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Synthesis of 4- and 6-substituted nitroindoles

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Abstract—Enolizable ketones react with *m*-nitroaniline in the presence of strong base such as *t*-BuOK to give 4- and 6-substituted nitroindoles. The reaction proceeds via oxidative nucleophilic substitution of hydrogen in *m*-nitroaniline with enolate anions in positions *ortho* to the amino group giving anionic σ^H adducts that are additionally stabilized by intramolecular interaction between the amino and the carbonyl group. Spontaneous oxidation of the σ^H adducts followed by the Bayer type condensation of the produced *ortho*-aminonitrobenzyl ketones gives 4- and 6-substituted nitroindoles. The scope of this reaction and its basic mechanistic features are discussed.

Numerous important natural products, drugs, plant protection agents, dyes, etc.[1,2] contain the indole ring system and, therefore, great attention is continuously directed towards novel, efficient methods of indole synthesis.[3] Although many methods of construction of the indole ring system are known, new and simple processes serving this purpose are in great demand.[4] Of particular interest are simple and efficient methods of the synthesis of indoles containing various substituents in defined positions of the five and six membered rings of the indole. Since the nitro group is one of the most versatile substituents, which can be converted into many other functionalities and also can promote numerous reactions,[5] synthesis of nitroindoles deserves special attention.[6] There are many ways of synthesising nitroindoles: via nitration of indoles under various conditions,[7] Fischer cyclization of starting materials containing the nitro group,[8] Bergman approach, utilizing 2-methyl-3-nitroanilines, etc.[9] One of the most general and versatile approach to the nitroindole ring construction appears to be nucleophilic substitution of hydrogen (NSH) in nitroarenes with carbon nucleophiles and subsequent cyclizations.[10] Thus, vicarious nucleophilic substitution of hydrogen (VNS) in *m*-nitrobenzoisonitriles with chloromethyl aryl sulfones followed by cyclization directly gives substituted 4- and/or 6-nitroindoles.[11a] To this category belongs the cyclization of 3-nitroanilides of chloroacetic acid via intramolecular VNS,[11b] and intramolecular oxidative nucleophilic substitution of hydrogen (ONSH) in *m*-nitroacetanilides and their analogues, leading to nitrooxindoles.[11c]

In our preliminary communication, we reported a much simpler method of synthesis of 4- and/or 6-nitroindoles—the direct condensation of 3-nitroanilines with ketones.[12]

A similar reaction of 3-nitroaniline **1a** with aliphatic nitriles results in formation of 2-amino-4-nitro- and 2-amino-6-nitroindoles.[13] The reaction apparently proceeds via ONSH in the nitroaromatic ring with the respective carbanions, followed by intramolecular reaction of the amino group with the carbonyl or the cyano groups. The process seems to be directed and assisted by an interaction between these groups within the σ^H adduct and/or in the course of the addition process.

In this paper, a full account of our studies on the synthesis of nitroindoles via this interesting and useful reaction between ketones and nitroanilines is presented.

Nucleophilic substitution of hydrogen in nitroarenes with carbon, nitrogen or oxygen nucleophiles is a well known and established process. Formation of anionic σ^H adducts and further oxidative or eliminative transformations of these short lived intermediates are accepted mechanistic features.[14,15]

Reactions of enolate anions with nitroarenes have been studied for more than 100 years. Reaction of acetone enolate with *m*-dinitrobenzene to form a σ^H adduct and its subsequent oxidation with an excess of the nitroarene to dinitrobenzyl methyl ketone are known as the Janovsky and the Zimmerman reactions, respectively.[16] ONSH in simple mononitroarenes: nitrobenzene, *p*-chloronitrobenzene etc. with the enolate of acetophenone was reported by Hamana.[17] Fluoride anion promoted reaction of trimethylsilyl enol ethers with nitroarenes produces σ^H adducts of the respective enolates that appear to be additionally stabilized by *O*-silylation of the nitro group. These σ^H adducts can be

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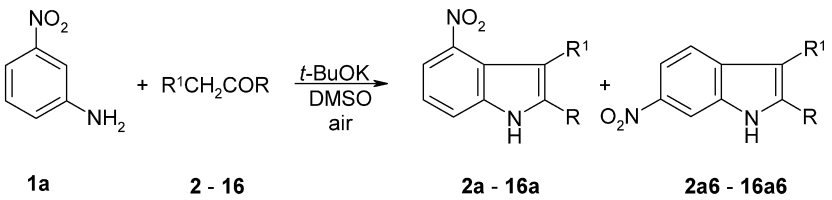
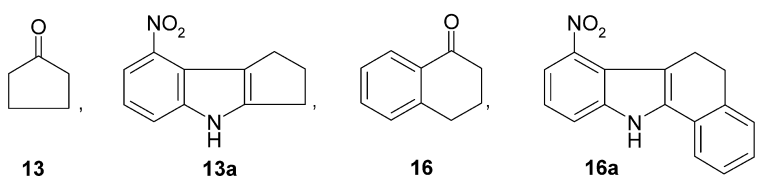


1a **2 - 16** **2a - 16a** **2a6 - 16a6**

Ketones **2-16**

Compound	R^1	R	Compound	R^1	R
2	H	Me	**10**	Me	Me
3	H	*cyclo*-C_3H_5	**11**	Me	Et
4	H	*t*-Bu	**12**	Me	Ph
5	H	Ph	**13**		-$(CH_2)_3$-
6	H	2-Py	**14**		-$(CH_2)_4$-
7	H	2-furyl	**15**		-$(CH_2)_5$-
8	H	2-thienyl	**16**		-$(CH_2)_2C_6H_4$-
9	H	2-(*N*-Me)pyrryl			

Exemplification of structures of some starting ketones and the corresponding products:



13 **13a** **16** **16a**

Scheme 1.

further oxidized to give products of ONSH in nitroarenes with enolate anions.[18] Reductive cyclization of the *o*-nitrobenzyl ketones obtained in this way provides the corresponding indoles.[18] Addition of enolates of some α-haloketones to nitroarenes leads to σ^H adducts that undergo base induced β-elimination of hydrogen halide giving products of VNS–nitrobenzyl ketones.[19] There are many examples of reactions of polynitroarenes with ketones producing bi- and tricyclic adducts, some of them found application in synthesis.[20] However, to the best of our knowledge, there are no preceeding reports on reactions of enolates with *m*-nitroanilines.

1. Results and discussion

Treatment of a solution of 3-nitroaniline **1a** and acetone **2** in DMSO with *t*-BuOK results in a moderately exothermic reaction and dark-red coloration of the mixture. Acidification of the mixture and standard work up gave 2-methyl-4-nitroindole **2a** with a minor amount of the isomeric 6-nitroindole. Thus, the overall result is that hydrogen in position 2- and 6- of **1a** (*ortho*- and *para*- to the NO_2 and *ortho*- to the NH_2 group) has been replaced with the acetone moiety. This unusual orientation in the reaction-preference of the nucleophilic addition of the enolate to the most hindered position 2- of 3-nitroaniline is well precedented in the nucleophilic substitution of hydrogen in nitroarenes. During our previous studies of the VNS reaction in nitroarenes containing a variety of substituents Z in position 3- we have observed a strong preference for replacement of hydrogen in position 2- for Z=halogens, OMe, Me, NMe_2, etc. and discussed reasons for such orientation.[21]

Under similar conditions a variety of other ketones react with **1a** giving 4- and 6-nitroindoles. The DMSO/*t*-BuOK system appears to be a reagent of choice for this transformation. Indeed, acetophenone reacts satisfactorily with **1a** in the presence of *t*-BuOK in DMSO, whereas in THF, Et_2O, PhCl and CH_2Cl_2 only traces of the expected indoles were produced, and most of the reactants were recovered. DMF and HMPT are acceptable, but less practical solvents, because of decomposition of the former and toxicity of the latter. The reactions of **1a** with a variety of ketones **2**–**16** in DMSO are presented in Scheme 1 and Table 1.

All methyl ketones CH_3COR in which R does not contain acidic hydrogen atoms, in the reaction with **1a** form predominantly 4-nitro-2-*R*-indoles **2a**–**9a** resulted from addition of the enolates to position 2- of 3-nitroaniline. The observation that these ketones react exclusively in position 2-, reported in our preliminary communication,[12] was only partially confirmed in the present studies. Thus, in the reaction of **1a** with acetone **2** and acetophenone **5** we were also able to isolate minor quantities (7 and 8%), of 6-nitro-2-methyl and 6-nitro-2-phenyl-indoles **2a6** and **5a6**. One cannot exclude that in the reactions of **1a** with some other methyl ketones small quantities of substituted 6-nitroindoles are also formed, but they were not isolated in

Table 1. Substituted 4- and 6-nitroindoles obtained from **1a** and ketones **2**–**16** as in Scheme 1

Ketone	Products and yields (%)		Ketone	Products and yields (%)	
2	**2a**, 58	**2a6**, 7	**10**	**10a**, 32	**10a6**, 26
3	**3a**, 60	[a]	**11**	**11a**, 33	**11a6**, 30
4	**4a**, 42	[a]	**12**	**12a**, 16	**12a6**, 38
5	**5a**, 67	**5a6**, 8	**13**	**13a**, 16	**13a6**, 12
6	**6a**, 53	[a]	**14**	**14a**, 34	**14a6**, 13
7[b]	**7a**, 50	[a]	**15**	**15a**, 23	**15a6**, 13
8[b]	**8a**, 50	[a]	**16**	**16a**, 24	**16a6**, 12
9[c]	**9a**, 12	[a]			

[a] Small amounts (<5%) of 6-nitroindoles are perhaps formed but not isolated and identified.
[b] Reactions were performed with 3-fold excess of **1a** to ketone.
[c] Reaction with 2-acetylpyrrole failed, ketone was *N*-methylated with CH_3I and then reaction with **1a** and *t*-BuOK was performed.

routine column chromatography separation technique. Interestingly, the reaction of **1a** with methyl ethyl ketone **10**, gave two isomeric products, 4- and 6-nitro-2,3-dimethylindoles **10a**, and **10a6**, derived from the secondary enolate, produced via deprotonation of the methylenic group. We failed to find any evidence of the presence of 4- or 6-nitro-2-ethyl-indoles, which would be derived from the reaction of the isomeric primary enolate. Preference for the reactions of thermodynamically controlled secondary enolates over those kinetically controlled is a well established phenomenon.[22] The addition of the more sterically demanding secondary enolate occurs in both positions 2- and 6- of **1a** giving a mixture of 2,3-dimethyl-4-nitro- and 2,3-dimethyl-6-nitro indoles **10a** and **10a6**. Similarly, diethyl ketone **11** and propiophenone **12** in the reaction with **1a** gave two isomeric products: 2-ethyl-3-methyl-4-nitro- and -6-nitroindoles **11a** and **11a6** and 3-methyl-4-nitro-2-phenyl- and -6-nitroindoles **12a** and **12a6**, respectively. Interestingly, the ratio of the two isomeric 4- and 6-nitroindoles produced from the aliphatic ketones **10** and **11** was close to 1 (1.2 and 1.1), whereas in the reaction of propiophenone **12** the 6-nitroisomer was the major product, ratio **12a/12a6**≈0.4. The reaction of secondary enolates of cyclic ketones **13**, **14**, **15** and **16** also proceeds via the addition to positions 2-and 6- of 3-nitroaniline giving substituted 4- and 6-nitroindoles, always the 4-nitroisomer being isolated in larger yield (ratio 4-/6-nitro between 1.5 and 2.6). Thus, even sterically bulky secondary enolates attack preferentially the more sterically hindered position 2- of 3-nitroaniline.

3-Nitroanilines containing halogens also enter the reaction with a variety of enolates giving the corresponding halonitroindoles. Thus, in the reaction of 6-chloro-3-nitroaniline **1b** with ketones substituted 4-nitro-7-chloroindoles were produced. In no cases did we observe formation of the indoles resulting from nucleophilic displacement of the halogen in **1b**, namely 6-nitroindoles. However, in the majority of experiments some amounts of side products of dechlorination, 4-nitroindoles, were obtained. These compounds were identical to the indoles produced in the analogous reaction of **1a** itself. In separate experiments, chloronitroindole **5b** was subjected to the standard reaction conditions and was recovered unreacted, without loss of Cl. Therefore, we concluded that dechlorination took place at an intermediate stage, whereas the final products—the chloronitroindoles are stable under the reaction conditions. As one could expect the dehalogenation process proceeded to a much higher degree in the case of the analogous bromoaniline. The reaction of 6-bromo-3-nitroaniline **1c** with acetophenone **5** gave the expected 2-phenyl-4-nitro-7-bromoindole **5c** and the debrominated product **5a** in almost equal amounts. Similarly to chloroindole **5b**, bromoindole **5c** was stable under the reaction conditions, and the debromination product **5a** was not detected by TLC when **5a** was treated with *t*-BuOK in DMSO.

The reactions of enolates with fluoronitro anilines were somewhat more complicated, because of the competing process of nucleophilic substitution of halogen. The observed formation of the expected fluoronitroindoles via ONSH reaction was the major process, however, nitroindoles derived from S_NAr of fluorine were also isolated. Thus, in the reaction of 6-fluoro-3-nitro aniline **1d** with acetophenone **5** besides the expected 7-fluoro-2-phenyl-4-nitro-indole **5d** some amount of 6-nitro-2-phenylindole **5a**, identical to that obtained from **1a** and **5**, was produced (Scheme 2, Table 2).

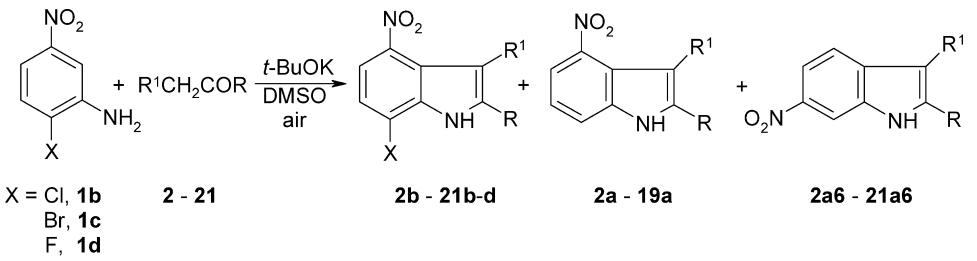
On the other hand, the reaction of 4-fluoro-3-nitroaniline **1e** with enolate anions via ONSH process can occur at positions 2- or 6- giving 5-fluoro-4- and 6-nitroindoles. Acetone was found to react with **1e** in the same manner as with **1a**, via addition to the most sterically hindered position giving 5-fluoro-2-methyl-4-nitroindole **2e**, whereas secondary enolates of diethyl ketone **11** and butyrophenone **22** gave predominantly or exclusively 6-nitroindoles **11e6** and **22e6** (Scheme 3, Table 2).

Usually the reaction of enolates with fluoro nitro anilines gave lower yields of nitroindoles, perhaps because of some competing reactions of substitution of fluorine by other nucleophiles present in the system. It is worth noting, that in the reaction of fluoronitroanilines **1d** and **1e** dehalogenation

Table 2. Substituted halonitroindoles obtained from halo-*m*-nitroanilines **1b**–**e** and ketones **2**–**21** as in Schemes 2 and 3

Aniline	Ketone	Products and yields (%)	
1b	**2**	**2b**, 51	
1b	**5**	**5b**, 61	**5a**, 5
1b	**7**	**7b**, 43	**7a**, 13
1b	**8**	**8b**, 60	**8a**, 7
1b	**11**	**11b**, 61	**11a**, 7
1b	**14**	**14b**, 30	**14a**, 1
1b	**16**	**16b**, 50	**16a**, 13
1b	**17**	**17b**, 55	
1b	**18**	**18b**, 46	**18a**, 16
1b	**19**	**19b**, 42	**19a**, 9
1b	**20**	**20b**, 27	
1b	**21**	**21b**, 23	
1c	**5**	**5c**, 37	**5a**, 33
1d	**2**	**2d**, 33	**2a6**, 3[a]
1d	**5**	**5d**, 50	**5a6**, 7[a]
1d	**11**	**11d**, 40	**11a6**, 15[a]
1d	**22**	**22d**, 34	**22a6**, 12[a]
1d	**19**	**19d**, 34	**19a6**, 12[a]
1e	**2**	**1e**, 21	
1e	**18**	**18e**, 5	**18e6**, 20
1e	**22**		**22e6**, 22

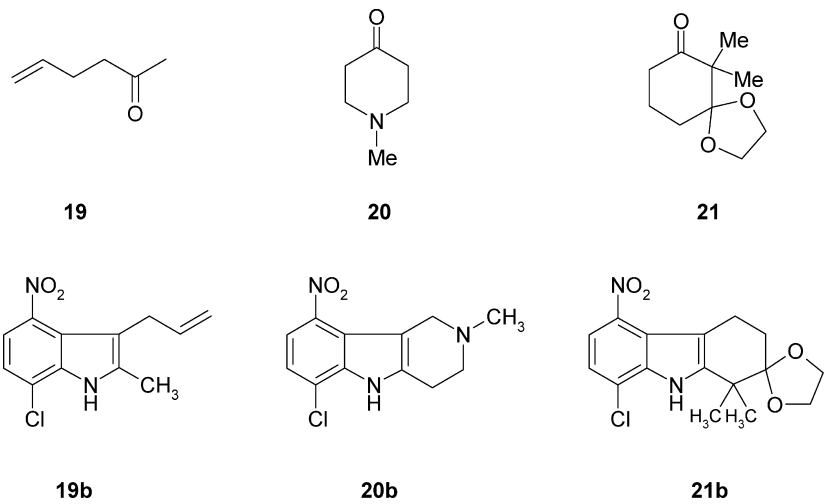
[a] Formed via substitution of F.



Ketones **17**-**22** not listed in scheme 1

R^1	R	No
H	1-Naphthyl	**17**
Et	*n*-Pr	**18**
Allyl	Me	**19**
—$CH_2N(Me)CH_2CH_2$—		**20**
—$(CH_2)_2$ $C(CH_3)_2$—		**21**

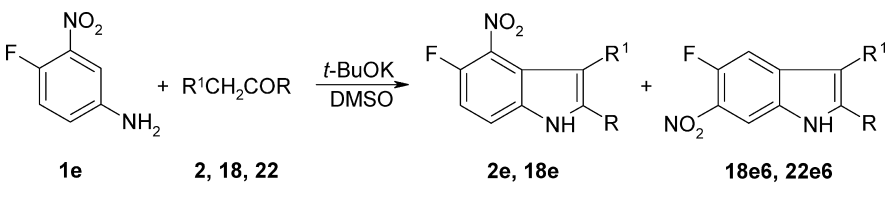
Exemplification of structures of some ketones and products:



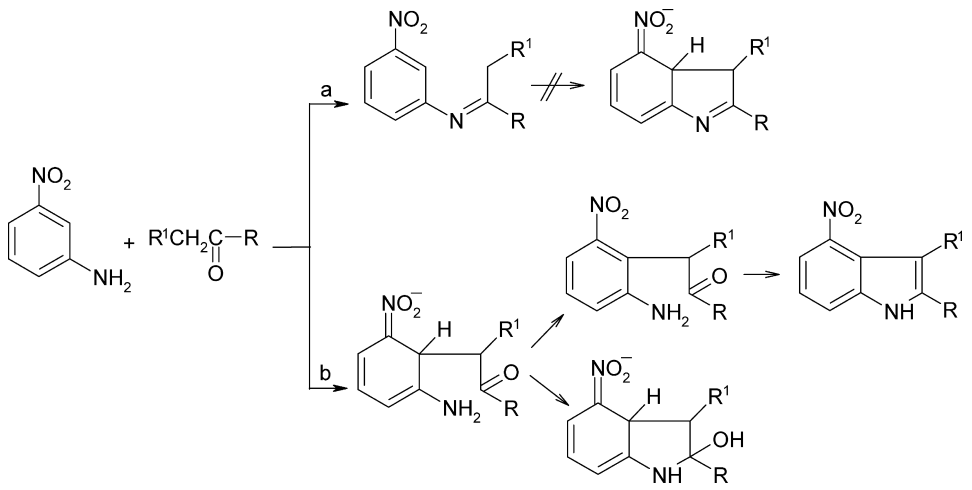
Scheme 2.

was not observed. Indoles **2a6**–**22a6** that do not contain fluorine were formed as the result of nucleophilic substitution of fluorine and further cyclization.

Formation of the indole ring in the base-induced reaction of ketones with **1a** can, in principle, occur in two ways: (a) initial condensation of the amino functionality with the carbonyl group of the ketones giving 3-nitroaryl imines, which upon treatment with base form carbanions that enter intramolecular ONSH resulting in the indole ring closure; (b) initial addition of the enolate anions to the nitroaromatic ring (*ortho*- or *para*- to the nitro group and *ortho*- to the



Scheme 3.

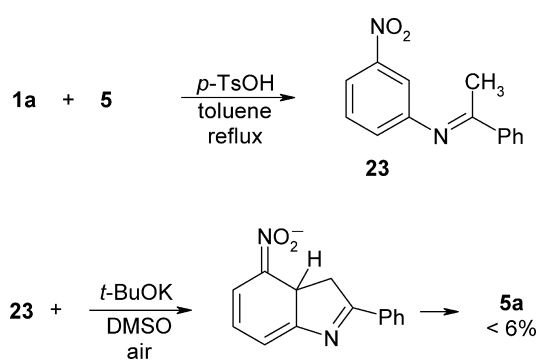


Scheme 4.

amino group) followed by oxidation of the produced σ^H adducts resulting in ONSH to form *ortho*-aminonitrobenzyl ketones, further intramolecular condensation of which gives nitroindoles.[23] These alternative pathways are shown in Scheme 4.

In order to clarify which of these alternative series of transformations is the actual reaction pathway, the corresponding imine **23** was prepared from acetophenone and 3-nitroaniline and subjected to the reaction conditions (Scheme 5).

However, the expected 4-nitro-2-phenylindole **5a** was found in the reaction mixture in less than 6% overall yield, moreover, it appears that in this case the indole was formed due to decomposition of the imine to the aniline and ketone followed by the reaction as in Scheme 1. This result indicates that the path a (Scheme 4), including initial condensation between the amino and the carbonyl group is not the reaction pathway and should be excluded from further consideration. The alternative path b, should, therefore, be considered as an actual reaction pathway. The absence of acylic products of this reaction *ortho*- to the nitro group and *para*- to the amino group indicates that there is a strong preference for the ONSH reaction in the vicinity of the amino group. This can be rationalized by the supposition that formation of a σ^H adduct is assisted by either non-covalent interaction between the amino and the carbonyl group or stabilization of the σ^H adduct by formation of cyclic aminal takes place. Further oxidation

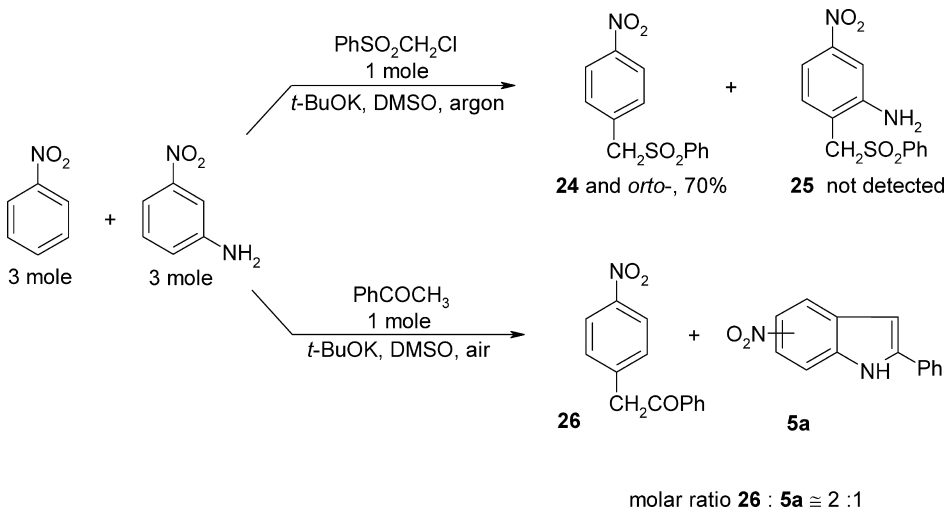


Scheme 5.

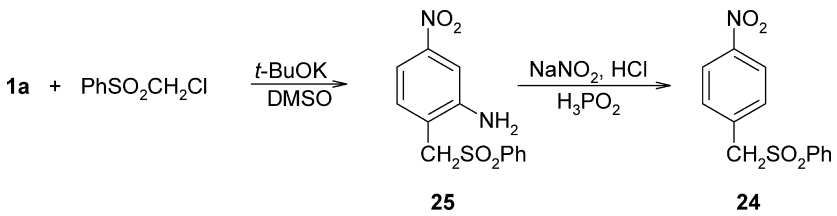
of the σ^H adducts gives the corresponding ONSH products–nitrobenzyl ketones which subsequently undergo the Baeyer type cyclisation[23] to give nitroindoles. Oxidation of the σ^H adducts in the form of aminal should give the same final results. Differentation between these two possible ways of stabilization of σ^H adducts was not attempted in our studies.

Additional stabilization of the σ^H adducts explains the relatively high activity of 3-nitroanilines as electrophilic partners in the reaction with enolate anions. It was observed earlier that **1a** is of rather low activity in its reactions with carbanions, due to the presence of the strong electrondonating amino group that deactivates the aromatic ring towards nucleophilic addition. Moreover, partial deprotonation of the amino group should enhance this effect substantially. The hypothesis that there is a specific tendency to form and stabilize σ^H adducts of enolates to **1a** in vicinity of the amino groups was verified experimentally in competitive experiments. In these experiments, we have directly compared rates of the VNS reaction in nitrobenzene and **1a** with the carbanion of chloromethyl phenyl sulfone, which is unable to form intramolecular bonding with the amino group, and rates of the ONSH reaction in nitrobenzene and **1a** with acetophenone (Scheme 6).

Results of these competitive experiments, presented in Scheme 6, indicate that the rate of VNS in nitrobenzene with the carbanion of chloromethyl phenyl sulfone is more than 100 times higher than the rate of this reaction with **1a**. In fact, the product of the latter process was not detected in the reaction mixture. On the other hand, the ONSH reaction with the enolate of acetophenone in nitrobenzene is only about two times faster than formation of the nitroindole via ONSH in **1a**, which suggests that the deactivating effect of the amino group on the electrophilic activity of **1a** is compensated by the additional stabilization of the σ^H adduct. Thus, as we have supposed, addition of the enolate to **1a** is favored, apparently because the corresponding σ^H adduct is additionally stabilized, and upon its oxidation forms 4-nitro-2-phenylindole. Although these data are only qualitative they indicate unambiguously that there is a strong effect promoting addition of enolates to **1a**. Such an effect does not operate in the reaction of carbanions unable to experience additional interactions with amino groups, for



Scheme 6.



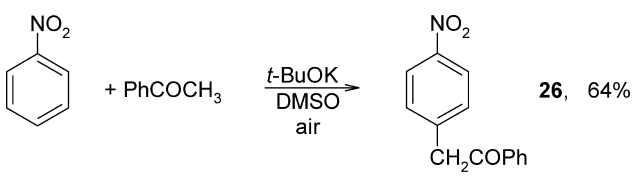
Scheme 7.

instance, those generated from chloromethyl phenyl sulfone.

The carbanion of chloromethyl phenyl sulfone is our standard nucleophile for the VNS reaction with nitroarenes. In the presence of *t*-BuOK in DMSO and also in other base–solvent systems it reacts with nitrobenzene to give a mixture of *ortho*- and *para*-nitrobenzyl phenyl sulfones **24**.[24] Since the VNS reaction of this sulfone with **1a** was not reported (we reported earlier that this reaction does occur with 3-nitro-*N*,*N*-dimethylaniline)[21] we have shown in a separate experiment that the VNS reaction of chloromethyl phenyl sulfone with **1a** proceeds satisfactorily giving a single product **25** (Scheme 7).

For unambiguous identification, compound **25** was diazotized and the diazonium salt reduced in situ with hypophosphorous acid, giving *para*-nitrobenzyl phenyl sulfone **24**, identical to that reported in our early paper.[24] Thus, VNS in **1a** proceeded in a position *para*- to the nitro group giving 2-amino-4-nitrobenzyl phenyl sulfone **25**. Under similar conditions, nitrobenzene reacts with acetophenone to give *para*-nitrobenzyl phenyl ketone **26** (Scheme 8).

This reaction under somewhat different conditions, was reported by Hamana[17] to give a mixture of *ortho*- and *para*-

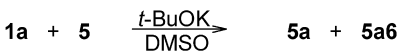


Scheme 8.

nitrobenzyl phenyl ketones. Some discrepancy in the orientation of ONSH in nitrobenzene with acetophenone enolate is apparently due to the differences in the conditions. The results presented in Scheme 6 indicate that there is an effect promoting the reaction of enolates with **1a** which does not operate in the case of nitrobenzene and which we assign to an interaction between the carbonyl and the amino groups as shown in Scheme 4.

Another important question is identity of the oxidant oxidizing the σ^H adducts of enolates to **1a**. We believe that these σ^H adducts are oxidized by the air oxygen always present in the reaction mixtures. Indeed when the reaction of acetophenone **5** with **1a** was carried out in the strictly deoxygenated solvent under argon yields of the indoles were substantially lower. On the other hand saturation of the system with oxygen does not change the outcome substantially as shown in Scheme 9

The identity of the oxidizing agents and effect of conditions on the oxidation process need further studies.



	Isolated yields, %	
air (open flask)	67	8
oxygen bubbled	66	4
degassed solvent, argon	28	4

Scheme 9.

In conclusion, the reported method of synthesis of nitroindoles from inexpensive and readily available starting materials offers the simplest and the most efficient approach to these valuable intermediates, particularly taking into account that as well as of standard transformations of the nitro group, further reactions of nucleophilic substitution of hydrogen such as VNS in nitroindoles[25] are possible so polycyclic heterocyclic systems can be readily produced.[26]

2. Experimental

Unless otherwise noted all reagents and solvents were used commercial without further purification. Chromatographic columns were filled with silica gel 60 (0.040–0.063 mm, 230–400 mesh). ^{1}H NMR spectra were recorded at 200 MHz.

The nitroindoles are stable yellow to dark-red crystalline compounds, however some of them show instability in solution on prolonged storage. 4-Nitroisomers are usually less soluble and produce orange to brown spots on TLC, while 6-nitroisomers are better soluble and produce lighter spots on TLC. Halogenated indoles are less polar (TLC) and better soluble.

The reactions were monitored by TLC (aluminium sheets, silica gel 60 F_{254}, Merck) using toluene as eluent. For the reaction with *N*-methyl-4-piperidone, methylene chloride–methanol, (4:1) was used as eluent. Samples of the reaction mixtures for TLC were treated with aqueous NH_4Cl and extracted with EtOAc. Usually, all the reactions were complete within 2 h, however, we recommend stopping the reaction when starting *m*-nitroaniline is not detected by TLC in the reaction mixture.

Typical TLC retention factors (R_f, toluene) components of the reaction mixture: *m*-nitroaniline=0.25 (yellow spot, UV lamp helps to find trace amounts), 6-NO_2 indoles=0.30–0.40 (yellow to orange spots), 4-NO_2 indoles=0.40–0.45 (orange to brown spots).

For methyl aryl ketones (for example see reaction of **1a** with **5**), retention factors of the both isomers are very close. Due to low abundance of 6-NO_2 isomer in the reaction mixture and low solubility of 4-nitroisomer ('diffusion' of sample) detection of 6-NO_2 isomer often becomes difficult. For these cases hexane–ethyl acetate (2:1) should be used as an eluent, where order of elution of isomers is reversed (R_f, hexane–ethyl acetate, 2:1): 4-NO_2 indoles=0.35–0.40 (orange to brown spots), 6-NO_2 indoles=0.45–0.50 (yellow to orange spots).

2-Bromo-5-nitroaniline **1c** was obtained by simple bromination of **1a** in glacial acetic acid at 10 °C and subsequent recrystallization from ethanol (yield 25%) mp 136–139 °C (lit.[27] 140 °C) similarly to the procedure described.[27]

Chloromethylphenylsulfone was obtained from bromochloromethane and benzenesulfinic acid sodium salt.[28]

Ethylene glycol monoacetal of dimedone (2,2-dimethylcyclohexane-1,3-dione) **21** was prepared as reported.[29]

2.1. General procedure

To a stirred solution of *m*-nitroaniline (5 mmol) and ketone (7 mmol) in DMSO (15 mL) at 15–20 °C (water bath), *t*-BuOK (12 mmol) was added in one portion. All operations were made in open flask under air. Deep red or red-violet colour indicated the reaction progress. After 2 h of stirring aqueous NH_4Cl (60 mL) was added, the mixture was extracted with ethyl acetate (3×50 mL) and the extract dried with $MgSO_4$. Chromatographic separation on silica gel with hexane–toluene (1:1) eluent, then pure toluene on 20 cm×5 cm column is efficient for 5 mmol scale preparations. We do not recommend hexane–ethyl acetate eluent for separation of crude reaction mixtures after workup. For reaction of **1a** with methylaryl ketones **5**–**9** procedure for isolation of minor amounts of 6-NO_2 isomers is recommended. Analytical samples were finally purified by recrystallization from heptane–toluene mixture.

2.2. General procedure for isolation of minor amounts of 6-NO_2 isomers

Reaction was performed as in general procedure. Combined extracts were dried with $MgSO_4$, filtered, silica gel was added to the solution and solvent was evaporated. Gel was put on chromatographic column with toluene (5×5 cm, silica gel). Large amount (up to 1 L) of toluene was passed through and solvent was evaporated. Residue was crystallized from heptane–toluene mixture (left in well isolated can in refrigerator for slow cooling). Precipitated crystals were filtered, washed with heptane–toluene mixture and dried to obtain 4-nitroindole derivatives (for **5a** 57%). Solution was evaporated with silica gel and put on chromatographic column with hexane–ethyl acetate (4:1 then 1:1) (5×15 cm, silica gel). After collection and evaporation of fractions 6-nitroindole derivatives (for **5a6** 8%) (first eluted product) and 4-nitroindole derivatives (for **5a** 10%) (second eluted product) were obtained.

2.2.1. Reaction with *N*-methyl-2-acetylpyrrole. To a stirred mixture of 2-acetylpyrrole (597 mg, 5.5 mmol) and *t*-BuOK (614 mg, 5.5 mmol) in DMSO (10 mL) at 20 °C, CH_3I (2.5 g, 17.6 mmol) was added in one portion. Reaction was moderately exothermic. After 1.5 h, TLC showed that reaction was completed and excess of CH_3I was removed in vacuo. To this solution *m*-nitroaniline **1a** (765 mg, 5.5 mmol) and *t*-BuOK (1368 mg, 12.2 mmol) were added consecutively. After 2 h of stirring in open flask under air aqueous NH_4Cl (60 mL) was added and product isolated as in general procedure to give 4-nitro-2-(*N*-methyl-pyrrol-2-yl)-indole **9a** (150 mg, 12%).

2.2.2. Reactions with 2-acetylthiophene and 2-acetylfuran. Reactions were performed as in general procedure, but 3-fold excess of *m*-nitroaniline was used (15 mmol) on ketone (5 mmol).

2.2.3. Reaction with α-tetralone. To a stirred solution of *m*-nitroaniline **1a** (693 mg, 5 mmol) and α-tetralone **16** (1040 mg, 7.1 mmol) in DMSO (15 mL) at 17 °C, *t*-BuOK (1127 mg, 10.1 mmol) was added in one portion. Deep blue colour appeared and after 45 min of stirring in open flask

under air aqueous NH_4Cl (60 mL) was added. Insoluble solid product was filtered and dried. Filtrate was extracted with ethyl acetate (2×25 mL) and dried with $MgSO_4$. Dried solid was added to extracts, silica gel was added to the mixture and then solvent was evaporated. Residue adsorbed on gel was put on 3 cm layer of silica gel. Then toluene and ethyl acetate was passed through. Solvent was evaporated and 40 mL of toluene was added. Mixture was heated to boiling for 10 min, then cooled, and the precipitate was filtered, washed with toluene and dried to obtain 5,6-dihydro-7-nitrobenzo[*a*]carbazole **16a** (416 mg, 31%). Organic solutions were put on chromatographic column with toluene and separated to obtain: 5,6-dihydro-7-nitrobenzo[*a*]carbazole **16a** (78 mg, 6%) and 5,6-dihydro-9-nitrobenzo[*a*]carbazole **16a6** (249 mg, 19%).

2.2.4. Synthesis of imine 23 and attempts of cyclization (Scheme 5). *m*-Nitroaniline **1a** (416 mg; 3 mmol), acetophenone **5** (127 mg; 1.06 mmol) and *p*-toluenesulphonic acid (TsOH; 7 mg; 3%) in toluene (50 mL) were refluxed overnight with Soxlet apparatus filled with well-dried molecular sieves. The solvent was evaporated and the residue separated by flash chromatography (toluene, silica gel (25 g) treated with NEt_3 (5 g) in 50 mL toluene overnight, then washed with 200 mL toluene on column). Evaporation of solvent and recrystallization from hexane gave *N*-(3-nitrophenyl)-*N*-[(*E*)-1-phenylethylidene]amine **23** as yellow-brown crystals (0.108 g; 43%), mp 90–91 °C, ^{1}H NMR δ (500 MHz, $CDCl_3$) 2.27 (s, 3H, CH_3), 7.13 (ddd, *J*=7.9, 2.0, 2.0 Hz, 1H), 7.45–7.54 (m, 3H), 7.67 (dd, *J*=2.0, 2.0 Hz, 1H), 7.95 (ddd, *J*=8.0, 2.0, 2.0 Hz, 1H), 7.97–8.00 (m, 2H). EIMS *m/e* (relative intensity): 240 (M^+, 54), 225 (100), 179 (55). Anal. Calcd for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66. Found: C, 70.15; H, 4.96; N, 11.58.

To a solution of *N*-(3-nitrophenyl)-*N*-[(*E*)-1-phenylethylidene]amine **23** (119 mg; 0.5 mmol) in DMSO (5 mL), *t*-BuOK (133 mg; 1.2 mmol) was added in one portion and the mixture was stirred for 2 h in open flask under air, aqueous NH_4Cl (25 mL) was added, extracted with ethyl acetate (2×25 mL) and combined organic layers were dried with $MgSO_4$. Separation by column chromatography on toluene gave 4-nitro-2-phenylindole **5a** (7 mg; 6%, structure confirmed by ^{1}H NMR) as the only isolable product.

2.2.5. Competitive reaction of 1a and nitrobenzene with chloromethyl phenyl sulfone (Scheme 6). Nitrobenzene (375 mg, 3 mmol), *m*-nitroaniline **1a** (416 mg, 3 mmol) and chloromethylphenylsulfone (208 mg, 1 mmol) were dissolved in degassed DMSO (9 mL) under argon. Then *t*-BuOK, 0.224 g (2 mmol) was added in one portion and the mixture was stirred at 20 °C for 20 min. After this aqueous NH_4Cl (60 mL) was added and the mixture was extracted with ethyl acetate (2×30 mL), and extracts were treated with 2×100 mL HCl_{aq} (1:1), washed with water dried with $MgSO_4$. After evaporation of solvent residue was separated on short column (toluene then toluene–ethyl acetate 10:1) to give the mixture of *ortho*- and *para*-nitrobenzyl phenyl sulfones (194 mg, 70%, detected by TLC and confirmed by ^{1}H NMR). The acidic solution was made alkaline with KOH and extracted with ethyl acetate (3×25 mL) to give *m*-nitroaniline **1a** (394 mg, 95%). Product of the reaction with *m*-nitroaniline (**25**) was not detected by TLC and ^{1}H NMR in organic phase nor in aqueous extracts.

2.2.6. Competitive reaction of 1a and nitrobenzene with 5 (Scheme 6). To a solution of nitrobenzene (370 mg, 3 mmol), *m*-nitroaniline **1a** (414 mg, 3 mmol) and acetophenone **5** (119 mg, 1 mmol) in DMSO (9 mL), *t*-BuOK (224 mg, 2 mmol) was added in one portion and the mixture was stirred at open flask under air for 20 min at 20 °C. The mixture was diluted with aqueous NH_4Cl (60 mL), extracted with ethyl acetate (3×25 mL), the combined extracts were treated with HCl_{aq} (1:1, 2×100 mL), washed with water and dried with $MgSO_4$. After evaporation of the solvent residue was separated on short column (toluene then toluene–ethyl acetate 10:1) to give mixture of nitroindoles (**5a**, **5a6**) and *p*-nitrobenzyl phenyl ketone **26** (166 mg, about 60% of all compounds). Basification of the acidic solution with KOH and extraction with ethyl acetate (3×25 mL) gave *m*-nitroaniline **1a** (330 mg, 80%).

^{1}H NMR analysis of the crude reaction mixture showed *p*-nitrobenzyl phenyl ketone **26** to nitroindoles (**5a**, **5a6**) ratio close to 2:1.

2.2.7. Reaction of 1a with chloromethylphenylsulfone (synthesis of 25, Scheme 7). *m*-Nitroaniline **1a** (416 mg, 3 mmol) and chloromethylphenylsulfone (193 mg, 1 mmol) were dissolved in degassed DMSO (9 mL) under argon and *t*-BuOK (225 mg, 2 mmol) was added in one portion. The mixture was stirred for 20 min at 20 °C, aqueous NH_4Cl (60 mL) was added and extracted with ethyl acetate (3×30 mL). Separation on short column with toluene then toluene–ethyl acetate (10:1) gave 5-nitro-2-[(phenyl sulfonyl)methyl]aniline **25** (164 mg, 56%) as yellow solid. Mp 216–218 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.74 (s, 2H), 5.80 (s, 2H), 7.06 (d, *J*=8.4 Hz, 1H), 7.24 (dd, *J*=8.4, 2.4 Hz, 1H), 7.44 (d, *J*=2.4 Hz, 1H), 7.58–7.62 (m, 2H), 7.70–7.75 (m, 1H), 7.78–7.82 (m, 2H). EIMS *m/e* (relative intensity): 292 (M^+, 8), 151 (100). IR (cm^{-1}, KBr): 3473, 3390, 1636, 1510, 1353, 1300, 1145, 1081, 750, 725, 694, 594, 517. Anal. Calcd for $C_{13}H_{12}N_2O_4S$: C, 53.42; H, 4.14; N, 9.58; S 10.97. Found: C, 53.42; H, 4.06; N; 9.58; S 10.91.

2.2.8. Conversion of 25 into 24 (Scheme 7). To a suspension of 5-nitro-2-[(phenylsulfonyl)methyl]aniline **25** (97 mg, 0.33 mmol) in a mixture of 36% aqueous HCl (3.3 g) and 50% aqueous H_3PO_2 (3.2 g) at −5 °C aqueous solution of $NaNO_2$ (120 mg, 1.7 mmol in 600 mg of water) was added slowly. The mixture was warmed to room temperature during 1 h. Water (50 mL) was added and the mixture was extracted with ethyl acetate (2×30 mL) combined organic layers were washed with brine (2×100 mL) and dried with $MgSO_4$. Column chromatography (toluene then toluene–ethyl acetate 10:1) gave 4-nitrobenzyl phenyl sulfone **24** (42 mg, 46%) mp 210–210.5 °C (lit.[24] 207 °C) (confirmed by ^{1}H NMR spectrum).

2.2.9. Reaction of 5 with nitrobenzene (synthesis of 26, Scheme 8). To a solution of nitrobenzene (373 mg, 3 mmol) and acetophenone **5** (117 mg, 1 mmol) in DMSO (9 mL) *t*-BuOK (233 mg, 2.1 mmol) was added in one portion. The mixture was stirred in open flask under air for 20 min at

20 °C and then aqueous solution of NH_4Cl (50 mL) was added, the whole was extracted with ethyl acetate (2×30 mL) and dried. Separation on short column with hexane–ethyl acetate (20:1 to 4:1) gave *p*-nitrobenzyl phenyl ketone **26** as white solid (151 mg, 64%), mp 141.5–143 °C (lit.[30] 138–140 °C). ^{1}H NMR δ ($CDCl_3$) 4.42 (s, 2H), 7.40–7.67 (m, 5H), 7.98–8.06 (m, 2H), 8.16–8.24 (m, 2H). LSIMS *m/z*: 242 [M^++1]. Anal. Calcd for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.60; N, 5.81. Found: C, 70.07; H, 4.59; N, 5.92 and unidentified yellow product (EIMS: M^+343) (19 mg).

2.2.10. Influence of oxygen on the reaction (Scheme 9). The reactions **1a** with **5** were performed according to the general procedure for isolation of minor amounts of 6-NO_2 isomers. For experiment without oxygen, DMSO was dried with CaH_2 overnight, distilled in a stream of argon under reduced pressure, degassed by 3-fold repeated freeze–pump–thaw technique (see Ref. 31) and argonated before experiment. Experiment with oxygen was performed with continuous bubbling of oxygen through the reaction mixture 10 min before and during the reaction.

2.3. Physicochemical and spectral data

Representative IR spectra are given for compounds **2a**, **2a6**, **5a**, **5a6**, **12a** and **12a6**.

2.3.1. 2-Methyl-4-nitroindole (2a). Mp 202 °C (lit.[9b] 197–198 °C). IR (cm^{-1}, KBr): 3301, 1580, 1505, 1478, 1321, 1231, 980, 779, 735.

2.3.2. 2-Methyl-6-nitroindole (2a6). Mp 118–119 °C (lit.[32] 113.5–114.5 °C). IR (cm^{-1}, KBr): 3314, 1589, 1543, 1501, 1463, 1316, 1069, 821, 733. ^{1}H NMR ($CDCl_3$) δ 2.55 (d, *J*=0.8 Hz, 3H), 6.35–6.37 (m, 1H), 7.53 (d, *J*=8.8 Hz, 1H), 8.01 (dd, *J*=8.8, 2.2 Hz, 1H), 8.29–8.31 (m, 1H), 8.55 (s br, 1H). EIMS *m/e* (relative intensity): 176 (M^+, 100), 146 (28), 130 (55). Anal. Calcd for $C_9H_8N_2O_2$: C, 61.36; H, 4.58; N, 15.90. Found: C, 61.51; H, 4.41; N, 15.80.

2.3.3. 7-Chloro-2-methyl-4-nitroindole (2b). Mp 208–209 °C. ^{1}H NMR δ ($CDCl_3$) 2.57 (d, *J*=0.9 Hz, 3H), 7.03–7.06 (m, 1H), 7.17 (d, *J*=8.7 Hz, 1H), 8.05 (d, *J*=8.7 Hz, 1H), 8.50 (br s, 1H). EIMS *m/e* (relative intensity): 210, 212 (M^+, 100, 34), 180, 182 (40, 14), 164, 166 (47, 15). Anal. Calcd for $C_9H_7ClN_2O_2$: C, 51.32; H, 3.35; N, 13.30. Found: C, 51.45; H, 3.23; N, 13.06.

2.3.4. 7-Fluoro-2-methyl-4-nitroindole (2d). Mp 228–229 °C. ^{1}H NMR ($CDCl_3$) δ 2.56 (d, *J*=0.8 Hz, 3H), 6.89 (dd, *J*=9.7, 8.9 Hz, 1H), 7.02–7.07 (m, 1H), 8.09 (dd, *J*=8.9, 4.3 Hz, 1H), 8.45 (br s, 1H). EIMS *m/e* (relative intensity): 194 (M^+, 100), 164 (28), 148 (52). Anal. Calcd for $C_9H_7N_2O_2F$: C, 55.67; H, 3.63; N, 14.43. Found: C, 55.87; H, 3.50; N, 14.30.

2.3.5. 5-Fluoro-2-methyl-4-nitroindole (2e). Mp 194–195 °C. ^{1}H NMR δ (DMSO-d_6) 2.48 (s, 3H), 6.65–6.69 (m, 1H), 7.20 (dd, *J*=12.5, 8.7 Hz, 1H), 7.68 (ddd, *J*=8.7, 3.8, 0.8 Hz, 1H), 11.94 (br s, 1H). EIMS *m/e* (relative intensity): 194 (M^+, 100), 164 (42), 148 (69). Anal. Calcd for $C_9H_7FN_2O_2$: C, 55.67; H, 3.63; N, 14.43. Found: C, 55.66; H, 3.39; N, 14.26.

2.3.6. 2-Cyclopropyl-4-nitroindole (3a). Mp 192–193 °C. ^{1}H NMR δ ($CDCl_3$) 0.87–1.01 (m, 2H), 1.03–1.17 (m, 2H), 1.96–2.11 (m, 1H), 6.88–6.92 (m, 1H), 7.16 (dd, *J*=8.0, 8.0 Hz, 1H), 7.57 (ddd, *J*=8.0, 0.9, 0.9 Hz, 1H), 8.09 (dd, *J*=8.1, 0.9 Hz, 1H), 8.42 (br s, 1H). EIMS *m/e* (relative intensity): 202 (M^+, 100), 185 (89), 155 (95), 128 (64). Anal. Calcd for $C_{11}H_{10}N_2O_2$: C, 65.34; H, 4.98; N, 13.85. Found: C, 65.23; H, 4.87; N, 14.04.

2.3.7. 2-*tert*-Butyl-4-nitroindole (4a). Mp 173 °C (lit.[12] 173 °C).

2.3.8. 2-Phenyl-4-nitroindole (5a). Mp 205 °C (lit.[9b] 203–206 °C). IR (cm^{-1}, KBr): 3339, 1500, 1481, 1454, 1374, 1325, 1272, 983, 766.

2.3.9. 2-Phenyl-6-nitroindole (5a6). Mp 214.5–216 °C. ^{1}H NMR (DMSO-d_6) δ 7.16 (s, 1H), 7.38–7.60 (m, 3H), 7.72 (d, *J*=8.8 Hz, 1H), 7.82–7.99 (m, 3H), 8.29 (d, *J*=2.0 Hz, 1H), 12.36 (s br, 1H). EIMS *m/e* (relative intensity): 238 (M^+, 100), 208 (35), 192 (44), 165 (28). IR (cm^{-1}, KBr): 3323, 1502, 1487, 1461, 1298, 1065, 757, 731. Anal. Calcd for $C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76. Found: C, 71.47; H, 4.29; N, 11.62.

2.3.10. 7-Chloro-4-nitro-2-phenylindole (5b). Mp 200–202 °C. ^{1}H NMR δ (DMSO-d_6) 7.40 (d, *J*=8.6 Hz, 1H), 7.43–7.60 (m, 4H), 8.07 (d, *J*=8.6 Hz, 1H), 8.06–8.14 (m, 2H), 12.42 (br s, 1H). EIMS *m/e* (relative intensity): 272, 274 (M^+, 100, 37), 242, 244 (25, 9), 226, 228 (21, 7), 191 (27). Anal. Calcd for $C_{14}H_9ClN_2O_2$: C, 61.66; H, 3.33; N, 10.27. Found: C, 61.81; H, 3.01; N, 10.08.

2.3.11. 7-Bromo-4-nitro-2-phenylindole (5c). Mp 197.5–198 °C. ^{1}H NMR ($CDCl_3$) δ 7.43 (d, *J*=8.6 Hz, 1H), 7.42–7.60 (m, 3H), 7.67 (d, *J*=2.5 Hz, 1H), 7.78–7.85 (m, 2H), 8.05 (d, *J*=8.6 Hz, 1H), 8.81 (s br, 1H). EIMS *m/e* (relative intensity): 316, 318 (M^+, 100, 97), 286, 288 (28, 27), 270, 272 (25, 24), 191 (99). Anal. Calcd for $C_{14}H_9N_2O_2Br$: C, 53.02; H, 2.86; N, 8.83; Br, 25.20. Found: C, 53.30; H, 2.67; N, 8.84; Br, 24.76.

2.3.12. 7-Fluoro-4-nitro-2-phenylindole (5d). Mp 204–206 °C. ^{1}H NMR δ (DMSO-d_6) 7.19 (dd, *J*=10.2, 8.9 Hz, 1H) 7.41–7.60 (m, 4H), 8.03–8.10 (m, 2H), 8.11 (dd, *J*=8.9, 4.1 Hz, 1H), 12.77 (br s, 1H). EIMS *m/e* (relative intensity): 256 (M^+, 100), 226 (27), 210 (42). Anal. Calcd for $C_{14}H_9FN_2O_2$: C, 65.62; H, 3.54; N, 10.93. Found: C, 65.53; H, 3.29; N, 10.78.

2.3.13. 4-Nitro-2-(2-pyridyl)indole (6a). Mp 167 °C (lit.[12] 167 °C).

2.3.14. 2-(Furan-2-yl)-4-nitroindole (7a). Mp 211–212 °C. ^{1}H NMR (DMSO-d_6) δ 6.73 (dd, *J*=3.4, 1.8 Hz, 1H), 7.17 (dd, *J*=3.4, 0.6 Hz, 1H), 7.32 (dd, *J*=8.0, 8.0 Hz, 1H), 7.33 (dd, *J*=2.2, 0.8 Hz, 1H), 7.85 (dt, *J*=8.0, 0.9 Hz, 1H), 7.92 (dd, *J*=1.8, 0.7 Hz, 1H), 8.07 (dd, *J*=8.0, 0.8 Hz, 1H), 12.49 (s, 1H). EIMS *m/e* (relative intensity): 228 (M^+, 100), 198 (8), 182 (34). Anal. Calcd for $C_{12}H_8N_2O_3$: C, 63.16; H, 3.53; N, 12.28. Found: C, 63.30; H, 3.32; N, 12.30.

2.3.15. 7-Chloro-2-(2′-furyl)-4-nitroindole (7b). Mp 209–210 °C. ^{1}H NMR δ ($CDCl_3$) 6.60 (dd, *J*=3.4, 1.7 Hz, 1H),

6.92 (dd, *J*=3.4, 0.6 Hz, 1H), 7.24 (d, *J*=8.6 Hz, 1H), 7.49–7.62 (m, 2H), 8.10 (d, *J*=8.6 Hz, 1H), 8.97 (br s, 1H). EIMS *m/e* (relative intensity): 262, 264 (M^+, 100, 34), 232, 234 (22, 7), 216, 218 (47, 16). Anal. Calcd for $C_{12}H_7ClN_2O_3$: C, 54.88; H, 2.69; N, 10.67. Found: C, 54.60; H, 2.53; N, 10.52.

2.3.16. 4-Nitro-2-(2′-thienyl)-indole (8a). Mp 220–221 °C. ^{1}H NMR (DMSO-d_6) δ 7.24 (dd, *J*=5.0, 3.7 Hz, 1H), 7.29 (dd, *J*=2.2, 0.8 Hz, 1H), 7.31 (dd, *J*=8.0, 8.0 Hz, 1H), 7.72 (dd, *J*=5.0, 1.2 Hz, 1H), 7.75 (dd, *J*=3.7, 1.2 Hz, 1H), 7.85 (ddd, *J*=8.0, 0.8, 0.8 Hz, 1H), 8.07 (dd, *J*=8.0, 0.8 Hz, 1H), 12.50 (s br, 1H). EIMS *m/e* (relative intensity): 244 (M^+, 100), 214 (27), 198 (44). Anal. Calcd for $C_{12}H_8N_2O_2S$: C, 59.01; H, 3.30; N, 11.47. Found: C, 59.20; H, 3.14; N, 11.42.

2.3.17. 7-Chloro-4-nitro-2-(2′-thienyl)indole (8b). Mp 211–213 °C. ^{1}H NMR δ (acetone-d_6) 7.21 (dd, *J*=5.1, 3.7 Hz, 1H), 7.36 (d, *J*=8.6 Hz, 1H), 7.43 (d, *J*=2.0 Hz, 1H), 7.66 (dd, *J*=5.1, 1.1 Hz, 1H), 7.82 (dd, *J*=3.7, 1.1 Hz, 1H), 8.08 (d, *J*=8.7 Hz, 1H), 11.50 (br s, 1H). EIMS *m/e* (relative intensity): 278, 280 (M^+, 100, 37), 248, 250 (40, 15). Anal. Calcd for $C_{12}H_7ClN_2O_2S$: C, 51.71; H, 2.53; N, 10.05. Found: C, 51.63; H, 2.26; N, 10.02.

2.3.18. 4-Nitro-2-(1-methyl-1*H*-pyrrol-2-yl)-1*H*-indole (9a). Mp 216–218 °C. ^{1}H NMR (DMSO-d_6) δ 3.91 (s, 3H), 6.18 (dd, *J*=3.8, 2.6 Hz, 1H), 6.71 (dd, *J*=3.8, 1.8 Hz, 1H), 7.02 (dd, *J*=2.1, 2.0 Hz, 1H), 7.17 (d, *J*=1.5 Hz, 1H), 7.26 (dd, *J*=8.0, 8.0 Hz, 1H), 7.79 (d, *J*=7.9 Hz, 1H), 8.03 (dd, *J*=8.1, 0.7 Hz, 1H), 12.03 (s, 1H). EIMS *m/e* (relative intensity): 241 (M^+, 100), 195 (36). Anal. Calcd for $C_{13}H_{11}N_3O_2$: C, 64.72; H, 4.60; N, 17.42. Found: C, 64.48; H, 4.42; N, 17.57.

2.3.19. 2,3-Dimethyl-4-nitroindole (10a). Mp 173 °C (lit.[33] 175 °C).

2.3.20. 2,3-Dimethyl-6-nitroindole (10a6). Mp 142 °C (lit.[34] 142 °C).

2.3.21. 2-Ethyl-3-methyl-4-nitroindole (11a). Mp 175 °C (lit.[8d] 175 °C).

2.3.22. 2-Ethyl-3-methyl-6-nitroindole (11a6). Mp 165 °C (lit.[8d] 164 °C).

2.3.23. 7-Chloro-2-ethyl-3-methyl-4-nitroindole (11b). Mp 150–151 °C. ^{1}H NMR δ ($CDCl_3$) 1.34 (t, *J*=7.6 Hz, 3H), 2.29 (s, 3H), 2.85 (q, *J*=7.6 Hz, 2H), 7.11 (d, *J*=8.5 Hz, 1H), 7.72 (d, *J*=8.5 Hz, 1H), 8.35 (br s, 1H). EIMS *m/e* (relative intensity): 238, 240 (M^+, 41, 14), 221, 223 (69, 25), 191, 193 (100, 39). Anal. Calcd for $C_{11}H_{11}ClN_2O_2$: C, 55.36; H, 4.65; N, 11.74. Found: C, 55.64; H, 4.78; N, 11.59.

2.3.24. 2-Ethyl-7-fluoro-3-methyl-4-nitroindole (11d). Mp 155–156 °C. ^{1}H NMR δ ($CDCl_3$) 1.33 (t, *J*=7.7 Hz, 3H), 2.30 (s, 3H), 2.84 (q, *J*=7.6 Hz, 2H), 6.82 (dd, *J*=9.5, 8.8 Hz, 1H), 7.78 (dd, *J*=8.8, 4.5 Hz, 1H), 8.40 (br s, 1H). EIMS *m/e* (relative intensity): 222 (M^+, 44), 205 (62), 175 (100). Anal. Calcd for $C_{11}H_{11}FN_2O_2$: C, 59.46; H, 4.99; N, 12.61. Found: C, 59.41; H; 4.84; N, 12.61.

2.3.25. 2-Ethyl-5-fluoro-3-methyl-4-nitroindole (11e). Mp 162–163 °C. ^{1}H NMR δ ($CDCl_3$) 1.30 (t, *J*=7.6 Hz, 3H), 2.11 (s, 3H), 2.78 (q, *J*=7.6 Hz, 2H), 6.92 (dd, *J*=10.4, 8.8 Hz, 1H), 7.33 (dd, *J*=8.8, 3.9 Hz, 1H), 8.10 (br s, 1H). EIMS *m/e* (relative intensity): 222 (M^+, 50), 205 (48), 175 (100). Anal. Calcd for $C_{11}H_{11}FN_2O_2$: C, 59.46; H, 4.99; N, 12.61. Found: C, 60.48; H, 5.15; N, 12.45.

2.3.26. 2-Ethyl-5-fluoro-3-methyl-6-nitroindole (11e6). Mp 197–198 °C. ^{1}H NMR δ ($CDCl_3$) 1.32 (t, *J*=7.7 Hz, 3H), 2.21 (s, 3H), 2.82 (q, *J*=7.7 Hz, 2H), 7.21 (d, *J*=12.1 Hz, 1H), 8.09 (d, *J*=6.1 Hz, 1H), 8.23 (br s, 1H). EIMS *m/e* (relative intensity): 222 (M^+, 100), 207 (48), 192 (31), 161 (51). Anal. Calcd for $C_{11}H_{11}FN_2O_2$: C, 59.46; H, 4.99; N, 12.61. Found: C, 60.49; H, 5.24; N, 12.18.

2.3.27. 3-Methyl-4-nitro-2-phenylindole (12a). Mp 207–208 °C (lit.[35] 205–206 °C), ^{1}H NMR δ ($CDCl_3$) 2.43 (s, 3H), 7.20 (d, *J*=8.0 Hz, 1H), 7.40–7.62 (m, 5H), 7.62 (dd, *J*=8.1, 0.9 Hz, 1H), 7.78 (dd, *J*=7.9, 0.9 Hz, 1H), 8.40 (br s, 1H). EIMS *m/e* (relative intensity): 252 (M^+, 63), 235 (37), 205 (100). IR (cm^{-1}, KBr): 3357, 1504, 1328, 1286, 1055, 993, 810, 764, 772, 700. Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.25; H, 4.64; N, 10.97.

2.3.28. 3-Methyl-6-nitro-2-phenylindole (12a6). Mp 208–210 °C (lit.[35] 205–206 °C), ^{1}H NMR δ ($CDCl_3$) 2.48 (s, 3H), 7.39–7.66 (m, 6H), 8.06 (dd, *J*=8.8, 2.0 Hz, 1H), 8.34 (dd, *J*=2.0, 0.5 Hz, 1H), 8.45 (br s, 1H). EIMS *m/e* (relative intensity): 252 (M^+, 100), 222 (23), 206 (24). IR (cm^{-1}, KBr): 3339, 1495, 1464, 1297, 1238, 1062, 775, 755, 709. Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.69; H, 4.46; N, 10.82.

2.3.29. 8-Nitro-1,2,3,4-tetrahydro-cyclopent[*b*]indole (13a). Mp 198–199 °C (lit.[36a] 199 °C).

2.3.30. 6-Nitro-1,2,3,4-tetrahydro-cyclopent[*b*]indole (13a6). Mp 139–141 °C (lit.[36a] 153 °C), ^{1}H NMR (DMSO-d_6) δ 2.41–2.58 (m, 2H), 2.72–2.85 (m, 2H), 2.85–2.97 (m, 2H), 7.45 (d, *J*=8.8 Hz, 1H), 7.85 (dd, *J*=8.8, 2.2 Hz, 1H), 8.22 (d, *J*=2.2 Hz, 1H), 11.69 (s, 1H). EIMS *m/e* (relative intensity): 202 (M^+, 100), 172 (13), 156 (35). Anal. Calcd for $C_{11}H_{10}N_2O_2$: C, 65.34; H, 4.98; N, 13.85. Found: C, 65.36; H, 5.21; N, 13.76.

2.3.31. 5-Nitro-1,2,3,4-tetrahydrocarbazole (14a). Mp 152 °C (lit.[36b] 153–156 °C).

2.3.32. 7-Nitro-1,2,3,4-tetrahydrocarbazole (14a6). Mp 169 °C (lit.[36b] 170–171 °C).

2.3.33. 8-Chloro-5-nitro-1,2,3,4-tetrahydrocarbazole (14b). Mp 208–209 °C (lit.[37] 214 °C), ^{1}H NMR δ ($CDCl_3$) 1.77–2.00 (m, 4H), 2.79–2.96 (m, 4H), 7.10 (d, *J*=8.5 Hz, 1H), 7.79 (d, *J*=8.5 Hz, 1H), 8.35 (br s, 1H). MS: 250, 252 (M^+, 32, 10), 233, 235 (100, 32), 203, 205 (77, 26). Anal. Calcd for $C_{12}H_{11}ClN_2O_2$: C, 57.50; H, 4.42; N, 11.17. Found: C, 57.46; H, 4.19; N, 11.10.

2.3.34. 1-Nitro-5,6,7,8,9,10-hexahydro-cyclohepta[*b*]indole (15a). Mp 147–148 °C (lit.[35] 148–149 °C).

2.3.35. 3-Nitro-5,6,7,8,9,10-hexahydro-cyclohepta[*b*] indole (15a6). Mp 134–136 °C (lit.[35] 135–136 °C).

2.3.36. 5,6-Dihydro-7-nitrobenzo[*a*]carbazole (16a). Mp 258–259 °C (dec.). ^{1}H NMR (DMSO-d_6) δ 2.93–3.15 (m, 4H), 7.25 (dd, *J*=8.0, 8.0 Hz, 1H), 7.30–7.41 (m, 3H), 7.70–7.78 (m, 2H), 7.82 (dd, *J*=8.0, 1.0 Hz, 1H), 12.36 (br s, 1H). EIMS *m/e* (relative intensity): 264 (M^+, 32), 247 (68), 217 (100). Anal. Calcd for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.58; N, 10.60. Found: C, 72.57; H, 4.28; N, 10.41.

2.3.37. 5,6-Dihydro-9-nitrobenzo[*a*]carbazole (16a6). Mp 253–254 °C (lit.[38] 226–228 °C), ^{1}H NMR (DMSO-d_6) δ 2.96–3.16 (m, 4H), 7.30–7.48 (m, 3H), 7.72 (d, *J*=8.8 Hz, 1H), 7.76–7.83 (m, 1H), 7.97 (dd, *J*=8.8, 2.1 Hz, 1H), 8.32 (d, *J*=2.1 Hz, 1H), 12.35 (br s, 1H). EIMS *m/e* (relative intensity): 264 (M^+, 100), 234 (22), 217 (90). Anal. Calcd for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.58; N, 10.60. Found: C, 72.71; H, 4.37; N, 10.69.

2.3.38. 10-Chloro-5,6-dihydro-7-nitrobenzo[*a*]carbazole (16b). Mp 206–207 °C. ^{1}H NMR δ (DMSO-d_6) 2.91–3.11 (m, 4H), 7.33 (d, *J*=8.5 Hz, 1H), 7.31–7.38 (m, 3H), 7.84 (d, *J*=8.5 Hz, 1H), 8.06–8.14 (m, 1H), 12.35 (br s, 1H). MS: 298, 300 (M^+, 38, 13), 281, 283 (100, 33), 251, 253 (65, 23). Anal. Calcd for $C_{16}H_{11}ClN_2O_2$: C, 64.33; H, 3.71; N, 9.38. Found: C, 64.61; H, 3.62; N, 9.01.

2.3.39. 7-Chloro-2-(1′-naphtyl)-4-nitroindole (17b). Mp 213–214 °C. ^{1}H NMR δ (DMSO-d_6) 7.36 (d, *J*=2.1 Hz, 1H), 7.47 (d, *J*=8.6 Hz, 1H), 7.58–7.86 (m, 4H), 8.05–8.20 (m, 3H), 8.13 (d, *J*=8.6 Hz, 1H), 12.80 (br s, 1H). EIMS *m/e* (relative intensity): 322, 324 (M^+, 100, 34), 276, 278 (20, 6). Anal. Calcd for $C_{18}H_{11}ClN_2O_2$: C, 66.99; H, 3.44; N, 8.68. Found: C, 67.14; H, 3.20; N, 8.42.

2.3.40. 3-Ethyl-4-nitro-2-*n*-propylindole (18a). Mp 144–145 °C. ^{1}H NMR δ ($CDCl_3$) 0.98–1.11 (m, 6H) 1.61–1.81 (m, 2H), 2.72–2.86 (m, 4H), 7.12 (dd, *J*=7.9 Hz, 1H), 7.52 (dd, *J*=7.9, 1.0 Hz, 1H), 7.74 (dd, *J*=7.9, 1.0 Hz, 1H), 8.27 (br s, 1H). EIMS *m/e* (relative intensity): 232 (M^+, 100), 215 (65). Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.42; H, 6.98; N, 12.05.

2.3.41. 7-Chloro-3-ethyl-4-nitro-2-*n*-propylindole (18b). Mp 151–152 °C. ^{1}H NMR δ ($CDCl_3$) 0.98–1.11 (m, 6H), 1.65–1.86 (m, 2H), 2.73–2.87 (m, 4H), 7.12 (d, *J*=8.5 Hz, 1H), 7.72 (d, *J*=8.5 Hz, 1H), 8.38 (br s, 1H). EIMS *m/e* (relative intensity): 266, 268 (M^+, 100, 33), 249, 251 (70, 23), 221, 223 (39, 14). Anal. Calcd for $C_{13}H_{15}ClN_2O_2$: C, 58.54; H, 5.67; N, 10.50. Found: C, 58.38; H, 5.70; N, 10.51.

2.3.42. 3-Allyl-2-methyl-4-nitroindole (19a). Mp 129–130 °C. ^{1}H NMR δ ($CDCl_3$) 2.44 (s, 3H), 3.54–3.59 (m, 2H), 4.71–4.84 (m, 1H), 4.86–4.95 (m, 1H), 5.82–6.03 (m, 1H), 7.12 (dd, *J*=8.0 Hz, 1H), 7.52 (dd, *J*=8.0, 1.0 Hz, 1H), 7.74 (dd, *J*=8.0, 1.0 Hz, 1H), 8.35 (br s, 1H). EIMS *m/e* (relative intensity): 216 (M^+, 27), 199 (64), 168 (100). Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.95. Found: C, 66.47; H, 5.65; N, 12.75.

2.3.43. 3-Allyl-2-methyl-6-nitroindole (19a6). Mp 119–121 °C. ^{1}H NMR δ ($CDCl_3$) 2.45 (s, 3H), 3.41–3.50 (m, 2H), 4.96–5.03 (m, 1H), 5.05–5.08 (m, 1H), 5.84–6.06 (m, 1H), 7.50 (d, *J*=8.8 Hz, 1H), 7.98 (dd, *J*=8.8, 2.0 Hz, 1H), 8.25 (d, *J*=2.0 Hz, 1H), 8.37 (br s, 1H). EIMS *m/e* (relative intensity): 216 (M^+, 100), 201 (20), 189 (51). Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.95. Found: C, 66.51; H, 5.56; N, 12.82.

2.3.44. 3-Allyl-7-chloro-2-methyl-4-nitroindole (19b). Mp 136–137 °C. ^{1}H NMR δ ($CDCl_3$) 2.48 (s, 3H), 3.53–3.58 (m, 2H), 4.71–4.84 (m, 1H), 4.87–4.96 (m, 1H), 5.81–6.02 (m, 1H), 7.13 (d, *J*=8.5 Hz, 1H), 7.71 (d, *J*=8.5 Hz, 1H), 8.49 (br s, 1H). EIMS *m/e* (relative intensity): 250, 252 (M^+, 54, 18), 233, 235 (83, 38), 209, 211 (100, 32). Anal. Calcd for $C_{12}H_{11}ClN_2O_2$: C, 57.50; H, 4.42; N, 11.17. Found: C, 57.31; H, 4.24; N, 11.00.

2.3.45. 3-Allyl-7-fluoro-2-methy-4-nitroindole (19d). Mp 119–120 °C. ^{1}H NMR δ ($CDCl_3$) 2.47 (s, 3H), 3.55–3.62 (m, 2H), 4.70–4.84 (m, 1H), 4.87–4.97 (m, 1H), 5.82–6.04 (m, 1H), 6.84 (dd, *J*=9.3, 8.9 Hz, 1H), 7.78 (dd, *J*=8.8, 4.5 Hz, 1H), 8.52 (br s, 1H). EIMS *m/e* (relative intensity): 234 (M^+, 37), 217 (70), 186 (100). Anal. Calcd for $C_{12}H_{11}FN_2O_2$: C, 61.53; H, 4.73; N, 11.96. Found: C, 61.31; H, 4.62; N, 11.82.

2.3.46. 8-Chloro-5-nitro-1,2,3,4-tetrahydro-γ-carboline (20b). Mp 189–190 °C. ^{1}H NMR δ ($CDCl_3$) 2.57 (s, 3H), 2.78–2.87 (m, 2H), 2.93–3.03 (m, 2H), 3.91 (t, *J*=1.6 Hz, 2H), 7.14 (d, *J*=8.6 Hz, 1H), 7.91 (d, *J*=8.6 Hz, 1H), 8.65 (br s, 1H). EIMS *m/e* (relative intensity): 265, 267 (M^+, 9, 3), 248, 250 (100, 32), 218, 220 (88, 30). Anal. Calcd for $C_{12}H_{12}ClN_3O_2$: C, 54.25; H, 4.55; N, 15.81. Found: C, 54.48; H, 4.48; N, 15.59.

2.3.47. Ethylene glycol monoacetal of 8-chloro-1,1-dimethyl-5-nitro-1,2,3,4-tetrahydro-carbazol-2-one (product of reaction of ethylene glycol monoacetal of dimedone with 2-chloro-5-nitroaniline) (21b). Mp 234–236 °C. ^{1}H NMR ($CDCl_3$) δ 1.44 (s, 6H), 2.04 (t, *J*=6.6 Hz, 2H), 3.07 (t, *J*=6.6 Hz, 2H), 3.99–4.15 (m, 4H), 7.14 (d, *J*=8.5 Hz, 1H), 7.82 (d, *J*=8.5 Hz, 1H), 8.28 (br s, 1H). EIMS *m/e* (relative intensity): 336, 338 (M^+, 41, 14), 319, 321 (25, 9), 250, 252 (100, 33). Anal. Calcd for $C_{16}H_{17}N_2O_4Cl$: C, 57.06; H, 5.09; N, 8.32. Found: C, 57.05; H, 5.17; N, 8.11.

2.3.48. 3-Ethyl-5-fluoro-6-nitro-2-phenylindole (22e6). Mp 164–165 °C. ^{1}H NMR δ ($CDCl_3$) 1.31 (t, *J*=7.6 Hz, 3H), 2.87 (q, *J*=7.6 Hz, 2H), 7.40 (d, *J*=12 Hz, 1H), 7.44–7.61 (m, 5H), 8.19 (d, *J*=6.1 Hz, 1H), 8.37 (br s, 1H). EIMS *m/e* (relative intensity): 284 (M^+, 71), 269 (100), 223 (48). Anal. Calcd for $C_{16}H_{13}FN_2O_2$: C, 67.60; H, 4.61; N, 9.85. Found: C, 67.77; H, 4.39; N, 9.89.

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