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Synthesis of 1-Hydroxyindoles and Indoles from *ortho*-Nitroarylethanes

Zbigniew Wróbel and Mieczysław Mąkosza*

Institute of Organic Chemistry, Polish Academy of Sciences
ul. Kasprzaka 44, 01-224 Warsaw, Poland

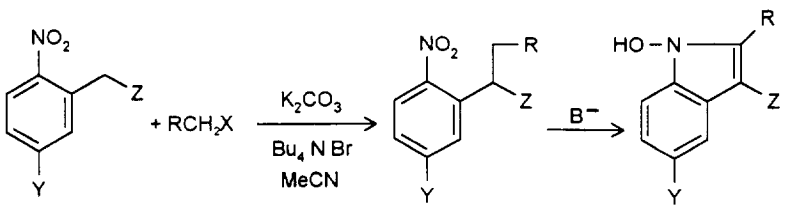
Abstract: Cyclization of substituted *ortho*-nitroarylethanes to 1-hydroxyindoles and their further reduction to indoles is described. The mechanism of cyclization is discussed. © 1997 Elsevier Science Ltd.

Processes involving neighboring group interaction in *ortho* substituted nitrobenzene derivatives are well-known in organic chemistry.[1] Many of them are of unquestionable synthetic value. Since nitroarenes containing functionalized substituents in *ortho* positions are readily available *via* the Vicarious Substitution of Hydrogen (VNS), a reaction developed in our laboratory,[2] we are interested in investigation of further transformations of these valuable starting materials.

One such process is the base-catalyzed cyclization of α,ß-disubstituted *ortho*-nitroarylethanes to 2,3-disubstituted 1-hydroxyindoles.[1,3] Reactions of this type provide probably the best general route to 1-hydroxyindoles. In our preliminary communication we have reported a new method of synthesis of 1-hydroxy-3-cyano-2-vinylindoles based on the cyclization of 2-allyl-2-(*o*-nitroaryl)acetonitriles effected by action of triethylamine and chlorotrimethylsilane in DMF solution.[4] Here we give a full report on our investigations undertaken to extend the scope of this reaction and for elucidation of its mechanistic features . First of all we have found that the base induced cyclization to 1-hydroxyindoles is not limited to allyl derivatives of *o*-nitroarylacetonitriles but is a general process for compounds **3** where Z denotes CN, COOR or SO_2Ar, and R denotes: vinyl, aryl, carboalkoxyl and even alkyl substituents, provided proper basic conditions are chosen. The reaction sequence from the VNS products **1** via alkylation with RCH_2X **2** to **3** and the cyclization to **4** is shown in eq.1. Results are collected in Table 1.

The starting *o*-nitroarylmethyl derivatives **1** were prepared from corresponding nitroarenes *via* the VNS reaction.[2] Alkylation of **1** to give **3** was efficiently carried out in solid-liquid PTC system as described earlier.[5] Compounds **3** can be transformed into **4** under various basic conditions which should be properly chosen, depending on the acidity of substrates **3**. Nitriles **3a-i** undergo smooth cyclization with Et_3N/Me_3SiCl/DMF (conditions A), methanolic NaOH (conditions B) or even methanolic triethylamine (conditions C) (entry 1). For the cyclization of less acidic sulfones **3l-n** NaOH/DMSO (conditions E) is the system of choice (entries 12-14). Sometimes the transformation of **3** into 1-hydroxyindole takes place directly during the alkylation of **1** to **3**. For example when 1-nitro-2-cyanomethyl-naphthalene **5** was alkylated with allyl bromide under the standard conditions ($K_2CO_3/Bu_4N^+Br^-$/MeCN)[5] a complicated mixture of products was formed which was neither separated nor analyzed. The same reaction carried out in methanol without PT-catalyst resulted in the formation of two products: **4r** and its O-allylated derivative **6** (eq. 2). Similar transformations of *o*-nitroanilines to 1-alkoxy-2-alkyl-

benzimidazoles on treatment with alkyl halides in the presence of sodium hydride in THF have been described recently.[6,7]



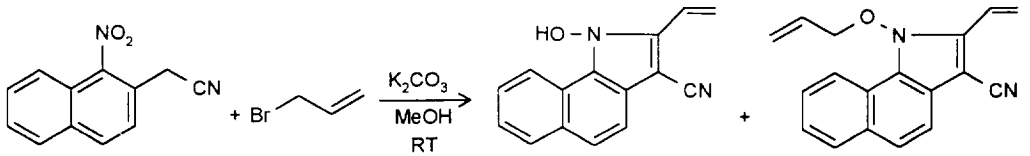
(1)

1 2 3 4

Table 1

Entry	Y	Z	R	3, yield %	4	3->4 conditions[a], yield %		
						A	B	other
1	Cl	CN	$CH=CH_2$	**3a** 66	**4a**	54	63	45(C)
2	Cl	CN	$C(Me)=CH_2$	**3b** 66	**4b**	54	-	-
3	Cl	CN	CH=CHPh	**3c** 66	**4c**	91	-	-
4	Br	CN	$CH=CH_2$	**3d** 77	**4d**	55	62	-
5	OMe	CN	$CH=CH_2$	**3e** 95	**4e**	26	-	-
6	OMe	CN[b]	$CH=CH_2$	**3f** 94	**4f**	34	49	-
7	Cl	CN	CO_2Et	**3g** 56	**4g**	85	0[c]	-
8	Cl	CN	$CONMe_2$	**3h** 54	**4h**	30(60)[d]	30	-
9	Cl	CN	$3,4\text{-}Cl_2C_6H_3$	**3i** 84	**4i**	53	-	-
10	Cl	$CO_2Bu\text{-}t$	$CH=CH_2$	**3j** 87	**4j**	25	0	-
11	Cl	$CO_2Bu\text{-}t$	$CO_2Bu\text{-}t$	**3k** 80	**4k**	0	-	54(D)
12	Cl	Tos	$CH=CH_2$	**3l** 91	**4l**	0	-	74(E)
13	OMe	Tos	Ph	**3m** 85	**4m**	-	-	94(E)
14	OMe	SO_2Ph	$CH=CH_2$	**3n** 86	**4n**	-	-	69(E)
15	Cl	CN	$n\text{-}C_7H_{15}$	**3o** 66	**4o**	-	58	-
16	Cl	CN	C_2H_5	**3p** 81	**4p**	-	61	-

a) Conditions: A: Me_3SiCl/Et_3N/DMF/RT; B: NaOH/MeOH/RT; C: Et_3N/MeOH/reflux, D: NaOH/t-BuOH/RT; E: NaOH/DMSO/RT; b) 2-methoxy-5-nitropyridine, c) the ester function was hydrolysed ; d) based on consumed substrate.



(2)

5 (1 eq.) **4r** (10%) **6** (30%)

1-Hydroxyindoles **4** can be readily reduced to the corresponding indoles **7** in good yields upon treatment with Zn dust in refluxing glacial acetic acid (eq. 3,Table 2). Thus the sequence: VNS, alkylation, cyclization and reduction provides an attractive way to these important intermediates in organic synthesis.

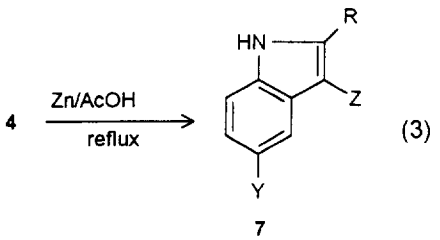


Table 2

Substrate	Y	Z	R	Product	Yield(%)
4a	Cl	CN	$CH=CH_2$	**7a**	69
4b	Cl	CN	$C(Me)=CH_2$	**7b**	65
4c	Cl	CN	CH=CHPh	**7c**	80
4d	Br	CN	$CH=CH_2$	**7d**	64
4i	Cl	CN	$3,4\text{-}Cl_2C_6H_3$	**7e**	58
4l	Cl	Tos	$CH=CH_2$	**7f**	53

At the beginning of the mechanistic discussion it should be mentioned that stoichiometry of the transformation of **3** to **4** corresponds to overall dehydration process - two hydrogen atoms of the removed water molecule are coming from α and ß positions of the side chain and the oxygen atom from the nitro group.

Although there are some examples of base induced cyclization of α,ß-disubstituted *o*-nitroarylethanes into 1-hydroxyindoles described in literature[1,3] the only mechanism considered for this transformation consists in formation of ß-positioned carbanion and its intramolecular addition to the nitro group.[3] This mechanism, barely acceptable for **3** possessing electronwithdrawing substituents R (Table 1, entries 7,8,11), can not be accepted for the reaction of **3** when R is vinyl, aryl or particularly alkyl (entry 15, 16) substituents. In our previous paper[4] we proposed, that the transformation of **3** into **4** in Me_3SiCl/Et_3N system consists of deprotonation of **3** in α-position, O-silylation of the formed ambident anion, deprotonation of the silyl derivative at ß-position and subsequent intramolecular addition of this new carbanion (Scheme 1, structure **10A**, $M=SiMe_3$), to the positively charged nitrogen atom followed by departure of the silanol anion to give **4.**

However, as similar results where observed under protic conditions and in the presence of Me_3SiCl (Table 3), hence it appears that a similar mechanism should operate in both these cases. It is known that trimethylsilyl group is known to behave as a "bulky proton" in many other reactions.[8] Because of the potential importance of

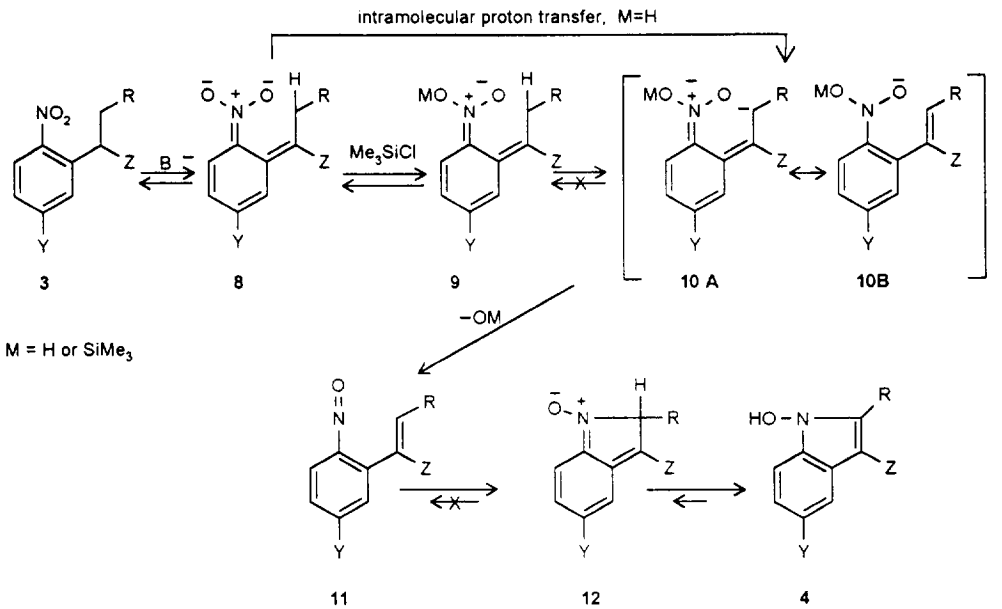
Table 3. Cyclization of **3a** into **4a** under different conditions

Entry	System[a)]	time[b)]	Yield (%)[c)]
1	NaOH(2eq.)/MeOH	<5 min	63
2	Et_3N(5eq.)/MeOH	4 weeks	73
3	Et_3N(5eq.)/DMF	1week	19
4	Et_3N(5eq.)/Me_3SiCl(5eq.)/DMF	<20 min	54
5	NaOH(2eq.)/DMSO	<5 min	20

a) reactions carried out at RT; b) time of disappearance of **3a** roughly estimated by t.l.c.; c) isolated via column chromatography

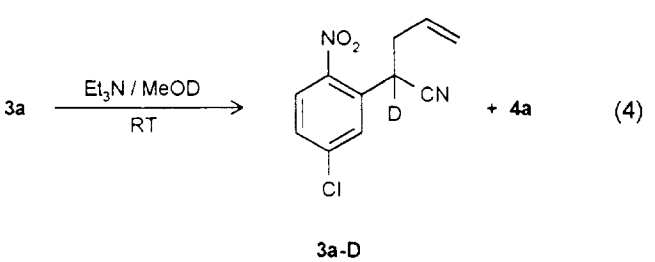
this process in indole synthesis it seems necessary to learn more about its mechanism. As our earlier short mechanistic hypothesis [4] is unsatisfactory, we present here a revised and expanded version of the mechanistic scheme. The reaction starts with reversible deprotonation of **3** in α -position to form anion **8** in which the intramolecular proton transfer from β-position to oxygen of the NO_2 group takes place giving **10** (in the case of Me_3SiCl assisted reaction this step is replaced by O-silylation and inter molecular deprotonation in β-position). Subsequent elimination of OH (or $OSiMe_3$) anion results in formation of nitroso- intermediate **11** which cyclizes

Scheme 1



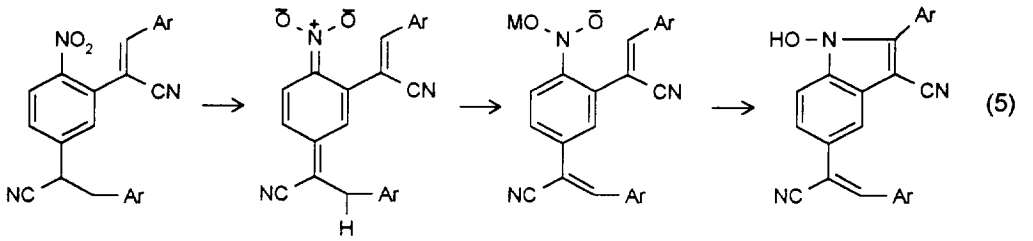
to nitrone **12** rearranging spontaneously to more stable **4** (Scheme 1). This mechanistic route is supported by the following observations:

1. The presence of base is necessary to induce the transformation of **3** to **4** thus it is reasonable to suppose that reversible deprotonation of **3** is the first step of the reaction. Indeed α-deuterated substrate **3a-D** was partially recovered along with **4a** after **3a** was treated with Et_3N in MeOD (eq. 4). It should be pointed out that deuterium enters *only* in the α-position, this suggests that further reaction steps should be irreversible.



(4)

2. The supposition that the β-proton is transferred to the oxygen of the NO_2 group *via* intramolecular process whereas in the Me_3SiCl assisted reactions the related step can occur intermolecularly is supported with experiments in which the model compound **13**[9] in which both α and β protons are located in *para* position to the NO_2 group, was investigated (eq 6). When **13** was treated with NaOH/MeOH system no reaction occurred although anion **14** was probably formed as could be judged by deep blue color of the reaction mixture characteristic for stabilized nitrobenzylic anions.[2] Use of triethylamine in methanol a base sufficiently strong for deprotonation, resulted in slow decomposition of the substrate without formation of any defined isolable product. On the other hand $Et_3N/Me_3SiCl/DMF$ converted 13 into 16 within 1h at room temperature. This suggests that the silylated intermediate is deprotonated to form **15** *via* an intermolecular process. This also proved that formation of **10** (M = H, $SiMe_3$) from **8** does not proceed *via* the dianion intermediate (**10**, M=Na^+ or Et_3N^+H). Taking into



(5)

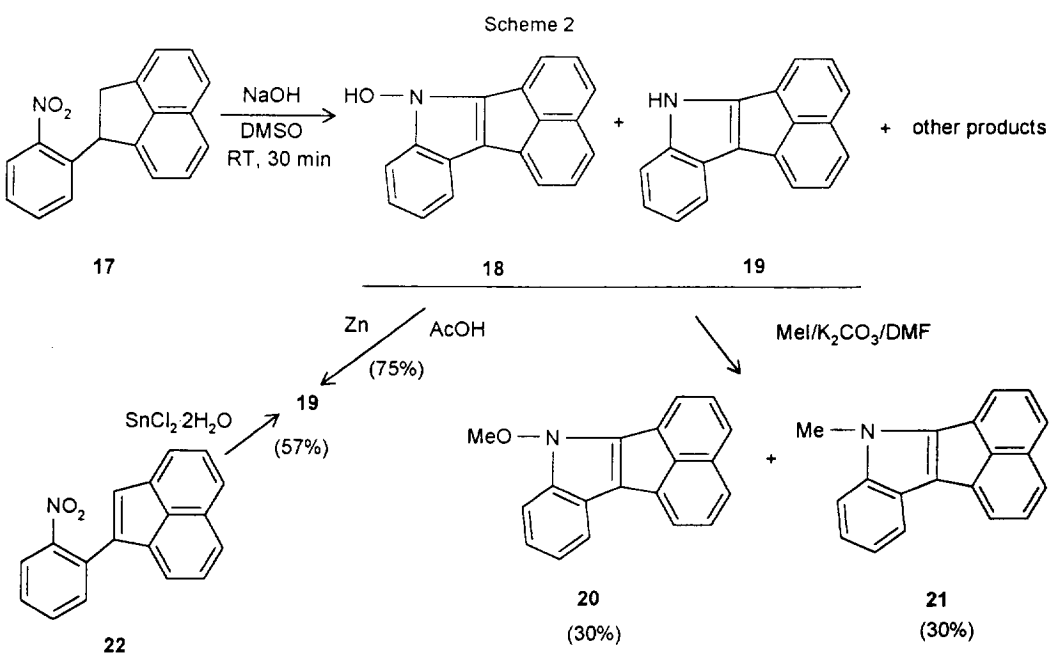
13 **14** **15** **16**

M = H, $SiMe_3$ Ar = *p*-ClC_6H_4

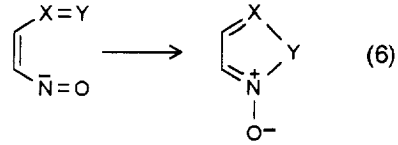
conditions: (A) Et_3N/Me_3SiCl/DMF/RT/1h 95% of **16**
(B) NaOH/MeOH/RT/3h 96% recovery of **13**
(C) Et_3N/ MeOH/RT slow decomp. of **13**; no **16**

account that both inductive and mesomeric effects should increase the acidity of the ß-proton in **14,** compared with **8,** one could expect formation of **15** (M= H, $SiMe_3$) from **14** via **15** ($M=Na^+$ or Et_3N^+H) in both (B) and (C) conditions because these systems work in the case of **8**. Since **10** is formed irreversibly and converts to **4** there is no reason to expect different behavior for **15,** which is a particular case of **10**. Moreover, since Et_3N/DMF (C) is a less basic system than NaOH/MeOH (B), there is also no reason to expect formation of dianion preceding silylation in this system. Thus, since conversion of **13** to **16** does not occur under conditions (B) and (C) the reaction cannot proceed *via* dianion.

Scheme 2

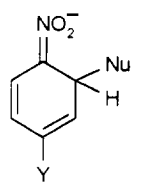


3.The hypothesis that nitrosocompound **11** is the key intermediate in the transformation of **3** to **4** is supported by results presented on Scheme 2. The model acenaphthenone derivative **17** (synthesized *via* nitroarylation of acenaphthenone with 2-fluoronitrobenzene followed by reduction of the carbonyl function), which does not contain an electron withdrawing substituent in the side chain cyclizes readily when treated with NaOH in DMSO. In this process a mixture of products, difficult to separate *via* TLC and column chromatography, was formed. The NMR spectrum of this mixture in DMSO-d_6 shows two singlets 11.82, and 11.95 (ratio 4:1) downfield to the aromatic region. On treatment with Zn/AcOH this mixture was transformed to pure **19** in 75% yield (δ_{NH} = 11.95), whereas methylation (MeI/K_2CO_3/DMF/RT) yielded O-methylated N-hydroxy **20** and N-methylated indole **21** derivatives which were isolated and identified indicating that both **18** (δ_{OH} = 11.82) and the indole **19** must be present in the reaction mixture. Polar variants of the cyclization step namely addition of the nucleophilic β-carbon atom to the positively charged nitrogen atom (see structure **10A**) as well as Michael type addition of the nucleophilic N-atom to activated carbon-carbon double bond (structure **10B**), considered earlier,[4] and similar reactions[10,11] would require the presence of an electronwithdrawing substituent adjacent to α-carbon atom to compensate the negative charge generated there during the addition suggesting that the cyclization of **17** to **18** does not proceed *via* this type of addition. Thermal electrocyclic reactions of nitroso compounds in which nitroso group forms conjugated 6π-electrons 5-atoms system containing at least one additional heteroatom are well known (eq. 7)[12] and it is possible that an electrocyclic reaction of the nitroso compound occurs as shown on Scheme 1. A similar mechanistic pathway was considered for the thermal rearrangement of 2-azidopyridine oxides to N-hydroxy-2-cyanopyrroles (X=Y : C=C).[13] Electrocyclization of the nitroso intermediate was supported by reductive ring closure in **22** to form **19** in nitrene excluding[14] conditions. On the other hand structure **8** is a vinylog

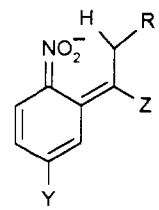


(6)

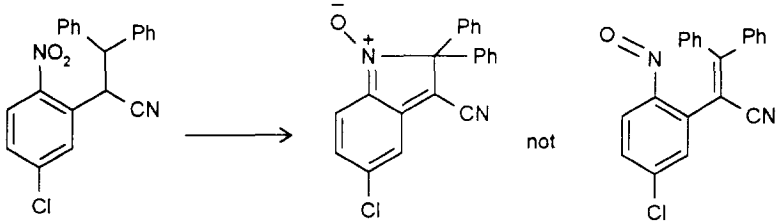
X=Y : N=N, N=C, N=O



σ^H – adduct



8



23 **24** **25**

(A) Et_3N/Me_3SiCl/DMF/RT/ 20 min 95%
(B) NaOH/MeOH/RT/5 min 95%

(7)

of the σ^H adduct formed in Davis[15-17] and von Richter[18] reactions. Since some σ^H adducts can be converted to nitroso compounds in protic media, it is reasonable to expect the similar behaviour for their vinylog and we believe

that this conversion proceeds stepwise *via* the mesomeric **10**.

4. Formation of 1-hydroxyindole was probably preceded by generation of nitrone **12.** Isomerisations of nitrones to N-hydroxyenamines are known.[19] In fact nitrone **24** was isolated, as the only product when the starting *o*-nitroaryl derivative **23** had ß-position blocked and isomerization to the 1-hydroxyindole was not possible (eq. 8). No evidence (^{13}C-NMR, ^{14}N-NMR) was found for the presence of uncyclized nitroso compound **25** which suggests irreversibility of the electrocyclization step.

EXPERIMENTAL

Melting points are uncorrected. The ^{1}H and ^{13}C NMR spectra were measured on Varian Gemini (200 MHz) and Bruker (500 MHz) when stated. Chemical shifts were expressed in ppm using TMS as an internal standard, coupling constants in hertz. The mass spectra were obtained on AMD-604 (AMD Intectra GmbH Germany).Starting *o*-nitroarylmethyl derivatives **1** were prepared according to known procedures.[2] Alkylations of **1** with **2** were effected in the presence of K_2CO_3 and catalytic amount of Bu_4NBr in MeCN (at room temperature for nitriles and reflux for sulfones and esters) as described.[5]

3a: mp 62-64°C (MeOH); ^{1}H-NMR see ref.[4]; Anal. calcd for $C_{11}H_9N_2O_2Cl$: C, 55.82; H, 3.83; N, 11.84%; found: C, 56.09; H, 3.54; N, 12.02%.

3b: mp 64-66°C (MeOH); ^{1}H-NMR ($CDCl_3$): 1.86 (s, 3H), 2.49-2.69 (m, 2H), 4.89-4.97 (m, 2H), 5.02 (t, J=1.4, 1H), 7.51 (dd, J=8.8, 2.3, 1H), 7.80 (d, J=2.3, 1H), 8.05 (d, J=8.8, 1H); MS (m/e): 250, 233, 220, 178, 153, 125, 114; Anal. cald for $C_{12}H_{11}N_2O_2Cl$: C, 57.49; H, 4.42; N, 11.18%; found: C, 57.46; H, 4.47; N, 11.18%.

3c: mp 130-132°C (EtOH); ^{1}H-NMR ($CDCl_3$): 2.71-2.97 (m, 2H), 4.89 (dd, J=8.5, 5.4, 1H), 6.21 (dt, J=15.7, 7.3, 1H), 6.54 (d, J=15.7, 1H), 7.28-7.38 (m, 5H), 7.51 (dd, J=8.8, 2.2, 1H), 7.78 (d, J=2.2, 1H), 8.06 (d, J=8.8, 1H); MS (m/e): 312, 295, 278, 242, 217, 196, 179, 169, 149; Anal. calcd for $C_{17}H_{13}N_2O_2Cl$: C, 65.28; H, 4.19; N, 8.95%; found: C, 65.07; H, 4.15; N, 9.05%.

3d: mp 77-79°C (EtOH-hexane); ^{1}H-NMR ($CDCl_3$): 2.54-2.82 (m, 2H), 4.82 (dd, J=8.4, 5.3, 1H), 5.17-5.30 (m, 2H), 5.75-5.96 (m, 1H), 7.68 (dd, J=8.7, 2.1, 1H), 7.91 (d, J=2.1, 1H), 7.97 (d, J=8.7, 1H); MS (m/e): 282,280, 265, 263, 248, 224, 210, 208, 199, 197, 186, 184; Anal. calcd for $C_{11}H_9N_2O_2Br$: C, 47.00; H, 3.23; N, 9.97%; found: C, 47.02; H, 3.08; N, 10.95%.

3e: oil, ^{1}H-NMR ($CDCl_3$): 2.51-2.81 (m, 2H), 3.94 (s, 3H), 4.99 (dd, J=8.5, 5.1, 1H), 5.19-5.27 (m, 2H), 5.77-5.98 (m, 1H), 6.95 (dd, J=9.1, 2.6, 1H), 7.22 (d, J=2.6, 1H), 8.17 (d, J=9.1, 1H); MS (m/e): 215, 202, 191, 186, 159, 144;LSIMS:255(M+Na), 233(M+H);LSIMSHR: 233.0934 (M^+), Calcd for $C_{12}H_{12}N_2O_3$: 233.0926.

3f: mp 49-52°C (EtOH-hexane); ^{1}H-NMR ($CDCl_3$): 2.77-2.85 (m, 2H), 4.12 (s, 3H), 5.05 (t, J=7.1, 1H), 5.18-5.28 (m, 2H), 5.81-6.01 (m, 1H), 6.84 (d, J=9.0, 1H), 8.35 (d, J=9.0, 1H); MS (m/e): 233, 216, 204, 193, 176, 160, 147; Anal. calcd for $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.76; N, 18.02%; found: C, 56.55; H, 4.69; N, 17.96%.

3g: mp 53-55°C (MeOH); ^{1}H-NMR ($CDCl_3$): 1.28 (t, J=7.2, 3H), 3.02 (d, J=7.4, 2H), 4.21 (q, J=7.2, 2H), 5.12 (t, J=7.4, 1H), 7.54 (dd, J=8.8, 2.2, 1H), 7.81 (d, J=2.2, 1H), 8.08 (d, J=8.8, 1H); Anal. calcd for $C_{12}H_{11}N_2O_4Cl$: C, 50.98; H, 3.92; N, 9.91%; found: C, 50.94; H, 3.76; N, 9.94%.

3h: mp 136-137°C (EtOH); ^{1}H-NMR ($CDCl_3$): 2.97 (s, 3H), 2.98 (s, 3H), 3.03 (d, J=6.2, 1H), 3.05 (d, J=7.4, 1H), 5.17 (dd, J=7.4, 6.2, 1H), 7.51 (dd, J=8.8, 2.2, 1H), 7.82 (d, J=2.2, 1H), 8.03 (d, J=8.8, 1H); LSIMS: 282 (M+H); Anal. calcd for $C_{12}H_{12}N_3O_3Cl$: C, 51.16; H, 4.30; N, 14.92%; found: C, 51.32; H, 4.51; N, 15.18%.

3i: mp 170-171°C (EtOH-benzene); ^{1}H-NMR ($CDCl_3$): 3.02 (dd, J=13.5, 9.8, 1H), 3.30 (dd, J=13.5, 4.5, 1H), 4.94 (dd, J=9.8, 4.5, 1H), 7.18 (dd, J=8.3, 2.2, 1H), 7.40 (d, J=2.0, 1H), 7.46 (d, J=8.3, 1H), 7.55 (dd, J=8.8, 2.2, 1H),

7.72 (d, J=2.2, 1H), 8.12 (d, J=8.8, 1H); MS (m/e): 354, 322, 286, 237, 201, 179, 159; Anal. calcd for $C_{15}H_9N_2O_2Cl_3$: C, 50.66; H, 2.55; N, 7.88%; found: C, 50.61; H, 2.36; N, 7.84%.

3j: oil; ^{1}H-NMR (acetone-d_6): 1.39 (s, 9H), 2.59-3.02(m, 2H), 4.19(dd, J=8.0, 7.1, 1H), 5.00(dq, J=10.1, 1.6, 1H), 5.07(dq, J=17.8, 1.6, 1H), 5.69-5.90(m, 1H), 7.60(dd, J=8.7, 2.3, 1H), 7.65(d, J=2.2, 1H), 8.01(d, J=8.7, 1H).

3k: oil; ^{1}H-NMR ($CDCl_3$): 1.40 (s, 9H), 1.41 (s, 9H), 2.74 (dd, J=16.6, 7.2, 1H), 3.14 (dd, J=16.6, 7.4, 1H), 4.53 (dd, J=7.4, 7.2, 1H), 7.40 (dd, J=8.7, 2.2, 1H), 7.45 (d, J=2.2,1H), 7.95 (d, J=8.7,1H).

3l: mp 124.5-125.5°C (MeOH-H_2O-DMF); ^{1}H-NMR (DMSO-d_6): 2.40 (s,3H), 2.80-3.10 (m, 2H), 4.98 (dq, J=10.1, 1.5, 1H), 5.10 (dq, J=17.1, 1.5, 1H), 5.31 (dd, J=9.4, 6.2, 1H), 5.46-5.68 (m,1H), 7.38-7.49 (m,4H), 7.69-7,76 (m,2H), 7.95 (d, J=9.4, 1H); MS (m/e): 365, 348, 335, 319, 279, 266, 210, 180. Anal. calcd for $C_{17}H_{16}NO_4SCl$: C, 55.81; H, 4.41; N, 3.83%; found: C, 55.83; H, 4.37; N, 3.79%.

3m: mp 160-162°C (EtOH-H_2O-DMF); ^{1}H-NMR (DMSO-d_6): 2.39 (s, 3H), 3.51- 3.55 (m, 2H), 3.88 (s,3H), 5.82-5.98 (m, 1H), 7.06 (dd, J=9.1, 2.8, 1H), 7.10-7.22 (m, 5H), 7.30 (d, J=2.8, 1H), 7.35-7.44 (m, 2H), 7.48-7.56 (m, 2H), 7.84 (d, J=9.1, 1H); Anal. calcd for $C_{22}H_{21}NO_5S$: C, 64.22; H, 5.15; N, 3.40%; found: C, 64.23; H, 5.14; N, 3.00%.

3n: mp 109-110°C (MeOH-H_2O-DMF); ^{1}H-NMR (DMSO-d_6): 2.88-3.11 (m, 2H), 3.88 (s, 3H), 4.96 (dd, J=10.1, 1.7, 1H), 5.09 (dd, J=17.2, 1.7, 1H), 5.48-5.69 (m, 2H), 7.09-7.16 (m, 2H), 7.56-7.64 (m, 4H), 7.68-7.80 (m, 1H), 7.91-7.98 (m, 1H); Anal. calcd for $C_{17}H_{17}NO_5S$: C, 58.77; H, 4.93; N, 4.03%; found: C, 58.59; H, 4.88; N, 3.68%.

3o: waxy solid mp 36-37°C; ^{1}H-NMR (DMSO-d_6): 0.86 (apparent t, 3H), 1.20-1.55 (m, 12H), 1.80-2.10 (m, 2H), 4.65 (dd, J=9.6, 5.4, 1H), 7.73 (dd, J=8.8, 2.3, 1H), 7.86 (d, J=2.3, 1H), 8.11 (d, J=8.8, 1H); MS (m/e): 308, 291, 273, 264, 246; HRMS: 308.1292 (M^+); calcd for $C_{16}H_{21}N_2O_2Cl$: 308.1291.

3p: mp 44-45°C (hexane); ^{1}H-NMR (DMSO-d_6): 0.95 (t, J=7.3, 3H), 1.31-1.68 (m, 2H), 1.78-2.14 (m, 2H), 4.67 (dd, J=9.7, 5.3, 1H), 7.73 (dd, J=8.8, 2.3, 1H), 7.86 (d, J=2.3, 1H), 8.12 (d, J=8.8, 1H). MS (m/e): 238, 221, 211,203, 194, 179; Anal. calcd for $C_{11}H_{11}N_2O_2Cl$: C, 55.35; H, 4.65; N, 11.74%; found: C, 55.40; H, 4.63; N: 11.56%.

Conversion of **3a-p** *into* **4a-p** *(Table 1). General procedures*:

System A: Substrate **3** (1 mmol) was dissolved in dry DMF (5 mL). Et_3N (5 mmol, 0.73 mL) and then Me_3SiCl (5 mmol, 0.63 mL) was added and the reaction mixture was stirred at room temperature until completion (t.l.c. control; 5 min to 3 h). After aqueous work-up product was isolated *via* column chromatography.

System B: Substrate **3** (1 mmol) was dissolved or suspended in MeOH (3 mL), treated with 1M solution of NaOH in MeOH (2 mL), stirred at room temperature until completion and worked-up as above. For **3o** and **3p** better results were obtained with a lower concentration of the substrate so 10 mL of MeOH and 3 mL of 1N methanolic solution of NaOH *per* 1 mmol of substrate was employed.

System C: Substrate **3** (1 mmol) was dissolved in MeOH (5 mL), treated with Et_3N (5 mmol, 0.73 mL) and refluxed in dry atmosphere. After completion the reaction mixture was evaporated to dryness and applied directly on the chromatography column.

System D: Substrate **3** (1 mmol) was dissolved in dry t-butyl alcohol (5 mL) and treated with powdered NaOH (100 mg, 2.5 mmol). Work-up as for systems A or B.

System E: Substrate **3** (1 mmol) was dissolved in dry DMSO (5 mL) and treated with powdered NaOH (120 mg, 3 mmol). Work-up as above.

4a: mp 170-174°C dec. (AcOEt); ^{1}H-NMR ($CDCl_3$) see lit.[4]; ^{1}H-NMR (DMSO-d_6): 5.92 (d, J=12.6, 1H), 6.46 (d, J=17.9, 1H), 6.96 (dd, J=17.9, 12.6, 1H), 7.36 (dd, J=8.8, 1.9, 1H), 7.58 (d, J=8.8, 1H), 7.66 (d, J=1.9, 1H), 12.3 (broad s, 1H); MS (m/e): 218, 202, 189, 174, 166, 155, 139, 114.

4b: mp 171-172.5°C dec. (AcOEt); ^{1}H-NMR (acetone-d_6): 2.33 (dd, J=1.6, 0.9, 3H), 5.66-5.77 (m, 2H), 7.35 (dd, J=8.8, 0.9, 1H), 7.58 (dd, J=8.8, 0.5, 1H), 7.62 (dd, J=0.9, 0.5, 1H); MS (m/e): 232, 216, 203, 189, 179, 168; Anal. calcd for $C_{12}H_9N_2OCl$: C, 61.94; H, 3.90; N, 12.04%; found: C, 61.58; H, 3.74; N, 11.72%.

4c: mp 218-220°C dec. (AcOEt); ^{1}H-NMR (acetone-d_6): 7.31-7.51 (m, 5H), 7.58 (d, J=8.7, 1H), 7.64 (d, J=1.8,1H), 7.69-7.75 (m, 2H), 7.95 (d, J=16.7, 1H); MS (m/e): 294, 278, 263, 251, 242, 217; Anal. calcd for $C_{17}H_{11}N_2OCl$: C, 69.27; H, 3.76; N, 9.51%; found: C, 68.87; H, 3.60; N, 9.36%.

4d: dec. at ~ 150°C (AcOEt); ^{1}H-NMR (acetone-d_6): 5.89 (dd, J=11.8, 0.9, 1H), 6.53 (dd, J=18.0, 0.9, 1H), 7.02 (dd, J=18.0, 11.8, 1H), 7.47 (dd, J=8.7, 1.6, 1H), 7.54 (dd, J=8.7, 0.7, 1H), 7.78 (dd, J=1.6, 0.7, 1H); MS (m/e): 264, 262, 248, 246, 237, 235, 220, 218, 209, 207, 166, 155; HRMS: 261.9743 (M^+); calcd for $C_{11}H_7N_2O^{79}Br$: 261.9742.

4e: dec. at ~ 165°C (AcOEt); ^{1}H-NMR (acetone-d_6): 3.88 (s, 3H), 5.77 (dd, J=11.8, 1.0, 1H), 6.45 (dd, J=18.0, 1.0, 1H), 6.90-7.07 (m, 3H), 7.43 (dd, J=8.9, 0.6, 1H); MS (m/e): 214, 198, 183, 155, 128; HRMS: 214.0737 (M^+); calcd for $C_{12}H_{10}N_2O_2$: 214.0742.

4f: mp ~ 166-168°C dec (AcOEt); ^{1}H-NMR (acetone-d_6): 3.97 (s, 3H), 5.84 (dd, J=11.8, 0.9, 1H), 6.50 (dd, J=18.0, 0.9, 1H), 6.75 (d, J=8.8, 1H), 7.02 (dd, J=18.0, 11.8, 1H), 7.84 (d, J=8.8, 1H); MS (m/e): 215, 198, 186, 170, 156, 143, 129; HRMS: 215.0689 (M^+); calcd for $C_{11}H_9N_3O_2$: 215.06948.

4g: mp 136-139°C (AcOEt-hexane); ^{1}H-NMR (acetone-d_6): 1.43 (t, J=7.1, 3H), 4.49 (q, J=7.1, 2H), 7.52 (dd, J=8.9, 1.9, 1H), 7.72 (dd, J=8.9, 0.7, 1H), 7.77 (dd, J=1.9, 0.7, 1H); MS (m/e): 264, 248, 218, 202,174, 164, 148, 139; Anal. calcd for $C_{12}H_9N_2O_3Cl$: C, 54.45; H, 3.45; N, 10.59%; found: C, 54.48; H, 3.12; N, 10.51%.

4h: mp 207-209°C dec. (EtOH-H_2O); ^{1}H-NMR (acetone-d_6): 3.11 (s, 3H), 3.16 (s, 3H), 7.43 (dd, J=8.8, 1.9, 1H), 7.63 (dd, J=8.8, 0.6, 1H), 7.67 (dd, J=1.9, 0.6, 1H); MS (m/e): 263, 247, 218, 203, 190, 176, 148; HRMS: 263.0462 (M^+), calcd for $C_{12}H_{10}N_3O_2Cl$: 263.0461.

4i: mp 248-250°C (AcOEt); ^{1}H-NMR (acetone-d_6 + DMSO-d_6): 7.42 (dd, J=8.8, 1.9, 1H), 7.68 (dd, J=8.8, 0.6, 1H), 7.70 (dd, J=1.9, 0.6, 1H), 7.86 (dd, J=8.4, 0.5, 1H), 7.93 (dd, J=8.4, 1.9. 1H), 8.16 (dd, J=1.9, 0.5, 1H); MS (m/e): 336, 320, 301, 285, 273, 258, 250; Anal. calcd for $C_{15}H_7N_2OCl_3$: C, 53.36; H, 2.09; N, 8.30%; found: C, 53.11; H, 1.99; N, 8.13%.

4j: dec. at 134°C (AcOEt); ^{1}H-NMR (acetone-d_6): 1.65 (s, 9H), 5.67 (dd, J=12.3, 1.8, 1H), 6.52 (dd, J=18.3, 1.8, 1H), 7.26 (dd, J=8.7, 2.1, 1H), 7.49 (dd, J=8.7, 0.6, 1H), 7.59 (dd, J=18.3, 12.3, 1H), 8.09 (dd, J=2.1, 0.6, 1H); MS (m/e): 293, 277, 237, 220, 204, 192; HRMS: 293.0817 (M^+), calcd for $C_{15}H_{16}NO_3Cl$: 293.08619.

4k: mp 183-185°C dec. (hexane); ^{1}H-NMR (acetone-d_6): 1.61 (s, 9H), 1.63 (s, 9H), 7.34 (dd, J=8.8, 2.0, 1H), 7.54 (dd, J=8.8, 0.6, 1H), 8.08 (dd, J=2.0, 0.6, 1H), 11.25 (broad s, 1H); Anal. calcd for $C_{18}H_{22}NO_5Cl$: C, 58.77; H, 6.21; N, 3.79%;found: C, 58.75; H, 6.21; N, 3.70%.

4l: mp 196-197°C dec. (MeCN-H_2O); ^{1}H-NMR (DMSO-d_6): 2.32 (s, 3H), 5.91 (dd, J=12.3, 1.6, 1H), 6.56 (dd, J=17.9, 1.6, 1H), 7.27-7.43 (m, 4H), 7.55 (d, J=8.7, 1H), 7.75-7.82 (m, 2H), 7.99 (d, J=1.9, 1H), 12.27 (s, 1H); MS (m/e): 347, 331, 301, 283, 266, 231, 217; Anal. calcd for $C_{17}H_{14}NO_3SCl$: C, 58.70; H, 4.06; N, 4.03%; found: C, 58.60; H, 3.87; N, 4.30%.

4m: mp 176-177°C (AcOEt-hexane); ^{1}H-NMR (DMSO-d_6): 2.29 (s, 3H), 3.85 (s, 3H), 7.00 (dd, J=8.9, 2.4, 1H), 7.21-7.29 (m, 2H), 7.41-7.56 (m, 9H), 11.71 (s, 1H); Anal. calcd for $C_{22}H_{19}NO_4S$: C, 67.16; H, 4.87; N, 3.56%; found: C, 67.11; H, 4.70; N, 3.63%.

4n: dec. at 185°C (MeCN); ^{1}H-NMR (DMSO-d_6): 3.84 (s, 3H), 5.81 (dd, J=12.3, 1.7, 1H), 6.42 (dd, J=18.0, 1.7, 1H), 6.99 (dd, J=9.0, 2.4, 1H), 7.36 (dd, J=18.0, 12.3, 1H), 7.42 (d, J=9.0, 1H), 7.47 (d, J=2.4, 1H), 7.50-7.62 (m, 3H), 7.86-7.93 (m, 2H), 12.07 (s, 1H); Anal. calcd for $C_{17}H_{15}NO_4S$: C, 61.99; H, 4.59; N, 4.25%; found: C,

61.61; H, 4.48; N, 4.97%.

4o: mp 114-115°C (CCl_4-hexane); ^{1}H-NMR (DMSO-d_6): 0.85 (apparent t, 3H), 1.14-1.42 (m, 8H), 1.66-1.80 (m, 2H), 2.90 (t, J=7.4, 2H), 7.31 (dd, J=8.7, 1.9, 1H), 7.53 (dd, J=8.7, 0.6, 1H), 7.60 (dd, J=1.9, 0.6, 1H), 12.06 (s, 1H); MS (m/e): 290, 274, 261, 245, 231, 217, 206, 189; Anal. calcd for $C_{16}H_{19}N_2OCl$: C, 66.08; H, 6.59; N, 9.64%; found: C, 65.96; H, 6.78; N, 9.39%.

4p: mp 188-189°C (AcOEt-CCl_4); ^{1}H-NMR (DMSO-d_6): 1.32 (t, J=7.5, 3H), 2.93 (q, J=7.5, 2H), 7.31 (dd, J=8.7, 1.9, 1H), 7.54 (dd, J=8.7, 0.6, 1H), 7.61 (dd, J=1.9, 0.6, 1H), 12.07 (s, 1H); MS (m/e): 220, 205, 192, 189, 177, 164, 153, 140. Anal. calcd for $C_{11}H_9N_2OCl$: C, 59.87; H, 4.11; N, 12.69%; found: C, 59.47; H, 3.91; N, 12.50%.

Reduction of N-hydroxyindoles **4** *to indoles* **7** *(Table 2). General procedure*: suspension of Zn dust (325 mg, 5 mmol, 10-fold excess) and 1-hydroxyindole (0.5 mmol) in 3 mL of glacial acetic acid was stirred at reflux until completion of the reaction (3-5 h). After quenching with 10% aq. HCl followed by the extraction with AcOEt product was isolated *via* column chromatography.

7a: mp 204-205°C (AcOEt-hexane); ^{1}H-NMR see ref.4; MS (m/e): 202, 189, 174, 167, 140; Anal. calcd for $C_{11}H_7N_2Cl$: C, 65.19; H, 3.48; N, 13.83%; found: C, 64.80; H, 3.53; N, 13.93%.

7b: mp 190-194°C (AcOEt-hexane); ^{1}H-NMR (acetone-d_6): 2.34 (dd, J=1.5, 0.9, 3H), 5.54-5.56 (m, 1H), 5.95-5.97 (m, 1H), 7.28 (dd, J=8.7, 2.0, 1H), 7.51 (dd, J=8.7, 0.6, 1H), 7.62 (dd, J=2.0, 0.6, 1H), 11.4 (broad s, 1H); MS (m/e): 216, 203, 194, 181, 166, 154; Anal. calcd for $C_{12}H_9N_2Cl$: C, 66.52; H, 4.19; N, 12.93%; found: C, 66.67; H, 4.20; N, 12.62%.

7c: mp 295-298°C (AcOEt-hexane); ^{1}H-NMR (acetone-d_6): 7.29 (dd, J=8.7, 2.0, 1H), 7.34 (d, J=16.6, 1H), 7.40-7.56 (m, 4H), 7.62 (d, J=16.6, 1H), 7.63 (dd, J=2.0, 0.4, 1H), 7.67-7.73 (m, 2H); Anal. calcd for $C_{17}H_{11}N_2Cl$: C, 73.25; H, 3.98; N, 10.05%; found: C, 73.28; H, 3.76; N, 9.99%.

7d: mp 222-224°C (AcOEt-hexane); ^{1}H-NMR (acetone-d_6): 5.75 (d, J=11.3, 1H), 6.24 (d, J=17.8, 1H), 6.95 (dd, J=17.8, 11.3, 1H), 7.42 (dd, J=8.7, 1.7, 1H), 7.55 (dd, J=8.7, 0.8, 1H), 7.79 (dd, J=1.7, 0.8, 1H), 11.54 (broad s, 1H); MS (m/e): 248, 246, 235, 233, 167, 154, 140; Anal. calcd for $C_{11}H_7N_2Br$: C, 53.46; H, 2.86; N, 11.34%; found: C, 53.32; H, 2.80; N, 11.18%.

7e: mp above 250°C; ^{1}H-NMR (acetone-d_6 DMSO-d_6): 7.34 (dd, J=8.7, 2.0, 1H), 7.62 (dd, J=8.7, 0.6, 1H), 7.67 (d, J=2.0, 0.6, 1H), 7.87 (d, J=8.5, 1H), 8.06 (dd, J=8.5, 2.1, 1H), 8.26 (d, J=2.1, 1H). Anal. calcd for $C_{15}H_7N_2Cl_3$: C, 56.01; H, 2.20; N, 8.71%; found: C, 56.11; H, 2.12; N, 8.70%.

7f: mp 193-195°C (EtOH-DMF-H_2O); ^{1}H-NMR (acetone-d_6): 2.36 (s, 3H), 5.72 (d, J=11.6, 1H), 6.10 (d, J=18.0, 1H), 7.25 (dd, J=8.6, 2.0, 1H), 7.35-7.41 (m, 2H), 7.45 (dd, J=8.6, 0.6, 1H), 7.65 (dd, J=18.0, 11.6, 1H), 7.85-7.92 (m, 2H), 8.05 (dd, J=2.0, 0.6, 1H); Anal. calcd for $C_{17}H_{14}NO_2SCl$: C, 61.53; H, 4.25; N, 4.22%; found: C, 61.47; H, 4.30; N, 4.33%.

Allylation of 1-nitro-2-cyanomethylnaphthalene (eq. 2): 1-nitro-2-cyanomethylnaphthalene **5** (424 mg, 2 mmol) was dissolved in 7.5 mL of MeOH and treated with NaOH (200 mg, 5 mmol). After stirring for 10 min the deep blue solution was treated with allyl bromide (260 μL, 3 mmol) and stirred at room temperature for 3.5 h. After acidic work-up the mixture was chromatographed on silica gel to yield **4r** (54 mg, 11.5%) and **6** (167 mg, 30.5%).

4r: dec. at 180°C; ^{1}H-NMR (acetone-d_6): 5.80 (dd, J=11.8, 1.9, 1H), 6.47 (dd, J=17.9, 1.2, 1H), 7.11 (dd, J=17.9, 11.8, 1H), 7.51-7.67 (m, 2H), 7.68 (d, J=8.7, 1H), 7.75 (d, J=8.7, 1H), 8.00-8.06 (m, 1H), 8.91-8.96 (m, 1H), 11.45 (broad s, 1H); MS (m/e): 234, 218, 217, 205, 190, 164; HRMS: 234.0803 (M^+); calcd for $C_{15}H_{10}N_2O$: 234.0804.

6: oil; NMR ($CDCl_3$): 4.87 (dd, J=1.2, 0.9, 1H), 4.90 (dd, J=1.2, 0.9, 1H), 5.48 (ddd, J=10.3, 1.5, 0.8, 1H), 5.58 (ddd, J=17.2, 2.8 1.4, 1H), 5.88 (dd, J=12.2, 0.8, 1H), 6.19-6.39 (m, 1H), 6.49 (dd, J=17.8, 0.8, 1H), 7.08 (dd,

J=17.8, 12.8, 1H), 7.56-7.74 (m, 2H), 7.70 (d, J=8.8, 1H), 7.79 (d, J=8.8, 1H), 8.07 (dd, J=8.0, 1.5, 1H), 8.66 (ddd, J=8.2, 1.4, 0.6, 1H); MS (m/e): 274, 257, 244, 233, 217, 205, 190, 178, 164; HRMS: 274.1130 (M^+); calcd for $C_{18}H_{14}N_2O$: 274.1134.

Conversion of **3a** *to* **4a** *in various base-solvent systems (Table 3).* Reactions were carried out as described above (see procedures A-E).

Reaction of **3a** *with triethylamine in CH_3OD (eq. 4)*: Substrate **3a** (118 mg, 0.5 mmol) was dissolved in CH_3OD (2.5 mL,99.5% of D-atoms, Fluka), treated with triethylamine (0.36 mL, 2.5 mmol) and kept at 55°C for 2 h. After this time silica gel (~0.5 g) was added, the mixture evaporated to dryness and chromatographed to yield **3a-D** (60 mg, 50%) and **4a** (33 mg, 30%).

3a-D: ^{1}H-NMR (500 MHz, $CDCl_3$): 2.67 (two groups of 4 signals, 2H, allyl CH_2), 5.21-5.27 (m, 1H, vinyl CH), 5.81-5.90 (m, 10 signals, 2H, vinyl CH_2), 7.50 (dd, J=8.8, 2.2, 1H), 7.75 (d, J=2.2, 1H), 8.06 (d, J=8.8, 1H). For comparison: **3a**: ^{1}H-NMR (500 MHz, $CDCl_3$): 2.67 (two groups of 5 signals, everyone with subtle splitting structure, 2H, allyl CH_2), 4.84 (dd, J=8.5, 5.2, 1H, benzyl CH), 5.21-5.27 (m, 1H, vinyl CH), 5.81-5.90 (m, 10 signals, 2H, vinyl CH_2), 7.50 (dd, J=8.8, 2.2, 1H), 7.75 (d, J=2.2, 1H), 8.06 (d, J=8.8, 1H).

Preparation of the model compound **13.**[9]

Condensations of 4-chlorobenzaldehyde with 5-fluoro-2-nitrophenylacetonitrile and methyl cyanoacetate were performed under standard conditions with catalytic amount of piperidine and acetic acid and benzene as azeotroping agent.

26: yield 66%; mp 152-154°C (MeOH-benzene); ^{1}H-NMR (DMSO-d_6): 7.60-7.71 (m, 3H), 7.81 (s, 1H), 7.83 (dd, J=9.0, 2.8, 1H), 7.90-7.98 (m, 2H), 8.33 (dd, J=9.2, 5.1, 1H); Anal. calcd for $C_{15}H_8N_2O_2ClF$: C, 59.52; H, 2.66; N, 9.25%; found: C, 59.80; H, 2.40; N, 9.27%.

27: mixture of geometric isomers ,yield 94%; mp 116-119°C (EtOH); ^{1}H-NMR (acetone-d_6): 3.91 (s, 3H), 6.63-7.71 (m, 2H), 8.02 (s, 0.2 H), 8.09-8.16 (m, 2H), 8.36 (s, 0.8H); Anal. calcd for $C_{11}H_8NO_2Cl$: C, 59.61; H, 3.64; N, 6.32%; found: C, 59.60; H, 3.36 N, 6.51%.

Reduction of 4-chlorobenzylidene derivative **27**. The reaction was carried out similarly to the described procedure[20]. Compound **27** (1.7 g, 7.7 mmol) was suspended in dry DMF (5 ml) treated with 99% formic acid (0.87 mL) and Et_3N (1.28 mL), then heated at 60°C with stirring until gas evolution ceased (about 4 h). The reaction was then evaporated to drynes, the residue dissolved in CH_2Cl_2, washed with water, dried and evaporated to yield 1.52 g of **28** (88%) sufficiently pure for the next step. ^{1}H-NMR ($CDCl_3$): 3.22 (ABX, J_{AB}≈13.0, J_{AX}=8.0, J_{BX}=5.9, 2H), 3.73 (dd, J_{AX}=8.0, J_{BX}=5.9, 1H), 3.80 (s, 3H), 7.19-7.35 (m, 4H).

Reaction of 26 with 28 to form 13: Compounds **26** (750 mg, 2.48 mmol) and **28** (1378 mg, 6.18 mmol) in dry MeCN (25 mL) were treated with Et_3N (4.5 mL, 32 mmol) and heated to reflux for 1.5h with the exlusion of moisture. After that time substrate **26** was completly consumed (tlc control). The reaction mixture was evaporated to dryness and passed through a short column (silica gel, hexane-AcOEt system (4:1) as eluent) to remove tars. The two-components mixture thus obtained was dissolved in MeOH (100 mL), treated with concd. aq. ammonia (20 mL) and heated to reflux for 30 s. After cooling and acidifation the reaction mixture was extracted with methylene diachloride and produced separated *via* column chromatography to yield 225 mg of **13** (20% on **26**).

13: mp 160-162°C (EtOH-AcOEt-hexane); ^{1}H-NMR ($CDCl_3$): 3.22 (d, J=6.8, 1H), 3.24 (d, J=7.0, 1H), 4.17 (t, J=7.0, 6.8, 1H), 6.93 (s, 1H), 7.01-7.08 (m, 2H), 7.22 (d, J=2.1, 1H), 7.30-7.37 (m, 2H), 7.44-7.51 (m, 2H), 7.50 (dd, J=8.6, 2.1, 1H), 7.78-7.86 (m, 2H), 8.16 (d, J=8.6, 1H); MS (m/e): 447, 413, 290, 125. Anal. calcd for $C_{24}H_{15}N_3O_2Cl_2$: C, 64.44; H, 3.16; N, 9.40%; found: C, 64.44; H, 3.04; N, 9.41%.

Reactions of **13** in different systems were performed as described above. Product **16** was isolated after dilution

of the reaction mixture with aq. HCl, filtering the precipitate and recrystallization from aq. DMF (95% yield). **16**: dec. >250°C (DMF-H_2O); ^{1}H-NMR (500 MHz, DMSO-d_6): 7.61 (d, J=8.5, 1H), 7.70-7.83 (m, 4H), 7.91-8.02 (m, 6H), 8.14 (s, 1H), 12.48 (broad s, 1H); MS (m/e): 429, 413, 377, 343, 315; HRMS: 429.0438 (M^+), calcd for $C_{24}H_{13}N_3OCl_2$: 429.0436.

Synthesis of compound 17. (i) *Reaction between 1-acenaphthenone and 2-fluoronitrobenzene*: A solution of 1-acenaphthenone (840 mg, 5 mmol) in dry DMF (3 mL) was added to a stirred suspension of NaH (5.5 mmol) in dry DMF (3 mL) at RT. After gas evolution ceased (30 min), the resulting blue solution was treated with 2-fluoronitrobenzene (530 µL, 5 mmol) in dry DMF (2 mL) and stirred at RT for 20 min. Acidic work-up and chromatograpy on silica gel (CCl_4-AcOEt (100:1) as eluent) yielded 800 mg (55%) of 2-(2-nitrophenyl)acenaphthenone: mp 110-112°C (AcOEt); NMR (500 MHz, DMSO-d_6): 5.76 (s, 1H), 7.30-7.36 (m, 1H), 7.46-7.51 (m, 1H), 7.61-7.67 (m, 2H), 7.71-7.79 (m, 1H), 7.88 (dd, J=8.1, 7.0, 1H), 8.00 (d, J=8.5, 1H), 8.02 (d, J=7.0, 1H), 8.06 (dd, J=8.1, 1.2, 1H), 8.33 (d, J=8.1, 1H); MS (m/e): 289, 288, 272, 271, 259, 244, 228; Anal. calcd for $C_{18}H_{11}NO_3$: C, 74.73; H, 3.83; N, 4.84%; found: C, 74.78; H, 3.56; N, 4.76%.

(ii) *Reduction of 2-(2-nitrophenyl)acenaphthenone*: substrate (289 mg, 1 mmol) was dissolved in trifluoroacetic acid (2.5 mL) and the red solution formed was treated with triethylsilane (700 µL, 4.4 mmol). After stirring overnight ar RT the reaction was evaporated to drynes and chromatographed to give oil which triturated with hexane yielded 40 mg (14.5%) of **17** as yellow crystals.

17: mp 68-70°C (hexane); NMR (500 MHz, DMSO-d_6): 3.33 (dd, J=17.7, 3.9, 1H), 4.04 (dd, J=17.7, 8.7, 1H), 5.28 (dd, J=8.7, 3.9, 1H); 6.99 (ddd, J=7.8, 1.3, 1H), 7.15 (dd, J=7.4, 0.5, 1H), 7.38 (dd, J=7.4, 0.4, 1H), 7.48-7.52 (m, 2H), 7.53-7.58 (m, 2H), 7.73 (dd, J=8.2, 0.5, 1H), 7.75 (d, J=5.2, 1H), 7.97 (dd, J=8.2, 1.3, 1H): MS (m/e): 275, 274, 258, 256, 246, 241, 226, 215; Anal. calcd for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09%; found: C, 78.39; H, 4.68; N, 5.08%.

Synthesis of 2-(2-nitrophenyl)acenaphthylene **22**:

(i) *Reduction of 2-(2-nitrophenyl)acenaphthenone*: The title compound (145 mg, 0.5 mmol) was dissolved in hot MeOH (25 mL) and treated with $NaBH_4$ (about 50 mg) added in one portion. Initial deep navy-blue colour vanished after a few minutes indicating the end of the reaction. After acidic work-up followed by column chromatography 141 mg (97%) of 1-hydroxy-2-(2-nitrophenyl)acenaphthene was obtained: mp 123-124°C (AcOEt-hexane); NMR (500 MHz, DMSO-d_6): 4.49 (d, J=6.9, 1H), 5.59 (d, J=7.1, 1H), 5.82 (, J=7.0, 1H), 6.98 (dd, J=7.5, 1.0, 1H), 7.19 (d, J=7.0. 1H), 7.46-7.53 (m, 3H), 7.56 (dd, J=8.2, 7.0, 1H), 7.65 (dd, J=8.2, 6.9, 1H), 7.79 (d, J=8.2, 1H), 7.84 (d, J=8.2, 1H), 8.05 (dd, J=7.0, 1.6, 1H); MS (m/e): 291, 290, 272, 256, 246, 228, 215; Anal. calcd for $C_{18}H_{13}NO_3$; C, 74.21; H, 4.50; N, 4.81%; found: C, 74.32; H, 4.29; N, 4.50%.

(ii) *Dehydration of 1-hydroxy-2-(2-nitrophenyl)acenaphthene to 2-(2-nitrophenyl)acenaphthylene* **22**: Starting alcohol (740 mg, 2.54 mmol) dissolved in CH_2Cl_2 (30 mL) and dry pyridine (1 mL) was treated at O°C with methanesulfonyl chloride (0.25 mL, ~2.8 mmol). After stirring at RT for 5h, acidic work-up and column chromatography 416 mg (60%) of **22** was obtained: mp 119-120°C (EtOH-hexane); NMR (500 MHz, DMSO-d_6): 7.26 (s, 1H), 7.51 (d, J=6.8, 1H), 7.61 (dd, J=8.1, 7.0, 1H), 7.67 (dd, J=8.2, 6.9, 1H), 7.71 (m, 1H), 7.80 (dd, J=7.6, 1.4, 1H), 7.85 (m, 1H), 7.89 (d, J=6.8, 1H), 8.00 (dd, J=8.1, 6.0, 2H), 8.11 (dd, J=8.1, 1.1, 1H); MS (m/e): 273, 272, 256, 244, 226, 213, 200, 189; Anal. calcd for $C_{18}H_{11}NO_2$; C, 79.11, H, 4.06; N, 5.13%, found: C, 79.03; H, 4.10; N, 5.16%.

Reaction of **17** *in NaOH/DMSO system*: To **17** (180 mg, 0.665 mmol) dissolved in dry DMSO (3 mL), powdered NaOH (130 mg, 3.25 mmol) was added. After stirring at ambient temperature for 1h the reaction mixture was worked-up and chromatographed yielding 130 mg of product which shows one spot on tlc. MS (m/e): 241;

LSIMS: 257, 241. NMR (500 MHz, DMSO-d_6): 6.62-8.31 (complicated sets of multiplets), 11.82 and 11.95 (two s, ratio 4:1)

(i) *Reduction* of the above mixture was performed as follows: 30 mg of the mixture and 100 mg of Zn dust were stirred and refluxed in glacial acetic acid (2 mL) for 4h. Work-up followed by column chromatography yield 22 mg of pure **19** (about 75%).

19: mp 232-235°C (AcOEt-hexane); NMR (500 MHz, DMSO-d_6): 7.03-7.13 (m, 1H); 7.44-7.48 (m, 1H), 7.51 (dd, J=8.3, 6.8, 1H), 7.57 (dd, J=7.8, 7.2, 1H), 7.64 (dd, J=8.3, 0.5, 1H), 7.78-7.87 (m, 5H), 11.95 (s, 1H); MS (m/e): 241, 213, 187; calcd for $C_{18}H_{11}N$: C, 89.60; H, 4.60; N, 5.80%; found: C, 89.54; H, 4.62; N, 5.60%.

(ii) *Methylation* of the mixture was performed as follows: 32 mg of the mixture and K_2CO_3 (50 mg) were stirred in DMF (0.5 mL) while 0.1 mL of methyl iodide was added. The resulted mixture was stirred about 40 h at room temperature, worked-up and chromatographed to yield **20** 12 mg, about 30%) and **21** (12 mg, about 30%).

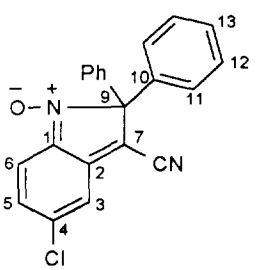
20: mp 128-129°C; NMR (500 MHz, DMSO-d_6): 4.27 (s, 3H), 7.21-7.29 (m, 2H), 7.56-7.60 (m, 2H), 7.67 (dd, J=8.2, 6.9, 1H), 7.75 (d, J=6.9, 1H), 7.91-7.98 (m, 4H); MS (m/e): 271, 240, 213; HRMS: 271.0996 (M^+) Anal. calcd for: $C_{19}H_{13}NO$: 271.0997.

21: mp 182-184°C; NMR (500 MHz, DMSO-d_6): 4.10 (s, 3H), 7.15-7.21 (m, 2H), 7.54-7.57 (m, 2H), 7.62 (dd, J=8.2, 6.9, 1H), 7.68 (dd, J=7.9, 0.4, 1H), 7.85 (d, J=8.2, 1H), 7.87 (d, J=7.6, 1H), 7.89 (ddd, J=8.3, 1.3, 0.7, 1H), 8.06 (d, J=7.0, 1H); MS (m/e): 255, 240, 226, 213; HRMS: 255.1050 (M^+); calcd for $C_{19}H_{13}N$: 255.1048.

Reduction of compound **22** *with* $SnCl_2 2H_2O$: $SnCl_2 2H_2O$ (680 mg, 3 mmol) was added to a solution of **22** (82 mg, 0.75 mmol). The resulted mixture was heated to reflux for 3h , worked-up and chromatographed to yield 41 mg of crude **19** (57%). ^{1}H-NMR spectrum confirmed the structure of **19** accompanied with some impurities.

Synthesis of compound **23**. 5-Chloro-2-nitrophenyl acetonitrile (983 mg, 5 mmol) was dissolved in 10 mL of dry MeCN and treated succesively with K_2CO_3 (1.8 g, 15 mmol), tetrabutyl-ammonium bromide (30 mg) and an excess of benzhydryl chloride (2.5 mL). After stirring for 5 h the reaction was worked-up and product separated from multicomponent mixture via column chromatography. Yield 325 mg (18%).

23: mp 100-102°C (MeOH-H_2O); NMR ($CDCl_3$): 4.42 (d, J=7.9, 1H), 5.77 (d, J=7.9, 1H), 7.13-7.42 (m, 12H), 7.87 (d, J=9.2, 1H).



Conversion of **23** to **24** was carried out according to procedures A or B (95%).

24: mp 129-130°C (MeOH); NMR (500 MHz, $CDCl_3$): 7.00 (d, J=1.6, 1H), 7.24-7.27 (m, 5H), 7.40 (dd, J=1.6, 1.0, 1H), 7.45-7.51 (m, 6H); MS (m/e): 344, 327, 315, 300, 292, 277. HRMS: 344.0768 (M^+), calcd for $C_{21}H_{13}N_2OCl$: 344.0769; ^{13}C-NMR (see picture): 142.03 (C-2), 140.94 (C-4), 140.60 (C-1), 134.91 (C-10), 132.40 (C-3), 129.56 (C-13), 129. 14 (C-11), 128.26 (C-12), 120.55 (C-5), 117.80 (C-6), 114.47 (C-8), 104.98 (C-7), 92.88 (C-9); ^{14}N-NMR ($CDCl_3$): 0-150 (broad signal with max. about - 80 ppm), -71.2 (sharp signal, CN).

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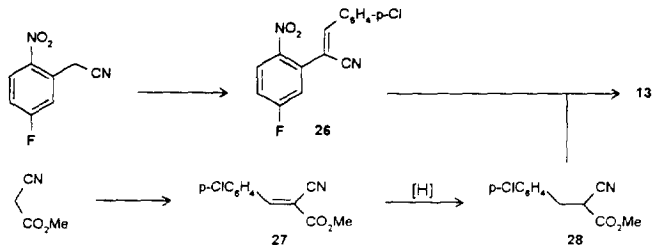
9. This compound was synthesized according to the scheme:



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