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# STUDY OF THE REACTIONS OF FOUR INDOLIC 1-AZADIENES WITH A FEW ENOIC, YNOIC, AND AZO DIENOPHILES

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## STUDY OF THE REACTIONS OF FOUR INDOLIC 1-AZADIENES WITH A FEW ENOIC, YNOIC, AND AZO DIENOPHILES

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#### ABSTRACT

Four indolic 1-azadienes (**1a–c**, **2**) underwent Diels–Alder reaction, dienophile-catalysed addition–elimination reaction, Michael reaction or hydrolysis with three enoic, two ynoic and one azo dienophiles, leading to a  $\gamma$ -carboline, various 3-cyanoindoles, 3-formylindole and several nitrones.

*Key Words:* 1-Azadienes; Hetero D.-A. reaction;  $\gamma$ -Carboline; Nitrones

Hetero Diels–Alder reactions constitute a powerful tool for the construction of six-membered heterocycles.<sup>[1,2]</sup> Of the various dienes used, azadienes represent a significant class. Of the two possible types of 1-azadienes,

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1-aza-1,3-dienes, although usually considered as poor  $4\pi$ -components, have been studied extensively and reviewed recently.<sup>[3]</sup> We were interested in the D.–A. reactions of 1-azadienes in which the C=C bond is a part of a heteroarene. Despite an early success,<sup>[4]</sup> several subsequent attempts towards the D.–A. reactions of azadienes of this type were thwarted.<sup>[5–8]</sup> Later, however, Kusurkar and we were the first to accomplish the  $[4\pi + 2\pi]$  cycloaddition of furfuraldoxime<sup>[9]</sup> and the *N*,*N*-dimethylhydrazone (NNDMH) of 1-ethoxycarbonylindole-3-carboxaldehyde (**1a**)<sup>[10]</sup> (Figure 1), respectively.

In continuation of our interest, we wanted to study the reaction of 1a, its *N*-benzoyl analogue 1b, the parent unacylated NNDMH 1c and indole-3-carboxaldehyde oxime (2) with a few enoic, ynoic and azo dienophiles. FMO considerations, based on  $\pi$ -VE-SCF-MO calculations<sup>[11]</sup> on the 1-methoxycarbonyl analogue of 1a, predicted that (i) the azadiene system is nearly co-planar, (ii) its  $E_{HOMO}$  is sufficiently high to permit a normal electron-demand D.–A. reaction with conventional electron-deficient dienophiles, and (iii) the very high  $\pi$ -electron density and the resulting highest nucleophilicity at the dimethylamino nitrogen may trigger dienophilecatalysed addition-elimination reactions, leading to nitriles. Although FMO calculations were not carried out on 2, the reported previous success with furfuraldoxime<sup>[9]</sup> induced us to use this azadiene as well. Accordingly, the targeted reactions were carried out and the results have been briefly presented in this communication.

We had earlier achieved the cycloaddition of **1a** with *N*-methylmaleimide (NMM), furnishing the  $\gamma$ -carboline **3a** (**3b**, R=CO<sub>2</sub>Et).<sup>[10]</sup> When **1b** was similarly refluxed with NMM in xylene containing catalytic amount of *para*-toluene sulphonic acid (PTS), the new annulated  $\gamma$ -carboline **3b** was formed in low yield (Scheme 1). In all likelihood, a  $[4\pi + 2\pi]$  cycloaddition, followed by elimination of dimethylamine and dehydrogenation, resulted in **3b**. Since no reaction took place in absence of PTS, the latter may be considered as promoting both D.-A. reaction and elimination. The known tendency of cyclic enamines to undergo decomposition and the thermal instability of **3b** are largely responsible for the observed low yield.

When **1a** was similarly treated with diethyl azodicarboxylate (DEAZD) without the use of any catalyst (Scheme 2), almost equal amounts of the

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Scheme 3.

corresponding 3-cyanoindole **4a** and N,N'-diethoxycarbonylhydrazine (**5**) were formed in moderate overall yield (49%). The azadiene **1b** reacted similarly with DEAZD to furnish **4b** and **5** in a lower overall yield (34%).

The compound **5** had previously been reported as a by-product of the reaction of DEAZD with two ketone phenylhydrazones<sup>[12]</sup> and with the NNDMH's of two araldehyde oximes.<sup>[7]</sup> Neither of these reports contained NMR and mass spectral data in support of the derived structure **5**, nor did they provide any literature reference to it. This situation necessitated a complete spectral identification of **5**, which we have carried out (vide Experimental). Moreover, the mechanism of the formation of **5** was not suggested in any of these reports. We like to explain the genesis of both **4a/b** and **5** together in the following manner (Scheme 3).

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Scheme 4.

 $1a/b + HC \equiv C-CO_2Me \xrightarrow{CH_3CN; 60^{\circ}} 4a/b$ (MP) PTS; 18 hr (13/33%)(13/33%)

Scheme 5.

The cyanoindoles **4a** and **4b** were most likely formed by a dienophilecatalysed addition-elimination reaction, depicted below, just as the formation of certain 2-cyanoarenes from the reaction of dimethyl acetylenedicarboxylate (DMAD) with the NNDMH's of the respective 2-formylarenes was explained.<sup>[6]</sup> The initially formed, unisolated intermediate **5'** is likely to have undergone thermal elimination of *N*-methylformaldimine to give **5** as the stable product. The liberated aldimine may have polymerised in a manner similar to the trimerisation of acetaldimine.

In contrast, the unacylated azadiene 1c did not react with DEAZD or diethyl acetylenedicarboxylate (DEAD) in refluxing xylene, even in presence of PTS or Montmorillonite K10 clay. However, in the reaction of 1c with DEAZD in acetonitrile solution at  $60^{\circ}$  in presence of PTS, the regeneration of 3-formylindole in good yield was observed (Scheme 4).

Because of the very high resonance energy of 1c, its C(2)=C(3) bond cannot behave as an olefin. In other words, the C(2)=C(3)-CH=N system of 1c does not have sufficient azadiene character to permit its participation in D.–A. reaction. This is the reason, we believe, for the observed failure.

Both 1a and 1b reacted with methyl propiolate (MP) in acetonitrile solution at 60° to furnish once again the respective 3-cyanoindoles 4a and 4b(Scheme 5). The presence of PTS was not found to be essential for the conversion of 1a to 4a, but it appeared to enhance the rate of the reaction (not detailed in the Experimental). PTS was found to be ineffective for the conversion of 1b to 4b, but the catalytic presence of M. K10 clay appeared to be necessary.

The parent azadiene **1c** reacted fast with MP in acetonitrile to furnish two products, of which 3-cyanoindole (**4c**) was the major one (Scheme 6). While trying to arrive at the individual <sup>1</sup>H and <sup>13</sup>C NMR assignments of **4c** by analysing its HMQC and GHMBC spectra (CDCl<sub>3</sub>), a 3-bond <sup>13</sup>C<sup>-1</sup>H HMBC correlation was recorded between a carbon at  $\delta$  87.6 and H-2 ( $\delta$  7.74),

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Scheme 6.

$$4\mathbf{c} + \mathrm{MP} \xrightarrow{\mathrm{CH}_3\mathrm{CN}; \, \mathrm{rt}} \mathbf{6} \, (64\%)$$

Scheme 7.

which suggested the former to be the 3-cyano carbon. But a perusal of the <sup>13</sup>C chemical shifts of various nitriles<sup>[13]</sup> strongly advocated that another chemical shift at  $\delta$  115.7 be assigned to CN, thereby ascribing  $\delta$  87.6 to C-3 of the indole ring. These values reasonably agreed with those, viz.  $\delta$  116.0 and  $\delta$  84.6 (d<sub>6</sub>-DMSO), respectively, retrieved from an online search.<sup>[14]</sup> The referred correlation thus transpired to be a two-bond <sup>13</sup>C<sup>-1</sup>H correlation.

The minor product was identified as the new 3-cyanoindole **6**, which clearly stemmed from both dienophile-catalysed addition-elimination reaction and Michael addition of MP at N-1 of the indole nucleus. The placement of the 3-substituted methacrylate moiety at N-1 of 3-cyanoindole was deduced from the combined 1D and 2D NMR experiments and the nOe's of H-7 ( $\delta$  7.66) and H-2' ( $\delta$  6.15) signals, observed when H-3' ( $\delta$  8.22) and H-2 ( $\delta$  7.90), respectively were irradiated.

The simultaneous formation of both 4c and 6 suggested that elimination was the first step (leading to 4c), followed by Michael reaction, leading to 6. When 4c was similarly treated with MP, 6 was formed, but the reaction took conspicuously long time (23 h) for completion (Scheme 7). This suggested that both elimination and Michael reaction were taking place simultaneously, with the former taking place at a much faster rate.

In view of the successful D.–A. reaction of furfuraldoxime,<sup>[9]</sup> we studied the reaction of the indolic oxime **2** with acrylonitrile (AN), acrylamide (AA), DMAD, MP and DEAZD. As apprehended, the targeted D.–A. reaction did not take place with any of these dienophiles. Instead, the reaction took different courses for the enoic and the ynoic dienophiles. Thus, the reaction of **2** with AN and AA in refluxing benzene furnished the respective nitrones **7a** and **7b** (Scheme 8), whose structures received support from their following characteristic <sup>1</sup>H NMR data:  $\delta$  4.18/4.10 and

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CHAKRABARTY ET AL.  $C_6H_6; \Delta$ H2 12/14 hr ĊH2R 85/80 % Ĥ 2 AN: R = CN7a(R = CN) $AA: R = CONH_2$ 7b ( $R = CONH_2$ ) Scheme 8. 2 + DMAD/MP  $\xrightarrow{\text{CH}_3\text{CN}; 60^\circ}$  3-Formylindole + (22/21%)4c (11/15%)Scheme 9.

 $\delta$  3.12/2.70 (2H, t each, *J* 6.5/7 Hz) for CH<sub>2</sub>N<sup>+</sup> and CH<sub>2</sub>R groups, respectively. These nitrones are expected to have resulted from a formal Michael addition via the nitrogen lone pair (1,3-azaprotio cyclotransfer)<sup>[15]</sup> to the activated alkenes, as shown above.

Similar nitrones have recently been reported to be formed by the reaction of 2 with methyl acrylate, methyl vinyl ketone and NMM.<sup>[16]</sup>

The reaction of **2** with DMAD, MP and DEAZD, carried out in acetonitrile at  $60^{\circ}$ , furnished two products in each case, 3-formylindole being the common product. The second product from each of DMAD and MP was 3-cyanoindole (**4c**) (Scheme 9).

We propose to explain the formation of 3-formylindole and 4c as follows. Any oxime, e.g., 2 is known to exist in equilibrium with the corresponding NH nitrone, 2' in this case, generated by 1,2-prototropy (Scheme 10).<sup>[17]</sup> Alternatively, the oxime may experience a formal Michael addition through the lone pair of its oxime nitrogen to the ynoic dienophiles, leading to the nitrone 2''. Water present in the LR grade acetonitrile used in the reaction brings about the hydrolysis of either of the nitrones, 2' and 2'', to furnish 3-formylindole. When the oxime itself was stirred in acetonitrile at  $60^{\circ}$  for 12 h, no reaction took place. This rules out the possibility of the hydrolysis of the NH-nitrone 2', thereby pointing to the hydrolysis of 2'' as the possible pathway. As in the case of the NNDMH's **1a–c**, a dienophilecatalysed addition-elimination reaction of 2 is likely to have led to the formation of **4c**.

The second product of the reaction of 2 with DEAZD was identified as the hydrazine 5 (Scheme 11), which may have been formed in a manner

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stated in the reaction of 1a/b with DEAZD. We were, however, baffled by the lack of formation of 3-cyanoindole as one of the products.

In fine, both the predictions from  $\pi$ -VE-SCF-MO calculations came partly true. Thus, 1b (and previously 1a) underwent Diels-Alder reaction with only NMM, while 1a, 1b, 2 and partly 1c displayed dienophileaddition-elimination reactions, catalysed furnishing the related 3-cyanoindoles with the ynoic and the azo dienophiles. The formation of 5 from the reactions with DEAZD and that of nitrones from the reactions of **2** have precedence in the case of other azadienes. To our knowledge, the present communication is the first record of the formation of a product resulting from both addition-elimination reaction and Michael addition occurring at different sites of the same substrate.

#### **EXPERIMENTAL**

Uncorrected Melting points (in Celsius) were determined on a Toshniwal apparatus. IR spectra (KBr) were recorded on a Nicolet Impact 410, Shimadzu 408, JAFCO 410 or Perkin Elmer 1600 spectrophotometers, electron impact mass spectra on AEI MS 3074 (LR) or JEOL-JMS AX505H (LR, HR) instruments, and <sup>1</sup>H and <sup>13</sup>C NMR spectra, both 1D and 2D, on Bruker AM 300L, Varian XL-400 or Bruker DRX 500 NMR spectrometers. Complete <sup>1</sup>H and <sup>13</sup>C NMR assignments, whenever stated, were derived from <sup>1</sup>H, <sup>13</sup>C, spin decoupling, nOe, HMQC and GHMBC spectra. Microanalyses were carried out on a Dr. Hans Hoesli Analyser at the Department of Pure Chemistry, University of Calcutta, Calcutta. Analytical and preparative TLC's were carried out on silica gel G plates XX

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(Merck, India). Spots were identified by iodine vapour and 0.5% KMnO<sub>4</sub> in aq. 1(N) NaOH. All the dienophiles, NH<sub>2</sub>NMe<sub>2</sub>, NH<sub>2</sub>OH·HCl and Montmorillonite K10 clay were procured commercially. For reactions with methyl propiolate, a stock solution (1 mL in 49 mL CH<sub>3</sub>CN) was used. Petrol refers to petroleum ether, b.p. 60–80°. The NNDMH's **1a**<sup>[10]</sup>, **1b**,<sup>[10]</sup> **1c**<sup>[10]</sup> and 3-formylindole<sup>[18]</sup> were prepared by literature procedures. The unreported spectral data of 2 have been presented here.

**Preparation of 2:** An aq. solution (1 mL) of NH<sub>2</sub>OH.HCl (105 mg) was neutralised with 50% aq. NaOH, added to a solution of 3-formylindole (145 mg; 1 mM) in ethanol (4 mL) and refluxed for 0.5 h. The solution at rt was diluted with water and neutralised with 1 : 1 aq. AcOH. The resulting precipitate was filtered, washed, dried and crystallised from rectified spirit to furnish pure 2: colourless needles, m.p. 196–198° (Lit.<sup>[19]</sup> m.p. 197–198°); yield: 0.146 g (91%); IR: 3384, 3164, 1642, 753 cm<sup>-1</sup>; MS: m/z 160 (M<sup>+</sup>; 20%), 142 (100), 115 (50); <sup>1</sup>H NMR (500 MHz; d<sub>6</sub>-DMSO):  $\delta$ 11.51 & 11.21 (1H, s each, NH & OH), 8.18 (1H, d, J 2.5 Hz, CH=N), 7.81 & 7.40 (1H, d each, J 8 Hz, H-4 & 7, respectively), 7.74 (1H, s, H-2), 7.12 & 7.06 (1H, t each, J 7.5 Hz, H-6 & 5, respectively); <sup>13</sup>C NMR (125 MHz):  $\delta$  135.7 (C-7a), 127.1 (C-3a), 107.2 (C-3), 139.2, 131.3, 122.7, 120.7, 119.0, 112.6 (all Ar–CH).

**Reaction of 1b with NMM:** A solution of **1b** (90 mg; 0.3 mM) and NMM (83 mg; 0.75 mM) in dry xylene (10 mL) containing PTS (5 mg) was refluxed under nitrogen blanket for 12 h. Xylene was distilled off under reduced pressure, the residue dissolved in little CHCl<sub>3</sub> and diluted with excess petrol. The resulting ppt. (49 mg) was purified by prep. TLC in C<sub>6</sub>H<sub>6</sub>:EtOAc (2:3) to furnish **3b** (Rf 0.48), yellowish solid, m.p. 248–250° (petrol–CHCl<sub>3</sub>); yield: 16 mg (15%); anal. Found: C, 70.88; H, 3.65; N, 11.80; calc. for C<sub>21</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub>: C, 70.98; H, 3.66; N, 11.83%; IR: 1772, 1708, 748 cm<sup>-1</sup>; MS: m/z 355 (M<sup>+</sup>; 11%), 165 (7), 105 (100), 77 (48), 51 (10); <sup>1</sup>H NMR (100 MHz):  $\delta$  3.16 (3H, s, NMe), 7.30–7.80 (6H), 7.84–8.04 (2H) & 8.16–8.40 (1H) (all m; 9 × Ar–CH), 9.64 (1H, s, CH=N).

**Reaction of 1a with DEAZD: 1a** (63 mg; 0.25 mM), dissolved in 8 mL xylene, was treated with DEAZD (0.1 mL; 0.5 mM) and refluxed in nitrogen atmosphere for 32 h. Xylene was distilled off under reduced pressure, and the residue was separated into its components by PTLC in petrol–EtOAc (13:7) to furnish **1a** (15 mg), **4a** (Rf 0.55) and **5** (Rf 0.48).

**4a**; Viscous mass which, when kept in fridge, solidified; m.p.  $65-66^{\circ}$  (Lit.<sup>[10]</sup> m.p.  $66^{\circ}$ ); yield: 11 mg (25%).

5: Light brown needles, m.p.  $128-130^{\circ}$  (petrol–CHCl<sub>3</sub>) (Lit.<sup>[10]</sup> m.p.  $131-132^{\circ}$ ); yield: 21 mg (24%); IR: 3246, 1753, 1699 cm<sup>-1</sup>; MS: *m/z* 176 (M<sup>+</sup>; 31%), 131 (28), 130 (17), 104 (100), 103 (58); <sup>1</sup>H NMR (400 MHz): δ 6.45 (1H, br, NH), 4.2 (2H, q) & 1.24 (3H, t, *J* 5 Hz; CO<sub>2</sub>Et); <sup>13</sup>C NMR (100 MHz): δ 151.7 (*C*O<sub>2</sub>Et), 57.3 (CH<sub>2</sub>), 9.4 (CH<sub>3</sub>).

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# **Reaction of 1b with DEAZD:** A solution of **1b** (88 mg; 0.3 mM) in xylene (8 mL) was refluxed with DEAZD (0.8 mM) under nitrogen blanket for 30 h. Removal of xylene and PTLC of the residue in petrol–EtOAc (13:7) furnished **4b** (Rf 0.58), **1b** (19 mg) and **5** (Rf 0.48) (20 mg; 14%) in pure state. **4b**: Colourless needles, m.p. 106–108° (Lit.<sup>[10]</sup> m.p. 108–110°); vield: 12 mg (20%).

**Reaction of 1c with DEAZD:** A solution of **1c** (20 mg; 0.1 mM) and PTS (5 mg) in CH<sub>3</sub>CN (3 mL) was stirred at 60° for 11 h. Removal of solvent and purification of the residue by PTLC in petrol–EtOAc (13:7) furnished 3-formylindole (Rf 0.4) as buff-coloured needles, m.p. 197–198° (aq. EtOH) (Lit.<sup>[19]</sup> m.p. 197–199°); yield: 12 mg (77%).

**Reaction of 1a with MP:** MP (3 mL stock soln.; 0.6 mM) was added to a solution of **1a** (0.5 mM) in CH<sub>3</sub>CN (10 mL) and stirred at  $60^{\circ}$  for 34 h. A similar work-up and PTLC in petrol–EtOAc (13:7) furnished **4a** (14 mg; 13%).

**Reaction of 1b with MP:** A solution of **1b** (0.1 mM) in CH<sub>3</sub>CN (5 mL) containing Montmorillonite K 10 clay (5 mg) and MP (0.12 mM) was stirred at 60° for 38 h. The solution was filtered through a bed of celite and the residue obtained by evaporation of the filtrate was purified by PTLC to give **4b** in 33% yield (8 mg).

**Reaction of 1c with MP:** A solution of **1c** (40 mg; 0.2 mM) and MP (0.25 mM) in CH<sub>3</sub>CN (5 mL) was stirred for 3.5 h. Removal of CH<sub>3</sub>CN and purification by PTLC in petrol–EtOAc (3:1) furnished pure **4c** (Rf 0.5) and **6** (Rf 0.3).

**4c:** Fluffy, colourless needles, m.p. 178–180° (petrol–CH<sub>2</sub>Cl<sub>2</sub>) (Lit.<sup>[20]</sup> m.p. 179–182°); yield: 16 mg (55%); IR: 3218, 2216 cm<sup>-1</sup>; MS: m/z 142 (100%), 115 (61), 114 (28), 88 (27); <sup>1</sup>H NMR (400 MHz):  $\delta$  8.74 (1H, br, NH), 7.78 (1H, m, H-4), 7.74 (1H, d, J 3 Hz, H-2), 7.48 (1H, ddd, J 8, 2, <1 Hz, H-7), 7.34 & 7.31 (1H, dt each, J 8, 2 Hz, H-6 & 5, respectively); <sup>13</sup>C NMR (100 MHz):  $\delta$  134.8 (C-7a), 126.9 (C-3a), 115.5 (CN), 87.6 (C-3), 131.7 (CH-2), 124.3 (CH-6), 122.4 (CH-5), 119.7 (CH-4), 112.0 (CH-7).

**6:** Off-white flakes, m.p. 102–104° (petrol–CHCl<sub>3</sub>); yield: 12 mg (22%); IR: 2223, 1730, 1650, 940 cm<sup>-1</sup>; MS: m/z 226.0742 (C<sub>13</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>; M<sup>+</sup>; 100%), 197 (20), 195.0558 (C<sub>12</sub>H<sub>7</sub>N<sub>2</sub>O; 82), <sup>1</sup>H NMR (400 MHz): δ 8.22 (H<sub>A</sub>) & 6.15 (H<sub>B</sub>) (1H, d each, J 16 Hz, NCH<sub>A</sub>=CH<sub>B</sub>), 7.90 (1H, s, H-2), 7.78 and 7.65 (1H, br d each, J 8 Hz, H-4 & 7, respectively), 7.48 & 7.41 (1H, dt each, J 8, 2 Hz, H-6 & 5, respectively); <sup>13</sup>C NMR (100 MHz): δ 166.5 (CO<sub>2</sub>), 135.1 (C-7a), 127.8 (C-3a), 114.0 (CN), 93.0 (C-3), 135.8 (N-CH=), 130.2 (CH-2), 126.0 (CH-6), 124.3 (CH-5), 120.4 (CH-4), 110.8 (CH-7), 105.2 (=*C*H–CO<sub>2</sub>).

**Reaction of 4c with MP:** A solution of 4c (0.2 mM) and MP (0.2 mM) in CH<sub>3</sub>CN (5 mL) was stirred at rt for 23 h. CH<sub>3</sub>CN was then boiled off and the residue was crystallised from CHCl<sub>3</sub> to furnish **6** in 64% yield (29 mg).

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**Reaction of 2 with AN:** A solution of **2** (33 mg; 0.2 mM) and AN (22 mg; 0.4 mM) in dry C<sub>6</sub>H<sub>6</sub> (5 mL) was refluxed for 12 h and then left overnight at rt. The resulting crystals were filtered under suction and dried to furnish pure **7a**: fluffy, white needles, m.p. 176° (C<sub>6</sub>H<sub>6</sub>) (Rf 0.6) in EtOAc–MeOH (4:1); yield: 36 mg (85%); anal. found: C, 67.57; H, 5.18; N, 19.75; calc. for C<sub>12</sub>H<sub>11</sub>N<sub>3</sub>O: C, 67.61; H, 5.16; N, 19.72%; IR: 3344, 2258, 1611, 749 cm<sup>-1</sup>; MS: *m/z* 213 (M<sup>+</sup>; 100%), 197 (78), 173 (40); <sup>1</sup>H NMR (500 MHz; d<sub>6</sub>-DMSO):  $\delta$  11.74 (1H, s, NH), 8.83 (1H, d, *J* 1.5 Hz, CH=N<sup>+</sup>), 8.31 (1H, s, H-2), 7.78 & 7.45 (1H, d each, *J* 8 Hz, H-4 & 7, respectively), 7.17 & 7.13 (1H, t each, *J* 7.5 Hz, H-6 & 5, respectively), 4.17 & 3.12 (2H, t each, *J* 6.5 Hz, N<sup>+</sup>CH<sub>2</sub> & CH<sub>2</sub>CN, respectively); <sup>13</sup>C NMR (125 MHz):  $\delta$  136.3 (C-7a), 126.7 (C-3a), 119.5 (CN), 107.8 (C-3), 129.6, 129.3, 123.3, 120.9, 118.9, 112.9 (all CH), 59.3 (CH<sub>2</sub>N<sup>+</sup>), 16.8 (CH<sub>2</sub>CN).

**Reaction of 2 with AA:** A solution of **2** (0.4 mM) and AA (43 mg; 0.6 mM) in dry  $C_6H_6$  (8 mL) was refluxed for 14 h and left overnight at rt. The resulting solid was filtered and dried to give **7b**: white needles, m.p. 216–218° ( $C_6H_6$ ) (Rf 0.2 in EtOAc-MeOH=4:1); yield: 74 mg (80%); anal. found: C, 62.39; H, 5.65; N, 18.21; calc. for  $C_{12}H_{13}N_3O_2$ : C, 62.34; H, 5.63; N, 18.18%; IR: 3365, 3201, 1663, 745 cm<sup>-1</sup>; MS: *m/z* 231 (M<sup>+</sup>; 78%), 215 (100), 214 (77), 197 (25), 187 (18); <sup>1</sup>H NMR (500 MHz; d<sub>6</sub>-DMSO):  $\delta$  11.55 (1H, s, NH), 8.78 (1H, d, J 2.5 Hz, CH=N<sup>+</sup>), 8.16 (1H, s, H-2), 7.77 & 7.43 (1H, d each, *J* 8 Hz, H-4 & 7, respectively), 7.16 & 7.11 (1H, t each, *J* 7.3 Hz, H-6 & 5, respectively), 7.45 & 6.87 (1H, br s each, CONH<sub>2</sub>), 4.10 & 2.70 (2H, t each, *J* 7 Hz, CH<sub>2</sub>N<sup>+</sup> & CH<sub>2</sub>CO, respectively); <sup>13</sup>C NMR (125 MHz):  $\delta$  172.6 (CO), 136.2 (C-7a), 126.6 (C-3a), 108.1 (C-3), 129.0, 128.3, 123.1, 120.7, 118.9, 112.8 (all Ar–CH), 60.5 (CH<sub>2</sub>N<sup>+</sup>), 33.9 (CH<sub>2</sub>CO).

**Reaction of 2 with DMAD:** A solution of 2 (0.5 mM) in CH<sub>3</sub>CN (5 mL) containing DMAD (107 mg; 0.75 mM) was stirred at 60° for 12 h. The solvent was boiled off and the residue was purified by PTLC in petrol–EtOAc (2:1) to furnish **4c** (Rf 0.3) (8 mg; 11%) and 3-formylindole (Rf 0.2) (16 mg; 22%).

**Reaction of 2 with MP:** A solution of **2** (0.5 mM) and MP (1.5 mM) in CH<sub>3</sub>CN (5 mL) was stirred at 60° for 12 h. The removal of solvent, followed by PTLC of the residue in C<sub>6</sub>H<sub>6</sub>–MeOH (9:1) furnished **4c** (Rf 0.5) (11 mg; 15%) and 3-formylindole (Rf 0.4) (15 mg; 21%).

**Reaction of 2 with DEAZD:** A solution of **2** (0.2 mM) and DEAZD (0.3 mM) in CH<sub>3</sub>CN (4 mL) was stirred at 60° for 8 h. The removal of solvent and purification of the resulting residue by PTLC in petrol–EtOAc (13:7) furnished 23 mg of a solid (Rf 0.3), m.p. 115° which was shown by <sup>1</sup>H NMR spectrum to be a mixture of 3-formylindole and **5** (in 7:93 ratio), also supported by TLC in petrol–C<sub>6</sub>H<sub>6</sub>–EtOAc (1:1:3): **5** (Rf 0.6) and 3-formylindole (Rf 0.5).

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#### FOUR INDOLIC 1-AZADIENES

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