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Michael reaction of indoles with 3-(2′-nitrovinyl)indole under solvent-free conditions and in solution. An efficient synthesis of 2,2-bis(indolyl)nitroethanes and studies on their reduction

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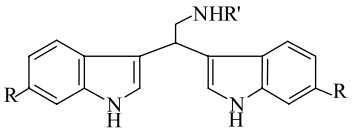
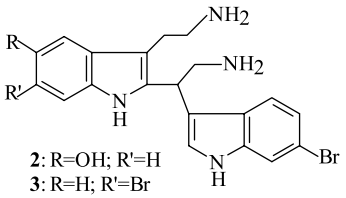
Abstract—Michael reaction of 3-(2′-nitrovinyl)indole with eight 3-unsubstituted indoles on TLC-grade silica gel furnished unsymmetrical bis(indolyl)nitroethanes in 7–12 min under microwave irradiation and in 8–14 h at rt. In contrast, the *p*-TsOH-catalysed reaction of the nitrovinylindole with the 3-unsubstituted and two 3-substituted indoles in solution under reflux furnished both unsymmetrical and symmetrical bis(indolyl)nitroethanes, the latter resulting from novel tandem Michael addition–elimination–Michael addition reactions. The synthesis of a 2′,3″-bis(indolyl)nitroethane, the precursor core structure of two bioactive marine metabolites, and the reduction of 2,2-bis(3′-indolyl)nitroethane to the corresponding ethylamine, isolated as its *N*-acetyl derivative, have been achieved. Significantly, attempted hydrolysis of three nitronates, derived from the corresponding bis(indolyl)nitroethanes, with buffered aqueous $TiCl_3$ has led to the first isolation of oximes (*syn*/*anti*-mixture) as the only products.

1. Introduction

Bis(indolyl)alkanes, -alkylamines, -alkanols, -alkanals and -alkanoic acids, often with bromo and hydroxy substituents in the benzenoid rings, constitute a small group of bisindoles of synthetic as well as natural origins (both terrestrial and marine). Some of these compounds are reported to be significantly bioactive as, for example, coronary dilator,[1] plant hormone,[2a,b] hallucinogen,[3] antibacterial,[4] DNA-damaging,[5] antiserotonin activity, strong affinity for somatostatin and neuropeptide Y receptors in recepter-binding assays[6] and anticarcinogen.[7a,b] In our recent review on this class of compounds,[8] we stated that bioactive 2,2-bis(indolyl)ethylamines (BIEAs), earlier reported to be only of synthetic origin,[1] have recently been reported from marine sources as well, for example, the BIEAs **1** from a tunicate[9] and **2** and **3** from a sponge.[6]



1: R=Br; R'=H
4: R=H; R'=COPh



2: R=OH; R'=H
3: R=H; R'=Br

Although a BIEA (**4**) was first synthesised by the reaction of 3-indolylmagnesium iodide with benzamidoacetaldehyde,[10] the first general synthesis of BIEAs, only symmetrical ones, involved mainly the acid-catalysed reaction of indoles with *N*,*N*-dialkylaminoalkanals or their diethylacetals.[1] The second synthesis of BIEAs comprised the reaction of indoles with nitrones or 3-indolylhydroxylamines using trimethylsilyl chloride as an activator.[11a,b] But both these routes often required long reaction periods (up to 60 h) and furnished BIEAs in very low (e.g., 7%) or wide ranging yields (31–92%). We, therefore, intended to synthesise 2,2-bis(indolyl)nitroethanes (BINEs) which, upon subsequent reduction, should furnish BIEAs.

In this context, our attention was drawn to the fact that, although the Michael addition of nucleophilic indoles to nitroolefins has been well studied,[12a–c] the use of 3-(2′-nitrovinyl)indole (**5**) as a Michael acceptor in its reaction

Keywords: 3-(2′-Nitrovinyl)indole; Indoles; Michael reaction; Bis(indolyl)nitroethanes; Reduction; Oximes (*syn*/*anti*-).
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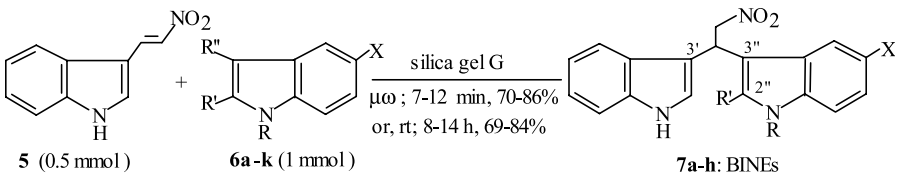


Scheme 1.

Table 1. Reaction of **5** with **6** on TLC-grade silica gel (5 g)

Indoles (**6**)					BINEs (**7**)			
Sl. No.	R	R′	R″	X	μω		rt	
					Time (min)	Yield (%)	Time (h)	Yield (%)
6a	H	H	H	H	10	86	14	82
6b	Me	H	H	H	9	85	9	84
6c	Me	H	H	Br	9	73	10	72
6d	Et	H	H	H	8.5	71	8	70
6e	^{i}Pr	H	H	H	9	75	9.5	72
6f	H	Me	H	H	7	70	8	69
6g	H	H	H	Br	10	83	9	82
6h	Me	Me	H	H	12	78	11	76
6i[a]	H	H	Me	H	—	—	—	—
6j[a]	Me	H	Me	H	—	—	—	—
6k[a]	Ac	H	H	H	—	—	—	—

[a] No reaction occurred.

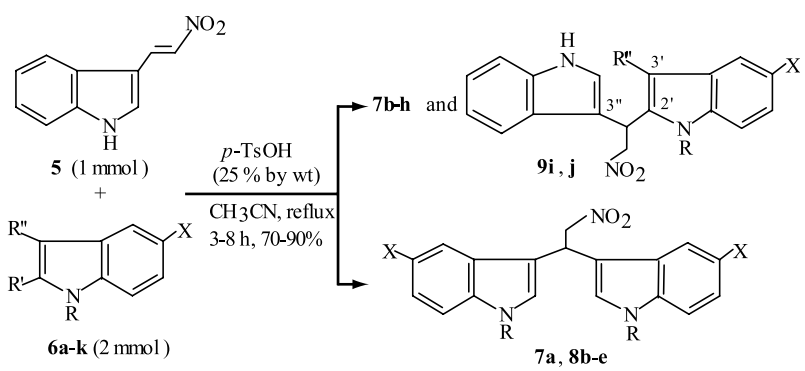
with indoles as nucleophiles has never been reported. We, therefore, developed an efficient synthesis of BINEs by the Michael reaction of **5** with 3-unsubstituted indoles (**6a**–**f**) on TLC-grade silica gel (acting as a mild acidic catalyst) under microwave irradiation or at rt to furnish in high yields the BINEs **7a**–**f**,[13] all but one (**7a**) of which were unsymmetrical. We have now extended this reaction to other substrates and have overcome the failures encountered in some cases by carrying out the Michael reaction in conventional solution phase in the presence of a protic acid catalyst to furnish both unsymmetrical and symmetrical BINEs, the latter resulting from novel tandem reactions. We applied our solution phase protocol for the synthesis of a 2′,3″-BIEA which forms the precursor to the core structure of two naturally occurring bioactive BIEAs. Further, as originally targeted, a BINE was successfully reduced to the corresponding BIEA. Moreover, while trying to convert some of the BINEs to the respective bis(indolyl)alkanals with aqueous $TiCl_3$, the respective oximes were isolated as the only products for the first time. The significance of these observations and the results are presented in this report.

2. Results and discussion

In our preliminary communication,[13] we reported that when **5**,[14] prepared by Henry reaction of 3-formylindole, was allowed to react with indole (**6a**) and the 3-unsubstituted indoles (**6b**–**f**) on TLC-grade silica gel, only the unsymmetrical BINEs (**7b**–**f**; also **7a**, which is clearly a symmetrical BINE) were formed in high yields, expeditiously (7–12 min) under microwave irradiation and in a much longer period (8–14 h) at rt. The reaction with **5** has now been extended to 5-bromoindole (**6g**), 1,2-dimethylindole (**6h**), skatole (**6i**), 1-methylskatole (**6j**) and 1-acetylindole (**6k**). 1-Acetylindole (**6k**) failed to react obviously due to its lack of nucleophilicity. Surprisingly, however, both the 3-methylindoles (**6i**,**j**) also met with failure, which is rather baffling. The results are shown in Scheme 1, Table 1.

In order to account for this failure, we reasoned that silica gel is not acidic enough to bring about the desired Michael addition of **6i** and **6j** at their less nucleophilic site, C-2, to **5**. To overcome this difficulty, the reaction of **5** with **6a**–**k** in general was studied in acetonitrile solution under reflux using *para*-toluene sulfonic acid (*p*-TsOH; 25% by wt) as the catalyst. As expected, except **6k** which failed to react this time too, all other indoles furnished unsymmetrical BINEs (**7b**–**h**,**9i**,**9j**). But surprisingly, the 1-alkylindoles **6b**–**e** additionally furnished the symmetrical bis(1-alkylindolyl)nitroethanes **8b**–**e** (Scheme 2, Table 2), whose formation must involve tandem reactions.

Regarding the formation of **8b**–**e**, we envisaged that the corresponding unsymmetrical BINEs **7b**–**e** were the initial reaction products in these cases too. Once formed, these BINEs underwent acid-catalysed elimination of an indole



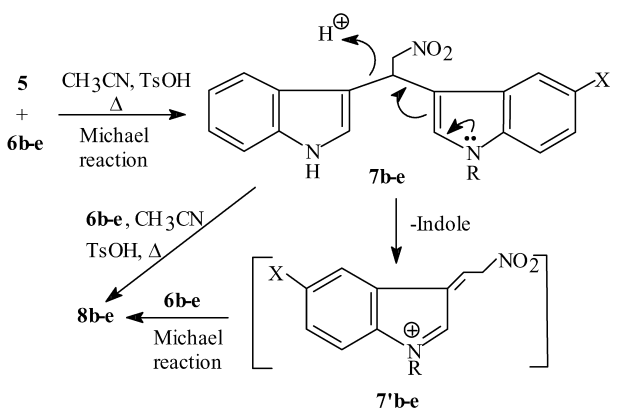
Scheme 2.

Table 2. Reaction of **5** with **6** in CH_3CN solution using *p*-TsOH

Indoles (**6**)					BINEs				
Sl. No.	R	R′	R″	X	Time (h)	Yield (%)			
						7	**8**	**9**	Overall
6a	H	H	H	H	8	84	—	—	84
6b	Me	H	H	H	5	63	27	—	90
6c	Me	H	H	Br	6	56	20	—	76
6d	Et	H	H	H	4	51	22	—	73
6e	^{i}Pr	H	H	H	4	52	26	—	78
6f	H	Me	H	H	6	70	—	—	70
6g	H	H	H	Br	7	81	—	—	81
6h	Me	Me	H	H	5	78	—	—	78
6i	H	H	Me	H	4	—	—	82	82
6j	Me	H	Me	H	3	—	—	80	80
6k[a]	Ac	H	H	H	—	—	—	—	—

[a] No reaction occurred.

molecule, resulting in the indoleninium cations **7′b–e**. Michael addition of 1-alkylindoles (**6b–e**) to **7′b–e** soon after their formation lead to the rearranged symmetrical BINEs **8b–e**. Since only the 1-alkylindoles **6b–e** furnished the rearranged BINEs **8b–e**, the increased electron density at the indolic nitrogen, arising from 1-alkylation, may be considered to have triggered the elimination of indole molecules to form the crucial indoleinium compounds **7′b–e**. This mechanistic proposition of tandem Michael addition–elimination–Michael addition received support from the slow formation of the respective BINEs (**8b–e**) in 15–30% yields when each of **7b–e** was separately refluxed with the corresponding alkylindole (**6b–e**) in solution under similar conditions (CH_3CN, *p*-TsOH, △) (Scheme 3).



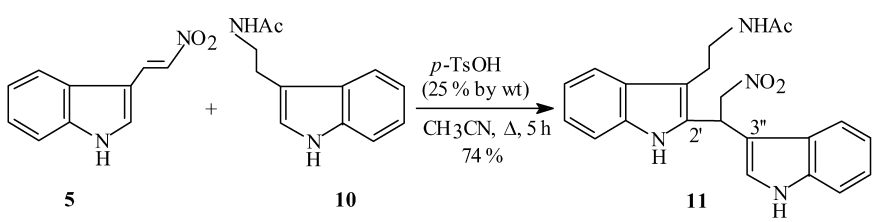
Scheme 3.

It is not clear to us as to why a similar product of tandem reactions was not formed from the reaction of 1,2-dimethylindole (**6h**), although the initial Michael addition product **7h** was formed in comparable yield.

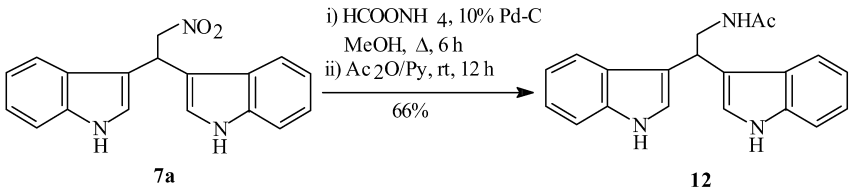
Our methodology could be well utilised for the synthesis of the BINE **11**, which can be reduced to the core BIEA structure of the marine metabolites **2** and **3**. Thus, when **5** was treated with *N*-acetyltryptamine (**10**) in the solution phase (CH_3CN, *p*-TsOH, △), the 2′,3″-BINE **11** was obtained in high yield (Scheme 4).

Since various types of BINEs could now be easily and efficiently prepared by our method, it only remained to be seen if the BINEs could be reduced to the corresponding BIEAs, the original target molecules. We, therefore, attempted the reduction of the representative BINE **7a**, the simplest member of the group, by some of the reagents reported for this purpose,[15a] viz. $LiAlH_4$, $NiCl_2{\cdot}6H_2O$/$NaBH_4$, Zn/HCl, H_2/Pd–C (1 atm), NiB_2/$NH_2NH_2.H_2O$,[16] In/NH_4Cl.[17] But none of these reagents worked. We, therefore, tried another method, viz. transfer hydrogenation using HCO_2NH_4/Pd–C under reflux[18a,b] (Scheme 5), when **7a** was smoothly reduced to the corresponding amine, isolated as its *N*-acetyl derivative (**12**).

In order to widen the utility of the present synthesis, the conversion of the BINEs into the corresponding 2,2-bis(indolyl)alkanals was aimed at because the latter can be converted into the corresponding alkanols and alkanoic acids which are natural products. The obvious choice, the Nef reaction,[19] could not be employed since it involves the use of sulfuric acid. Although the conversion of nitroalkanes

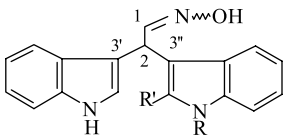


Scheme 4.



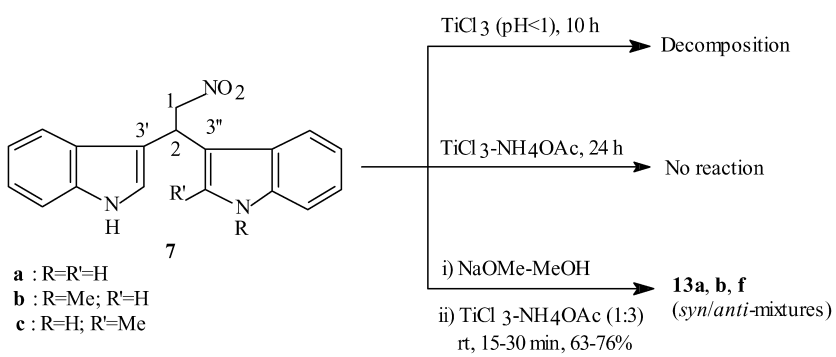
Scheme 5.

to aldehydes or ketones has been reported to be accomplished by several other reagents,[15b] we opted for McMurry's method of using aqueous $TiCl_3$ in buffered or unbuffered media on the nitroalkanes or the nitronates derived therefrom.[20a,b] Accordingly, when the BINE **7a** was treated with aqueous $TiCl_3$ (pH<1) at rt under nitrogen atmosphere and later in the presence of ammonium acetate, it caused decomposition and no change, respectively. However, when the nitronate derived (NaOMe/MeOH) from **7a** was treated with aqueous $TiCl_3$ in a buffered medium (pH~5–6) in methanol under nitrogen atmosphere at rt, the reaction was complete (TLC) within 30 min. Contrary to our expectation, the product was identified as the corresponding aldoxime **13a** (a mixture of the *syn*- and *anti*-isomers: 2:1; ^{1}H NMR) and no aldehyde could be isolated even after repeated trials. An attempt to drive the reaction towards the formation of the alkanal by stirring the reaction mixture for a longer period (2 h) led only to decomposition. In order to test the generality of this observation, we carried out the reaction with two more substrates, viz. **7b** and **7f**. In each case, a mixture of the *syn*- and *anti*-isomers of the corresponding aldoxime (**13b**,**f**) was obtained (Scheme 6; Table 3). Attempts were made to separate the two isomeric products in all three cases, but only the *anti*-isomer of **13a** could be isolated in 20% yield, i.e. with 80% recovery.



a : R=R'=H
b : R=Me; R'=H
c : R=H; R'=Me

The configurations of the *syn*- and the *anti*-isomers of the oximes were ascertained from their ^{1}H NMR spectroscopic data. A survey of the literature[21a–c] revealed that the aldehydic proton of alkenyl or aryl aldoximes appears downfield in the *syn*-isomers compared to their chemical shifts in the *anti*-isomers. Based on the chemical shift of the aldehydic proton of the pure *anti*-isomer of **13a**, it was noted that the C*H*=N appears at δ 7.23, 7.16 and 7.28 for the *anti*-isomers and δ 7.82, 7.79 and 7.91 for the *syn*-isomers of **13a**,**b** and **f**, respectively. A perusal of the ^{13}C NMR chemical shifts of the isomers of **13a**,**b**,**f** revealed that in each case the two isomers can be very well differentiated also from the chemical shifts of the Ar_2CH carbons. Thus, the Ar_2CH appears at around δ 29 for the *anti*-isomers and around δ 35 for the *syn*-isomers (vide Section 4).



a : R=R'=H
b : R=Me; R'=H
c : R=H; R'=Me

Scheme 6.

Table 3. Reaction of BINEs (**7**) with buffered aqueous $TiCl_3$

BINEs (**7**)	Oximes (**13**)		
	Time (min)	*syn*/*anti* (^{1}H NMR)	Overall yield (%)
7a	30	2:1	76
7b	15	2:1	63
7f	25	3:2	72

The formation of the oximes was indeed surprising and significant too. In view of an earlier report on the reduction of oximes by aqueous $TiCl_3$ to the imines and their subsequent hydrolysis to the carbonyl compounds,[22] McMurry suggested[20] that the conversion of primary and secondary nitroalkanes to the aldehydes and ketones, respectively by titanium(III) proceeds through the intermediacy of the oximes. But, to our knowledge, no oxime has yet been reported to be isolated from such a reduction. Thus, the isolation of the oximes **13a**,**b** and **f** is significant because

it constitutes the first direct evidence in support of the intermediacy of the oximes in McMurry's conversion of nitroalkanes, BINEs in this case, by aqueous $TiCl_3$. The failure to isolate any bis(indolyl)acetaldehyde from these reactions is probably due to the instability of the corresponding oximes under the reaction conditions.

3. Conclusions

A novel Michael reaction of 3-(2′-nitrovinyl)indole (**5**) with 3-unsubstituted indoles (**6a**–**h**) furnished only the addition products (BINEs **7a**–**h**, all but **7a** of which are unsymmetrical) using dry reaction conditions on TLC-grade silica gel, but both **7a**–**e** and symmetrical BINEs (**8b**–**e**) were obtained when the reactions were carried out in acetonitrile solution in presence of *p*-TsOH. A new sequence of tandem Michael addition–elimination–Michael addition reactions has been proposed for the formation of **8b**–**e**. This methodology has also been employed for the preparation of a 2′,3″-BINE (**11**), thereby opening a new avenue to the synthesis of naturally occurring BIEAs, for example, **2** and **3**, which would, of course, require a subsequent reduction. Further, the BINE **7a** was efficiently reduced by transfer hydrogenation (HCO_2NH_4, Pd–C) to the corresponding BIEA **12**, which thus provides access to a general synthesis of both symmetrical and unsymmetrical BIEAs. Finally, treatment of three BINEs (**7a**,**b**,**f**) with buffered aqueous $TiCl_3$ afforded the corresponding oximes (**13a**,**b**,**f**; *syn*- and *anti*-mixtures), which constitutes the first evidence in support of the previously predicted[20] intermediacy of oximes in the $TiCl_3$-mediated conversion of primary nitroalkanes to alkanals.

4. Experimental

4.1. General

Solvents were dried and purified using standard techniques. The glass apparatus for the anhydrous reactions were dried in an oven and assembled hot before use. Melting points (in Celcius) were determined on a Toshniwal apparatus and are uncorrected. IR spectra were recorded on a Nicolet Impact 410 and Nicolet Magnus 750 Series II spectrophotometer, LR EI-MS in a AEI MS 30 and LR EI-MS as well as HR MS, both EI and FAB (*m*-nitrobenzyl alcohol as liquid matrix), on JEOL JMS-AX505HA and JEOL JMS-700 MStation mass spectrometers and ^1H (500 MHz) and ^{13}C (125 MHz) NMR spectra, both 1D and 2D including DEPT-135, on a Bruker DRX 500 NMR spectrometer. Individual ^1H and ^{13}C NMR assignments, wherever made, are based on HMQC and HMBC spectral analyses. Silica gel G (Merck, India) was used for carrying out the dry reactions as well as for TLCs, both analytical and preparative, and silica gel (60–120 mesh; Qualigens, India) was used for column chromatography (CC). Elemental analyses were performed in a Dr. Hans Hoesli Analyser (Type A1; No. 1058).

4.2. General procedure for the synthesis of BINEs

Under microwave irradiation. A solution of **5** (0.5 mmol) and an 3-unsubstituted indole (**6a**–**h**; 1 mmol) in EtOAc (5 mL) was adsorbed on silica gel G (5 g) and the solvent was allowed to evaporate off at rt. The resulting dry mass was irradiated with microwave (BPL-SANYO, domestic multimode oven, 800 W, 50% power). When **5** was consumed (TLC), the reaction mixture was allowed to cool down to rt, the organic matter leached with EtOAc (3×25 mL), filtered through a bed of celite and the residue obtained by removal of solvent from the filtrate was purified by prep. TLC or CC to furnish the BINEs **7a**–**h**.

At rt. The reactants adsorbed on silica gel G as above was left at rt until **5** was consumed. The products were isolated as above and identified by comparison (mp, mmp, co-TLC) with samples obtained from the microwave-assisted experiments.

4.2.1. 2,2-Bis(3′-indolyl)nitroethane (7a). Brown solid; yield: μω, 86%; rt, 82%; mp 64–66 °C (pet. ether–CH_2Cl_2); IR (KBr) 3414, 1548, 1378, 745 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.08 (2H, d, J=8 Hz), 5.49 (1H, t, J=8 Hz), 7.03 (2H, d, J=2 Hz), 7.09 and 7.20 (2H, t each, J=7.5 Hz), 7.35 and 7.59 (2H, d each, J=8 Hz), 8.01 (2H, br s); ^{13}C NMR: δ 34.2 (Ar_2CH), 79.5 (CH_2NO_2), 111.8 (2×), 119.4 (2×), 120.2 (2×), 122.7 (2×), 122.9 (2×) (all Ar–CH), 114.7 (2×), 126.5 (2×), 136.9 (2×) (all Ar–C); MS: *m*/*z* (%) 305 (M^+, 18), 258 (35), 257 (23), 245 (50), 243 (37), 142 (27), 130 (97), 115 (100), 89 (86), 77 (52). Anal. calcd for $C_{18}H_{15}N_3O_2$: C, 70.82; H, 4.91; N, 13.77. Found C, 70.74; H, 4.93; N, 13.74.

4.2.2. 2-(3′-Indolyl)-2-(1″-methyl-3″-indolyl)nitroethane (7b). Orange crystals; yield: μω, 85%; rt, 84%; mp 174 °C (pet. ether–$CHCl_3$); IR (KBR), ^1H and ^{13}C NMR ($CDCl_3$) and EI–MS data have earlier been reported by us.[13]

4.2.3. 2-(3′-Indolyl)-2-(5″-bromo-1″-methyl-3″-indolyl)-nitroethane (7c). Waxy; yield: μω, 73%; rt, 72%; IR ($CHCl_3$) 3429, 1560, 1381, 758 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.65 (3H, s, NCH_3), 4.98 (1H, dd, J=8, 6.25 Hz, CH_AH_B-NO_2), 5.04 (1H, dd, J=7.5, 6.25 Hz, $CH_AH_BNO_2$), 5.38 (1H, dd, J=8, 7.5 Hz, Ar_2CH), 6.89 (1H, s, H-2″), 6.99 (1H, d, J=2 Hz, H-2′), 7.08 (1H, t, J=7.5 Hz, H-5′), 7.12 (1H, d, J=9 Hz, H-7″) 7.18 (1H, t, J=7.5 Hz, H-6′), 7.27 (1H, dd, J=9, 2 Hz, H-6″), 7.33 (1H, d, J=8 Hz, H-7′), 7.54 (1H, d, J=8 Hz, H-4′), 7.66 (1H, d, J=2 Hz, H-4″), 8.05 (1H, br s, NH); ^{13}C NMR: δ 33.3 (NCH_3), 34.0 (Ar_2CH), 79.4 (CH_2NO_2), 111.5 (CH-7″), 111.9 (CH-7′), 113.2 (CH-5″), 119.2 (CH-4″), 120.3 (CH-5′), 121.9 (CH-4″), 122.6 (CH-2′), 123.0 (CH-6′), 125.3 (CH-6″), 128.5 (CH-2″); 112.6 (C-3″), 114.4 (C-3′), 126.4 (C-3′a), 128.6 (C-3″a), 136.4 (C-7″a), 137.0 (C-7′a); MS: *m*/*z* (%) 399 (22), 397 (M^+, 21), 352 (44), 350 (33), 339 (100), 337 (95), 257 (45). Anal. calcd for $C_{19}H_{16}N_3O_2Br$: C, 57.28; H, 4.02; N, 10.55. Found C, 57.20; H, 4.01; N, 10.59.

4.2.4. 2-(3′-Indolyl)-2-(1″-ethyl-3″-indolyl)nitroethane (7d). Brown crystals; yield: μω, 71%; rt, 70%; mp 135–136 °C (pet. ether–CH_2Cl_2); IR (KBr) 3400, 1541, 1379, 758, 744 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.40 (3H, t, J=7.0 Hz, NCH_2CH_3), 4.09 (2H, dq, J=3, 7 Hz, NCH_2), 5.09 (2H, d, J=7.75 Hz, CH_2NO_2), 5.50 (1H, t, J=7.75 Hz, Ar_2CH), 6.97 (1H, s, H-2″), 7.03 (1H, d, J=2 Hz, H-2′), 7.10 (1H, t,

J=7.5 Hz, H-5″), 7.11 (1H, t, J=7.5 Hz, H-5′) 7.21 (1H, t, J=7.5 Hz, H-6′), 7.24 (1H, t, J=7.5 Hz, H-6″), 7.34 (2H, d, J=8.0 Hz, H-7′, 7″), 7.61 (2H, d, J=8 Hz, H-4′, 4″), 8.06 (1H, br s, NH); ^{13}C NMR: δ 15.8 (CH_3), 34.2 (Ar_2CH), 41.3 (NCH_2), 79.7 (CH_2NO_2), 110.0 (CH-7″), 111.8 (CH-7′), 119.4 and 119.5 (CH-4′, 4″), 119.6 (CH-5″), 120.1 (CH-5′), 122.2 (CH-6″), 122.80 and 122.84 (CH-2′, 6′), 125.7 (CH-2″); 113.1 (C-3″), 114.8 (C-3′), 126.6 (C-3′a), 127.1 (C-3″a), 136.8 (C-7″a), 137.0 (C-7′a); MS: m/z (%) 333 (M^+, 24), 286 (36), 273 (96), 272 (80), 271 (100), 256 (41), 243 (32). Anal. calcd for $C_{20}H_{19}N_3O_2$: C, 72.07; H, 5.70; N, 12.61. Found C, 72.18; H, 5.73; N, 12.56.

4.2.5. 2-(3′-Indolyl)-2-(1″-isopropyl-3″-indolyl)nitroethane (7e). Reddish brown crystals; yield: μω, 75%; rt, 72%; mp 142 °C (pet. ether–EtOAc); IR (KBr) 3406, 1537, 1377, 740 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.46 and 1.49 (3H, d each, J=7 Hz, NCHMe_2), 4.63 (1H, septet, J=7 Hz, NCHMe$_2$), 5.10 (2H, d, J=7.5 Hz, CH_2NO_2), 5.51 (1H, t, J=7.5 Hz, H-2), 7.04 (1H, d, J=2 Hz, H-2′), 7.094 (1H, t, J=8 Hz, H-5″), 7.097 (1H, s, H-2″), 7.11 (1H, t, J=8 Hz, H-5′), 7.21 (1H, t, J=8 Hz, H-6′) 7.22 (1H, t, J=8 Hz, H-6″), 7.35 (1H, d, J=8 Hz, H-7′), 7.38 (1H, d, J=8 Hz, H-7″), 7.60 (1H, d, J=7.5 Hz, H-4″), 7.61 (1H, d, J=7.5 Hz, H-4′), 8.02 (1H, br s, NH); ^{13}C NMR: δ 23.10 and 23.14 (NCHMe_2), 34.4 (Ar_2CH), 79.7 (CH_2NO_2), 47.5 (NCHMe$_2$), 110.2 (CH-7″), 111.8 (CH-7′), 119.4 (CH-4′), 119.61 (CH-4″), 119.67 (CH-5″), 120.1 (CH-5′), 122.1 (CH-6″), 122.3 (CH-2″), 122.83 (CH-6′), 122.85 (CH-2′); 113.1 (C-3″), 114.9 (C-3′), 126.6 (C-3′a), 127.1 (C-3″a), 136.6 (C-7″a), 137.0 (C-7′a). MS: m/z (%) 347 (M^+, 50), 300 (44), 287 (100), 257 (29), 243 (61). Anal. calcd for $C_{21}H_{21}N_3O_2$: C, 72.62; H, 6.05; N, 12.10. Found C, 72.50; H, 6.03; N, 12.14.

4.2.6. 2-(3′-Indolyl)-2-(2″-methyl-3″-indolyl)nitroethane (7f). Orange crystals; yield: μω: 70%; rt, 69%; mp 207–208 °C (pet. ether–EtOAc); IR (KBr) 3413, 1550, 1378, 747 cm^{-1}; ^{1}H NMR (d_6-DMSO): δ 2.43 (3H, s, CH_3), 5.22 (1H, dd, J=9.5, 6.5 Hz), 5.31 (1H, dd, J=12.5, 9.5 Hz), 5.44 (1H, dd, J=12.5, 6.5 Hz), 6.82, 6.92 and 7.0 (1H, t each, J=7.5 Hz), 6.86 (1H, d, J=7.5 Hz), 7.19, 7.30 and 7.48 (1H, d each, J=8 Hz), 7.27 (1H, t, J=8 Hz), 7.42 (1H, d, J=2 Hz), 10.82 and 10.93 (1H, br s each); ^{13}C NMR: δ 12.4 (CH_3), 33.3 (Ar_2CH), 79.3 (CH_2NO_2), 111.4, 112.3, 119.11, 119.14, 119.15, 119.3, 120.8, 122.0, 122.7 (all Ar–CH), 108.8, 114.1, 127.2, 127.5, 133.4, 136.1, 137.1 (all Ar–C); MS: m/z (%) 319 (M^+, 24), 272 (33), 259 (76), 257 (100), 256 (57), 243 (27). Anal. calcd for $C_{19}H_{17}N_3O_2$: C, 71.47; H, 5.33; N, 13.16. Found C, 71.60; H, 5.30; N, 13.21.

4.2.7. 2-(3′-Indolyl)-2-(5″-bromo-3″-indolyl)nitroethane (7g). Reddish brown solid; yield: μω, 83%; rt, 82%; mp 86–88 °C (pet. ether–CH_2Cl_2); IR (nujol) 3405, 1544, 1376, 744 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.01 (1H, dd, J=12.5, 8.3 Hz), 5.06 (1H, dd, J=12.5, 7.5 Hz), 5.40 (1H, t, J=7.5 Hz), 6.98 and 7.03 (1H, d each, J=2 Hz), 7.09 (1H, t, J=7.5 Hz), 7.19 (1H, d, J=8.5 Hz), 7.199 (1H, t, J=8.5 Hz), 7.25 (1H, dd, J=8.5, 1.5 Hz), 7.35 and 7.55 (1H, d each, J=8 Hz), 7.67 (1H, d, J=1.2 Hz), 8.11 and 8.17 (1H, br s each); ^{13}C NMR: δ 34.0 (Ar_2CH), 79.3 (CH_2NO_2), 111.9, 113.3, 119.2, 120.3, 121.9, 122.7, 123.0, 123.9, 125.8 (all Ar–CH), 113.5, 114.21, 114.27, 126.3, 128.2, 135.6, 137.0 (all Ar–C). Anal. calcd for $C_{18}H_{14}N_3O_2Br$: C, 56.25; H, 3.64; N, 10.94. Found C, 56.35; H, 3.61; N, 10.90.

4.2.8. 2-(3′-Indolyl)-2-(1″,2″-dimethyl-3″-indolyl)nitroethane (7h). Dark brown solid; yield: μω, 78%; rt, 76%; mp 128–130 °C (pet. ether–EtOAc); IR (nujol) 3409, 1546, 1374, 738 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.41 (3H, s, CH_3), 3.63 (3H, s, NCH_3), 5.10 (1H, dd, J=12, 9.5 Hz), 5.23 (1H, dd, J=12.5, 6 Hz), 5.45 (1H, dd, J=9, 6 Hz), 7.01, 7.13 and 7.17 (1H, t each, J=7.5 Hz), 7.05 (1H, s), 7.07 (1H, t, J=8 Hz), 7.25 and 7.32 (1H, d each, J=8 Hz), 7.52 and 7.53 (1H, d each, J=7.5 Hz), 8.0 (1H, br s); ^{13}C NMR: δ 10.8 (2″-CH_3), 30.0, 34.1, 79.0 (CH_2NO_2), 109.4, 111.7, 119.17, 119.19, 119.4, 120.2, 121.1, 122.4, 122.8 (all Ar–CH), 108.2, 114.9, 126.5, 126.8, 134.8, 136.8, 137.4 (all Ar–C); MS: m/z (%) 333 (M^+, 38), 287 (9), 273 (100), 170 (25), 160 (29), 148 (31), 145 (23); HR EI-MS: calcd for $C_{20}H_{19}N_3O_2$ 333.1496. Found 333.1487.

4.3. General procedure for the synthesis of BINEs in solution phase

To a solution of **5** (1 mmol) and the indoles (**6a–k**,**10**, 2 mmol) in CH_3CN (10 mL) containing p-TsOH (25% by wt) was refluxed until **5** was consumed. The solution was poured into satd. aq. $NaHCO_3$ and extracted with EtOAc (3×25 mL). The pooled solvent phase was washed, dried (Na_2SO_4), solvent distilled off and the resulting residue purified by prep. TLC to furnish the BINEs (**7a–h**, **8b–e**, **9i–j** and **11**), as shown in Table 2.

4.3.1. 2,2-Bis(1′-methyl-3′-indolyl)nitroethane (8b). Ochre yellow flakes; yield: 27%; mp 165–166 °C (pet. ether–$CHCl_3$); IR (KBr) 1546, 1377, 1332, 746 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.69 (6H, s, 2×NCH_3), 5.04 (2H, d, J=7.5 Hz, CH_2NO_2), 5.47 (1H, t, J=7.5 Hz, Ar_2CH), 6.89 (2H, s, H-2′), 7.09 and 7.22 (2H, t each, J=7.5 Hz, H-5′ and -6′, respectively), 7.29 and 7.59 (2H, d each, J=8 Hz, H-7′ and -4′, respectively); ^{13}C NMR: δ 33.2 (2×; NCH_3), 34.1 (Ar_2CH), 79.7 (CH_2NO_2), 109.9 (2×; CH-7′), 119.5 (2×; CH-4′), 119.7 (2×; CH-5′), 122.4 (2×; CH-6′), 127.4 (2×; CH-2′); 113.2 (2×; C-3′) 127.0 (2×; C-3′a), 137.7 (2×; C-7′a); MS: m/z (%) 333 (M^+, 28), 290 (22), 288 (32), 276 (54), 275 (100), 273 (27), 259 (34). Anal. calcd for $C_{20}H_{19}N_3O_2$: C, 72.07; H, 5.70; N, 12.61. Found C, 72.18; H, 5.68; N, 12.56.

4.3.2. 2,2-Bis(5′-bromo-1′-methyl-3′-indolyl)nitroethane (8c). Orange solid; yield: 20%; mp 76–78 °C (pet. ether–CH_2Cl_2); IR (nujol) 1560, 1381, 804 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.69 (6H, s, 2×NCH_3), 4.98 (2H, d, J=8 Hz, CH_2NO_2), 5.32 (1H, t, J=8 Hz, Ar_2CH), 6.88 (2H, s, H-2′), 7.15 (2H, d, J=9 Hz, H-7′), 7.29 (2H, dd, J=9, 1.75 Hz, H-6′), 7.65 (2H, d, J=2 Hz, H-4′); ^{13}C NMR: δ 33.4 (2×; NCH_3), 33.7 (Ar_2CH), 79.3 (CH_2NO_2), 111.5 (2×; CH-7′), 113.2 (2×; CH-5′), 121.8 (2×; CH-4′), 125.4 (2×; CH-6′), 128.41 (2×; CH-2′); 112.4 (2×; C-3′), 128.47 (2×; C-3′a), 136.5 (2×; C-7′a); MS: m/z (%) 493 (6), 491(11), 489 (M^+, 6), 446 (8), 444 (12), 442 (7), 433 (18), 431 (37), 429 (21), 223 (29), 142 (61), 128 (77), 115 (100). Anal. calcd for $C_{20}H_{17}N_3O_2Br_2$: C, 48.88; H, 3.46; N, 8.55. Found C, 48.98; H, 3.48; N, 8.52.

4.3.3. 2,2-Bis(1′-ethyl-3′-indolyl)nitroethane (8d). Orange granular crystals; yield: 22%; mp 146 °C (pet. ether–$CHCl_3$); IR (KBr) 1546, 1375, 748 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.40 (6H, t, J=7.5 Hz, 2×CH_3), 4.09 (4H, dq, J=2, 7.0 Hz, NCH_2), 5.06 (2H, d, J=8 Hz, CH_2NO_2), 5.47 (1H, t, J=7.5 Hz, Ar_2CH), 6.96 (2H, s, H-2′), 7.08 (2H, t, J=7.5 Hz, H-5′), 7.21 (2H, t, J=7.5 Hz, H-6′), 7.32 (2H, d, J=8.5 Hz, H-7′), 7.59 (2H, d, J=8 Hz, H-4′); ^{13}C NMR: δ 15.8 (2×; CH_3), 34.3 (Ar_2CH), 41.3 (2×; NCH_2), 79.3 (CH_2NO_2), 110.0 (2×; CH-7′), 119.62 and 119.65 (2×; CH-4′, 5′), 122.2 (2×; CH-6′), 125.7 (2×; CH-2′); 113.2 (2×; C-3′) 127.2 (2×; C-3′a), 136.8 (2×; C-7′a); MS: m/z (%) 361 (M^+, 23), 314 (24), 301 (100), 271 (16), 256 (16), 130 (35), 115 (19). Anal. calcd for $C_{22}H_{23}N_3O_2$: C, 73.13; H, 6.37; N, 11.63. Found C, 73.20; H, 6.40; N, 11.60.

4.3.4. 2,2-Bis(1′-isopropyl-3′-indolyl)nitroethane (8e). Yellowish brown flakes; yield: 26%; mp 138 °C (pet. ether–$CHCl_3$); IR (KBr) 1545, 1375, 742 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.45 and 1.47 (6H, dd each, J=6.5, 1.5 Hz, 2×NCH*Me*$_2$), 4.612 and 4.616 (1H, septet each, J=6.5 Hz, NC*H*Me_2), 5.07 (2H, dd, J=7.5, 2.5 Hz, CH_2NO_2), 5.47 (1H, td, J=7.5, 2.5 Hz, Ar_2CH), 7.06 (2H, t, J=7 Hz, H-5′), 7.07 (2H, d, J=2.5 Hz, H-2′), 7.19 (2H, t, J=7 Hz, H-6′), 7.35 (2H, d, J=8 Hz, H-7′), 7.57 (2H, dd, J=7.5, 1.5 Hz, H-4′); ^{13}C NMR: δ 23.11 and 23.16 (2×; NCH*Me*$_2$), 34.6 (Ar_2CH), 79.9 (CH_2NO_2), 47.5 (2×; N*C*HMe_2), 110.2 (2×; CH-7′), 119.61 and 119.65 (2×; CH-4′, 5′), 122.0 and 122.4 (2×; CH-2′, 6′); 113.3 (2×; C-3′), 127.2 (2×; C-3′a), 136.6 (2×; C-7′a); MS: m/z (%) 389 (M^+, 24), 342 (25), 330 (55), 329 (100), 246 (43), 244 (49). Anal. calcd for $C_{24}H_{27}N_3O_2$: C, 74.03; H, 6.94; N, 10.79. Found C, 74.21; H, 6.92; N, 10.83.

4.3.5. 2-(3′-Methyl-2′-indolyl)-2-(3″-indolyl)nitroethane (9i). Brown crystals; yield: 82%; mp 98–100 °C (pet. ether–$CHCl_3$); IR (KBr) 3410, 1550, 1376, 745 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.42 (3H, s, CH_3), 4.88 (1H, dd, J=12.5, 7 Hz, C$H_AH_BNO_2$), 5.06 (1H, dd, J=12.5, 7.5 Hz, CH_AH_B-NO_2), 5.49 (1H, t, J=7.5 Hz, Ar_2CH), 7.03 (1H, t, J=7.5 Hz, H-5″), 7.06–7.15 (4H, m, H-2″, 5′, 6′, 7′), 7.18 (1H, t, J=7.5 Hz, H-6″), 7.33 (1H, d, J=8 Hz, H-7″), 7.36 (1H, d, J=8 Hz, H-4″), 7.53–7.54 (1H, m, H-4′) 7.67 (1H, br s, H-1′), 8.11 (1H, br s, H-1″); ^{13}C NMR: δ 9.0 (CH_3), 34.2 (Ar_2CH), 78.3 (CH_2NO_2), 111.9 (CH-7″), 111.2, 119.8, 121.8, 122.4 (CH-2″, 5′, 6′, 7′), 119.0 (CH-4′), 119.2 (CH-4″), 120.7 (CH-5″), 123.4 (CH-6″); 109.2 (C-3′), 112.4 (C-3″), 126.4 (C-3′a), 129.7 (C-3′a), 131.3 (C-2′), 135.9 (C-7′a), 136.9 (C-7″a); MS: m/z (%) 319 (M^+, 13), 272 (8), 259 (32), 257 (31), 243 (8), 130 (87), 117 (100). Anal. calcd for $C_{19}H_{17}N_3O_2$: C, 71.47; H, 5.33; N, 13.16. Found C, 71.40; H, 5.31; N, 13.11.

4.3.6. 2-(1′,3′-Dimethyl-2′-indolyl)-2-(3″-indolyl)nitroethane (9j). Yellowish brown solid; yield: 80%; mp 82–84 °C (pet. ether–CH_2Cl_2); IR (nujol) 3396, 1546, 1374, 744 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.37 (3H, s, CH_3), 3.61 (3H, s, NCH_3), 5.06 (1H, dd, J=13, 9 Hz), 5.22 (1H, dd, J=13, 7 Hz), 5.60 (1H, dd, J_1=J_2=7.5 Hz), 6.90 (1H, d, J=1 Hz), 7.03 and 7.18 (1H, t each, J=7.5 Hz), 7.10 (1H, td, J=7, 2 Hz), 7.20 (1H, d, J=7 Hz), 7.21 (1H, td, J=7.5, 0.75 Hz), 7.30, 7.32 and 7.55 (1H, d each, J=7.5 Hz), 8.07 (1H, d, J=2.5 Hz); ^{13}C NMR: δ 9.9 (3′-CH_3), 30.5 (1′-CH_3), 33.9 (Ar_2CH), 77.9 (CH_2NO_2), 109.4, 111.8, 119.0, 119.08, 119.4, 120.6, 122.2, 122.4, 123.2 (all Ar–CH), 109.1, 122.5, 126.3, 128.8, 132.3, 137.0, 137.4 (all Ar–C); MS: m/z (%) 333 (M^+, 73), 304 (100), 289 (94), 273 (66), 257 (18), 160 (41), 149 (43), 144 (60), 130 (34); HR EI-MS: calcd for $C_{20}H_{19}N_3O_2$ 333.1492. Found 333.1485.

4.3.7. 2-{3′-(β-Acetamidoethyl)-2′-indolyl}-2-(3″-indolyl)nitroethane (11). Orange solid; yield: 74%; mp 128–132 °C (pet. ether–EtOAc); IR (KBr) 3403, 3273, 1648, 1549, 1374, 745 cm^{-1}; ^1H NMR (d_6-DMSO): δ 1.75 (3H, s), 2.88–2.92 (2H, m), 3.12–3.16 and 3.21–3.27 (1H, m each), 5.29–5.35 (2H, m), 5.38–5.45 (1H, m), 6.94, 6.95, 7.02 and 7.05 (1H, t each, J=7.5 Hz), 7.27, 7.33, 7.39 and 7.54 (1H, d each, J=8 Hz), 7.46 (1H, d, J=7.5 Hz), 7.95 (1H, t, J=5.5 Hz), 10.92 and 11.08 (1H, br s each); ^{13}C NMR: δ 23.5 and 25.3 (CH_2CH_2), 79.1 (CH_2NO_2), 33.3 (Ar_2CH), 111.8, 112.4, 118.9, 119.0, 119.3, 119.7, 121.8, 122.2, 123.7 (all Ar–CH), 109.7, 112.6, 126.7, 128.5, 134.3, 136.5, 136.8, 170 (all Ar–C); MS: m/z (%) 390 (M^+, 1), 344 (50), 343 (35), 329 (35), 286 (47), 271 (63), 270 (40), 257 (100), 187 (4), 156 (11), 143 (12), 130 (32). Anal. calcd for $C_{22}H_{22}N_4O_3$: C, 67.69; H, 5.64; N, 14.35. Found C, 67.60; H, 5.62; N, 14.40.

4.4. Reduction of the BINE 7a

To a stirred solution of **7a** (319 mg, 1 mmol) in dry MeOH (20 mL), was added 10% Pd/C (60 mg) at rt, followed by anhydrous HCO_2NH_4 (315 mg, 5 mmol) in a single portion under nitrogen atmosphere. The resulting mixture was heated to 60 °C for 1 h. After the completion of the reaction (TLC), the catalyst was removed by filtration through a celite bed, washed with methanol, the pooled filtrates concentrated and poured into water, extracted with EtOAc (3×20 mL) and dried (Na_2SO_4). The solvent on evaporation furnished a residue which was dissolved in pyridine (1 mL) and Ac_2O (2 mL) and kept overnight. The reaction mixture was poured into excess water and washed successively with 2 M aq. HCl, satd. aq. $NaHCO_3$ and extracted with EtOAc (3×20 mL) and dried (Na_2SO_4). The removal of the solvent furnished **12** as a brown solid (209 mg; 66%), mp. 116–118 °C (pet. ether–CH_2Cl_2). All data of **12** were in agreement with those reported earlier for it from our laboratory.[23]

4.5. General procedure for the reduction of the nitronates, derived from 7a,b,f by aqueous $TiCl_3$ at pH 5–6

The BINE (**7a**,**b**,**f**) (1 mmol) was dissolved in dry methanol (20 mL) and treated with NaOMe (1.1 equiv.) and stirred for 1 h. A buffered $TiCl_3$–NH_4OAc solution, prepared by adding NH_4OAc (0.95 g, 12 mmol) in water (3 mL) to 15% aqueous $TiCl_3$ (3 mL, 4.5 mmol), was then added rapidly to the above solution at rt under nitrogen atmosphere. After the indicated period (Table 3), the reaction mixture was poured into water and extracted with EtOAc (3×20 mL). The organic extracts were combined, washed with aq. $NaHCO_3$, dried (Na_2SO_4) and the solvent distilled off. The resulting residue was purified by prep. TLC to furnish the oximes **13a**,**b** and **f**, each a mixture of the *syn*- and *anti*-isomers. For **13b** and **13f**, the designatory letters mj and mn stand for the major and the minor isomers, respectively.

4.5.1. 2,2-Bis(3′-indolyl)ethanaloxime (13a; *syn/anti*-mixture). *anti*-Isomer (pure). Dark brown solid; yield: 20%; mp 226–228 °C (pet. ether–EtOAc); IR (nujol) 3454, 3412, 3400, 3193, 1614, 918, 745 cm^{-1}; ^1H NMR (d_6-DMSO): δ 6.06 (1H, d, J=8 Hz, Ar_2CH), 6.91 and 7.04 (2H, t each, J=7.5 Hz), 7.14 (2H, s), 7.23 (1H, d, J=8 Hz, CH=N), 7.34 (2H, d, J=8 Hz), 7.49 (2H, d, J=7.5 Hz), 10.89 (2H, s, 2×NH), 10.95 (1H, s, =NOH); ^{13}C NMR: δ 29.9 (Ar_2CH), 112.3 (2×), 119.1 (2×), 119.7 (2×), 121.8 (2×), 123.7 (2×) (all Ar–CH), 151.7 (CH=N), 115.0 (2×), 127.2 (2×), 137.2 (2×) (all Ar–C); MS: *m/z* (%) 289 (M^+, 44), 272 (100), 271 (59), 245 (87), 243 (50); HR EI-MS: calcd for $C_{18}H_{15}N_3O$ 289.1215. Found 289.1212.

syn-Isomer (^1H NMR assignments ascertained by subtraction of data of pure *anti*-isomer from those of the *syn/anti*-mixture). Yield: 76%; *syn/anti*=2:1; IR (KBr) 3406, 1618, 742 cm^{-1}; ^1H NMR (d_6-DMSO): δ 5.24 (1H, d, J=8 Hz, Ar_2CH), 6.88 and 7.01 (2H, t each, J=7.5 Hz), 7.11 (2H, s), 7.31 (2H, d, J=8 Hz), 7.46 (2H, d, J=7.5 Hz), 7.82 (1H, d, J=7.5 Hz, CH=N), 10.42 (1H, br s, =NOH), 10.82–10.95 (2H, m, 2×NH); ^{13}C NMR: δ 35.8 (Ar_2CH), 112.3 (2×), 119.1(2×), 119.8 (2×), 121.8 (2×), 123.75 (2×) (all Ar–CH), 151.6 (CH=N), 115.4 (2×), 127.1 (2×), 137.3 (2×) (all Ar–C); MS: *m/z* (%) 289 (M^+, 29), 272 (100), 245 (68), 243 (70).

4.5.2. 2-(3′-Indolyl)-2-(1″-methyl-3″-indolyl)ethanaloxime (13b; *syn/anti*-mixture). Yield: 62%; *syn*:*anti*=2:1; IR ($CHCl_3$) 3474, 3413, 1613, 769 cm^{-1}; ^1H NMR (d_6-DMSO): δ 3.67 (3H mj+3H mn, s, 2×NMe), 5.24 (mj) and 6.02 (mn) (1H, d each, J=8 Hz, 2×Ar_2CH), 6.88 and 6.92 (1H mj+1H mn, t each, J=7 Hz), 7.01 (1H mj+1H mn, t, J=7 Hz), 7.04–7.11 (1H mj+1H mn, m), 7.07 (1H mj+1H mn, s), 7.13 (1H mj+1H mn, s), 7.16 (mn) and 7.79 (mj) (1H, d each, J=8 Hz, 2×CH=N), 7.31 and 7.33 (1H mj+1H mn, d each, J=9 Hz), 7.45 (1H mj+1H mn, d, J=9 Hz), 7.47 (1H mj+1H mn, d, J=8.5 Hz), 10.43 (mj) and 10.92 (mn) (1H, s each, 2×NH), 10.86 (mn) and 10.88 (mj) (1H, s each, 2×=NOH); ^{13}C NMR: δ 29.7 (mn) and 35.6 (mj) (2×Ar_2CH), 33.1 (2×; NMe), 110.5 (mj+mn), 112.3 (mj+mn), 119.21 (mn), 119.23 (mj), 119.28 (mn), 119.3 (mj), 119.6 (mn), 119.7 (mj), 119.9 (mn), 120.0 (mj), 121.91 (mn), 121.92 (mj), 122.0 (mj+mn), 123.73 (mn), 123.77 (mj), 128.11 (mn) and 128.13 (mj) (all Ar–CH), 151.5 (mj) and 151.6 (mn) (2×CH=N), 114.4 (mn), 114.7 (mj) and 115.2 (mj+mn), 127.1 (mj), 127.2 (mn), 127.5 (mj) and 127.6 (mn), 137.2 (mn), 137.3 (mj), 137.70 (mn) and 137.74 (mj) (all Ar–C); MS: *m/z* (%) 303 (M^+, 82), 286 (100), 285 (63), 259 (100), 257 (88), 245 (44); HR FAB-MS: calcd for $C_{19}H_{17}N_3O$ 303.1372. Found 303.1350.

4.5.3. 2-(3′-Indolyl)-2-(2″-methyl-3″-indolyl)ethanaloxime (13f; *syn/anti*-mixture). Yield: 72%; *syn/anti*=3:2; IR (nujol) 3396, 3283, 1619, 744 cm^{-1}; ^1H NMR (d_6-DMSO): δ 2.33 (mj) and 2.37 (mn) (3H, s each, 2×NMe), 5.21 (mj) and 5.94 (mn) (1H, d each, J=7.5 Hz, 2×Ar_2CH), 6.77–6.87 (2H mj+2H mn, m), 6.91 and 6.93 (1H mj+1H mn, t each, J=7 Hz), 7.0 (1H mj+1H mn, t, J=7.5 Hz), 7.04 (mj) and 7.06 (mn) (1H, s each), 7.15–7.27 (2H mj+2H mn, m), 7.28 (1H mn, d, J=9 Hz, CH=N), 7.30 (1H mj+1H mn), 7.34 (mj) and 7.36 (mn) (2H, t each, J=7.5 Hz), 7.91 (1H mj, d, J=8 Hz, CH=N), 10.47 (1H mj), 10.78 (1H mn), 10.80 (1H mn), 10.82 (2H mj) and 10.91 (1H mn) (s each, 4×NH+2×OH); ^{13}C NMR: δ 12.6 (2×; CH_3), 29.6 and 35.3 (2×Ar_2CH), 111.4 (2×), 112.2 (2×), 119.0 (2×), 119.1 (2×), 119.3 (2×), 119.4, 119.6, 120.7, 120.8, 121.8 (2×), 123.2, 123.4 (all Ar–CH), 151.2 and 151.4 (2×CH=N), 110.3 (2×), 115.3 (2×), 127.4 (2×), 128.0, 128.1, 132.6, 132.7, 136.1 (2×), 137.2 (2×) (all Ar–C); MS: *m/z* (%) 303 (M^+, 29), 286 (49), 285 (31), 270 (23), 259 (61), 258 (71), 257 (100), 243 (28), 130 (43); HR EI-MS: calcd for $C_{19}H_{17}N_3O$ 303.1372. Found 303.1379.

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