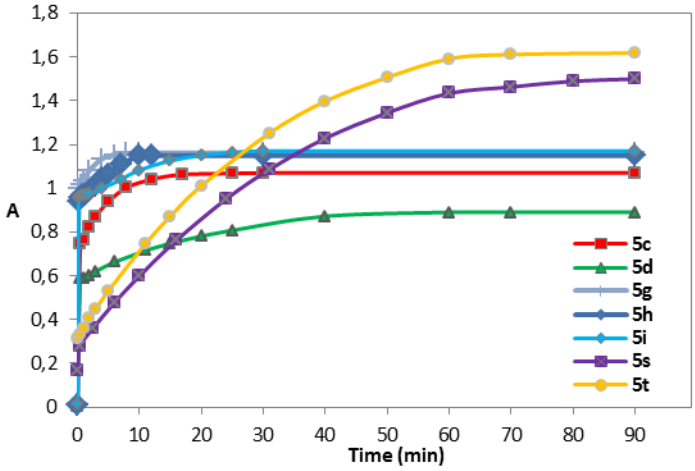


Fig. 3.9.5. Absorbance changes at 422 nm for **5c**,**d**,**g-i**,**s**,**t** (0.1 mM, 298 K) in a mixture of CH_3CN/phosphate buffer (Na_2HPO_4/NaH_2PO_4, 7.5 mM, pH 7.6) (19:1, v/v) after the addition of NaCN (10 equiv).

The response times of 6-((4-Nitrophenyl)diazenyl)spiro[chroman-2,2'-indole] derivatives **25a-d** were evaluated in analogous conditions, and the formation of the coloured adduct **39a-d** took from 5 to 15 minutes (*Fig. 3.11.6*).

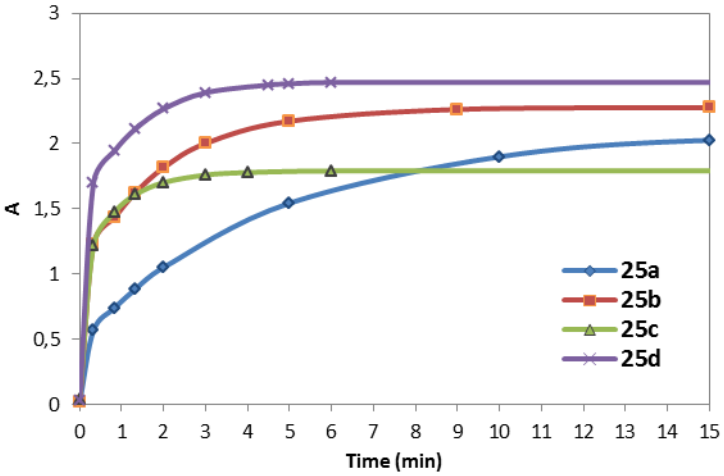


Fig. 3.9.6. Absorbance changes at 544, 574, 541 and 573 nm for **25a-d** respectively (0.1 mM, 298 K) in a mixture of CH_3CN/phosphate buffer (Na_2HPO_4/NaH_2PO_4, 7.5 mM, pH 7.6) (19:1, v/v) after the addition of NaCN (10 equiv).

3.9.2. Selectivity

To test the selectivity of chemosensors **5a**, **5e** and **25c**, parallel investigations were carried out with a series of other anions (specifically, F^-, Cl^-, Br^-, I^-, CH_3COO^-, $C_2O_4^{2-}$, HCO_3^-, HSO_3^-, HSO_4^-, NO_2^-, NO_3^-, SCN^-, SO_3^{2-}, SO_4^{2-}, $S_2O_3^{2-}$). The addition of excess amounts of the other anions did not result in significant absorbance spectral changes during UV–vis titration (*Fig. 3.9.7*), which indicates that this potential chemosensor demonstrates excellent selectivity over other common anions.

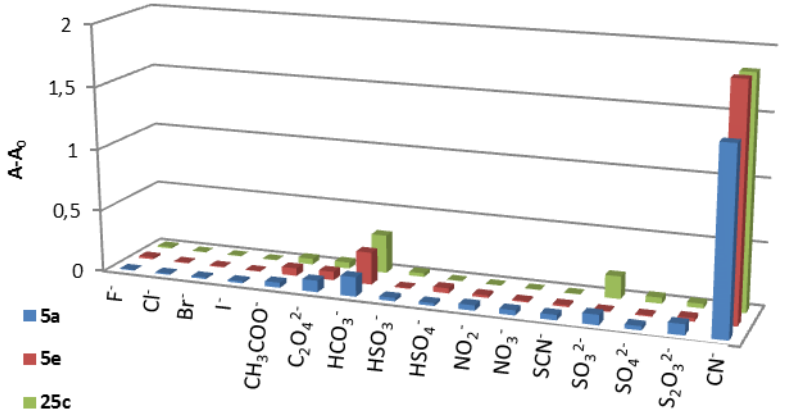


Fig. 3.9.7. Absorbance at 422 nm of **5a**,**e** and at 544 nm for **25c** (0.1 mM, 298 K) in a mixture of CH_3CN/phosphate buffer (Na_2HPO_4/NaH_2PO_4, 7.5 mM, pH 7.6) (19:1, v/v) in the presence of CN^- or other common anions (10 equiv); A_0 is the absorbance of **5a**,**e** at 422 nm and at 544 nm for **25c** in the absence of CN^-.

The high selectivity of chemosensing may be explained by the fact that only the addition of a cyanide anion on the indoline nucleus forms a strong enough covalent bond with the indole C(2) atom to afford stable nitriles **37** and **39** whereas the addition of the other aforementioned anions is a reversible process.

3.9.3. Sensitivity

World Health Organization recommends that water containing more than 0.07 mg/l (27×10^{-7}M) CN^- should not be used as domestic supply [90]. According to standards and specifications set in the *EU Drinking Water Directive* and applied in all the member states of the European Union, the maximum allowed value is 50 μg/l (19×10^{-7}M) CN^-[91]. These low limits mean that it is essential to use extremely sensitive methods for detecting and determining cyanide.

The calibration plot of cyanide concentration versus the most sensitive absorption for **5a**,**e**,**q** and **24c** (*Fig. 3.9.8*) shows that this potential chemosensor is sensitive in relatively low concentrations of CN^- and meets the established water quality control criteria.

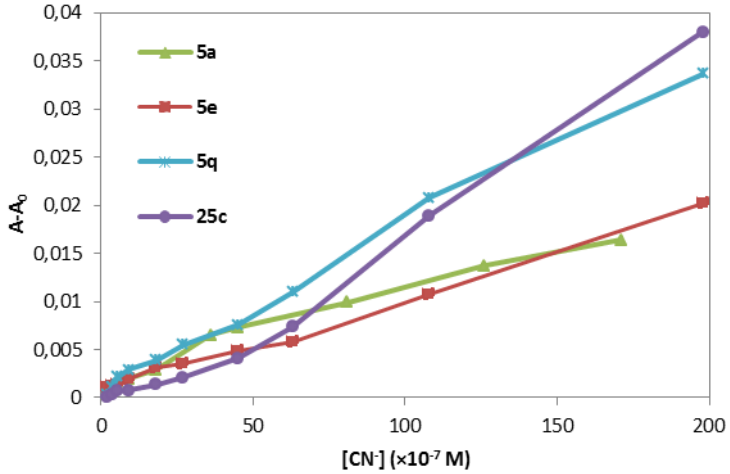


Fig. 3.9.8. Absorbance at 422 nm of **5a**,**e**,**q** and at 544 nm of **25c** (0.1 mM, 298 K) in a mixture of CH_3CN/phosphate buffer (Na_2HPO_4/NaH_2PO_4, 7.5 mM, pH 7.6) (19:1, v/v) in the presence of various concentrations of CN^- where A_0 is the absorbance of **5a**,**e**,**q** at 422 nm and at 544 nm of **25c** in the absence of CN^-(standard deviation 0.0002).

4. EXPERIMENTAL PART

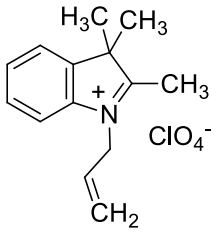
Materials and instruments

Unless otherwise stated, all the starting materials and reagents were obtained from commercial suppliers and used without further purification. Reactions were monitored by TLC analysis on precoated silica gel plates (Kieselgel $60F_{254}$, Merck). Compounds were visualized with UV light and charring after treatment with a 1% $KMnO_4$ solution spray. Column chromatography was performed on silica gel SI 60 (43-60 μm, E. Merck). Melting points were determined in open capillary tubes with a Büchi B-540 melting point apparatus and were uncorrected. Infrared spectra were recorded on a Perkin Elmer Spectrum One spectrometer using potassium bromide pellets. ^{1}H NMR spectra were recorded at 300 MHz on a Varian Unity Inova spectrometer at 400 MHz, and 700 MHz on Bruker Avance III spectrometers. ^{13}C NMR spectra were collected by using the same instruments at 75, 100 and 175 MHz. Chemical shifts are expressed in ppm downfield relative to TMS and coupling constants (*J*), referring to apparent peak multiplicity, are reported in Hz. High-resolution ESI-TOF mass spectra were measured on Bruker maXis and micrOTOF-Q III spectrometers. Diffraction data was collected on a Bruker-Nonius KappaCCD diffractometer at room temperature and at -100 °C by S.V. Belyakov (Latvian Institute of Organic Synthesis). The crystal structures were solved by using known programs [92]. Elemental analyses were conducted by employing Elemental Analyzer CE-440 (Exeter Analytical, Inc.) at the Microanalytical Laboratory, Department of Organic Chemistry, Kaunas University of Technology. UV/vis spectra were determined on a PerkinElmer Lambda 35 spectrometer using quartz cells with a light path length of 0.5 cm. Mass spectra were measured with a Waters ZQ ion spray instrument and a Shimadzu LCMS-2020. Microwave reactions were conducted by using a CEM Discover Synthesis Unit (CEM Corp., Matthews, NC). This machine consists of a continuous focused microwave power delivery system with the operator-selectable power output ranging from 0 to 300 W. The reaction was performed in glass vessels (capacity 10 mL) sealed with a septum. The pressure was controlled by a load cell connected to the vessel. The temperature of the contents of the vessel was monitored by using a calibrated infrared temperature control unit mounted under the reaction vessel. All the experiments were performed by using the stirring option whereby the contents of the vessel are stirred by means of a rotating magnetic plate located below the floor of the microwave cavity and a tefloncoated magnetic stir bar inside the vessel. An in-house flash-photolysis spectrometer was employed to collect transient absorption data in the nanosecond-to-microsecond time domain. Flash photolysis experiments were performed by using a Nd:YAG laser (EKSPLA NL30) while pulses of the third harmonic (wavelength -355 nm, duration – 3-6 ns) were applied for excitation. Difference absorption was registered by measuring the intensity of a Xe flash lamp's emission passing through a cuvette containing the sample. The collected time-resolved spectra and traces were analyzed by using global analysis techniques described in [93].

For the measurement of UV/vis absorption, compounds **5a-j**,**q**,**s-u** and **25a-d** were dissolved in a mixture of CH_3CN/phosphate buffer (Na_2HPO_4/NaH_2PO_4, 7.5 mM, pH 7.6) (19:1, v/v, 298 K). Each solution (0.1 mM) was transferred to a spectrophotometer quartz cell (0.5 cm light path length), and 0.025 mL 72 mM sodium cyanide solution was added. This volume was negligible compared to the initial volume of the solution in the cell (1.8 mL). The mixtures were shaken, and the absorption was measured from 200 to 600 nm against a CH_3CN/phosphate buffer (19:1, v/v, 298 K) blank. A 72 mM sodium cyanide stock solution was prepared from sodium cyanide and diluted to the levels of 36 mM, 3.6 mM and 0.72 mM. To construct a calibration curve of cyanide concentration versus the most sensitive absorption at 422 nm for **5a**,**e**,**q**, and at 544 nm for **25c**, various cyanide solutions (25, 50, 75, 125, 250, 500 μL of 0.72 mM and 25, 125, 250, 375 μL of 3.6 mM) were added to 100 mL of 0.1 mM **5a**,**e**,**q**, and **25c** solutions in CH_3CN/phosphate buffer. All of the added volumes of cyanide were negligible, with 0.875 mL as the highest volume compared to the initial volume of the **5a**,**e**,**q** and **25c** solutions.

Synthesis procedures and spectral data

1-Allyl-2,3,3-trimethyl-3*H*-indolium perchlorate **2c**



To a stirred solution of 2,3,3-trimethyl-3*H*-indolium chloride (0.975g, 5 mmol) in distilled water (15mL), sodium carbonate (1.06g, 10mmol) was added. The mixture became turbid and was extracted with diethyl ether (3 × 20 mL); the combined extract was dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure to give brown oily material which was disolved in acetone (4mL). Then, 3-bromoprop-1-ene (1.21g, 10 mmol) was added, and the obtained mixture was stirred for 5 hours at 60 °C; afterwards, the solvent was evaporated under reduced pressure. The residue was dissolved in ethanol, and 42% perchloric acid was added drop-wise until pH=2, and the mixture was kept at 5 °C for 18 hours. The formed crystals were separated by filtration and purified by recrystallization from ethanol. The yield measured 0.764 g (51%), mp 170–172 ºC.

^{1}H NMR (300 MHz, TFA-D): δ 1.67 (s, 6H, 2×3-CH_3), 2.84 (s, 3H, 2-CH_3), 5.15 (dt, *J* = 5.1 Hz, *J* = 1.5 Hz, 2H, N-CH_2), 5.34 (dt, *J* = 17.1 Hz, *J* = 1.5 Hz, 1H, =CH_2) 5.56(dt, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H, =CH_2), 6.01-6.13 (m, 1H, -CH=), 7.62-7.71(m, 4H, Ar-H).

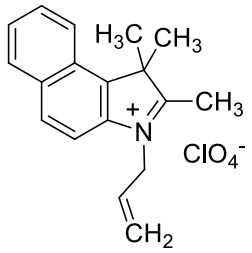
^{13}C NMR (75 MHz, TFA-D): δ 15.0, 23.9 (2×CH_3), 52.5, 57.4, 117.3, 123.0, 125.6, 128.5, 132.0, 133.2, 143.1, 144.0, 199.3.

IR (cm^{-1}): 3063, 2977, 1629 ($C=N^+$), 1095 (ClO_4^-), 624 (ClO_4^-).

MS m/z (%): 200 (M^+, 100).

Anal. Calcd for $C_{14}H_{18}ClNO_4$, %: C 56.10; H 6.05; N 4.67. Found: C 55.96; H 6.26; N 4.73.

3-Allyl-1,1,2-trimethylbenz[e]indolium perchlorate **2h**



To a solution of 1,1,2-trimethylbenz[*e*]indole (1.046 g, 5 mmol) in acetonitrile (10 mL), allyl bromide (1.815 g, 15 mmol) was added, and then the mixture was heated under reflux for 24 hours. Afterwards, the solvent was evaporated under reduced pressure. The residue was dissolved in ethanol, and 42% perchloric acid was added drop-wise until pH=2 and stored at 5 ℃ for 18 hours. The formed crystals were separated by filtration and purified by recrystallization from ethanol. The resulting yield was 0.437 g (25%), mp 197–200 ºC.

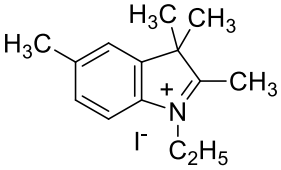
^{1}H NMR (400 MHz, TFA-D): δ 2.07 (s, 6H, 2×3-CH_3), 3.09 (m, 3H, 2-CH_3), 5.42 (d, *J* = 5.1 Hz, 2H), 5.49 (d, *J* = 17.2 Hz, 1H), 5.74 (d, *J* = 10.4 Hz, 1H), 6.30 (ddd, *J* = 17.3, 10.4, 5.2 Hz, 1H, -CH=), 7.99 – 7.81 (m, 3H), 8.40 – 8.23 (m, 3H).

^{13}C NMR (100 MHz, TFA-D): δ 14.5, 23.3 (2×CH_3), 52.3, 58.5, 113.5, 122.6, 124.6, 128.4, 130.1, 130.2, 131.0, 132.1, 133.9, 136.6, 139.5, 140.1, 198.5.

IR (cm^{-1}): 3087, 2982, 1635 (C=N$^+$).

ESI-HRMS: [M$^+$], found 250.1590. [$C_{18}H_{20}N^+$] requires 250.1590.

1-Ethyl-2,3,3,5-tetramethyl-3*H*-indolium iodide **2k**



To a solution of 2,3,3,5-tetramethyl-3*H*-indole (0.866 g, 5 mmol) in acetonitrile (5 mL), iodoethane (1.42 g, 10 mmol) was added, and the reaction mixture was heated at reflux. After 6 h, the resultant crystalline material was filtered and recrystallized from ethanol. The yield was 1.383 g (84%), mp 142–144 ºC.

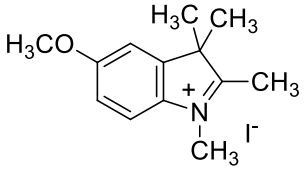
^{1}H NMR (400 MHz, TFA-D): δ 1.90 (s, 6H, 2×3-CH_3), 1.92 (t, *J* = 7.6 Hz, 3H, $CH_2\underline{CH_3}$), 2.81 (s, 3H), 3.10 (s, 3H), 4.82 (q, *J* = 7.6 Hz, 2H, $\underline{CH_2}CH_3$), 7.73 – 7.89 (m, 2H), 7.82 – 7.88 (m, 1H).

^{13}C NMR (100 MHz, TFA-D): δ 14.2, 14.9, 22.4, 24.0 (2×CH_3), 46.2, 57.0, 116.6, 126.3, 132.7, 140.5, 144.4, 145.2, 196.2.

IR (cm^{-1}): 3055, 2972, 1624 (C=N$^+$).

ESI-HRMS: [M$^+$], found 202.1590. [$C_{14}H_{20}N^+$] requires 202.1590.

1,2,3,3-Tetramethyl-5-methoxy-3*H*-indolium iodide **2q**



To a solution of 2,3,3-trimethyl-5methoxy-3*H*-indole (0.946 g 5 mmol) in acetonitrile (5 mL), iodomethane (1.42 g, 10 mmol) was added, and the reaction mixture was heated at reflux. After 12 h, the resultant crystalline material was filtered and recrystallized from ethanol. The yield was 1.241 g (75%) mp 192–194 ºC.

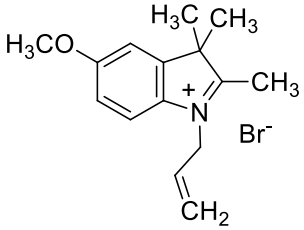
^{1}H NMR (400 MHz, TFA-D): δ 1.81 (s, 6H, 2×3-CH_3), 2.98 (s, 3H), 4.19 (s, 3H), 4.26 (s, 3H), 7.42 – 7.36 (m, 2H), 7.43 (d, *J* = 2.3 Hz, 1H).

^{13}C NMR (100 MHz, TFA-D): δ 14.9, 23.7 (2×CH_3), 36.5, 56.8, 57.8, 111.6, 117.1, 117.9, 122.7, 137.7, 145.8, 195.7.

IR (cm^{-1}): 3011, 2975, 1619 ($C=N^+$).

ESI-HRMS: [M^+], found 204.1383. [$C_{13}H_{18}NO^+$] requires 204.1383.

1-Allyl-2,3,3-trimethyl-5-methoxy-3*H*-indolium bromide **2r**



To a solution of 2,3,3-trimethyl-5methoxy-3*H*-indole (0.946 g 5 mmol) in acetonitrile (5 mL), 3-bromoprop-1-ene (1.21g, 10 mmol) was added and the reaction mixture was heated at reflux. After 15 h, acetone (6 mL) was added to the mixture. The resultant crystalline material was filtered, washed with acetone and recrystallized from ethanol. The yield was 0.465 g (30%), mp 189–191 ºC.

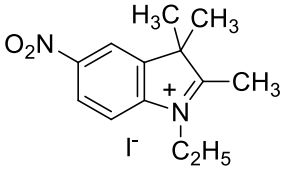
^{1}H NMR (400 MHz, TFA-D): δ 1.89 (s, 6H, 2×3-CH_3), 3.03 (s, 3H, 2-CH_3), 4.24 (s, 3H, -OCH_3), 5.33 (d, *J* = 5.3 Hz, 2H), 5.57 (dt, *J* = 17.2, 1.6 Hz, 1H), 5.79 (d, *J* = 10.5 Hz, 1H), 6.28 (ddd, *J* = 22.5, 10.6, 5.3 Hz, 1H), 7.44 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.50 (d, *J* = 2.4 Hz, 1H), 7.86 (d, *J* = 8.9 Hz, 1H).

^{13}C NMR (100 MHz, TFA-D): δ 14.5, 23.7 (2×CH_3), 52.3, 56.9, 57.7, 111.7, 117.2, 118.3, 122.9, 128.1, 136.5, 145.9, 163.9, 196.2.

IR (cm^{-1}): 3011, 2966, 1609 ($C=N^+$).

ESI-HRMS: [M^+], found 230.1539. [$C_{15}H_{20}NO^+$] requires 230.1539.

1-Ethyl-2,3,3-trimethyl-5-nitro-3*H*-indolium iodide **2t**



To a solution of 2,3,3-trimethyl-5-nitro-3*H*-indole (1.02 g 5 mmol) in acetonitrile (10 mL), iodoethane (1.56 g, 10 mmol) was added. The reaction mixture was heated at reflux. After 24 h, the resultant crystalline material was filtered and recrystallized from ethanol. The yield was 0.96 g, (53%), mp 202–204 ºC (with decomp.).

^{1}H NMR (400 MHz, TFA-*d*): δ 1.80 (t, *J* = 7.6 Hz, 3H, $CH_2\underline{CH_3}$), 1.87 (s, 6H, 2×3-CH_3), 3.12 (s, 3H, 2-CH_3), 4.82 (q, *J* = 7.6 Hz, 2H, $\underline{CH_2}CH_3$), 8.14 (d, *J* = 8.8 Hz, 1H, 7-H), 8.72 (s, 1H, 4-H), 7.73 (dd, *J* = 8.8, 2.0 Hz, 1H, 6-H).

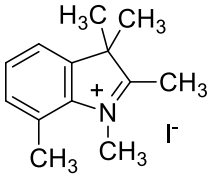
^{13}C NMR (100 MHz, TFA-*d*): δ 14.1, 16.4, 23.8 (2×CH_3), 47.5, 58.3, 118.8, 121.7, 128.5, 146.0, 147.4, 151.3, 204.0.

IR (cm^{-1}): 3027, 2978, 1627 (C=N$^+$), 1532 (NO_2-asymm.), 1348 (NO_2-symm.).

MS m/z (%): 233 (M^+, 100).

Anal. Calcd for $C_{13}H_{17}IN_2O_2$ (233.29): C 43.35; H 4.76; N 7.78. Found C 43.05; H 4.66; N 7.85.

1,2,3,3,7-Pentamethyl-3*H*-indolium iodide **2u**



To a stirred solution of 2,3,3,7-tetramethyl-3*H*-indole (0.866 g, 5 mmol) in acetonitrile (4 mL), iodomethane (1.42g, 10mmol) was added. The reaction mixture was heated at reflux for 24 hours. The formed crystals were separated by filtration and purified by recrystallization from ethanol. The yield was 1.056 g (67%), mp 248–250 ºC.

^{1}H NMR (300 MHz, TFA-D): δ 1.65 (s, 6H, 2×3-CH_3), 2.86 (s, 6H, 2-CH_3, 7-CH_3), 4.34 (s, 3H, N-CH_3), 7.41-7.59 (m, 3H, Ar-H).

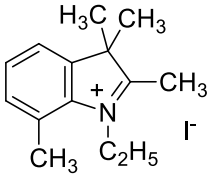
^{13}C NMR (75 MHz, TFA-D): δ 15.6, 20.8, 24.2 (2×C), 40.8, 56.3, 123.3, 129.7, 132.8, 135.9, 142.4, 144.8, 198.1.

IR (cm^{-1}): 3024, 2966, 1625 (C=N$^+$).

MS m/z (%): 188 (M^+, 100).

Anal. Calcd for $C_{13}H_{18}IN$, %: C 49.54; H 5.76; N 4.44. Found: C 49.61; H 5.37; N 4.24.

1-Ethyl-2,3,3,7-tetramethyl-3*H*-indolium iodide **2v**



To a stirred solution of 2,3,3,7-tetramethyl-3*H*-indole (0.866 g, 5 mmol) in acetonitrile (4mL), iodomethane (1.56 g, 10mmol) was added. The reaction mixture was heated at reflux for 24 hours. The formed crystals were separated by filtration and purified by recrystallization from ethanol. The yield was 0.642 g (39%), mp 208–210 ºC.

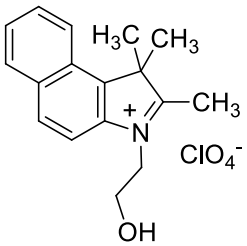
^{1}H NMR (400 MHz, TFA-D): δ 1.76 (s, 6H, 2×3-CH_3), 1.82 (t, *J* = 7.4 Hz, 3H, $CH_2\underline{CH_3}$), 2.98 (s, 3H, CH_3), 3.00 (s, 3H, CH_3), 4.89 (q, *J* = 7.4 Hz, 2H, $\underline{CH_2}CH_3$), 7.56 (d, *J* = 7.5 Hz, 1H), 7.64 (d, *J* = 6.9 Hz, 1H), 7.70 (t, *J* = 7.6 Hz, 1H).

^{13}C NMR (100 MHz, TFA-D): δ 14.5, 14.7, 19.8, 23.9 (2×C), 47.7, 56.0, 123.4, 128.9, 132.6, 136.0, 140.9, 145.1, 197.6.

IR (cm^{-1}): 3033, 2971, 1620 ($C=N^+$).

ESI-HRMS: [M^+], found 202.1590. [$C_{14}H_{20}N^+$] requires 202.1590.

3-(2-Hydroxyethyl)-1,1,2-trimethylbenz[*e*]indolium perchlorate **2x**



To a solution of 1,1,2-trimethylbenz[*e*]indole (1.046 g, 5 mmol) in acetonitrile (10 mL), 2-bromoethanol (1.875 g, 15 mmol) was added. The mixture was heated under reflux for 15 hours. Then the solvent was evaporated under reduced pressure. The residue was dissolved in ethanol and 42% perchloric acid was added drop-wise until pH=2 and stored at 5 ºC for 18 hours. The formed crystals were separated by filtration and purified by recrystallization from ethanol. The yield was 0.885 g (50%), mp 196–198 ºC.

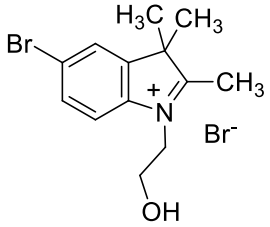
^{1}H NMR (400 MHz, TFA-D): δ 2.14 (s, 6H, 2×3-CH_3), 3.23 (s, 3H, 2-CH_3), 4.79 – 4.75 (m, 2H, CH_2), 5.19 – 5.14 (m, 2H, CH_2), 8.11 – 7.91 (m, 3H), 8.37 – 8.29 (m, 1H), 8.41 (d, *J* = 9.1 Hz, 1H), 8.45 (d, *J* = 8.5 Hz, 1H).

^{13}C NMR (100 MHz, TFA-D): δ 15.2, 23.5(2×C), 52.1, 58.6, 61.2, 113.2, 124.6, 130.1, 130.0, 130.9, 132.1, 133.9, 136.5, 139.5, 139.8, 200.2.

IR (cm^{-1}): 3505 (OH), 3075, 2981, 1634 ($C=N^+$).

ESI-HRMS: [M^+], found 254.1539. [$C_{17}H_{20}NO^+$] requires 254.1539.

5-Brom-1-(2-hydroxethyl)-2,3,3-trimethyl-3*H*-indolium bromide **2y**



2-Bromoethanol (1.875 g, 15 mmol) and 5-brom-2,3,3-trimethyl-3*H*-indole (1.19 g, 5 mmol) were added to a reaction vial and heated at 110ºC in a microwave system for 20 min and a ramp time of 4 min. The liquid was concentrated by using CH_2Cl_2. The residue was suspended in acetone, the solid was scraped and filtered, and then re-crystallized from ethanol. The yield was 1.724 g (95%), mp 202–204 ºC.

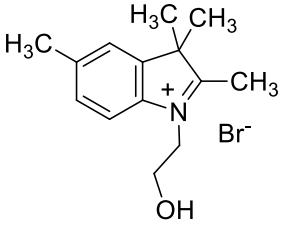
^{1}H NMR (400 MHz, TFA-D): δ 1.88 (s, 6H, 2×3-CH_3), 3.13 (s, 3H, 2-CH_3), 4.69 – 4.63 (m, 2H, CH_2), 5.06 – 5.00 (m, 2H, CH_2), 7.85 (d, *J* = 8.6 Hz, 1H), δ 8.02 (m, 2H).

^{13}C NMR (100 MHz, TFA-D): δ 15.8, 23.8 (2×C), 52.4, 57.4, 60.7, 118.2, 127.6, 129.2, 135.1, 141.8, 145.6, 201.0,

IR (cm^{-1}): 3440 (OH), 3079, 2973, 1625 (C=N$^+$).

ESI-HRMS: [M$^+$], found 282.0488. [$C_{13}H_{17}BrNO^+$] requires 282.0488.

1-(2-Hydroxethyl)-2,3,3,5-tetramethyl-3*H*-indolium bromide **2z**



2-Bromoethanol (1.875 g, 15 mmol) and 2,3,3,5-tetramethyl-3*H*-indole (0.866 g, 5 mmol) were added to a reaction vial and heated at 110ºC in a microwave system for 20 min and a ramp time of 4 min. The liquid was concentrated by using CH_2Cl_2. The residue was suspended in acetone, the solid was scraped and filtered, and then re-crystallized from ethanol. The yield was 0.701 g (47%), mp 180–182 ºC.

^{1}H NMR (400 MHz, TFA-D): δ 2.01 (s, 6H, 2×3-CH_3), 2.89 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 4.87 – 4.77 (m, 2H, CH_2), 5.20 – 5.11 (m, 2H, CH_2), 7.89 – 7.78 (m, 2H), 7.95 (d, *J* = 8.3 Hz, 1H).

^{13}C NMR (100 MHz, TFA-D): δ 15.4, 22.0, 23.9 (2×C), 52.0, 57.0, 60.8, 116.3, 126.0, 132.3, 140.5, 143.9, 144.9, 199.3.

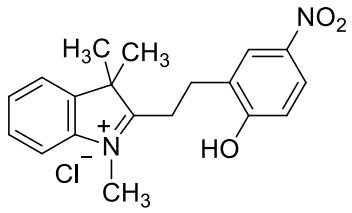
IR (cm^{-1}): 3419 (OH), 3046, 2965, 1627 (C=N$^+$).

ESI-HRMS: [M$^+$], found 218.1539. [$C_{14}H_{20}NO^+$] requires 218.1539.

*The general procedure for the preparation of 1-alkyl-[2-(2-hydroxy-5-nitrophenyl)ethyl-1]-3,3-dimethyl-3H-indolium chlorides (**4**)*

To a stirred solution of the corresponding iodide, bromide or perchlorate (**2a,b,e,j,k,m,u,w-z**) (5 mmol) in distilled water (15 mL) and ethanol (5 mL), sodium carbonate (1.06 g, 10 mmol) was added at rt. The mixture became turbid and was extracted with diethyl ether (3 × 20 mL). The combined organic phase was dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure to afford the corresponding 2-methylene-2,3-dihydro-1*H*-indole (**3a,b,e,j,k,m,u,w-z** respectively) as an oil (or solid in cases of **3e** and **3x**). The crude intermediate enamine obtained as a result of this procedure was dissolved in acetonitrile (3 mL), and 2-chloromethyl-4-nitrophenol (938 mg, 5 mmol) was added to the solution. The mixture was stirred at rt for 6 h except in the case of **3w** at 50ºC for 8 h. The resultant crystalline material was filtered, washed with cold acetonitrile (1 mL) and dried *in vacuo* to afford the title compound (**4a,b,e,j,k,m,u,w-z**).

[2-(2-Hydroxy-5-nitrophenyl)ethyl-1]-1,3,3-trimethyl-3*H*-indolium chloride **4a**



Whitish crystals were obtained with the yield of 0.704 g, (39%), mp 208–211 ºC.

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.61 (s, 6H, 2×3-CH_3), 2.96–3.07 (m, 2H, CH_2), 3.32–3.42 (m, 2H, CH_2), 4.13 (s, 3H, NCH_3), 7.26 (d, J = 9.0 Hz, 1H, Ar-H), 7.63–7.66 (m, 2H, Ar-H), 7.83–7.86 (m, 1H, Ar-H), 7.95–7.98 (m, 1H, Ar-H), 8.09 (dd, J = 9.0, 2.8 Hz, Ar-H), 8.35 (d, J = 2.8 Hz, 1H, Ar-H), 11.98 (s, 1H, OH).

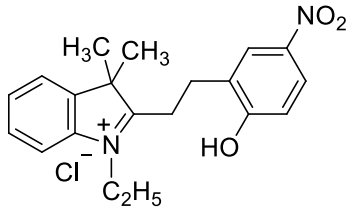
^{13}C NMR (75 MHz, DMSO-d_6): δ 21.3 (2×CH_3), 26.3, 26.5, 35.1, 54.5, 115.4, 115.5, 123.3, 124.8, 126.5, 126.7, 128.9, 129.7, 139.4, 141.8, 142.2, 162.3, 195.7.

IR (cm^{-1}): 3416 (O-H), 3041, 2976, 1517 (NO_2-asymm.), 1347 (NO_2-symm.).

MS m/z (%): 325.4 (M^+, 100).

Anal. Calcd (%) for $C_{19}H_{21}ClN_2O_3$ (360.83): C 63.24; H 5.87; N 7.76. Found: C 62.84; H 5.99; N 7.75.

1-Ethyl-[2-(2-hydroxy-5-nitrophenyl)ethyl-1]-3,3-dimethyl-3*H*-indolium chloride **4b**



Whitish crystals were obtained with the yield of 0.693 g (37%), mp 195-199 ºC.

^{1}H NMR (300 MHz, DMSO-d_6): 1.55 (t, J = 6.9 Hz, 3H, $CH_2\underline{CH_3}$), 1.64 (s, 6H, 2×3'-CH_3), 3.00–3.07 (m, 2H, CH_2), 3.33–3.44 (m, 2H, CH_2), 4.63–4.73 (m, 2H, $\underline{CH_2}CH_3$), 7.27 (d, J = 9 Hz, 1H, 3-H-Ph), 7.64–7.67 (m, 2H, Ar-H), 7.86–7.89 (m, 1H, Ar-H), 8.02–8.05 (m, 1H, Ar-H), 8.08 (dd, J = 9.0, 2.7 Hz, 1H, Ar-H), 8.38 (d, J = 2.7 Hz, 1H, Ar-H), 12.01 (s, 1H, OH).

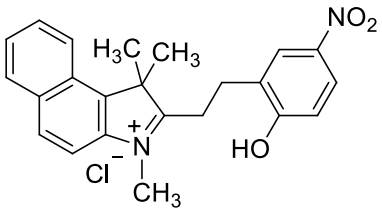
^{13}C NMR (75 MHz, DMSO-d_6): δ 21.5 (2×CH_3), 26.4, 26.9, 30.1, 43.5, 54.9, 115.4, 115.9, 123.5, 124.7, 126.4, 126.6, 129, 129.7, 139.3, 140.6, 142.6, 162.2, 195.8.

IR (cm^{-1}): 3462 (O-H), 3050, 2971, 1520 (NO_2-asymm.), 1338 (NO_2-symm.).

MS m/z (%): 339.4 (M^+, 100).

Anal. Calcd (%) for $C_{20}H_{23}ClN_2O_3$ (374.86): C 64.08; H 6.18; N 7.47. Found: C 63.98; H 6.25; N 7.31.

[2-(2-Hydroxy-5-nitrophenyl)ethyl-1]-1,1,3-trimethyl-1*H*-benz[*e*]indolium chloride **4e**



Off-white crystals were obtained with the yield of 0.86 g (42%), mp 219–222 ºC.

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.83 (s, 6H, 2×3'-CH_3), 3.06–3.12 (m, 2H, CH_2), 3.45–3.50 (m, 2H, CH_2), 4.27 (s, 3H, N-CH_3), 7.24 (d, J = 9.0 Hz, 1H, Ar–H), 7.70-7.82 (m, 2H, Ar–H), 8.08-8.41 (m, 6H, Ar–H), 11.95 (s, 1H, OH).

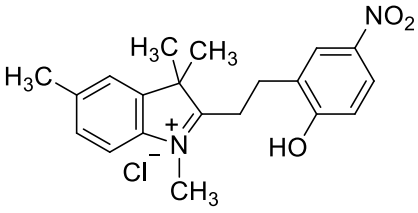
^{13}C NMR (75 MHz, DMSO-d_6): δ 20.6 (2×CH_3), 26.2, 26.5, 35.5, 55.8, 113.2, 115.3, 123.5, 124.7, 126.5, 126.7, 127.0, 127.2, 128.4, 129.7, 130.5, 133.2, 136.6, 139.4, 139.5, 162.4, 195.4.

IR (cm^{-1}): 3388 (O-H), 3057, 2938, 1521 (NO_2-asymm.), 1334 (NO_2-symm.).

MS *m/z* (%): 375 (M^+, 100).

Anal. Calcd (%) for $C_{23}H_{23}ClN_2O_3$ (410.89): C 67.23; H 5.64; N 6.82. Found: C 66.88; H 6.03; N 6.48.

[2-(2-Hydroxy-5-nitrophenyl)ethyl-1]-1,3,3,5-tetramethyl-3*H*-indolium chloride **4j**



Whitish crystals were obtained with the yield of 0.843 g (45%) mp 192–194 ºC.

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.58 (s, 6H, 2×3-CH_3), 2.45 (s, 3H, 5-CH_3), 2.99–3.05 (m, 2H, CH_2), 3.32–3.38 (m, 2H, CH_2), 4.10 (s, 3H, NCH_3), 7.27 (d, J = 9 Hz, 1H, Ar-H), 7.45 (d, J = 8.25 Hz, 1H, Ar-H), 7.66 (s, 1H, Ar-H), 7.83 (d, J = 8.25 Hz, 1H, Ar-H), 8.07 (dd, J = 9.0, 3.0 Hz, 1H, Ar-H), 8.34 (d, J = 3.0 Hz, 1H, Ar-H), 11.98 (s, 1H, OH).

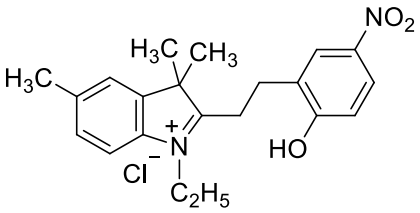
^{13}C NMR (75 MHz, DMSO-d_6): δ 21.1, 21.4 (2×CH_3), 26.2, 26.4, 35.1, 54.2, 115.1, 115.4, 123.7, 124.7, 126.5, 126.6, 129.3, 139.4, 139.9, 140.1, 141.9, 162.3, 194.5.

IR (cm^{-1}): 3394 (O-H), 3029, 2975, 1523 (NO_2-asymm.), 1337 (NO_2-symm.).

MS m/z (%): 339.4 (M^+, 90).

Anal. Calcd (%) for $C_{20}H_{23}ClN_2O_3$ (374.86): C 64.08; H 6.18; N 7.47. Found: C 63.51; H 6.33; N 7.39.

1-Ethyl-[2-(2-hydroxy-5-nitrophenyl)ethyl-1]-3,3,5-trimethyl-3*H*-indolium chloride **4k**



Whitish crystals were obtained with the yield of 1.530 g (79%), mp 195–197 ºC.

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.53 (t, J = 7.2 Hz, 3H, $CH_2\underline{CH_3}$), 1.61 (s, 6H, 2×3-CH_3), 2.45 (s, 3H, 5-CH_3) 3.00-3.05 (m, 2H, CH_2), 3.32–3.38 (m, 2H, CH_2), 4.63 (q, J = 7.2 Hz, 2H, $\underline{CH_2}CH_3$), 7.27 (d, J = 9.2 Hz, 1H, 3-H-Ph), 7.45 (d, J = 8.3 Hz, 1H, 6-H-Ar), 7.68 (s, 1H, 4-H-Ar), 7.98 (d, J = 8.3 Hz, 1H, 7-H-Ar), 8.07 (dd, J = 9.2 Hz, J = 2.6 Hz, 1H, 4-H-Ph), 8.37 (d, J = 2.6 Hz, 1H, 6-H-Ph), 12.02 (s, 1H, OH).

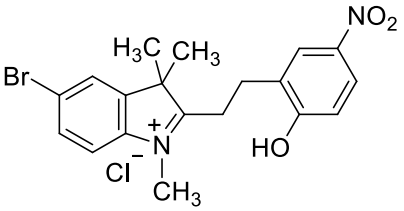
^{13}C NMR (75 MHz, DMSO-d_6): δ 13.6, 21.0, 21.6 (2×CH_3), 26.3, 26.9, 43.5, 54.4, 115.4, 115.5, 123.8, 124.7, 126.4, 126.6, 129.4, 138.4, 139.3, 139.9, 142.4, 162.2, 194.5.

IR (cm^{-1}): 3397 (O-H); 3055, 2973, 1520 (NO_2-asymm.); 1333 (NO_2-symm.).

MS m/z (%): 353 (M^+, 100).

Anal. Calcd (%) for $C_{21}H_{25}ClN_2O_3$ (388.89): C 64.86, H 6.48, N 7.2. Found: C 64.91, H 6.27, N 7.43.

5-Brom-[2-(2-hydroxy-5-nitrophenyl)ethyl-1]-1,3,3-trimethyl-3*H*-indolium chloride **4m**



Whitish crystals were obtained with the yield of 1.355 g (62%), mp 210–213 ºC.

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.62 (s, 6H, 2×3-CH_3), 2.97–3.08 (m, 2H, CH_2), 3.33–3.42 (m, 2H, CH_2), 4.11 (s, 3H, N-CH_3), 7.24 (d, *J* = 8.9 Hz, 1H, 3-H-Ph), 7.85–7.94 (m, 2H, 6-H-Ar, 4-H-Ar), 8.07 (dd, *J* = 8.9 Hz, *J* = 2.1 Hz, 4-H-Ph), 8.18 (s, 1H, 7-H-Ar), 8.34 (d, *J* = 2.1 Hz, 1H, 6-H-Ph), 11.98 (s, 1H, OH).

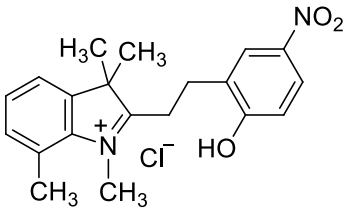
^{13}C NMR (75 MHz, DMSO-d_6): δ 21.0 (2×CH_3), 26.1, 26.6, 35.2, 54.7, 115.3, 117.4, 123.0, 124.7, 126.4, 126.5, 126.6, 131.8, 139.3, 141.5, 144.0, 162.2, 196.0.

IR (cm^{-1}): 3382 (OH), 3032, 2931, 1520 (NO_2-asymm.), 1336 (NO_2-symm.)

MS m/z (%):403, 405 (M^+, 100).

Anal. Calcd (%) for $C_{19}H_{20}BrClN_2O_3$ (439.73): C 51.90, H 4.58, N 6.37. Found: C 50.88, H 4.5, N 6.31.

[2-(2-Hydroxy-5-nitrophenyl)ethyl-1]-1,3,3,7-tetramethyl-3*H*-indolium chloride **4u**



Whitish crystals were obtained with the yield of 0.90 g (48%), mp 200–203 ºC.

^{1}H NMR (300 MHz, DMSO-d_6): δ=1.58 (s, 6H, 2×3'-CH_3), 2.78 (s, 3H, 7-CH_3), 2.95–3.01 (m, 2H, CH_2), 3.32–3.38 (m, 2H, CH_2), 4.31 (s, 3H, NCH_3), 7.31 (d, *J* = 8.9 Hz, 1H, Ar–H), 7.39 (d, *J* = 7.5 Hz, 1H, Ar–H), 7.5 (t, *J* = 7.5 Hz, 1H, Ar–H), 7.67 (d, *J* = 7.5 Hz, 1H, Ar–H), 8.07 (dd, *J* = 8.9, 2.5 Hz, 1H, Ar–H), 8.35 (d, *J* = 2.5 Hz, 1H, Ar–H), 12.1 (s, 1H, OH).

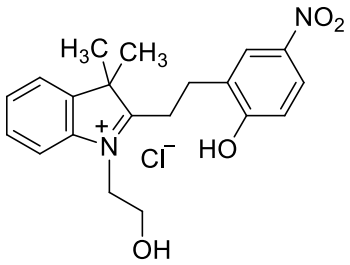
^{13}C NMR (75 MHz, DMSO-d_6): δ=19.1, 21.5 (2×CH_3), 26.2, 38.8, 39.0, 53.5, 115.3, 121.1, 124.6, 126.3, 126.6, 127.2, 129.3, 132.5, 139.2, 140.3, 142.8, 162.3, 195.3.

IR (cm^{-1}): 3624 (O-H), 3050, 2923, 1520 (NO_2-asymm.), 1345 (NO_2-symm.).

MS: *m/z* (%): 339 (M^+, 100).

Anal. Calcd (%) for $C_{20}H_{23}ClN_2O_3$ (374.86): C 64.08, H 6.18, N 7.47. Found: C 64.45, H 6.25, N 7.71.

1-(2-Hydroxyethyl)-[2-(2-hydroxy-5-nitrophenyl)ethyl-1]-3,3-dimethyl-3*H*-indolium chloride **4w**



Whitish crystals were obtained with the yield of 0.918 g (47%), mp 152–154 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 1.67 (s, 6H, 2×3-CH_3), 3.05–3.09 (m, 2H, CH_2), 3.42-3.46 (m, 2H, CH_2), 3.80 (br. s., 1H, CH_2CH_2OH), 3.91 (t, *J* = 4.4 Hz, 2H, CH_2CH_2OH), 4.75 (t, *J* = 4.8 Hz, 2H, CH_2CH_2OH), 7.20 (d, *J* = 9.2 Hz, 1H, 3-H-Ph), 7.65 (t, *J* = 3.6 Hz, 2H, Ar-H), 7.86-7.89 (m, 1H, Ar-H), 8.03-8.05 (m, 1H, Ar-H), 8.09 (dd, J = 9.2 Hz, *J* = 2.8 Hz, 1H, 4-H-Ph), 8.37 (d, *J* = 2.8 Hz, 1H, 6-H-Ph), 11.87 (s, 1H, OH).

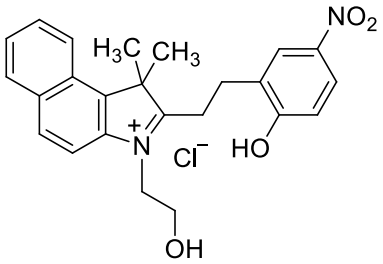
^{13}C NMR (100 MHz, DMSO-d_6): δ 21.9 (2×CH_3), 26.6, 26.9, 50.6, 54.8, 57.6, 115.4, 116.1, 123.4, 124.8, 126.6, 126.7, 128.9, 129.7, 139.4, 140.9, 142.2, 162.2, 197.4.

IR (cm^{-1}): 3282 (O-H); 3012, 2970, 1522 (NO_2-asymm.); 1333 (NO_2-symm.).

MS m/z (%): 355 (M^+, 100).

Anal. Calcd (%) for: $C_{20}H_{23}ClN_2O_4$ (390.86): C 61.46, H 5.93, N 7.17. Found: C 61.31, H 6.15, N 6.97.

1-(2-Hydroxyethyl)-[2-(2-hydroxy-5-nitrophenyl)ethyl-1]-1,1,3-trimethyl-1*H*-benz[*e*]indolium chloride **4x**



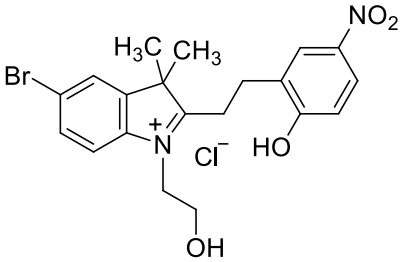
Whitish crystals were obtained with the yield of 1.083 g (43%), mp 188–190 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 1.65 (s, 6H, 2×3-CH_3), 3.13–3.02 (m, 2H, CH_2), 3.50–3.39 (m, 2H, CH_2), 3.96–3.87 (m, 2H, CH_2), 4.81–4.69 (m, 2H, CH_2), 5.36 (br.s, 1H, CH_2CH_2OH), 7.22 (d, *J* = 9.0 Hz, 1H), 7.69–7.58 (m, 3H), 7.92–7.80 (m, 2H), 8.12–8.01 (m, 2H), 8.36 (d, *J* = 2.8 Hz, 1H), 11.90 (s, 1H, OH).

^{13}C NMR (100 MHz, DMSO-d_6): δ 21.9 (2×CH_3), 22.1 , 26.6, 26.9, 54.8, 57.6, 115.4, 115.6, 116.1, 123.4, 124.8, 126.6, 128.8, 128.9, 129.3, 129.7, 139.4, 140.9, 141.2, 142.2, 143.0, 162.3, 197.4.

IR (cm^{-1}): 3296 (O-H); 3052, 2950, 1526 (NO_2-asymm.); 1333 (NO_2-symm.).
ESI-HRMS: [M^+], found 405.1809. [$C_{24}H_{25}N_2O_4^+$] requires 405.1809.

5-Brom-1-(2-hydroxyethyl)-[2-(2-hydroxy-5-nitrophenyl)ethyl-1]-3,3-dimethyl-3*H*-indolium chloride **4y**



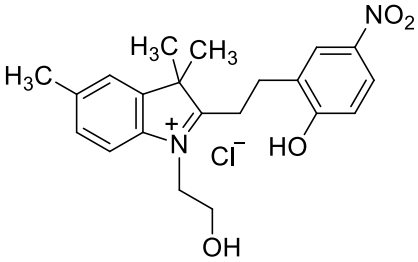
Whitish crystals were obtained with the yield 0.868 g (37%), mp 193–195 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 1.68 (s, 6H, 2×3-CH_3), 3.13–2.99 (m, 2H, CH_2), 3.48–3.32 (m, 2H, CH_2), 3.96–3.77 (m, 2H, CH_2), 4.80–4.68 (m, 2H, CH_2), 5.36 (br.s, 1H, CH_2CH_2OH), 7.19 (d, *J* = 9.0 Hz, 1H), 7.86 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 8.6 Hz, 1H), 8.08 (d, *J* = 11.8 Hz, 1H), 8.25–8.20 (m, 1H), 8.38–8.33 (m, *J* = 1.9 Hz, 1H), 11.87 (s, 1H, OH).

^{13}C NMR (100 MHz, DMSO-d_6): δ 21.7 (2×CH_3), 26.8, 27.1, 50.8, 55.1, 57.6, 115.4, 118.1, 123.1, 124.8, 126.5, 126.6, 126.8, 139.4, 140.4, 142.9, 144.5, 162.2, 197.8.

IR (cm^{-1}): 3361(O–H), 3039, 2965, 1512 (NO_2-asymm.), 1330 (NO_2-symm.).
ESI-HRMS: [M^+], found 433.0758. [$C_{20}H_{22}BrN_2O_4^+$] requires 433.0757.

1-(2-Hydroxyethyl)-[2-(2-hydroxy-5-nitrophenyl)ethyl-1]-3,3,5-trimethyl-3*H*-indolium chloride **4z**



Whitish crystals were obtained with the yield of 1.05 g (52%), mp 176–177 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 1.64 (s, 6H, 2×3-CH_3), 2.45 (s, 3H, CH_3), 3.04–3.08 (m, 2H, CH_2), 3.36–3.46 (m, 2H, CH_2), 3.89 (t, *J* = 19.2 Hz, 2H, CH_2CH_2OH), 4.71 (t, *J* = 20.8 Hz, 2H, CH_2CH_2OH), 5.53 (pl.s., 1H, CH_2CH_2OH), 7.22 (d, *J* = 8.8 Hz, 1H, 3-H-Ph), 7.44 (d, *J* = 8.4 Hz, 1H, Ar-H), 7.68 (s, 1H, Ar-H), 7.91 (d, *J* = 8.4 Hz, 1H, Ar-H), 8.08 (dd, *J* = 8.8 Hz, *J* = 2.4 Hz, 1H, 4-H-Ph), 8.36 (d, *J* = 2.4 Hz, 1H, 6-H-Ph), 11.89 (s, 1H, OH).

^{13}C NMR (100 MHz, DMSO-d_6): δ 21.1, 22.0 (2×CH_3), 26.5, 26.9, 50.6, 54.6, 57.6, 115.4, 115.8, 123.8, 124.8, 126.6, 126.6, 129.3, 138.8, 139.3, 139.9; 142.4, 162.3, 196.1.

IR (cm^{-1}): 3384(O–H), 3036, 2965, 1510 (NO_2-asymm.), 1333 (NO_2-symm.).

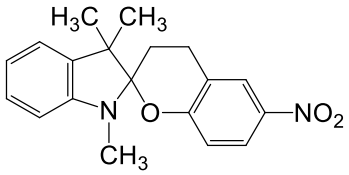
MS m/z (%): 369 (M^+, 100).

Anal. Calcd (%) for: $C_{21}H_{25}ClN_2O_4$ (404.89): C 62.30, H 6.22, N 6.92. Found: C 62.34, H 6.22, N 6.73.

*General procedures for the preparation of 1'-substituted 6-nitro-1,3',3,4-tetrahydrospiro[chromene-2,2'-indoles] (**5a,b,e,j,k,m,u,w-z**)*

A solution of the corresponding [2-(2-hydroxy-5-nitrophenyl)ethyl-1]-3*H*-indolium chloride (**4a,b,e,j,k,m,u,w-z**, 3 mmol) in ethanol (5 mL) was diluted with water (15 mL). Then aqueous ammonia solution (10%) was added to the mixture by drops under stirring till the mixture became turbid. The separated product was extracted with diethyl ether (3 × 20 mL), the combined extract was dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The solid residue was recrystallized from acetonitrile to give the title spiro[chromene-2,2'-indole] (**5a,b,e,j,k,m,u,w-z**).

1',3',3'-Trimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5a**



Yellowish crystals were obtained with the yield of 0.72 g (74%), mp 187–189 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (br s, 6H, 2×3'-CH_3), 2.35–2.41 (m, 2H, CH_2), 2.85 (s, 3H, NCH_3), 3.00–3.14 (m, 2H, CH_2), 6.60 (d, *J* = 7.5 Hz, 1H, 7'-H); 6.78 (d, *J* = 9.0 Hz, 1H, 8-H), 6.85 (dt, *J* = 7.5, 0.9 Hz, 1H, 5'-H), 7.06 (dd, *J* = 7.5, 0.9 Hz, 1H, 4'-H), 7.20 (dt, *J* = 7.5, 0.9 Hz, 1H, 6'-H), 7.98 (dd, *J* = 9.0, 2.7 Hz, 1H, 7-H), 8.04 (d, *J* = 2.7 Hz, 1H, 5-H).

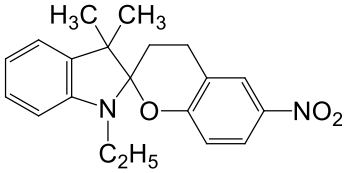
^{13}C NMR (75 MHz, $CDCl_3$): δ 22.1, 23.5, 24.2, 25.8, 28.5, 49.6, 104.5, 107.3, 116.9, 119.4, 121.4, 121.5, 124.3, 125.2, 128.0, 137.0, 140.6, 148.6, 162.0.

IR (cm^{-1}): 3068, 2965, 1509 (NO_2-asymm.), 1329 (NO_2-symm.).

Anal. Calcd (%) for $C_{19}H_{20}N_2O_3$ (324.37): C 70.35; H 6.21; N 8.64. Found: C 70.03; H 6.30; N 9.03.

ESI-HRMS: [M+H$^+$], found 325.1548. [$C_{19}H_{21}N_2O_3$ +H$^+$] requires 325.1547.

1'-Ethyl-3',3'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5b**



Yellowish crystals were obtained with the yield of 0.305 g (30%), mp 154–156 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.23 (t, *J* = 7.2 Hz, 3H, $CH_2\underline{CH_3}$), 1.25 (br s, 6H, 2×3'-CH_3), 2.21–2.48 (m, 2H, $\underline{CH_2}CH_3$), 2.95–3.44 (m, 4H, 2×CH_2), 6.58–6.61 (m, 1H, 7' -H), 6.76 (d, *J* = 9.3 Hz, 1H, 8-H), 6.82 (dt, *J* = 7.5, 0.9 Hz, 1H, 5'-H), 7.06 (dd, *J* = 7.5, 0.9 Hz, 1H, 4'-H), 7.19 (dt, *J* = 7.5, 0.9 Hz, 1H, 6'-H), 7.98 (dd, *J* = 9.0, 2.7 Hz, 1H, 7-H), 8.04 (d, *J* = 2.7 Hz, 1H, 5-H).

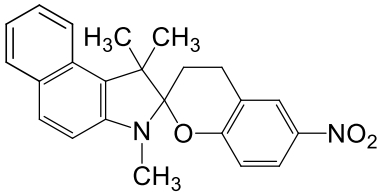
^{13}C NMR (75 MHz, $CDCl_3$): δ 15.1, 22.0, 23.6, 24.8, 25.9, 37.5, 49.7, 104.7, 106.5, 116.9, 118.8, 121.3, 121.4, 124.2, 125.2, 128.0, 136.7, 140.5, 147.6, 161.9.

IR (KBr, cm^{-1}): 3068, 2970, 1510 (NO_2-asymm.), 1331 (NO_2-symm.).

Anal. Calcd (%) for $C_{20}H_{22}N_2O_3$ (338.40): C 70.99; H 6.55; N 8.28. Found: C 70.57; H 6.61; N 8.24. Found: C 70.03; H 6.30; N 9.03.

ESI-HRMS: [M+H$^+$], found 339.1705. $C_{20}H_{23}N_2O_3$ requires 339.1703.

1',1',3'-Trimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-benz[*e*][2*H*]indole] **5e**



Yellowish crystals were obtained with the yield of 0.753 g (67%), mp 172–174 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.53 (br.s, 6H, 2×3'-CH_3), 2.43 (br.s, 2H, CH_2), 2.94 (s, 3H, N-CH_3), 3.11 (m, 2H, CH_2), 6.74 (d, *J* = 9.2 Hz, 1H, 8H), 7.02 (d, *J* = 8.4 Hz, 1H, 4'H), 7.22 (dt, *J* = 7.4 Hz, *J* = 1.2 Hz, 1H, 7'H), 7.40 (dt, *J* = 7.4 Hz, *J* = 1.2 Hz, 1H, 8'H), 7.76 (d, *J* = 7.4 Hz, 1H, 9'H), 7.80 (d, *J* = 8.4 Hz, 1H, 5'H), 7.93 (d, *J* = 7.4 Hz, 1H, 6'H), 7.98 (dd, *J* = 9.2 Hz, *J* = 2.8 Hz, 1H, 7H), 8.06 (d, *J* = 2.8 Hz, 1H, 5H).

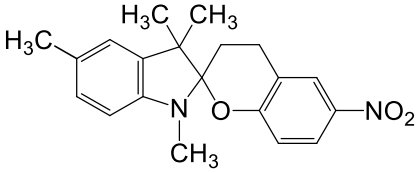
^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (2×CH_3), 23.5, 24.2, 28.9, 51.6, 105.0, 110.4, 116.7, 121.2, 121.5, 121.7, 124.3, 125.1, 125.7, 126.5, 129.4, 129.5, 129.6, 129.8, 140.5, 146.2, 162.2.

IR (cm^{-1}): 3051, 2967, 1518 (NO_2-asymm.), 1331 (NO_2-symm.).

Anal. Calcd (%) for $C_{23}H_{22}N_2O_3$ (374.43): C 73.78; H 5.92; N 7.48. Found: C 73.43; H 6.29; N 7.13.

ESI-HRMS: [M+H$^+$], found 375.1706. [$C_{23}H_{22}N_2O_3$+H$^+$] requires 375.1703.

1',3',3',5'-Tetramethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5j**



Yellowish crystals were obtained with the yield of 0.812 g (80%), mp 178–179 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (br s, 6H, 2×3'-CH_3), 2.32 (s, 3H, 5'-CH_3), 2.34–2.38 (m, 2H, CH_2), 2.83 (s, 3H, NCH_3), 3.01–3.12 (m, 2H, CH_2), 6.5 (d, *J* = 8.1 Hz, 1H, 7'-H); 6.78 (d, *J* = 9 Hz, 1H, 8H), 6.86-6.88 (m, 1H, 4'-H), 6.98-7.02 (m, 1H, 6'-H), 7.97 (dd, *J* = 9.0, 2.7 Hz, 1H, 7-H), 8.03 (d, *J* = 2.7 Hz, 1H, 5-H).

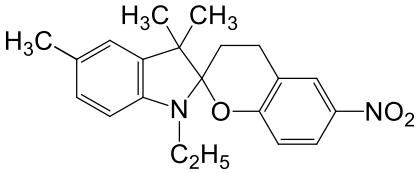
^{13}C NMR (75 MHz, $CDCl_3$): δ 21.1, 22.1, 23.6, 24.2, 25.8, 28.7, 49.7, 104.8, 107.2, 116.9, 121.6, 122.3, 124.3, 125.2, 128.3, 128.7, 137.2, 140.6, 146.5, 162.1.

IR (cm^{-1}): 3065, 2940, 1499 (NO_2-asymm.), 1332 (NO_2-symm.).

Anal. Calcd (%) for $C_{20}H_{22}N_2O_3$ (338.40): C 70.99; H 6.55; N 8.28. Found: C 70.60; H 6.60; N 8.45.

ESI-HRMS: [M+H^+], found 339.1708. [$C_{20}H_{23}N_2O_3$ +H^+] requires 339.1704.

1'-Ethyl-3',3',5'-trimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5k**



Yellowish crystals were obtained with the yield of 0.895 g (85%), mp 175–176 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.22 (t, *J* = 7.2 Hz, 3H, $CH_2\underline{CH_3}$), 1.24 (s, 6H, 2×3'-CH_3), 2.31 (s, 3H, 5'-CH_3), 2.35 (t, *J* = 6.6 Hz, 2H, 3-CH_2), 3.06 (t, *J* = 6.6 Hz, 2H, 4-CH_2), 3.3 (t, *J* = 7.2 Hz, 2H, $\underline{CH_2}CH_3$), 6.5 (d, *J* = 8.1 Hz, 1H, 7'-H), 6.75 (d, *J* = 9.0 Hz, 1H, 8-H), 6.87–6.88 (m, 1H, 4'-H), 6.97–7.00 (m, 1H, 6'-H), 7.97 (dd, *J* = 9.0 Hz, *J* = 2.8 Hz, 1H, 7-H), 8.04 (d, *J* = 2.8 Hz, 1H, 5-H).

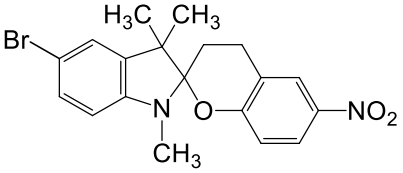
^{13}C NMR (75 MHz, $CDCl_3$): δ 14.9, 20.9, 23.5, 23.7, 24.8, 37.3, 37.5, 49.7, 106.2, 116.7, 121.3, 122.1, 122.2, 124.1, 125.1, 128.0, 128.1, 136.8, 140.4, 145.2, 161.9.

IR (cm^{-1}): 3068, 2966, 1502 (NO_2-asymm.), 1328 (NO_2-symm.).

MS m/z (%): 353 (M + H^+, 100).

Anal. Calcd (%) for $C_{21}H_{24}N_2O_3$ (352.43): C 71.57; H 6.86; N 7.95. Found: C 71.24; H 7.0; N 8.33.

5'-Brom-1',3',3'-trimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5m**



Yellowish crystals were obtained with the yield of 1.05 g (87%), mp 133–135 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.21 (s, 6H, 2×3'-CH_3), 2.24–2.42 (m, 2H, 3-CH_2), 2.82 (s, 3H, N-CH_3), 2.96–3.17 (m, 2H, 4-CH_2), 6.45 (d, *J* = 8.3 Hz, 1H, 7'-H), 6.77 (d, *J* = 9.0 Hz, 1H, 8-H), 7.12 (d, *J* = 2.1 Hz, 1H, 4'-H), 7.27 (dd, *J* = 8.3 Hz, *J* = 2.1 Hz, 1H, 6'-H), 7.98 (dd, *J* = 9.0 Hz, *J* = 2.7 Hz, 1H, 7-H), 8.03 (d, *J* = 2.7 Hz, 1H, 5-H).

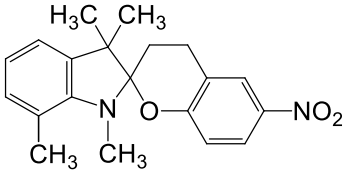
^{13}C NMR (75 MHz, $CDCl_3$): δ 21.7, 23.2, 23.9, 25.5, 28.4, 46.6, 104.1, 108.6, 111.0, 116.7, 121.2, 124.2, 124.5, 125.1, 130.5, 139.2, 140.6, 147.5, 161.5.

IR (cm^{-1}): 3059, 2977, 1512 (NO_2-asymm.); 1329 (NO_2-symm.).

MS m/z (%) 403, 405 ($M + H^+$, 100).

Anal. Calcd (%) for $C_{19}H_{19}BrN_2O_3$ (403.27): C 56.59; H 4.75; N 6.95. Found: C 56.98; H 4.78; N 6.95.

1',3',3',7'-Tetramethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5u**



Yellowish crystals were obtained with the yield of 0.518 g (51%), mp 206–209 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.24 (s, 6H, 2×3'-CH_3), 2.31–2.36 (m, 2H, CH_2), 2.5 (s, 3H, 7'-CH_3), 3.05–3.1 (m, 5H, CH_2, NCH_3), 6.76–6.82 (m, 2H, 5'-H, 8-H); 6.91–6.96 (m, 2H, 4'-H, 6'-H), 7.99 (dd, *J* = 9.0, 2.7 Hz, 1H, 7-H), 8.04 ppm (d, *J* = 2.7 Hz, 1H, 5-H).

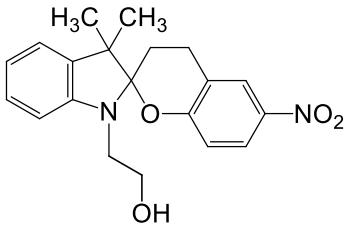
^{13}C NMR (75 MHz, $CDCl_3$): δ 20.1, 23.4, 24.0, 24.1, 25.6, 32.0, 48.8, 104.7, 116.7, 119.1, 119.2, 119.8, 121.5, 124.1, 125.1, 131.7, 137.6, 140.5, 146.5, 161.8.

IR (cm^{-1}): 3084, 2975, 1513 (NO_2-asymm.), 1330 cm^{-1} (NO_2-symm.).

Anal. Calcd (%) for $C_{20}H_{22}N_2O_3$: C 70.99; H 6.55; N 8.28; found: C 70.76; H 6.61; N 8.54.

ESI-HRMS: [$M+H^+$], found 339.1706. [$C_{20}H_{22}N_2O_3 + H^+$] requires 339.1703.

1'-(2-Hydroxyethyl)-3',3'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5w**



Yellowish crystals were obtained with the yield of 0.350 g **(**33%), mp = 132–133 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (s, 6H, 2×3'-CH_3), 1.98 (br.s, 1H, CH_2CH_2OH), 2.26–2.49 (m, 2H, 3-CH_2), 2.97–3.19 (m, 2H, 4-CH_2), 3.35–3.60 (m, 2H, CH_2CH_2OH), 3.80 (t, *J* = 5.4 Hz, 2H, CH_2CH_2OH), 6.68 (d, *J* = 7.8 Hz, 1H, 7'-H), 6.78 (d, *J* = 9.0 Hz, 1H, 8-H), 6.87 (t, *J* = 7.2 Hz, 1H, 5'-H), 7.07 (d, *J* = 6.6 Hz, 1H, 4'-H), 7,19 (dt, *J* = 7.7 Hz, *J* = 1.0 Hz, 1H, 6'-H), 7.98 (dd, *J* = 9.0 Hz, *J* = 2.7 Hz, 1H, 7-H), 8.04 (d, *J* = 2.6 Hz, 1H, 5-H).

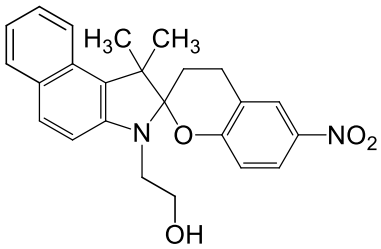
^{13}C NMR (100 MHz, $CDCl_3$): δ 22.0, 23.5, 25.0, 25.8, 45.6, 49.8, 61.3, 104.6, 107.2, 116.8, 119.7, 121.4, 121.6, 124.3, 125.3, 128.1, 136.8, 140.9, 147.8, 161.4.

IR (cm^{-1}): 3384 (O–H); 3036, 2965, 1510 (NO_2-asymm.); 1333 (NO_2-asymm.).

MS m/z (%): 355 ($M+H^+$, 100).

Anal. Calcd (%) for $C_{20}H_{22}N_2O_4$ (354.40): C 67.78; H 6.26; N 7.90. Found: C 67.72; H 6.33; N 7.59.

3'-(2-Hydroxyethyl)-1',1'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-benz[*e*][2*H*]indole] **5x**



Yellowish crystals were obtained with the yield of 0.618 g (51%), mp = 106–109 ºC.

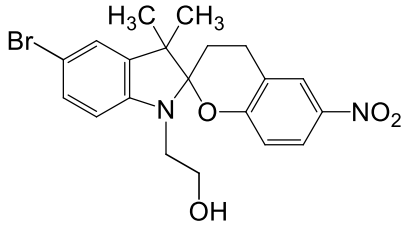
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54 (s, 6H, 2×1'-CH_3), 2.41–2.45 (m, 2H, 3-CH_2), 2.95 (br.s, 1H, CH_2CH_2OH), 3.09–3.12 (m, 2H, 4-CH_2), 3.55–3.58 (m, 2H, CH_2CH_2OH), 3.84 (t, *J* = 6.0Hz, 2H, CH_2CH_2OH), 6.72 (d, *J* = 9.0 Hz, 1H, Ar-H), 7.10 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.27–7.20 (m, 1H, Ar-H), 7.45–7.38 (m, 1H, Ar-H), 7.74 (t, *J* = 8.0 Hz, 1H, 7'H), 7.81 (t, *J* = 8.0 Hz, 1H, 8'H), 8.00 – 7.92 (m, 2H, Ar-H), 8.08 – 8.04 (m, 1H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 23.5, 23.6, 25.2, 45.7, 50.0, 51.9, 61.7, 105.6, 110.3, 116.8, 121.4, 121.6, 122.0, 124.5, 125.4, 125.6, 126.8, 129.7, 129.7, 129.8, 129.9, 140.8, 145.7, 161.9.

IR (cm^{-1}): 3379 (O–H), 3079, 2967, 1518 (NO_2-asymm.), 1336 (NO_2-symm.).

Anal. Calcd (%) for $C_{24}H_{24}N_2O_4$ (404.46) : C 71.27; H 5.98; N 6.93. Found: C 71.08; H 5.92; N 6.99.

5'-Brom-1'-(2-hydroxyethyl)-3',3'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5y**



Yellowish crystals were obtained with the yield of 0.742 g (57%), mp = 185–187 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.25 (s, 6H, 2×3'-CH_3), 1.86 (br.s, 1H, CH_2CH_2OH), 2.23–2.46 (m, 2H, 3-CH_2), 2.97–3.15 (m, 2H, 4-CH_2), 3.30–3.42 (m, 1H, CH_2), 3.48–3.58 (m, 1H, CH_2), 3.78 (t, *J* = 5.6 Hz, 2H, CH_2CH_2OH), 6.56 (d, *J* = 8.4 Hz, 1H, 7'-H), 6.77 (d, *J* = 8.8 Hz, 1H, 8-H), 7.13 (d, *J* = 2 Hz, 1H, 4'-H), 7.27 (dd, *J* = 8.4 Hz, *J* = 2.0 Hz, 1H, 6'-H), 7.99 (dd, *J* = 8.8 Hz, *J* = 2.8 Hz, 1H, 7-H), 8.04 (d, *J* = 2.8 Hz, 1H, 5-H).

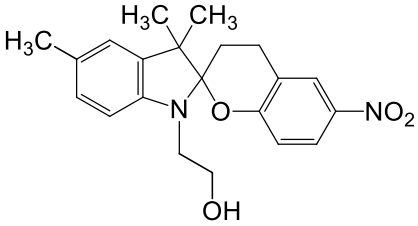
^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 23.3, 24.8, 25.6, 45.5, 49.8, 61.1, 104.4, 108.6, 111.4, 116.7, 121.2, 124.3, 124.7, 125.2, 130.5, 139.0, 140.9, 146.8, 161.0.

IR (cm^{-1}): 3422 (O–H); 3030, 2964, 1518 (NO_2-asymm.); 1336 (NO_2-symm.).

MS m/z (%): 432.9;434.9 ($M+H^+$, 95,100).

Anal. Calcd (%) for $C_{20}H_{21}BrN_2O_4$ (433.30): C 55.44; H 4.89; N 6.47. Found: C 55.23; H 4.78; N 6.49.

1'-(2-Hydroxyethyl)-3',3',5'-trimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5z**



Yellowish crystals were obtained with the yield of 0.202 g (18%), mp = 152–153 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (s, 6H, 2×3'-CH_3), 1.98 (br.s, 1H, CH_2CH_2OH), 2.32–2.56 (m, 5H, 3-CH_2, 5'-CH_3), 3.07 (br.s, 2H, 4-CH_2), 3.45–3.47 (m, 2H, CH_2CH_2OH), 3.79 (t, *J* = 5.6 Hz, 2H, CH_2CH_2OH), 6.59 (d, *J* = 8.0 Hz, 1H, 7'-H), 6.77 (d, *J* = 9.0 Hz, 1H, 8-H), 6.89 (s, 1H, 4'-H), 6.99 (d, *J* = 8.0 Hz, 1H, 6'-H), 7.98 (dd, *J* = 9.0 Hz, *J* = 2.7 Hz, 1H, 7-H), 8,04 (d, *J* = 2.7Hz, 1H, 5-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9, 22.1, 23.4, 23.5, 24.9, 45.7, 49.7, 61.2, 105.0, 106.9, 116.7, 121.3, 122.3, 124.2, 125.2, 128.2, 129.0, 136.8, 140.7, 145.5, 161.4.

IR (cm^{-1}): 3581 (O–H); 3066, 2978, 1517 (NO_2-asymm.), 1338 (NO_2-symm.).

MS m/z (%): 369 ($M+H^+$, 100).

Anal. Calcd (%) for $C_{21}H_{24}N_2O_4$ (368.43): C 68.46; H 6.57; N 7.60. Found: 68.26; H 6.57; N 7.52.

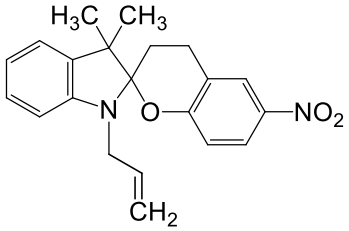
*General procedures for the preparation of 1'-substituted 6-nitro-1,3',3,4-tetrahydrospiro[chromene-2,2'-indoles] (**5c,d,f-i,l,n-t,v**)*

To a stirred solution of the corresponding iodide, bromide or perchlorate **2c,f-h,n,o,q-t,v** (5 mmol) in distilled water (15 mL) and ethanol (5 mL), sodium carbonate (1.06 g, 10 mmol) was added at rt. The mixture became turbid and was extracted with diethyl ether (3 × 20 mL). The combined organic phase was dried over anhydrous sodium sulfate, and then the solvent was evaporated under reduced pressure to afford the corresponding 2-methylene-2,3-dihydro-1*H*-indole (**3c,d,f-i,l,n-t,v** respectively) as an oil (or solid in cases of **3f-h**).

Indolium salts **2d,i,l,p**, (5 mmol) in CH_2Cl_2 (25 mL) were mixed with TEA (1.012 g, 1.39 mL, 10 mmol) and shaken well; the organic layer was washed with water (3×50 mL), dried over anhydrous sodium sulfate. As the next step, the solvent was evaporated under reduced pressure to afford the corresponding 2-methylene-2,3-dihydro-1*H*-indole (**3d,i,l,p** respectively) as an oil.

As a result of this sequence, the obtained crude intermediate enamine **3c,d,f-i,l,n-t,v** was dissolved in acetonitrile (5 mL) and then 2-chloromethyl-4-nitrophenol (938 mg, 5 mmol) was added to the solution. The mixture was stirred at rt for **3c,f-i,n,o,r-t,v** and at 80 ºC for **3d,l,p,q**. After 6 h, the reaction mixture was poured into water (50 mL) and an aqueous ammonia solution (10%) was added by drops under stirring till reaching pH≈8. The mixture became turbid, the separated product was extracted with diethyl ether (3 × 20 mL), the combined extract was consequently dried over anhydrous sodium sulfate and the resulting solvent was evaporated under reduced pressure. The residue was subjected to flash chromatography on silica gel to yield the title compounds (**5c,d,f-i,l,n-t,v**).

1'-Allyl-3',3'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5c**



R_f = 0.16 (hexane/acetone 7:1, v/v) recrystallized from acetonitrile resulted in the production of yellowish crystals with the yield of 0.490 g (28%), mp 160–161 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.29 (br s, 6H, 2×3'-CH_3), 2.35 (br s, 2H, 3-CH_2), 3.06 (br s, 2H, NCH_2), 3.88 (br s, 2H, 4-CH_2), 5.14 (dq, *J* = 10.2, 1.8 Hz, 1H, C=CH_2) 5.27(dq, *J* = 17.1, 1.8 Hz, 1H, C=CH_2), 5.94 (ddt, *J* = 17.1 Hz, *J* = 10.2 Hz,

J = 4.5 Hz, 1H, -CH=), 6.56 (d, *J* = 7.5 Hz, 1H, 7'-H), 6.78 (d, *J* = 9 Hz, 1H, 8-H), 6.85 (t, *J* = 7.5 Hz, 1H, 5'-H), 7.07 (d, *J* = 7.5 Hz, 1H, 4'-H), 7.17 (dt, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H, 6'-H), 7.98 (dd, *J* = 9 Hz, *J* = 3 Hz, 1H, 7-H), 8.04 (d, *J* = 3 Hz, 1H, 5-H).

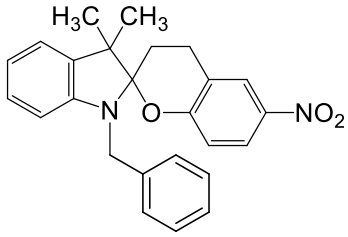
^{13}C NMR (75 MHz, $CDCl_3$): δ 22.0, 23.5, 24.9, 26.0, 45.8, 49.8, 104.6, 107.3, 115.3, 116.9, 119.3, 121.3, 121.4, 124.3, 125.2, 128.0, 135.2, 136.8, 140.6, 147.8, 161.8.

IR (cm^{-1}): 3031, 2935, 1511 (NO_2-asymm.), 1339 (NO_2-symm.).

Anal. Calcd (%) for $C_{21}H_{22}N_2O$ (350.41): C 71.98; H 6.33; N 7.99. Found: C 71.97; H 6.25; N 8.12. Found: C 70.03; H 6.30; N 9.03.

ESI-HRMS: [M+H$^+$], found 351.1709. [$C_{21}H_{23}N_2O_3$ +H$^+$] requires 351.1705.

1'-Benzyl-3',3'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5d**



R_f = 0.15 (hexane/acetone 6:1, v/v). The solid yellowish powder-like material was dried under high vacuum; the obtained yield was 0.581 g (29%), mp 62–64 ºC.

^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, TMS): δ 1.37 (s, 6H, 2×3'-CH_3), 2.35–2.42 (m, 2H, CH_2), 3.02–3.06 (m, 2H, CH_2), 4.55 (s, 2H, NCH_2), 6.51–6.53 (m, 1H, 7'-H), 6.83–6.93 (m, 2H, 5'-H, 8-H), 7.28–7.32 (m, 2H, 6'-H, 4'-H), 7.34–7.39 (m, 5H, Ph-H), 7.98–8.02 (m, 2H, 7-H, 5-H).

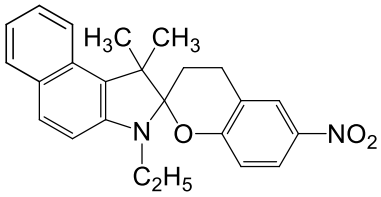
^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, TMS): δ 23.6, 23.7, 24.5, 25.2, 47.2, 50.1, 107.9, 116.7, 118.0, 120.1, 121.4, 122.5, 124.2, 125.1, 126.1, 126.5, 127.1, 127.5, 128.0, 128.7, 137.0, 138.7, 140.5, 147.6, 161.7.

IR (KBr): 3061, 2966; 1516 (NO_2-asymm.), 1337 cm^{-1} (NO_2-symm.).

Anal. Calcd (%) for $C_{25}H_{24}N_2O_3$: C 74.98; H 6.04; N 7.0; found: C 74.84; H 5.59; N 6.65.

ESI-HRMS: [M+H$^+$], found 401.1863. [$C_{25}H_{24}N_2O_3$+H$^+$] requires 401.1860.

3'-Ethyl-1',1'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-benz[*e*][2*H*]indole] **5f**



R_f = 0.2 (hexane/acetone 9:1, v/v) recrystallized from acetonitrile resulted in the production of yellowish crystals with the yield of 1.086g (56%), mp 168–169 ºC.

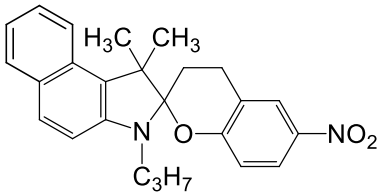
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28 (t, *J* = 9.6 Hz, 3H, $CH_2\underline{CH_3}$), 1.54 (s, 6H, 2×1'-CH_3), 2.44 (t, *J* = 7.6 Hz, 2H, 3-CH_2), 3.12 (t, *J* = 7.6 Hz, 2H, 4-CH_2), 3.43 (q, *J* = 9.6 Hz, 2H, $\underline{CH_2}CH_3$), 6.74 (d, *J* = 12.0 Hz, 1H, 8H), 7.02 (d, *J* = 11.4 Hz, 1H, 4'H), 7.22 (t, *J* = 10.4 Hz, 1H, 7'H), 7.41 (t, *J* = 10.4 Hz, 1H, 8'H), 7.77 (d, *J* = 10.4 Hz, 1H, 9'H), 7.81 (d, *J* = 11.4 Hz, 1H, 5'H), 7.93 (d, *J* = 10.4 Hz, 1H, 6'H), 7.99 (dd, *J* = 12.0 Hz, *J* = 3.2 Hz, 1H, 7H), 8.08 (d, *J* = 3.2 Hz, 1H, 5H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 15.5, 23.2, 23.4, 23.7, 25.0, 37.7, 51.8, 105.5, 109.9, 116.8, 121.2, 121.5 (2×C), 124.4, 125.2, 125.3, 126.5, 129.3, 129.5, 129.8 (2×C), 140.5, 145.4, 162.2. IR (cm^{-1}): 3056, 2967, 1519 (NO_2 asymm.), 1329 (NO_2 symm.).

Anal. Calcd (%) for $C_{24}H_{24}N_2O_3$ (388.46): C 74.21; H 6.23; N 7.21. Found: C 75.60; H 6.50; N 7.39.

ESI-HRMS: [M+H$^+$], found 389.1863. [$C_{24}H_{24}N_2O_3$+H$^+$] requires 389.1860.

1',1'-Dimethyl-3'-propyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-benz[*e*][2*H*]indole] **5g**



R_f = 0.14 (hexane/acetone 11:1, v/v) recrystallized from acetonitrile resulted in the production of yellowish crystals with the yield of 0.884g (44%). mp 151–152 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.0 (t, *J* = 9.8 Hz, 3H, $CH_2CH_2\underline{CH_3}$), 1.55 (s, 6H, 2×1'-CH_3), 1.68 (hex, *J* = 9.8 Hz, 2H, $CH_2\underline{CH_2}CH_3$), 2.44 (br.s, 2H, 3-CH_2), 3.12 (br.s, 2H, 4-CH_2), 3.43 (t, *J* = 9.8 Hz, 2H, $\underline{CH_2}CH_2CH_3$), 6.74 (d, *J* = 11.8 Hz, 1H, 8H), 7.01 (d, *J* = 11.2 Hz, 1H, 4'H), 7.21 (t, *J* = 11.0 Hz, 1H, 7'H), 7.41 (t, *J* = 11.0 Hz, 1H, 8'H), 7.76 (d, *J* = 11.0 Hz, 1H, 9'H), 7.81 (d, *J* = 11.2 Hz, 1H, 5'H), 7.93 (d, *J* = 11.0 Hz, 1H, 6'H), 7.99 (dd, *J* = 11.8 Hz, *J* = 3.6 Hz, 1H, 7H), 8.08 (d, *J* = 3.6 Hz, 1H, 5H).

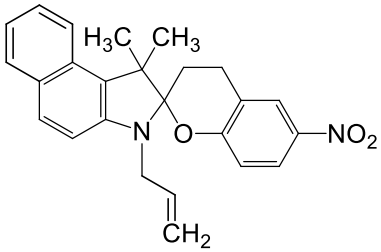
^{13}C NMR (100MHz, $CDCl_3$): δ 11.7(2×C), 23.5 (2×C), 23.7, 25.2, 45.2, 51.8, 105.4, 110.1, 116.8, 121.2, 121.5, 121.6, 124.4, 125.3 (2×C), 126.5, 129.5, 129.7, 129.8 (2×C), 140.6, 146.0, 162.3.

IR (cm^{-1}): 3059, 2964, 1519 (NO_2-asymm.), 1330 (NO_2-symm.).

Anal. Calcd (%) for $C_{25}H_{26}N_2O_3$ (402.48): C 74.60; H 6.51; N 6.96. Found: C 75.19; H 6.70; N 7.10.

ESI-HRMS: [M+H$^+$], found 403.2016. [$C_{25}H_{26}N_2O_3$+H$^+$] requires 403.2016.

3'-Allyl-1',1'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-benz[*e*][2*H*]indole] **5h**



R_f = 0.11 (hexane/acetone 11:1, v/v) recrystallized from acetonitrile resulted in the production of yellowish crystals with the yield of 0.52g (26%), mp 169–170 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.53 (s, 3H, 1'-CH_3), 1.63 (s, 3H, 1'-CH_3), 2.18–2.32 (m, 1H, 3-CH_2), 2.48–2.61 (m, 1H, 3-CH_2), 2.96–3.10 (m, 1H, 4-CH_2), 3.12–3.27 (m, 1H, 4-CH_2), 2.90 (AB-d, *J* = 18.2 Hz, 1H, N-CH_2), 4.03 (AB-d, *J* = 18.2 Hz, 1H, N-CH_2), 5.17 (d, *J* = 10.4 Hz, 1H, =CH_2) 5.29 (d, *J* = 17.2 Hz, 1H, =CH_2), 5.9 (m, 1H, -CH=), 6.75 (d, *J* = 10.2 Hz, 1H, 8H), 6.96 (d, *J* = 8.4 Hz, 1H, 4'H), 7.23 (t, *J* = 8.2 Hz, 1H, 7'H), 7.42 (t, *J* = 8.2 Hz, 1H, 8'H), 7.73 (d, *J* = 8.2 Hz, 1H, 9'H), 7.81 (d, *J* = 8.4 Hz, 1H, 5'H), 7.95 (d, *J* = 8.2 Hz, 1H, 6'H), 7.99 (dd, *J* = 10.2 Hz, *J* = 2.2 Hz, 1H, 7H), 8.07 (d, *J* = 2.2 Hz, 1H, 5H).

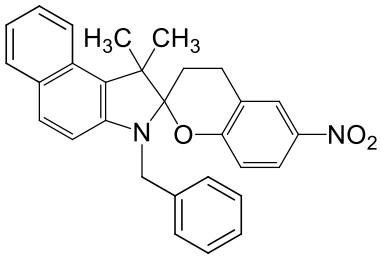
^{13}C NMR (100 MHz, $CDCl_3$): δ 23.1, 23.5, 24.1, 25.0, 45.8, 51.9, 105.2, 110.5, 115.4, 116.8, 121.3, 121.4, 121.7, 124.4, 125.3 (2×C), 126.6, 129.5, 129.7, 129.8 (2×C), 135.4, 140.6, 145.7, 162.1.

IR (cm^{-1}): 3075, 2960, 1513 (NO_2-asymm.), 1329 (NO_2-symm.).

Anal. Calcd (%) for $C_{25}H_{24}N_2O_3$ (400.47): C 74.98; H 6.04; N 7.00. Found: C 74.79; H 5.96; N 7.00.

ESI-HRMS: [M+H^+], found 401.1864. [$C_{25}H_{24}N_2O_3$+H^+] requires 401.1860.

3'-Benzyl-1',1'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-benz[e][2H]indole] **5i**



R_f = 0.15 (hexane/acetone 11:1, v/v) recrystallized from acetonitrile resulted in the production of yellowish crystals with the yield of 0.81 g (36%), mp = 180–181 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54 (s, 3H, 1'-CH_3), 1.60 (s, 3H, 1'-CH_3), 2.11–2.23 (m, 1H, 3-CH_2), 2.44–2.56 (m, 1H, 3-CH_2), 2.86–2.97 (m, 1H, 4-CH_2), 3.05–3.20 (m, 1H, 4-CH_2), 4.45 (AB-d, *J* = 16.2 Hz, 1H, N-CH_2), 4.56 (AB-d, *J* = 16.2 Hz, 1H, N-CH_2), 6.73 (d, *J* = 9.0 Hz, 1H, 8H), 6.77 (d, *J* = 8.6 Hz, 1H, 4'H), 7,17 (t, *J* = 8.0 Hz, 1H, 7'H),7.20–7.29 (m, 5H, Ph-H) 7.36 (t, *J* = 8.0 Hz, 1H, 8'H),

7.70 (d, *J* = 8.0 Hz, 1H, 9'H), 7.72 (d, *J* = 8.6 Hz, 1H, 5'H), 7,91 (d, *J* = 8.0 Hz, 1H, 6'H), 7,94 (dd, *J* = 9.0 Hz, *J* = 2.8 Hz, 1H, 7H), 7.98 (d, *J* = 2.8 Hz, 1H, 5H).

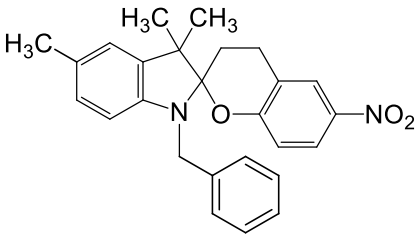
^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2, 23.5, 24.3, 25.2, 47.2, 52.0, 105.2, 110.5, 116.8, 121.3, 121.4, 121.9, 124.4, 125.3, 125.5, 126.2 (2×C), 126.6, 127.2 128.9 (2×C), 129.6, 129.7, 129.8, 129.9, 139.5, 140.7, 146.0, 162.2.

IR (cm^{-1}): 3056, 2962, 1515 (NO_2-asymm.), 1334 (NO_2-symm.).

Anal. Calcd (%) for $C_{29}H_{26}N_2O_3$ (450.53): C 77.31; H 5.82; N 6.22. Found: C 77.49; H 5.42; N 6.39.

ESI-HRMS: [M+H$^+$], found 451.2018. [$C_{29}H_{26}N_2O_3$+H$^+$] requires 451.2016.

1'-Benzyl-3',3',5'-trimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5l**



R_f = 0.15 (hexane/acetone 6:1, v/v) recrystallized from ethanol resulted in the production of yellowish crystals with the yield of 0.414 g (20%), mp 188–190 ºC.

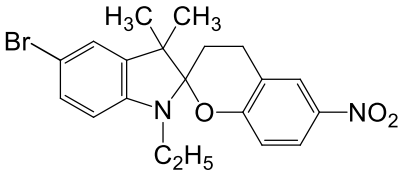
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.30 (s, 3H, 3'-CH_3), 1.39 (s, 3H, 3'-CH_3), 2.11–2.22 (m, 1H, CH_2), 2.32 (s, 3H, 5'-CH_3), 2.42–2.5 (m, 1H, CH_2), 2.9–2.98 (m, 1H, CH_2), 3.07–3.19 (m, 1H, CH_2), 4.33 (d, *J* = 17.4, 1H, N-CH_2), 4.55 (d, *J* = 17.4, 1H, N-CH_2), 6.34–6.37 (m, 1H, 7'-H), 6.82–6.85 (m, 1H, 8-H), 6.88–6.91 (m, 1H, 4'-H), 6.92–6.94 (m, 1H, 6'-H), 7.23–7.34 (m, 5H), 7.99–8.03 (m, 2H, 7-H, 5-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 20.9, 21.9, 23.3, 25.0, 26.1, 47.0, 49.7, 104.8, 107.2, 116.8, 121.2, 122.1, 124.1, 125.1, 126.1 (2×C), 126.9, 128.1, 128.6 (2×C), 128.7, 136.8, 139.4, 140.5, 145.9, 161.8.

IR (cm^{-1}): 3061, 2966, 1497 (NO_2-asymm.); 1332 (NO_2-symm.).MS m/z (%): 415 (M + H$^+$, 100).

Anal. Calcd (%) for $C_{26}H_{26}N_2O_3$(414.50): C 75.34; H 6.32; N 6.76. Found: C 75.63; H 6.52; N 6.47.

5'-Brom-1'-ethyl-3',3'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5n**



R_f = 0.17 (hexane/acetone 6:1, v/v) recrystallized from acetonitrile resulted in the production of yellowish crystals with the yield of 1.400 g (67%), mp 190–193 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.2 (t, *J* = 7.2 Hz, 3H, $CH_2\underline{CH_3}$), 1.23 (s, 6H, 2×3'-CH_3), 2.28–2.39 (m, 2H, 3-CH_2), 3.03–3.33 (m, 4H, N- CH_2, 4-CH_2), 6.44 (d, *J* = 8.2 Hz, 1H, 7'-H), 6.75 (d, *J* = 9.0 Hz, 1H, 8-H), 7.11 (d, *J* = 1.8 Hz, 1H, 4'-H), 7.25 (dd, *J* = 8.2 Hz, *J* = 1.8 Hz, 1H, 6'-H), 7.98 (dd, *J* = 9.0 Hz, *J* = 2.7 Hz, 1H, 7-H), 8.03 (d = 2.7 Hz, 1H, 5-H).

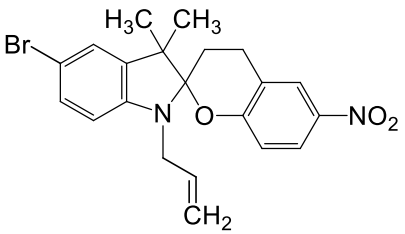
^{13}C NMR (75 MHz, $CDCl_3$): δ 14.6, 21.7, 23.4, 24.6, 25.6, 37.4, 49.7, 104.4, 107.8, 110.4, 116.7, 121.1, 124.2, 124.6, 125.1, 130.4, 139.0, 140.6, 146.5, 161.4.

IR (cm^{-1}): 3086, 2966, 1517 (NO_2-asymm.); 1336 (NO_2-symm.).

MS m/z (%): 417, 419 (M + H^+, 100).

Anal. Calcd (%) for $C_{20}H_{21}BrN_2O_3$ (417.30): C 57.56; H 5.07; N 6.71. Found: C 57.33; H 5.30; N 6.99.

5'-Brom-1'-allyl-3',3'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5o**



R_f = 0.16 (hexane/acetone 6:1, v/v) recrystallized from acetonitrile resulted in the production of yellowish crystals with the yield of 0.555 g (26%), mp 167–168 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.23 (s, 3H, 3'-CH_3), 1.3 (s, 3H, 3'-CH_3), 2.12–2.23 (m, 1H, 3-CH_2), 2.39–2.46 (m, 1H, 3-CH_2), 2.94–3.16 (m, 2H, N-CH_2), 3.66–3.74 (m, 1H, 4-CH_2), 3.90–3.98 (m, 1H, 4-CH_2), 5.14 (dq, *J* = 10.2 Hz, *J* = 1.8 Hz, 1H, =CH_2) 5.23 (dq, *J* = 17.1 Hz, *J* = 1.8 Hz, 1H, =CH_2), 5.9 (ddt, *J* = 17.1 Hz, *J* = 10.2 Hz, *J* = 4.5 Hz, 1H, -CH=), 6.41 (d, *J* = 8.5 Hz, 1H, 7'-H), 6.77 (d, *J* = 9.0 Hz, 1H, 8-H), 7.13 (d, *J* = 2.1 Hz, 1H, 4'-H), 7.24 (dd, *J* = 8.5 Hz, *J* = 2.1 Hz, 1H, 6'-H), 7.99 (dd, *J* = 9.0 Hz, *J* = 2.7 Hz, 1H, 7-H), 8.03 (d, *J* = 2.7 Hz, 1H, 5-H).

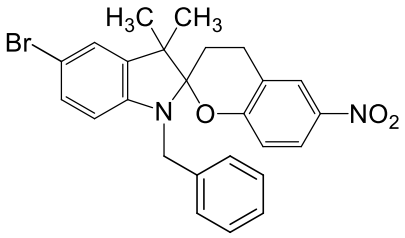
^{13}C NMR (75 MHz, $CDCl_3$): δ 21.8, 23.2, 24.6, 29.9, 45.5, 49.8, 104.3, 108.7, 110.9, 115.4, 116.7, 121.1, 124.2, 124.5, 125.1, 130.4, 134.5, 139.0, 140.7, 146.8, 161.3.

IR (cm^{-1}): 3066 (Alif. C-H); 2943 (Ar. C-H); 1515 (NO_2 asymm.); 1340 (NO_2-symm.).

MS m/z (%): 429, 431 (M + H^+, 100).

Anal. Calcd (%) for $C_{21}H_{21}BrN_2O_3$ (429.31): C 58.75; H 4.93; N 6.53. Found: C 58.41; H 4.91; N 6.47.

1'-Benzyl-5'-brom-3',3'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5p**



R_f = 0.2 (hexane/acetone 9:1, v/v) recrystallized from ethanol resulted in the production of yellowish crystals with the yield of 0.790 g (33%), mp 200–202 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.33 (s, 6H, 2×3'-CH_3), 2.21–2,4 (m, 2H, 3-CH_2), 2.96–3.08 (m, 2H, 4-CH_2), 4.3–4.56 (m, 2H, N-CH_2), 6.31–6.34 (m, 1H, 7'-H), 6.82–6.85 (m, 1H, 8-H), 7.17–7.21 (m, 2H, 6'-H, 4'-H), 7.26–7.37 (m, 5H), 7.99–8.03 (m, 2H, 7-H, 5-H).

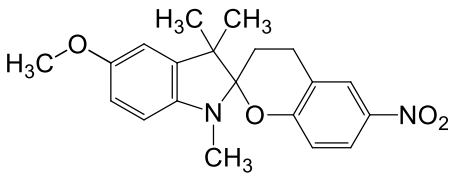
^{13}C NMR (75 MHz, $CDCl_3$): δ 23.3, 24.9 (2×C); 47.0 (2×C), 50.0, 109.0, 116.7, 121.1, 124.2, 124.6, 125.1, 126.0 (2×C), 127.2, 128.8 (2×C), 130.6, 138.5, 139.1, 140.7, 147.0, 161.3.

IR (cm^{-1}): 3053, 2976, 1514 (NO_2-asymm.), 1335 (NO_2-symm.).

MS m/z (%): 479, 481 (M + H$^+$, 100).

Anal. Calcd (%) for $C_{25}H_{23}BrN_2O_3$ (479.37): C 62.64; H 4.84; N 5.84. Found: C 62.64; H 5.07; N 5.95.

1',3',3'-Trimethyl-5'-methoxy-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5q**



R_f = 0.22 (hexane/acetone 5:1, v/v) recrystallized from acetonitrile resulted in the production of yellowish crystals with the yield of 0.372 g (21%), mp 137–138 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (s, 6H, 2×3'-CH_3), 2.35 (br.s, 2H, 3-CH_2), 2.81 (s, 3H, N-CH_3), 3.05 (br.s, 2H, 4-CH_2), 3.78 (s, 3H, OMe), 6.5 (d, *J* = 8.2 Hz, 1H, 7'H); 6,69 (d, *J* = 2.6 Hz, 1H, 4'H), 6.73 (dd, *J* = 8.2 Hz, *J* = 2.6 Hz, 1H, 6'H), 6.78 (d, *J* = 8.8 Hz, 1H, 8H), 7.98 (dd, *J* = 8.8 Hz, *J* = 2.8 Hz, 1H, 7H), 8.03 (d, *J* = 2.8 Hz, 1H, 5H).

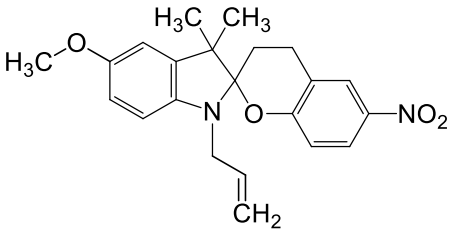
^{13}C NMR (100 MHz, $CDCl_3$): δ 21.9, 23.5, 24.3, 25.5, 28.9, 49.9, 50.1, 105.0, 107.5, 109.4, 111.8, 116.9, 121.6, 124.3, 125.2, 138.6, 140.6, 142.8, 154.0, 162.1.

IR (cm^{-1}): 3063, 2969, 1503 (NO_2-asymm.); 1329 (NO_2-symm.).

MS m/z (%): 355 (M + H$^+$, 100).

Anal. Calcd (%) for $C_{20}H_{22}N_2O_4$ (354.40): C 67.78; H 6.26; N 7.90. Found: C 68.02; H 6.38; N 8.23.

1'-Allyl-3',3'-dimethyl-5'-methoxy-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5r**



R_f = 0.17 (hexane/acetone 8:1, v/v) recrystallized from acetonitrile resulted in the production of yellowish crystals with the yield of 0.645 g (34%), mp 145–146 ºC.

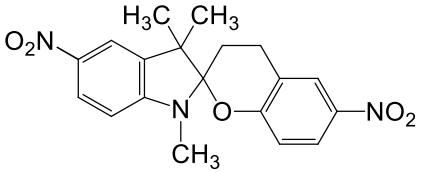
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (s, 3H, 3'-CH_3), 1.31 (s, 3H, 3'-CH_3), 2.11–2.25 (m, 1H, 3-CH_2), 2.38–2.48 (m, 1H, 3-CH_2), 2.92–3.03 (m, 1H, N-CH_2), 3.04–3.18 (m, 1H, N-CH_2), 3.62–3.74 (m, 1H, 4-CH_2), 3.78 (s, 3H, O-CH_3), 3.88–3.99 (m, 1H, 4-CH_2), 5.13 (dq, *J* = 10.4, *J* = 1.6 Hz, 1H, C=CH_2), 5.26 (dq, *J* = 17.2, *J* = 1.6 Hz, 1H, C=CH_2), 5.93 (ddt, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 4.4 Hz, 1H, -CH=), 6.45–6.48 (m, 1H, 7'-H), 6.69–6.72 (m, 2H, 4'-H, 6'-H), 6.77 (d, *J* = 9.0 Hz, 1H, 8-H), 7.98 (dd, *J* = 9.0 Hz, *J* = 2.4 Hz, 1H, 7-H), 8.03 (d, *J* = 2.4 Hz, 1H, 5-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 22.0, 23.5, 24.9, 26.1, 46.1, 50.0, 56.1, 105.2, 107.4, 109.4, 111.7, 115.2, 116.9, 121.4, 124.3, 125.2, 135.4, 138.3, 140.6, 142.1, 153.9, 161.9.

IR (cm^{-1}): 3060, 2969, 1505 (NO_2-asymm.); 1330 (NO_2-symm.).

ESI-HRMS: [M+H$^+$], found 381.1821. [$C_{22}H_{24}N_2O_4$+H$^+$] requires 381.1822.

1',3',3'-Trimethyl-5',6-dinitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5s**



R_f = 0.17 (hexane/acetone 4:1, v/v) recrystallized from acetonitrile resulted in the production of yellow crystals with the yield of 0.739 g (40%), mp 232–234 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ=1.28 (s, 6H, 2×3'-CH_3), 2.29–2.45 (m, 2H, CH_2), 2.96 (s, 3H, NCH_3), 3.03–3.17 (m, 2H, CH_2), 6.56 (d, *J* = 8.7 Hz, 1H, 7'-H); 6.79 (d, *J* = 9.0 Hz, 1H, 8-H), 7.91 (d, *J* = 2.4 Hz, 1H, 4'-H), 7.99 (dd, *J* = 9.0, 2.7 Hz, 1H, 7-H), 8.05 (d, *J* = 2.7 Hz, 1H, 5-H), 8.17 (dd, *J* = 8.7, 2.4 Hz, 1H, 6'-H).

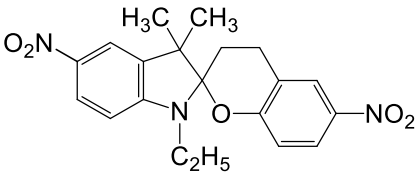
^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, TMS): δ=21.9, 23.3, 24.1, 25.7, 28.6, 49.3, 104.1, 106.0, 117.0, 118.2, 121.3, 124.5, 125.4, 126.5, 137.9, 140.8, 141.3, 154.0, 161.0.

IR (cm^{-1}): 3068, 2967, 1510 (NO_2-asymm.), 1322 cm^{-1} (NO_2-symm.).

Anal. Calcd (%) for $C_{19}H_{19}N_3O_5$: C 61.78; H 5.18; N 11.38; found: C 61.63; H 5.19; N 11.60.

ESI-HRMS: [M+H$^+$], found 370.1399. [$C_{19}H_{19}N_3O_5$ +H$^+$] requires 370.1397.

1'-Ethyl-3',3'-dimethyl-5',6-dinitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5t**



R_f = 0.11 (hexane/ethylacetate 9:1, v/v) recrystallized from acetonitrile resulted in the production of yellow crystals with the yield of 0.997 g (52%), mp 179–180 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (t, *J* = 7.2 Hz, 3H, $CH_2\underline{CH_3}$), 1.28 (s, 3H, 3'-CH_3), 1.29 (s, 3H, 3'-CH_3), 2.24–2.35 (m, 1H, ½ 3-CH_2), 2.42–2.52(m, 1H, ½ 3-CH_2), 3.0–3.20 (m, 2H, 4-CH_2), 3.33–3.52 (m, N-CH_2), 6.55 (d, *J* = 8.7 Hz, 1H, 7'-H); 6.78 (d, *J* = 9.0 Hz, 1H, 8-H), 7.91 (d, *J* = 2.3 Hz, 1H, 4'-H), 7.99 (dd, *J* = 9.0, 2.7 Hz, 1H, 7-H), 8.05 (d, *J* = 2.7 Hz, 1H, 5-H), 8.17 (dd, *J* = 8.7, 2.3 Hz, 1H, 6'-H).

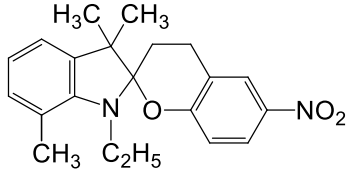
^{13}C NMR (100 MHz, $CDCl_3$): δ 14.6, 21.7, 23.3, 24.5, 25.7, 37.5, 49.3, 104.1, 105.1, 116.9, 118.1, 121.0, 124.4, 125.2, 126.5, 137.6, 140.3, 141.1, 152.9, 160.7.

IR (cm^{-1}): 3068, 2990, 1501 (NO_2-asymm.), 1321 (NO_2-symm.).

Anal. Calcd (%) for $C_{20}H_{21}N_3O_5$ (383.40): C 62.65; H 5.52; N 10.96. Found: C 62.03; H 5.48; N 11.33. Found: C 70.03; H 6.30; N 9.03.

ESI-HRMS: [M+H$^+$], found 384.1552. [$C_{20}H_{21}N_2O_5$ +H$^+$] requires 384.1554.

1'-Ethyl-3',3',7'-trimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5v**



R_f = 0.15 (hexane/ethylacetate 7:1, v/v) recrystallized from acetonitrile resulted in the production of yellow crystals with the yield of 0.440 g (25%) mp 211–213 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.22 (s, 6H, 2×3'-CH_3), 1.27 (t, *J* = 7.2 Hz, 3H, $CH_2\underline{CH_3}$), 2.36 (br.s, 2H, 3-CH_2), 2.51 (s, 3H, 7'-CH_3), 3.06 (br.s, 2H, N-CH_2), 3.55 (pl.s, 2H, 4-CH_2), 6.72–6.81 (m, 2H, 5'-H, 8-H), 6.9–6.95 (m, 2H, 4'-H, 6'-H), 8.0 (dd, *J* = 9.0 Hz, *J* = 2.6 Hz, 1H, 7-H), 8.04 (d, *J* = 2.6 Hz, 1H, 5-H).

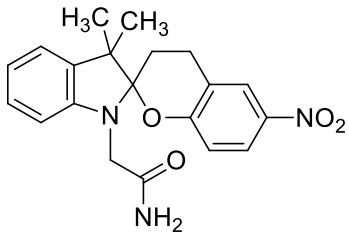
^{13}C NMR (75 MHz, $CDCl_3$): δ 17.7, 19.5, 22.1, 23.6, 24.9, 25.9, 37.7, 48.7, 104.8, 116.7, 117.4, 118.9, 119.2, 121.4, 124.1, 125.1, 132.0, 137.3, 140.3, 145,3, 161.9.

IR (cm^{-1}): 3077, 2970, 1508 (NO_2-asymm.), 1330 (NO_2-symm.).

MS m/z (%): 353 (M + H$^+$, 100)

Anal. Calcd (%) for $C_{21}H_{24}N_2O_3$, (352.43): C 71.57; H 6.86; N 7.95. Found: C 71.78; H 7.06; N 8.20.

1'-Carbamoylmethyl-3',3'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **11**



To a stirred solution of 1'-Carbamoylmethyl-3',3'-dimethyl-3*H*-indolium chloride (5 mmol) in distilled water (15 mL), sodium carbonate (1.06 g, 10 mmol) was added at 0 ºC. The mixture became turbid and was extracted with diethyl ether (3 × 20 mL). The combined organic phase was dried over anhydrous sodium sulfate. Then the solvent was evaporated under reduced pressure to afford the 1-carbamoylmethyl-2-methylene-2,3-dihydro-1*H*-indole as an oil.

The crude intermediate enamine obtained as a result of the above outlined procedure was dissolved in acetonitrile (15 mL). The powdered sodium carbonate (1.06 g, 10 mmol), anhydrous sodium sulfate (1.42 g, 10 mmol) and 2-chloromethyl-4-nitrophenol (938 mg, 5 mmol) were added to the solution. The mixture was stirred at rt. After 16 h, the reaction mixture was filtered, neorganic residue was washed with acetonitrile (3×5 mL). The filtrate was poured into water (50 mL). After the mixture became turbid, the separated product was extracted with diethyl ether (3 × 20 mL). Then the combined extract was dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The residue was subjected to flash chromatography on silica gel. R_f = 0.17 (hexane/acetone 4:1, v/v). After it was recrystallized from acetonitrile, yellow crystals were produced with the yield of 0.250 g (14%), mp 204–205 ºC.

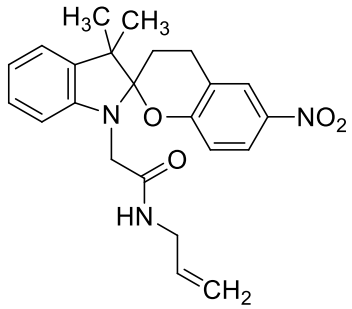
^{1}H NMR (400 MHz, $CDCl_3$,): δ 1.27 (s, 3H, 3'-CH_3), 1.32 (s, 3H, 3'-CH_3), 2.24–2.14 (m, 1H, CH_2), 2.55–2.44 (m, 1H, CH_2), 3.21–2.98 (m, 2H, CH_2), 3.81 (d, *J* = 18.6 Hz, 1H), 4.00 (d, *J* = 18.6 Hz, 1H), 6.06 (d, *J* = 2.6 Hz, 1H, -NH_2), 6.60 (d, *J* = 7.8 Hz, 1H), 6.67 (d, *J* = 2.6 Hz, 1H, -NH_2), 6.77 (d, *J* = 9.0 Hz, 1H), 6.95 (t, *J* = 8.2 Hz, 1H), 7.12 (d, *J* = 7.2 Hz, 1H), 7.21 (t, *J* = 7.7 Hz, 1H), 7.97 (dd, *J* = 9.0, 2.7 Hz, 1H), 8.03 (d, *J* = 2.6 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 22.1, 23.2, 24.9, 26.1, 47.6, 49.9, 103.8, 107.9, 116.8, 121.1, 121.2, 121.9, 124.4, 125.3, 128.3, 136.8, 141.1, 146.6, 160.8, 173.5.

IR (cm^{-1}): 3071, 2966, 1516 (NO_2-asymm.), 1342 (NO_2-symm.).

ESI-HRMS: [M+H^+], found 368.1605. [$C_{20}H_{21}N_3O_4$ +H^+] requires 368.1605.

1'-(N-Allylcarbamoylmethyl)-3',3'-dimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **16**



To a stirred solution of 1-allyl-9,9,9a-trimethylimidazo[1,2-a]indol-2-one (0.1 g, 0.39 mmol) in ethanol, hydrochloric acid (35%, 0.5 mL) was added and stirred for 1 min. The mixture was cooled to ~ 0 ºC; next, sodium carbonate (1.06 g, 10 mmol) was added, the resulting mixture became turbid, and the separated product was extracted with diethyl ether (3 × 20 mL). Then the combined extract was dried over anhydrous sodium sulfate, and 2-chloromethyl-4-nitrophenol (0.073 g, 0.39 mmol) was added to the solution. The resulting mixture was stirred at rt. After 6 h, the solvent was evaporated under reduced pressure. The residue was subjected to flash chromatography on silica gel. R_f = 0.11 (hexane/acetone 4:1, v/v) recrystallized from acetonitrile produced yellow crystals with the yield of 0.070 g (44%), mp 194–195 ºC.

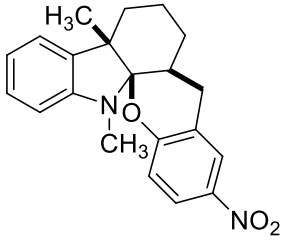
^{1}H NMR (400 MHz, $CDCl_3$,): δ 1.28 (s, 3H, 3'-CH_3), 1.33 (s, 3H, 3'-CH_3), 2.23–2.10 (m, 1H, CH_2), 2.51–2.39 (m, 1H, CH_2), 3.21–2.97 (m, 2H, CH_2), 4.08–3.74 (m, 4H, CH_2), 5.14–5.04 (m, 2H, CH_2), 5.87–5.71 (m, 1H, -CH=), 6.58 (d, *J* = 7.8 Hz, 1H), 6.72 (t, *J* = 5.6 Hz, 1H, NH), 6.77 (d, *J* = 9.0 Hz, 1H), 6.96 (t, *J* = 7.3 Hz, 1H), 7.12 (d, *J* = 7.2 Hz, 1H), 7.22 (td, *J* = 7.7, 1.1 Hz, 1H), 7.99 (dd, *J* = 9.0, 2.7 Hz, 1H), 8.04 (d, *J* = 2.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 22.07, 23.21, 24.88, 26.14, 41.61, 48.02, 49.86, 103.84, 107.91, 116.53, 116.86, 121.00, 121.11, 121.91, 124.42, 125.25, 128.38, 133.92, 136.87, 141.13, 146.84, 160.76, 169.61.

IR (cm^{-1}): 3058, 2973, 1519 (NO_2-asymm.), 1337 (NO_2-symm.).

ESI-HRMS: [M+H$^+$], found 408.1916. [$C_{23}H_{25}N_3O_4$ +H$^+$] requires 408.1918.

(5b*R**, 8a*R**, 14a*S**)-1,5b-Dimethyl-11-nitro-5b,6,7,8,8a,9-hexahydro-8*H*-indole[2,3-*c*]xantene **20a**



To a stirred solution of 4a,9-dimethyl-2,3,4,4a-tetrahydro-1*H*-carbazol-9-ium iodide **17a** (5 mmol) in distilled water (15 mL) and ethanol (5 mL), sodium

carbonate (1.06 g, 10 mmol) was added at rt. The mixture became turbid and was extracted with diethyl ether (3 × 20 mL). The combined organic phase was dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure to afford enamine **18a**. The crude intermediate enamine obtained as a result of the outlined procedure was dissolved in acetonitrile (5 mL), and then 2-chloromethyl-4-nitrophenol (938 mg, 5 mmol) was added to the solution. The mixture was stirred at 80 ºC. After 6 h the reaction mixture was poured into water (50 mL). When the mixture became turbid, the separated product was extracted with diethyl ether (3 × 20 mL), the combined extract was dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The residue was subjected to flash chromatography on silica gel, R_f = 0.16 (hexane/acetone 7:1, v/v). Recrystallization from acetonitrile produced yellow crystals with the yield of 0.352 g (20%), mp 137–139 ºC.

^{1}H NMR (300 MHz, $CDCl_3$,): δ 1.35 (s, 3H, 5a-CH_3), 1.37-1.54 (m, 2H, CH_2), 1.69 – 1.99 (m, 4H, 2×CH_2), 2.60 – 2.78 (m, 2H, CH_2), 2.80 (s, 3H, N-CH_3), 6.65 (d, *J* = 7.5 Hz, 1H, 13-H) 6.74 (d, *J* = 9.0 Hz, 1H, 2-H), 6.85 (t, *J* = 7.5 Hz, 1H, 11-H), 7.03 (d, *J* = 7.5 Hz, 1H, 10-H), 7.2 (dt, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H, 12-H), 7.95 (dd, *J* = 9.0 Hz, *J* = 2.7 Hz, 1H, 3-H), 8.00 (d, *J* = 2.7 Hz, 1H, 5-H).

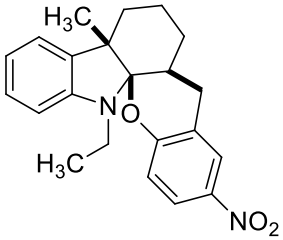
^{13}C NMR (75 MHz, $CDCl_3$): δ 16.1; 17.7; 27.9; 28.3; 28.5; 30.0; 40.9; 48.5; 105.8; 107.9; 116.2; 119.1; 120.3; 120.8; 122.2; 124.1; 124.7; 127.4; 138.2; 148.2; 161.5.

IR (cm^{-1}): 3050, 2927, 1515 (NO_2-asymm.), 1333 (NO_2-symm.).

MS m/z (%): 351 ($M + H^+$, 100).

Anal. Calcd (%) for $C_{21}H_{22}N_2O_3$, (350.41): C 71.98; H 6.33; N 7.99. Found: C 71.78; H 6.37; N 7.84.

(5b*R**, 8a*R**, 14a*S**)-1-Ethyl-5b-methyl-11-nitro-5b,6,7,8,8a,9-hexahydro-8*H*-indole[2,3-*c*]xantene **20b**



To a stirred solution of 9-ethyl-4a-methyl-2,3,4,4a-tetrahydro-1*H*-carbazol-9-ium iodide **17b** (5 mmol) in distilled water (15 mL) and ethanol (5 mL), sodium carbonate (1.06 g, 10 mmol) was added at rt. The mixture became turbid and was extracted with diethyl ether (3 × 20 mL). The combined organic phase was dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure to afford enamine **18b**. The crude intermediate enamine obtained as a result of the outlined procedure was dissolved in acetonitrile (5 mL), and 2-chloromethyl-4-nitrophenol (938 mg, 5 mmol) was added to the solution. The mixture was stirred at 80 ºC. After 6 h the reaction mixture was poured into water (50 mL). When the mixture became turbid, the separated product was extracted with diethyl ether (3 ×

20 mL), then the combined extract was dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The residue was subjected to flash chromatography on silica gel, R_f = 0.2 (hexane/ethylacetate 2:1, v/v), and after recrystallization from ethanol, yellow crystals were obtained with the yield of 0.769 g (42%), mp 150–152 ºC.

^{1}H NMR (300 MHz, $CDCl_3$,): δ 1.24 (t, *J* = 7.5 Hz, 3H, $CH_2\underline{CH_3}$), 1.36 (s, 3H, 5b-CH_3), 1.42-1.56 (m, 2H, CH_2), 1.88-2.01 (m, 4H, 2×CH_2), 2.59-2.68 (m, 1H, CH_2), 2.72-2.8 (m, 1H, CH_2), 3.16-3.42(m, 2H, CH_2), 6.66 (d, *J* = 7.5 Hz, 1H, 13-H) 6.71 (d, *J* = 9.2 Hz, 1H, 2-H), 6.83 (dt, *J* = 7.5 Hz, *J* = 0.9 Hz, 1H, 11-H), 7.03 (dd, *J* = 7.5 Hz, *J* = 0.9 Hz, 1H, 10-H), 7.19 (dt, *J* = 7.5 Hz, *J* = 0.9 Hz, 1H, 12-H), 7.95 (dd, *J* = 9.2 Hz, *J* = 2.7 Hz, 1H, 3-H), 8.01 (d, *J* = 2.7 Hz, 1H, 5-H).

^{13}C NMR ($CDCl_3$): δ 14.6; 16.2, 17.8; 28.6; 28.7; 30.7; 37.5; 41.0; 48.6; 106.3; 107.3; 116.2; 118.7; 120.3; 122.2; 124.0; 124.6; 127.4; 138.1; 140.3; 147.4; 161.2.

IR (cm^{-1}): 3048, 2936, 1516 (NO_2-asymm.), 1330 (NO_2-symm.).

MS m/z (%): 365 ($M + H^+$, 80).

Anal. Calcd (%) for $C_{22}H_{24}N_2O_3$, (364.44): C 72.5; H 6.64; N 7.69. Found: C 72.9; H 6.92; N 8.01.

*General procedure for preparation of alkylating agent **24g,h.***

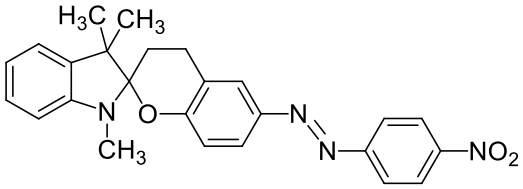
To a stirred solution of the corresponding alcohol (**23g,h**) (2 mmol) in ethyl acetate (10 mL), concentrated hydrochloric acid (2 mL) was added. The mixture was stirred at 70ºC for 4 h. After cooling to room temperature, the solvent was removed under reduced pressure, and the residue was dissolved in ethanol (15 mL), then poured into water (60 mL) and extracted with diethyl ether (3 × 20 mL). The combined organic phase was washed with water (2 × 30 mL), dried over anhydrous sodium sulfate, and then the solvent was evaporated under reduced pressure to afford the corresponding alkylating agent (**24g** and **24h,** respectively) as dark red resinous material, which was used for the further reaction without purification.

*General procedure for preparation of **25a-d***

To a stirred solution of the corresponding iodide (**2a,e**) (5 mmol) in distilled water (15 mL), sodium carbonate (1.06 g, 10 mmol) was added at rt. The mixture became turbid and was extracted with diethyl ether (3 × 20 mL). The combined organic phase was dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure to afford the corresponding 2-methylene-2,3-dihydro-1*H*-indole (**3a**,**e**) as a brownish oil in the case of **3a** and as a bright green solid material in the case of **3e**. The crude intermediate enamine obtained as a result of the outlined procedure was dissolved in acetonitrile (3 mL), and then the solution of alkylating agent **5g** or **5h** (5 mmol) in acetonitrile (15 mL) was added to the solution. The mixture was stirred at rt for 4 h. The resultant crystalline material was filtered, washed with cold acetonitrile (1 mL) and dried *in vacuo*. The solvent of the filtrate was evaporated under reduced pressure. The residue was subjected to flash chromatography on silica gel (hexane/acetone 10:1, v/v), combined with crystalline

material which had first crystallized from the reaction mixture and recrystallized from acetonitrile to afford compound **25a-d**.

1',3',3'-Trimethyl-6-[4''-nitrophenylazo]-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **25a**



R_f = 0.15 (hexane/acetone 10:1, v/v) produced orange crystals with the yield of 1.005 g (47%), mp 219–220 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28 (s, 6H, 2×3'-CH_3), 2.32-2.43 (m, 2H, 3-CH_2), 2.88 (s, 3H, N-CH_3), 3.0-3.24 (m, 2H, 4-CH_2), 6.59 (d, *J* = 7.6 Hz, 1H, 7'H), 6.85 (d, *J* = 7.8 Hz, 1H, 8H), 6.86 (t, *J* = 7.6 Hz, 1H 6'H), 7.06 (d, *J* = 7.6 Hz, 1H, 4'H), 7.20 (d, *J* = 7.6 Hz, 1H, 5'H), 7.77 (d, *J* = 7.8 Hz, 1H, 7H), 7.78 (s, 1H, 5H), 7.96 (d, *J* = 8.8 Hz, 2H, 2''H, 6''H), 8.35 (d, *J* = 8.8 Hz, 2H, 3''H, 5''H).

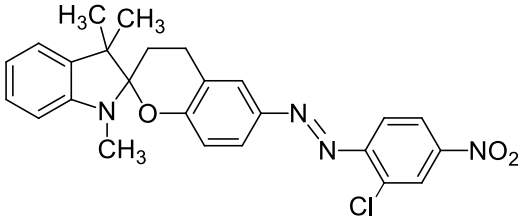
^{13}C NMR (100 MHz, $CDCl_3$): δ 22.0, 23.5, 24.4, 25.6, 28.5, 49.5, 103.8, 107.2, 117.3, 119.1, 121.3, 121.7, 123.0 (2×C), 124.1, 124.7 (2×C), 124.8, 127.8, 137.2, 146.2, 148.1, 148.7, 156.1, 160.5.

IR (cm^{-1}): 3048, 2967, 1520 (NO_2-asymm.), 1341 (NO_2-symm.).

Anal. Calcd for $C_{25}H_{24}N_4O_3$ (428.48): C 70.08; H 5.65; N 13.08. Found: C 69.65; H 5.24; N 13.64.

ESI-HRMS: [M+H^+], found 429.1925 [$C_{25}H_{24}N_4O_3$+H^+] requires 429.921.

1',3',3'-Trimethyl-6-[2''-chloro-4''-nitrophenylazo]-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **25b**



R_f = 0.15 (hexane/acetone 10:1, v/v) produced dark brown crystals with the yield of 1.412 g (61%), mp 190–191 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (s, 6H, 2×3'-CH_3), 2.27-2.49 (m, 2H, 3-CH_2), 2.89 (s, 3H, N-CH_3), 2.99-3.26 (m, 2H, 4-CH_2), 6.52-6.71 (m, 1H, 7'H), 6.76-6.96 (m, 2H, 8H, 6'H), 7.01-7.14 (m, 1H, 4'H), 7.15-7.26 (m, 1H, 5'H), 7.73 (d, *J* = 7.4 Hz, 1H, 6''H), 7.77-7.86 (m, 2H, 5H, 7H), 7.16 (d, *J* = 7.4 Hz, 1H, 5''H,), 8.40 (s, 1H, 3''H).

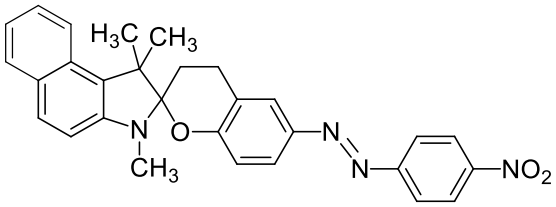
^{13}C NMR (100 MHz, $CDCl_3$): δ 22.1, 23.6, 24.4, 25.8, 28.5, 49.6, 103.9, 107.3, 117.5, 118.4, 119.2, 121.4, 121.9, 122.8, 125.0, 125.3, 126.2, 128.0, 134.8, 137.2, 146.7, 148.0, 148.8, 152.7, 161.2.

IR (cm^{-1}): 3095, 2961, 1520 (NO_2-asymm.), 1344 (NO_2-symm.).

Anal. Calcd for $C_{25}H_{23}ClN_4O_3$ (462.93): C 64.86; H 5.01; N 12.10. Found: C 64.19; H 10.10; N 12.44.

ESI-HRMS: [M+H$^+$], found 463.1536 [$C_{25}H_{23}ClN_4O_3$+H$^+$] requires 463.1532.

1',1',3'-trimethyl-6-[4"-nitrophenylazo]-1',3,3',4-tetrahydrospiro[chromene-2,2'-benz[*e*][2*H*]indole] **25c**



R_f = 0.17 (hexane/acetone 10:1, v/v) produced dark brown crystals with the yield of 1.003 (42 %), mp 199–201 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42-171 (m, 6H, 2×3'-CH_3), 2.47 (br.s, 2H, 3-CH_2), 2.99 (s, 3H, N-CH_3), 3.16 (br.s, 2H, 4-CH_2), 6.85 (d, *J* = 8.8 Hz, 1H, 8H), 7.04 (d, *J* = 8.4 Hz, 1H, 4'H), 7.23 (t, *J* = 6.8 Hz, 1H 7'H), 7.42 (t, *J* = 6.8 Hz, 1H 8'H), 7.75-7.86 (m, 4H, 9',5',6',7H), 7.96 (d, *J* = 8.2 Hz, 3H, 2", 6",5H), 8.36 (d, *J* = 8.2 Hz, 2H, 3"H, 5"H).

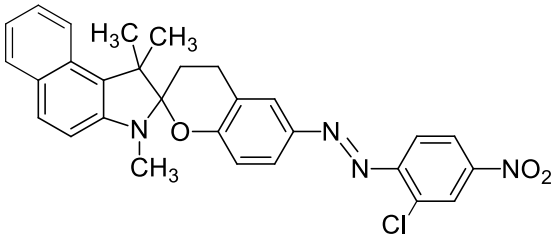
^{13}C NMR (100 MHz, $CDCl_3$): δ 23.7, 24.2, 24.6, 29.1, 29.4, 51.6, 104.4, 110.5, 117.3, 121.4, 121.6, 122.0, 123.1 (2×C), 123.2, 124.3 (2×C), 124.8, 124.9, 126.0, 126.5, 129.4, 129.8, 129.9, 146.3, 146.6, 148.2, 156.3, 160.9.

IR (cm^{-1}): 3055, 2970, 1520 (NO_2-asymm.), 1344 (NO_2-symm.).

Anal. Calcd for $C_{29}H_{26}N_4O_3$ (478.54): C 72.79, H 5.48, N 11.71. Found: C 73.10, H 5.43, N 11.64.

ESI-HRMS: [M+H$^+$], found 479.2083 [$C_{29}H_{26}N_4O_3$+H$^+$] requires 479.2078.

1',1',3'-trimethyl-6-[2"-chloro-4"-nitrophenylazo]-1',3,3',4-tetrahydrospiro[chromene-2,2'-benz[*e*][2*H*]indole] **25d**



R_f = 0.16 (hexane/acetone 10:1, v/v) produced dark brown crystals with the yield of 1.766 g (69 %), mp 200–202 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.41-1.72 (m, 6H, 2×3'-CH_3), 2.48 (br.s, 2H, 3-CH_2), 2.98 (s, 3H, N-CH_3), 3.08-3.29 (m, 2H, 4-CH_2), 6.85 (d, *J* = 8.0 Hz, 1H, 8H), 7.04 (d, *J* = 8.8 Hz, 1H, 4'H), 7.22 (t, *J* = 7.4 Hz, 1H 7'H), 7.41 (t, *J* = 7.4 Hz, 1H 8'H), 7.74-7.84 (m, 4H, 9',5',6',5,7H), 7.96 (d, *J* = 8.8 Hz, 1H, 6"H), 8.18 (dd, *J* = 8.8 Hz, *J* = 2.4 Hz 1H, 5"H,), 8.42 (d, *J* = 2.4 Hz, 1H, 3"H).

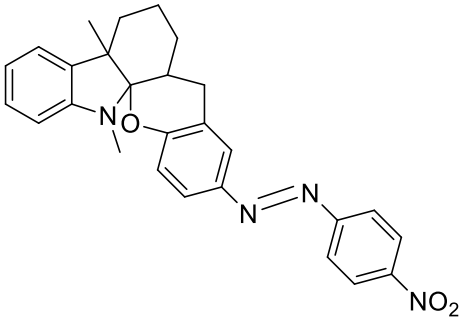
^{13}C NMR (100 MHz, $CDCl_3$): δ 23.4, 23.6, 23.7, 24.6, 29.1, 51.7, 104.6, 110.6, 117.4, 118.4 (2×C), 121.4, 121.7, 122.1, 122.8 (2×C), 125.2, 126.2 (2×C), 126.5, 129.5, 129.6, 129.8, 129.9, 134.8, 146.8, 148.1, 152.7, 161.5.

IR (cm^{-1}): 3051, 2978, 1522 (NO_2-asymm.), 1343 (NO_2-symm.).

Anal. Calcd (%) for $C_{29}H_{25}ClN_4O_3$ (512.97): C 67.90, H 4.91, N 10.92. Found: C 68.07, H 4.81, N 10.78.

ESI-HRMS: [M+H$^+$], found 513.1698 [$C_{29}H_{25}ClN_4O_3$+H$^+$] requires 513.1702.

(5b*R**, 8a*R**, 14a*S**)-1,5b-Dimethyl-11-(4'-nitrophenylazo)-5b,6,7,8,8a,9-hexahydro-8*H*-indole[2,3-*c*]xantene **26**



To a stirred solution of 4a,9-dimethyl-2,3,4,4a-tetrahydro-1*H*-carbazol-9-ium iodide **17a** (0.66 g, 2 mmol) in distilled water (15 mL) and ethanol (5 mL), sodium carbonate (0.53 g, 5 mmol) was added at rt. The mixture became turbid and was extracted with diethyl ether (3 × 20 mL). The combined organic phase was dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure to afford enamine **18a**. The crude intermediate enamine obtained as a result of the outlined procedure was dissolved in acetonitrile (5 mL), and the solution of alkylating agent **24g** (0.583 g, 2 mmol) in acetonitrile (5 mL) was added. The mixture was stirred at rt. After 6 h, the resultant crystalline precipitate was filtered and recrystallized from acetonitrile, dark orange crystals were produced with the yield of 0.260 g (28%), mp 195–197 ºC.

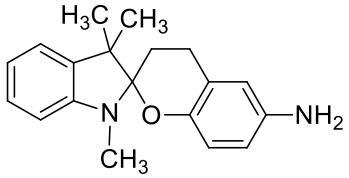
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39 (s, 3H, CH_3), 1.44–1.60 (m, 2H, CH_2), 1.74–1.86 (m, 2H, CH_2), 1.90–1.99 (m, 1H, CH_2), 2.66–2.87 (m, 5H, CH_2, CH_3), 3.31–3.38 (m, 1H, CH_2), 6.66 (d, *J* = 7.7 Hz, 1H), 6.80 – 6.89 (m, *J* = 8.3, 5.7 Hz, 2H), 7.04 (d, *J* = 7.1 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 6.4 Hz, 2H), 7.95 (d, *J* = 8.9 Hz, 2H), 8.35 (d, *J* = 8.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 17.9, 28.1, 28.6, 28.89, 30.4, 41.0, 48.6, 105.3, 108.1, 116.9, 119.1, 120.5, 122.7, 123.1 (2×C), 124.3, 124.5, 124.9 (2×C), 127.5, 138.6, 146.3, 148.2, 148.6, 156.3, 160.3.

IR (cm^{-1}): 3050, 2925, 1518 (NO_2-asymm.), 1340 (NO_2-symm.).

ESI-HRMS: [M+H$^+$], found 455.2078. [$C_{27}H_{26}N_4O_3$ +H$^+$] requires 455.2078.

6-Amino-1',3',3'-trimethyl -1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **27**



To a stirred solution of 1',3',3'-trimethyl-6-nitro-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **5a** (0.180 g, 0.555 mmol) in hydrochloric acid (7 mL) $SnCl_2 \cdot 2H_2O$ (0.621 g, 2.778 mmol) was added and the reaction mixture was heated at 60 ºC for 5 hours. The formed solid was separated by filtration and suspended in water (15 mL). Next, an aqueous ammonia solution (10%) was added by drops under stirring till reaching pH≈8. When the mixture became turbid, the separated product was extracted with diethyl ether (3 × 20 mL), and then the combined extract was dried over anhydrous sodium sulfate. Finally, the solvent was evaporated under reduced pressure. A brownish solid was produced with the yield of 0.13 g (80 %), mp 68–69 ºC.

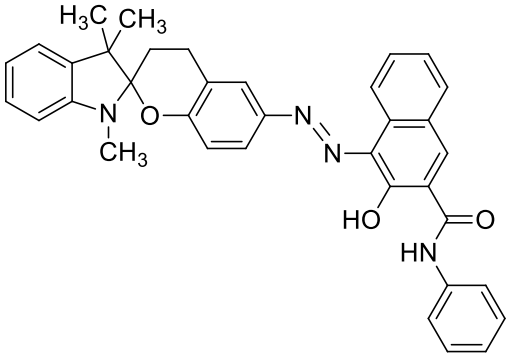
^{1}H NMR (700 MHz, $CDCl_3$): δ 1.22 (s, 3H, 3'-CH_3), 1.27 (s, 3H, 3'-CH_3), 2.23–2.30 (m, 2H, CH_2), 2.80–2.85 (m, 1H, CH_2), 2.83 (s, 3H, N- CH_3), 2.96–3.01 (m, 1H, CH_2), 3.33 (s, 2H, NH_2), 6.45–6.49 (m, 2H), 6.55 (d, *J* = 7.8 Hz, 1H), 6.57 (d, *J* = 8.3 Hz, 1H), 6.80 (t, *J* = 7.1 Hz, 1H), 7.04 (dd, *J* = 7.1, 0.6 Hz, 1H), 7.16 (td, *J* = 7.6, 1.1 Hz, 1H).

^{13}C NMR (176 MHz, $CDCl_3$): δ 22.0, 23.9, 24.8, 25.8, 28.6, 49.3, 101.7, 107.0, 115.5, 115.7, 117.0, 118.7, 121.3, 121.7, 127.7, 137.8, 138.5, 149.3, 149.4.

IR (cm^{-1}): 3059, 2952.

ESI-HRMS: [M+H$^+$], found 295.1808. [$C_{19}H_{23}N_2O$ +H$^+$] requires 295.1805.

1',3',3'-Trimethyl-6-[4"-azo-3"-hydroxy-N-phenylnaphthalene-2"-carboxamide]-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **30**



To a stirred solution of 6-amino-1',3',3'-trimethyl-1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] **27** (0.15 g, 0.5 mmol) in HBF_4 (1 mL, 48%) and H_2O (3 mL), a solution of $NaNO_2$ (0.036 g, 0.5 mmol) in H_2O was added by drops at 0 ºC. The mixture was stirred for 0.5 h at 0 ºC and then for 1 h allowing the temperature to rise to the ambient level. The diazonium salt suspension obtained as a result of the outlined procedure was added drop-wise to a suspension of 3-hydroxy-

N-phenylnaphthalene-2-carboxamide **29** (0.134 g, 0.5 mmol) in aqueuos KOH solution (20 mL, 1M) at 0 ºC. The mixture was stirred for 0.5 h at 0 ºC and then for 1 h in order to allow the temperature to rise to the ambient level. The resultant deep red suspension was neutralized with an aqueous ammonia solution (10%) and extracted with diethyl ether (3 × 20 mL), then the combined extract was dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The residue was subjected to flash chromatography on silica gel, R_f = 0.2 (hexane/acetone 6:1, v/v). Deep magenta-colored solid was produced with the yield of 0.019 g (6%), mp 155–156 ºC.

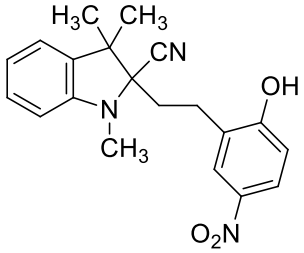
^{1}H NMR (400 MHz, $CDCl_3$,): δ 1.28 (s, 3H, 3'-CH_3), 1.31 (s, 3H, 3'-CH_3), 2.34–2.42 (m, 2H, CH_2), 2.89 (s, 3H, N-CH_3), 2.97–3.06 (m, 1H, CH_2), 3.10–3.20 (m, 1H, CH_2), 6.61 (d, *J* = 7.8 Hz, 1H), 6.55–6.81 (m, 3H), 7.07 (d, *J* = 7.0 Hz, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.19–7.24 (m, 1H), 7.27 (dt, *J* = 7.7, 1.1 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 3H), 7.45 (s, 1H), 7.48 (d, *J* = 2.3 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.82 (d, *J* = 7.8 Hz, 2H), 8.41 (d, *J* = 8.2 Hz, 1H), 8.90 (s, 1H, NH), 11.69 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$): δ 22.1, 24.4, 24.5, 27.0, 28.6, 49.5, 103.3, 107.2, 108.1, 118.0, 118.5, 119.0, 119.1, 120.6 (2×C), 121.4, 122.7, 124.1, 125.6, 126.0, 126.4, 127.8, 127.9, 129.1 (2×C), 130.8, 131.0, 134.9, 135.4, 137.3, 138.8, 145.8, 148.9, 156.8, 162.5, 173.8.

IR (cm^{-1}): 3185 (OH), 3049, 2959.

ESI-HRMS: [M+H^+], found 569.2547. [$C_{36}H_{32}N_4O_3$ +H^+] requires 569.2547.

2-[2-(2-Hydroxy-5-nitrophenyl)ethyl-1]-1,3,3-trimethyl-2,3-dihydro-1H-indole-2-carbonitrile **38**



To a stirred solution of **5a** (0.15 g, 0.462 mmol) in tetrahydrofuran (5 mL), sodium cyanide (0.045 g, 0.924 mmol) and a drop of distilled water were added. The mixture was stirred for 1 h at rt. The solvent was evaporated under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/acetone 6:1, v/v) to afford **38** as yellow solid, R_f = 0.12 with the yield of 0.079 g (49%), mp 176–178 ºC.

^{1}H NMR (700 MHz, DMSO-d_6,): δ 1.23 (s, 3H), 1.63 (s, 3H), 2.15 (td, *J* = 13.3, 4.8 Hz, 1H), 2.30 (td, *J* = 13.5, 4.1 Hz, 1H), 2.80 (s, 3H), 2.83 (td, *J* = 13.0, 4.1 Hz, 1H), 2.96 (td, *J* = 13.1, 4.9 Hz, 1H), 6.67 (d, *J* = 7.8 Hz, 1H), 6.82 (t, *J* = 7.4 Hz, 1H), 7.00 (d, *J* = 8.9 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 7.3 Hz, 1H), 8.04 (dd, *J* = 8.9, 2.8 Hz, 1H), 8.18 (d, *J* = 2.8 Hz, 1H), 11.26 ppm (s, 1H);

^{13}C NMR (176 MHz, DMSO-d_6): δ 23.30, 23.89, 25.34, 30.67, 31.10, 46.76, 76.75, 108.68, 115.09, 118.49, 119.97, 121.49, 124.23, 125.95, 127.99, 128.16, 136.83, 139.54, 148.52, 161.18 ppm;

IR (KBr): 3381 (OH), 3081, 2970, 2222 (C[tbond]N), 1525 (NO_2-asymm.), 1340 cm^{-1} (NO_2-symm.);

MS: m/z (%): 352 (100) [$M+H^+$];

Anal. Calcd (%) for $C_{20}H_{21}N_3O_3$: C 68.36; H 6.02; N 11.96. Found: C 68.56; H 6.07; N 11.61.

CONCLUSIONS

1. The reaction of 2-methylene-1,3,3-dimethyl-2,3-dihydro-1*H*-indoles with 2-chloromethyl-4-nitrophenol results in the formation of 1-alkyl-[2-(2-hydroxy-5-nitrophenyl)ethyl-1]-3,3-dimethyl-3*H*-indolium chlorides which undergo spirocyclization as a result of treatment with a base to afford 1',3,3',4-tetrahydrospiro[chromene-2,2'-indoles] which represent a new class of heterocyclic compounds.
2. The reaction of 2-methylene-1,3,3-dimethyl-2,3-dihydro-1*H*-indoles with 2-chlormethyl-4-(4'-nitrophenylazo)phenol or 2-chlormethyl-4-(2'-chloro-4'-nitrophenylazo)phenol yields 1',3,3',4-tetrahydro-6-((4-Nitrophenyl)diazenyl)spiro[chroman-2,2'-indole] derivatives.
3. Irradiation of 1',3,3',4-tetrahydrospiro[chromene-2,2'-indole] derivatives (0.1 mM solutions in acetonitrile) with nanosecond laser pulses yields cleavage of C-O bonds in the 3,4-dihydro-2*H*-pyran rings thus forming short-lived colored species identified as *p*-nitrophenolate chromophores. These compounds subsequently revert back to the ground state thermally.
4. 1',3,3',4-Tetrahydrospiro[chromene-2,2'-indole] derivatives detect cyanide with high specificity. These chemosensors show a distinct color change when treated with cyanide in acetonitrile solution buffered with sodium phosphate, and this procedure is fast, sensitive and not affected by the presence of other common anions

LIST OF PUBLICATIONS

Publications in the journals inscribed into the list approved by Information Scientific Institute (ISI)

1. Dagilienė, M., Martynaitis, V., Vengris, M., Redeckas, K., Voiciuk, Vl., Holzer, W. & Šačkus, A. (2013). Synthesis of 1',3,3',4-tetrahydrospiro[chromene-2,2'-indoles] as a new class of ultrafast light-driven molecular switch. Tetrahedron. Oxford: Pergamon-Elsevier Science Ltd. ISSN 0040-4020., Vol. 69, iss. 44, p. 9309-9315.
2. Dagilienė, M., Martynaitis, V., Kriščiūnienė, V., Krikštolaitytė, S. & Šačkus, A.. (2015). Colorimetric cyanide chemosensor based on 1',3,3',4-tetrahydrospiro[chromene-2,2'-indole]. ChemistryOpen. Weinheim: Wiley-VCH Verlag GmbH & Co. KGaA. ISSN 2191-1363, Vol. 4, Iss. 3, p. 363-369.

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1. Dagilienė, M., Steponavičiūtė, R., Martynaitis, V., Vengris, M., Šačkus, A. & Redeckas, K. (2012). Synthesis and photochromism of 4- and 8-arylindolo[2,1-b][1,3]benzoxazines. XXIV IUPAC: Symposium on Photochemistry 15-20 July, Coimbra, Portugal: abstract book. Coimbra: [s.n.], 2012. p. 277.
2. Dagilienė, M., Martynaitis, V., Redeckas, K., Vengris, M. & Šačkus, A. (2013). Spiro[chroman-2,2'-indolai] – naujo tipo greitieji fotochromai. Organinė chemija: mokslinės konferencijos pranešimų medžiaga = Organic chemistry: proceedings of scientific conference. Kauno technologijos universitetas. Kaunas: Technologija. ISSN 2029-6401. p. 87-88.
3. Dagilienė, M., Martynaitis, V., Vengris, M., Redeckas, K. & Šačkus, A. (2013). Synthesis of 1',3,3',4-tetrahydrospiro[chromene-2,2'-indoles] as a new class of ultrafast light-driven molecular switches. International Symposium on Photochromism, Humboldt University, Berlin, Germany, September 23-26, Book of Abstracts, p. 106
4. Martynaitis, V., Markuckaitė, G., Dagilienė, M., Krikštolaitytė, S. & Šačkus, A. Synthesis and photochromism of 4-methylindoline spirochromane derivatives. ISySyCat 2015: International Symposium on Synthesis and Catalysis, September 2-4, Èvora, Portugal: book of abstracts. Èvora: University of Èvora, p. 133.

Patents

1. Spiro[Chroman-2,2'-indole] derivatives as cyanide ion chemosensors/ Inventors: Algirdas Sackus, Vytas Martynaitis, Migle Dagiliene, Sonata Krikstolaityte, Greta Ragaite. Patent WO2014189348.
2. Spiro[chroman-2,2'-indolo] dariniai kaip cianido jonų chemosensoriai/ Inventors: Algirdas Šačkus, Vytas Martynaitis, Miglė Dagilienė, Sonata Krikštolaitytė, Greta Ragaitė; Applicant: Kaunas University of Technology. Patent LT 6105 B.
3. New photochromic compounds, method of production thereof and intermediate compounds/ Inventors: Algirdas Sackus, Vytas Martynaitis, Mikas Vengris, Kipras Redeckas, Migle Dagiliene; Applicants: Kaunas University of Technology. Patent EP 2718393 A1.
4. Nauji fotochrominiai junginiai, jų gamybos būdas ir tarpiniai junginiai jiems gauti/ Inventors: Algirdas Šačkus, Vytas Martynaitis, Miglė Dagilienė, Mikas Vengris, Kipras Redeckas; Applicants: Kaunas University of Technology. Patent LT 6024 B.

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