Tetrahedron 65 (2009) 6868–6872

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Preparation of *peri*-annulated indoles from polynitro compounds

Alexander V. Samet *, Alexei N. Yamskov [1], Yuri A. Strelenko, Victor V. Semenov

N. D. Zelinsky Institute of Organic Chemistry RAS, Leninsky Pr., 47, Moscow, 119991, Russian Federation

ARTICLE INFO

Article history:
Received 8 April 2009
Received in revised form 2 June 2009
Accepted 19 June 2009
Available online 24 June 2009

ABSTRACT

A novel *peri*-annulated heterocyclic system of 1,2-dihydrobenz[6,7]oxepino[4,3,2-*cd*]indole was prepared starting from TNT via 4,6-dinitro-1-tosylindoline as a key intermediate. Base-induced C=C bond shift in 1,2-dihydrobenz[6,7]oxepino[4,3,2-*cd*]indoles affords isomeric 2,11-dihydrobenz[6,7]oxepino[4,3,2-*cd*]indoles.

1. Introduction

Some natural biologically active compounds feature *peri*-annulated indole core.[1] Thus, well-known lysergic acid derivatives **A**[1b] contain an indole moiety fused with cyclohexane ring, while in the molecules of welwitindolinones **B**,[2] aurantioclavine,[3] clavicipitic acid[4] the indole fragment is *peri*-annulated with seven-membered carbo- and heterocycles (Fig. 1).

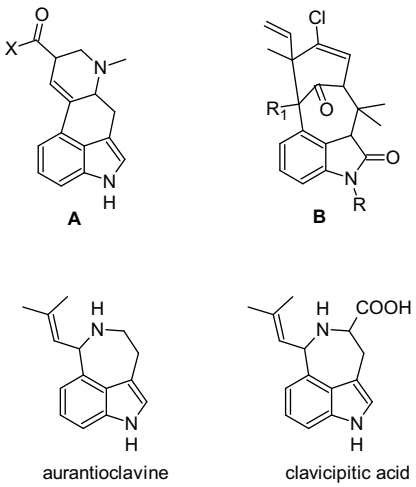
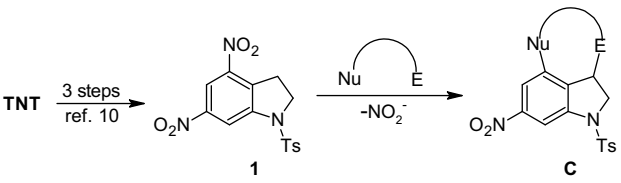


Figure 1. Some natural biologically active compounds with *peri*-annulated indole core.

In the course of investigations aimed at utilization of 2,4,6-trinitrotoluene (TNT)[5–9] earlier we synthesized 4,6-dinitro-1-tosylindoline **1**.[10,11] Its structure includes nitro groups, susceptible to nucleophilic displacement, and acidic benzylic CH-protons, apparently making it a promising intermediate in a synthesis of *peri*-annulated systems with indole fragment **C** under the action of reagents which molecules possess both nucleophilic and electrophilic centers (Scheme 1).[12]



Scheme 1.

Reaction of **1** with benzaldehyde in the presence of a base (piperidine) was previously shown to yield a product of Knoevenagel condensation—3-benzylidene-4,6-dinitro-1-tosylindoline.[13]

2. Results and discussion

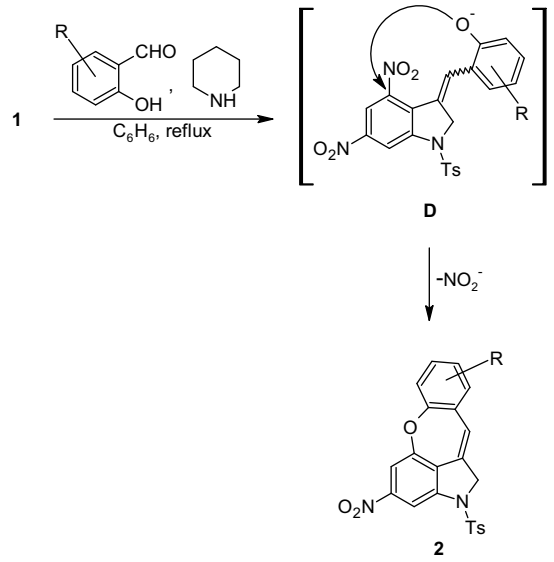
Meanwhile, the reaction with *ortho*-hydroxy benzaldehydes (where the OH-group is a nucleophilic center and the CHO-group is an electrophilic one) normally does not stop at condensation products **D** and is accompanied by intramolecular nucleophilic displacement of the nitro group with the phenolate-anion, resulting in oxepine ring closure (Scheme 2).[14]

The resulting red or orange 1,2-dihydrobenz[6,7]oxepino[4,3,2-*cd*]indoles **2** under the action of a stronger base (DBU) rearrange into colourless 2,11-dihydrobenz[6,7]oxepino[4,3,2-*cd*]indoles **3** with a shift of the C=C bond from the oxepine ring into the pyrrole (see Scheme 3 and Table 1). Energetic gain due to formation of the aromatic indole system is the driving force of the rearrangement.

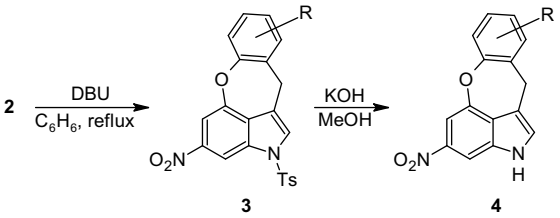
This approach to indole synthesis, featuring an endocyclic C-C double bond shift in 3-(alkylidene)indolines, is not very common, though such shifts induced by acids[15] or bases[16] are known.

* Corresponding author. Fax: +7 495 1355328.
E-mail address: sametav@server.ioc.ac.ru (A.V. Samet).
[1] Deceased.

0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.06.074



Scheme 2.



Scheme 3.

Table 1
Preparation of the compounds **2–4**

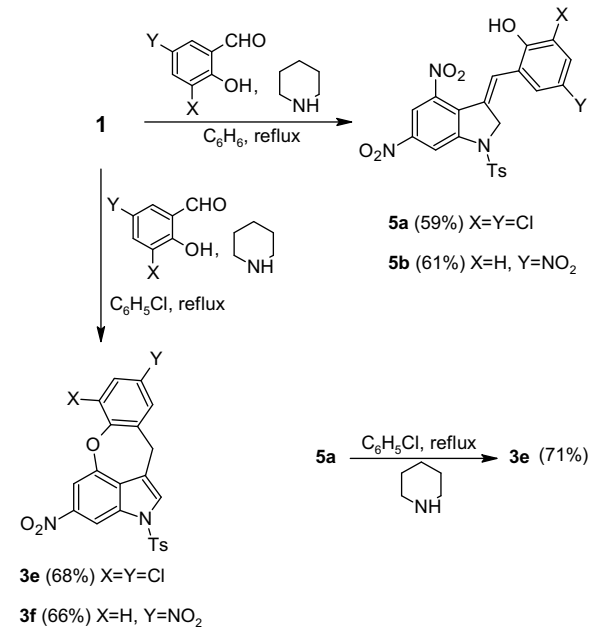
R	Yield of **2** (%)	Yield of **3** (%)	Yield of **4** (%)
H (**a**)	75	82	80
9-Br (**b**)	81	91	96
7-MeO (**c**)	68	92	90
7-allyl (**d**)	76	87	86
7,9-Cl_2 (**e**)		68[a]	96

[a] Prepared directly from **1** in refluxing C_6H_5Cl, see Scheme 4.

N-Tosylindoles **3** undergo smooth detosylation by KOH in MeOH furnishing NH-indoles **4**.

Under the same conditions, a reaction of the indoline **1** with 5-nitrosalicylic and 3,5-dichlorosalycilic aldehydes affords 3-(2-hydroxybenzylidene)indolines **5** instead of cyclization products (Scheme 4)—obviously, because of the lower nucleophilicity of the corresponding phenolate anions due to the electron-withdrawing substituents in the ring. However, the cyclization does take place at higher temperature (when refluxing chlorobenzene is used instead of benzene as a solvent). Under these conditions, the concomitant shift of the C=C bond occurs as well, and 2,11-dihydrobenz[6,7]oxepino[4,3,2-*cd*]indoles **3e**,**f** are formed directly (1,2-dihydro derivatives **2** were not isolated).

2D ^{1}H NOESY spectrum of the compound **5b** provides evidence for (*Z*)-configuration of 3-(2-hydroxybenzylidene)indolines **5** (Fig. 2). A cross-peak between the signals of H-2 (δ 5.11) and H-6′ (δ 8.14) is observed in the spectrum, while a cross-peak between the signals of H-2 and =CH (δ 7.12) is absent (for comparison, 2D ^{1}H NOESY spectrum of oxepinoindole **2a** features a strong cross-peak between the corresponding signals H-1 (δ 4.75) and H-11 (δ 6.49).



Scheme 4.

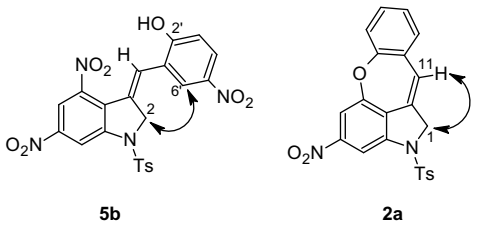
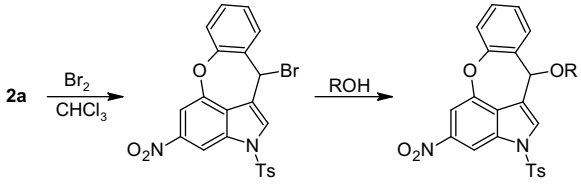


Figure 2. Key cross peaks in 2D ^{1}H NOESY spectra of **5b** and **2a**.

Thus, a base-induced (*Z*)-(*E*)-isomerization should apparently precede the cyclization of **5a**,**b** to **3e**,**f** (such isomerization seems quite plausible in the phenolates like **D**, see Scheme 2).

An interesting transformation of the oxepinoindoles **2** consists of their bromination and subsequent nucleophilic substitution. Bromination[17] of **2a** affords 11-bromo derivative **6**, which could be converted to ethers **7a**,**b** simply by refluxing it in the corresponding alcohols (MeOH, EtOH) (Scheme 5):



Scheme 5.

Probably, such a smooth alcoholysis is due to a S_N1 reaction mechanism and the high stability of the corresponding carbocation in the 11 position.[18]

3. Conclusion

Reaction of 4,6-dinitro-1-tosylindoline, prepared in 3 steps from TNT, with *o*-hydroxybenzaldehydes proceeds via intermediate (*Z*)-3-(*o*-hydroxybenzylidene)indolines (which were isolated in

some cases) and affords 1,2-dihydrobenz[6,7]oxepino[4,3,2-*cd*]indoles. Base-induced C=C bond shift in the latter results in isomeric 2,11-dihydrobenz[6,7]oxepino[4,3,2-*cd*]indoles, while bromination of 1,2-dihydrobenz[6,7]oxepino[4,3,2-*cd*]indoles and subsequent nucleophilic displacement yields 11-substituted derivatives. Thus, TNT could be used for a synthesis of a novel class of *peri*-annulated indoles.

4. Experimental

4.1. General

^{1}H NMR spectra were recorded on a Bruker AM-300 and Bruker DRX500 spectrometers (300.13 and 500.13 MHz, respectively); ^{13}C NMR spectra were recorded on a Bruker DRX500 spectrometer (125.75 MHz). Mass-spectra were measured on a Kratos MS-30 instrument (EI, 70 eV). IR spectra were obtained on a 'Specord M80–2' spectrometer.

4.2. Synthetic procedures

Caution. Both we and other researchers encountered no difficulties in working with multi-gram quantities of TNT[19] (the same is true for the compound **1** as well). Nevertheless, polynitroaromatic compounds are potential explosives, so proper protective measures (shields, glasses) should be used during experiments with these materials. Scale-up of the reported reactions requires appropriate chemical hazards testing.

*4.2.1. Preparation of N-tosyl-1,2-dihydrobenz[6,7]oxepino[4,3,2-cd]indoles **2a–d** and 3-(2-hydroxybenzylidene)indolines **5a,b** (general procedure)*

To a suspension of indoline 1 (1.82 g, 5 mmol) and the corresponding *ortho*-hydroxy benzaldehyde (5 mmol) in benzene (5 mL), piperidine (0.45 g, 5.3 mmol) was added, and the mixture was stirred at reflux for 30 min. The resulting thick suspension was cooled to rt, diluted with MeOH, and filtered. The precipitate was washed with MeOH (5 mL) and dried. For isolation of 3-(2-hydroxybenzylidene)indolines, the mixture was acidified with AcOH (1 mL) before filtration.

*4.2.1.1. 4-Nitro-2-(p-toluenesulphonyl)-1,2-dihydrobenz[6,7]oxepino-[4,3,2-cd]indole **2a**.* Yield 75%. Orange-red crystals, mp 236–238 °C (DMF).[13] ^{1}H NMR (DMSO-d_6, δ): 2.35 (s, 3H, Ts), 4.75 (s, 2H, H-1), 6.49 (br s, 1H, H-11), 7.06 (d, J=8.0 Hz, 1H, H-7), 7.09–7.14 (m, 2H), 7.30–7.33 (m, 1H), 7.43 (d, J=8.3 Hz, 2H, Ts), 7.50 (s, 1H, H-5), 7.78 (d, J=8.3 Hz, 2H, Ts), 7.92 (s, 1H, H-3). ^{13}C NMR (DMSO-d_6, δ): 21.1, 55.3, 105.0, 110.7, 122.2, 125.3, 126.1, 127.3 (2CH), 127.8, 128.1, 130.5 (2CH), 131.5, 131.6 (2CH), 132.5, 144.1, 145.4, 150.7, 152.3, 152.9. EIMS (70 eV) (m/z, I, %): 420 [M$^+$, 42], 265 [29], 219 [100], 91 [40]. Anal. Calcd for $C_{22}H_{16}N_2O_5S$: C, 62.85; H, 3.84; N, 6.66; S, 7.63. Found, %: C, 63.13; H, 3.66; N, 6.68; S, 7.78. IR (ν_{max}, KBr): 1524, 1368, 1336, 1160, 1124, 1100, 672.

*4.2.1.2. 9-Bromo-4-nitro-2-(p-toluenesulphonyl)-1,2-dihydrobenz[6,7]-oxepino[4,3,2-cd]indole **2b**.* Yield 81%. Bright-yellow needles, mp 268–270 °C (DMF). ^{1}H NMR (DMSO-d_6, δ): 2.43 (s, 3H, Ts), 4.68 (s, 2H, H-1), 6.34 (br s, 1H, H-11), 6.87 (d, J=8.0 Hz, 1H, H-7), 7.20 (s, 1H, H-10), 7.32 (d, J=8.0 Hz, 1H, H-8), 7.35–7.42 (m, 3H), 7.75 (d, J=8.3 Hz, 2H, Ts), 7.97 (s, 1H, H-3). ^{13}C NMR (DMSO-d_6, δ): 21.0, 55.3, 105.1, 110.5, 117.8, 123.6, 124.1, 127.2 (2CH), 130.2, 130.4 (2CH), 132.5, 133.0, 133.2, 133.5, 144.3, 145.4, 150.9, 152.0. EIMS (70 eV) (m/z, I, %): 500 [M$^+$, 24], 498 [M$^+$, 26], 345 [58], 343 [58], 299 [78], 297 [100], 91 [77]. Anal. Calcd for $C_{22}H_{15}BrN_2O_5S$: C, 52.92; H, 3.03; N, 5.61; S, 6.42. Found: C, 53.25; H, 2.88; N, 5.60; S, 6.20. IR (ν_{max}, KBr): 1536, 1368, 1340, 1168, 1104, 664, 580.

*4.2.1.3. 7-Methoxy-4-nitro-2-(p-toluenesulphonyl)-1,2-dihydrobenz-[6,7]oxepino[4,3,2-cd]indole **2c**.* Yield 68%. Red crystals, mp 246–248 °C (DMF). ^{1}H NMR (DMSO-d_6, δ): 2.42 (s, 3H, Ts), 3.85 (s, 3H, OMe), 4.70 (s, 2H, H-1), 6.42 (br s, 1H, H-11), 6.61 (d, J=8.0 Hz, 1H, H-8), 6.95–7.00 (m, 2H), 7.38 (d, J=8.2 Hz, 2H, Ts), 7.41 (s, 1H, H-5), 7.76 (d, J=8.2 Hz, 2H, Ts), 7.98 (s, 1H, H-3). EIMS (70 eV) (m/z, I, %): 450 [M$^+$, 56], 295 [60], 249 [100], 91 [82]. Anal. Calcd for $C_{23}H_{18}N_2O_6S$: C, 61.32; H, 4.03; N, 6.22; S, 7.12. Found: C, 61.11; H, 3.90; N, 6.54; S, 7.00. IR (ν_{max}, KBr): 1525, 1370, 1335, 1160, 1125, 1103, 665.

*4.2.1.4. 7-Allyl-4-nitro-2-(p-toluenesulphonyl)-1,2-dihydrobenz[6,7]-oxepino[4,3,2-cd]indole **2d**.* Yield 76%. Orange crystals, mp 240–242 °C (DMF). ^{1}H NMR (DMSO-d_6, δ): 2.41 (s, 3H, Ts), 3.48 (d, J=7.4 Hz, 2H), 4.69 (s, 2H, H-1), 5.03–5.08 (m, 2H), 5.94–5.97 (m, 1H), 6.42 (br s, 1H, H-11), 6.92 (d, J=8.1 Hz, 1H, H-10), 6.98 (t, J=8.0 Hz, 1H, H-9), 7.12 (d, J=8.0 Hz, 1H, H-8), 7.40 (m, 3H), 7.76 (d, J=8.3 Hz, 2H, Ts), 7.97 (s, 1H, H-3). ^{13}C NMR (DMSO-d_6, δ): 21.1, 55.3, 105.0, 110.9, 116.0, 125.7, 125.8, 127.2 (2CH), 128.2, 128.4, 129.8, 130.4 (2CH), 131.2, 132.5, 132.7, 136.8, 144.0, 145.4, 150.5, 152.0. EIMS (70 eV) (m/z, I, %): 460 [M$^+$, 50], 305 [54], 259 [81], 91 [100]. Anal. Calcd for $C_{25}H_{20}N_2O_5S$: C, 65.20; H, 4.38; N, 6.08; S, 6.96. Found: C, 64.85; H, 4.56; N, 6.32; S, 7.19. IR (ν_{max}, KBr): 1528, 1368, 1340, 1164, 1120, 664.

*4.2.1.5. 3-(2-Hydroxy-3,5-dichlorobenzylidene)-4,6-dinitro-1-(p-toluenesulphonyl)-2,3-dihydroindole **5a**.* Yield 59%. Orange powder, mp 216–217 °C (MeCN). ^{1}H NMR (DMSO-d_6, δ): 2.43 (s, 3H, Ts), 4.95 (br s, 2H, H-2), 7.17–7.23 (m, 2H), 7.36 (s, 1H), 7.40 (d, J=8.3 Hz, 2H), 7.86 (d, J=8.3 Hz, 2H), 8.28 (s, 1H), 8.43 (s, 1H), 9.90 (br s, 1H, OH). ^{13}C NMR (DMSO-d_6, δ): 21.1, 54.9, 111.0, 115.0, 122.4, 123.5, 123.7, 125.9, 127.0, 127.2, 127.5 (2CH), 128.3, 129.8, 130.5 (2CH), 132.6, 144.2, 145.3, 145.8, 147.9, 150.1. Anal. Calcd for $C_{22}H_{15}Cl_2N_3O_7S$: C, 49.27; H, 2.82; N, 7.83; S, 5.98. Found: C, 49.25; H, 2.95; N, 8.14; S, 5.71. IR (ν_{max}, KBr): 3504, 1536, 1372, 1344, 1172, 664.

*4.2.1.6. 3-(2-Hydroxy-5-nitrobenzylidene)-4,6-dinitro-1-(p-toluenesulphonyl)-2,3-dihydroindole **5b**.* Yield 61%. Orange powder, mp 227–230 °C (MeCN). ^{1}H NMR (DMSO-d_6, δ): 2.37 (s, 3H, Ts), 5.11 (d, J=3.1 Hz, 2H, H-2), 7.09 (d, J=8.9 Hz, 1H, H-3′), 7.12 (t, J=3.1 Hz, 1H, =CH), 7.42 (d, J=8.3 Hz, 2H, Ts), 7.83 (d, J=8.3 Hz, 2H, Ts), 8.14 (d, J=2.7 Hz, 1H, H-6′), 8.17 (dd, J=8.9, 2.7 Hz,1H, H-4′), 8.39 (d, J=2.0 Hz, 1H, H-7), 8.45 (d, J=2.0 Hz, 1H, H-5), 11.72 (br s, 1H, OH). ^{13}C NMR (DMSO-d_6, δ): 21.0, 54.9, 110.9, 114.8, 115.9, 122.2, 122.6, 124.7, 126.4, 127.1, 127.2 (2CH), 128.0, 130.4 (2CH), 132.5, 139.6, 144.1, 145.3, 145.6, 147.7, 161.5. Anal. Calcd for $C_{22}H_{16}N_4O_9S$: C, 51.56; H, 3.15; N, 10.93; S, 6.26. Found: C, 51.35; H, 2.97; N, 11.10; S, 6.49. IR (ν_{max}, KBr): 3497, 1534, 1515, 1370, 1338, 1168, 665.

*4.2.2. Preparation of N-tosyl-2,11-dihydrobenz[6,7]oxepino[4,3,2-cd]-indoles **3a–d** (general procedure)*

To a suspension of 1,2-dihydrobenz[6,7]oxepino[4,3,2-*cd*]indole **2a–d** (4 mmol) in benzene (10 mL), DBU (0.10 g, 0.65 mmol) was added and the mixture was refluxed for 1 h. The resulting homogeneous solution was evaporated to dryness, to the residue MeOH (5 mL) was added, the precipitate filtered off, washed with MeOH (5 mL), and dried.

*4.2.2.1. 4-Nitro-2-(p-toluenesulphonyl)-2,11-dihydrobenz[6,7]oxepino-[4,3,2-cd]indole **3a**.* Yield 82%. Mp 196–198 °C (benzene).[13] ^{1}H NMR (DMSO-d_6, δ): 2.36 (s, 3H, Ts), 4.16 (s, 2H, H-11), 7.11 (t, J=8.1 Hz, 1H), 7.20–7.30 (m, 2H), 7.33 (d, J=8.0 Hz, 1H), 7.37 (d, J=8.2 Hz, 2H, Ts), 7.80 (s, 1H), 7.84 (s, 1H), 7.88 (d, J=8.2 Hz, 2H, Ts), 8.45 (s, 1H, H-3). ^{13}C NMR (DMSO-d_6, δ): 21.1, 28.8, 105.2, 107.7, 118.7, 122.2, 125.6, 125.9, 126.9 (2CH), 127.3, 128.3, 128.7, 130.7 (2CH), 131.8, 133.8, 134.1, 145.5, 146.3, 150.4, 156.9. Anal. Calcd for $C_{22}H_{16}N_2O_5S$: C, 62.85; H, 3.84; N,

6.66; S, 7.63. Found: C, 62.98; H, 4.13; N, 6.39; S, 7.51. IR (ν_{max}, KBr): 1525, 1338, 1245, 1181, 1082, 675.

4.2.2.2. 9-Bromo-4-nitro-2-(p-toluenesulphonyl)-2,11-dihydrobenz-[6,7]oxepino[4,3,2-cd]indole ***3b***. Yield 91%. Mp 192–195 °C (benzene). ^{1}H NMR (DMSO-d_6, δ): 2.38 (s, 3H, Ts), 4.17 (s, 2H, H-11), 7.21 (d, J=8.2 Hz, 1H), 7.32–7.40 (m, 3H), 7.52 (s, 1H, H-10), 7.82 (s, 2H, H-1 and H-5), 7.88 (d, J=8.3 Hz, 2H, Ts), 8.48 (s, 1H, H-3). ^{13}C NMR (DMSO-d_6, δ): 21.0, 28.3, 105.4, 107.7, 117.6, 117.8, 124.5, 125.9, 126.8 (2CH), 130.6 (2CH), 131.3, 133.0, 133.7, 134.0, 134.3, 145.4, 146.3, 149.8, 156.1. EIMS (70 eV) (m/z, I, %): 500 [M$^+$, 95], 498 [M$^+$, 100], 299 [43], 297 [36], 155 [48], 91 [74]. Anal. Calcd for $C_{22}H_{15}BrN_2O_5S$: C, 52.92; H, 3.03; N, 5.61; S, 6.42. Found: C, 53.15; H, 2.91; N, 5.77; S, 6.26. IR (ν_{max}, KBr): 1524, 1336, 1240, 1176, 1124, 1088, 672, 580.

4.2.2.3. 7-Methoxy-4-nitro-2-(p-toluenesulphonyl)-2,11-dihydrobenz-[6,7]oxepino[4,3,2-cd]indole ***3c***. Yield 92%. Mp 229–231 °C (benzene). ^{1}H NMR (DMSO-d_6, δ): 2.37 (s, 3H, Ts), 3.86 (s, 3H, OMe), 4.14 (s, 2H, H-1), 6.86 (d, J=8.0 Hz, 1H, H-10), 6.91 (d, J=8.1 Hz, 1H, H-8), 7.03 (t, J=8.0 Hz, 1H, H-9), 7.37 (d, J=8.3 Hz, 2H, Ts), 7.80 (s, 2H, H-1 and H-5), 7.86 (d, J=8.3 Hz, 2H, Ts), 8.44 (s, 1H, H-3). ^{13}C NMR (DMSO-d_6, δ): 21.1, 28.7, 56.1, 105.5, 107.8, 112.0, 118.7, 121.6, 125.7, 126.0, 126.8 (2CH), 128.0, 130.7 (2CH), 133.3, 133.8, 134.1, 145.4, 145.7, 146.3, 150.3, 152.2. Anal. Calcd for $C_{23}H_{18}N_2O_6S$: C, 61.32; H, 4.03; N, 6.22; S, 7.12. Found, %: C, 61.08; H, 3.95; N, 6.37; S, 6.90. IR (ν_{max}, KBr): 1522, 1335, 1240, 1185, 1085, 671.

4.2.2.4. 7-Allyl-4-nitro-2-(p-toluenesulphonyl)-2,11-dihydrobenz[6,7]-oxepino[4,3,2-cd]indole ***3d***. Yield 87%. Mp 163–164 °C (benzene). ^{1}H NMR (DMSO-d_6, δ): 2.37 (s, 3H, Ts), 3.60 (d, J=7.4 Hz, 2H), 4.15 (s, 2H, H-11), 5.02–5.08 (m, 2H), 5.95–5.98 (m, 1H), 7.03 (t, J=8.0 Hz, 1H, H-9), 7.09 (d, J=8.1 Hz, 1H), 7.19 (d, J=8.0 Hz, 1H, H-8), 7.38 (d, J=8.3 Hz, 2H, Ts), 7.81 (s, 2H, H-1 and H-5), 7.88 (d, J=8.3 Hz, 2H, Ts), 8.45 (s, 1H, H-3). Anal. Calcd for $C_{25}H_{20}N_2O_5S$: C, 65.20; H, 4.38; N, 6.08; S, 6.96. Found: C, 65.00; H, 4.49; N, 6.23; S, 7.25. IR (ν_{max}, KBr): 1525, 1332, 1237, 1182, 1080, 672.

4.2.3. Preparation of N-tosyl-2,11-dihydrobenz[6,7]oxepino[4,3,2-cd]indoles ***3e,f*** *from indoline* ***1***

To a suspension of indoline **1** (1.82 g, 5 mmol) and the corresponding *ortho*-hydroxy benzaldehyde (5 mmol) in chlorobenzene (5 mL), piperidine (0.45 g, 5.3 mmol) was added, and the mixture was stirred at reflux for 2 h. The resulting thick suspension was cooled to rt, diluted with MeOH (5 mL), and filtered. The precipitate was washed with MeOH (5 mL) and dried.

4.2.3.1. 7,9-Dichloro-4-nitro-2-(p-toluenesulphonyl)-2,11-dihydrobenz-[6,7]oxepino[4,3,2-cd]indole ***3e***. Yield 68%. Mp 240–242 °C (benzene). ^{1}H NMR (DMSO-d_6, δ): 2.37 (s, 3H, Ts), 4.23 (s, 2H, H-11), 7.34–7.43 (m, 4H), 7.86–7.92 (m, 4H), 8.51 (s, 1H, H-3). ^{13}C NMR (DMSO-d_6, δ): 21.1, 28.5, 106.1, 107.9, 117.0, 126.4, 126.9 (2CH), 127.1, 127.8, 128.4, 129.2, 129.8, 130.7 (2CH), 133.7, 134.0, 135.7, 145.4, 146.4, 148.7, 151.0. Anal. Calcd for $C_{22}H_{14}Cl_2N_2O_5S$: C, 54.00; H, 2.88; N, 5.72; S, 6.55. Found: C, 53.71; H, 2.84; N, 6.09; S, 6.72. IR (ν_{max}, KBr): 1525, 1340, 1234, 1180, 1085, 670.

4.2.3.2. 4,9-Dinitro-2-(p-toluenesulphonyl)-2,11-dihydrobenz[6,7]-oxepino[4,3,2-cd]indole ***3f***. Yield 66%. Mp 270–275 °C (DMF) (decomp.). ^{1}H NMR (DMSO-d_6, δ): 2.32 (s, 3H, Ts), 4.38 (s, 2H, H-11), 7.43 (d, J=8.3 Hz, 2H, Ts), 7.66 (d, J=8.8 Hz, 1H), 7.95 (d, J=8.3 Hz, 2H, Ts), 8.02 (d, J=1.8 Hz, 1H, H-5), 8.04 (s, 1H, H-1), 8.19 (dd, J=8.8, 2.8 Hz, 1H), 8.36 (d, J=2.8 Hz, 1H), 8.50 (d, J=1.8 Hz, 1H, H-3). ^{13}C NMR (DMSO-d_6, δ): 21.1, 28.5, 105.7, 108.0, 117.2, 123.9, 124.2, 126.1, 126.6, 126.9 (2CH), 130.7 (2CH), 133.4, 133.6, 134.0, 144.3, 145.5, 146.4, 149.0, 161.4. EIMS (70 eV) (m/z, I, %): 465 [M$^+$, 49], 218 [30], 155 [77], 91 [100]. Anal. Calcd for $C_{22}H_{15}N_3O_7S$: C, 56.77; H, 3.25; N, 9.03; S, 6.89. Found: C, 56.62; H, 3.40; N, 8.82; S, 7.15. IR (ν_{max}, KBr): 1532, 1512, 1344, 1296, 1236, 1180, 1084, 672.

Using the same procedure, the compound **3e** could be prepared from **5a** in 71% yield.

4.2.4. Preparation of NH-2,11-dihydrobenz[6,7]oxepino[4,3,2-cd]-indoles ***4a–e*** *(general procedure)*

A suspension of *N*-tosyl-2,11-dihydrobenz[6,7]oxepino[4,3,2-*cd*]indole **3a–e** (4 mmol) and KOH (0.84 g, 15 mmol) in MeOH (20 mL) was refluxed for 40 min and poured into 1 N HCl (50 mL). The resulting precipitate was filtered off and dried.

4.2.4.1. 4-Nitro-2,11-dihydrobenz[6,7]oxepino[4,3,2-cd]indole ***4a***. Yield 80%. Mp 242–243 °C (MeCN). ^{1}H NMR (DMSO-d_6, δ): 4.21 (s, 2H, H-11), 7.14 (t, J=8.2 Hz, 1H), 7.28 (t, J=8.1 Hz, 1H), 7.35–7.39 (m, 2H), 7.55 (s, 1H), 7.58 (s, 1H), 8.08 (s, 1H), 11.59 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, δ): 29.5, 101.8, 104.9, 112.2, 122.3, 124.6, 125.2, 126.3, 128.2, 130.5, 133.8, 135.4, 142.7, 149.9, 157.2. Anal. Calcd for $C_{15}H_{10}N_2O_3$: C, 67.67; H, 3.79; N, 10.52. Found: C, 67.59; H, 3.93; N, 10.80. IR (ν_{max}, KBr): 3342, 1515, 1470, 1356, 1335.

4.2.4.2. 9-Bromo-4-nitro-2,11-dihydrobenz[6,7]oxepino[4,3,2-cd]indole ***4b***. Yield 96%. Mp 235–237 °C (MeCN). ^{1}H NMR (DMSO-d_6, δ): 4.21 (s, 2H, H-11), 7.33 (d, J=8.2 Hz, 1H, H-7), 7.45 (d, J=8.2 Hz, 1H, H-8), 7.55 (s, 1H), 7.59 (s, 1H), 7.63 (s, 1H, H-10), 8.09 (s, 1H), 11.62 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, δ): 28.9, 101.9, 105.1, 111.3, 116.9, 124.2, 124.6, 126.6, 130.8, 132.8, 135.4, 136.4, 142.6, 149.3, 156.5. Anal. Calcd for $C_{15}H_9BrN_2O_3$: C, 52.20; H, 2.63; N, 8.12. Found: C, 52.31; H, 2.64; N, 7.89. IR (ν_{max}, KBr): 3368, 1516, 1472, 1348, 1332.

4.2.4.3. 7-Methoxy-4-nitro-2,11-dihydrobenz[6,7]oxepino[4,3,2-cd]indole ***4c***. Yield 90%. Mp 234–238 °C (MeCN) (decomp.). ^{1}H NMR (DMSO-d_6, δ): 3.85 (s, 3H, OMe), 4.19 (s, 2H, H-11), 6.93 (d, J=8.0 Hz, 1H), 7.00 (d, J=8.0 Hz, 1H), 7.06 (t, J=8.0 Hz, 1H), 7.51 (s, 1H), 7.53 (s, 1H), 8.07 (s, 1H), 11.53 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, δ): 29.3, 56.1, 102.1, 105.0, 111.6, 112.1, 121.6, 125.2, 125.3, 126.3, 135.3, 135.4, 142.5, 145.9, 149.7, 152.4. EIMS (70 eV) (m/z, I, %): 296 [M$^+$, 100], 265 [59], 249 [55], 235 [31]. Anal. Calcd for $C_{16}H_{12}N_2O_4$: C, 64.86; H, 4.08; N, 9.46. Found: C, 65.01; H, 4.14; N, 9.20. IR (ν_{max}, KBr): 3328, 1512, 1472, 1332, 1296, 1080, 760.

4.2.4.4. 7-Allyl-4-nitro-2,11-dihydrobenz[6,7]oxepino[4,3,2-cd]indole ***4d***. Yield 86%. Mp 165–166 °C (MeCN). ^{1}H NMR (DMSO-d_6, δ): 3.63 (d, J=7.4 Hz, 2H), 4.19 (s, 2H, H-11), 5.05 (m, 2H), 6.01 (m, 1H), 7.06 (t, J=8.0 Hz, 1H, H-9), 7.14 (d, J=8.1 Hz, 1H), 7.24 (d, J=8.0 Hz, 1H), 7.53 (s, 1H), 7.59 (s, 1H), 8.08 (s, 1H), 11.56 (s, 1H, NH). Anal. Calcd for $C_{18}H_{14}N_2O_3$: C, 70.58; H, 4.61; N, 9.15. Found: C, 70.30; H, 4.82; N, 8.88. IR (ν_{max}, KBr): 3354, 1522, 1455, 1346, 1335, 1075.

4.2.4.5. 7,9-Dichloro-4-nitro-2,11-dihydrobenz[6,7]oxepino[4,3,2-cd]indole ***4e***. Yield 96%. Mp 295–298 °C (MeCN). ^{1}H NMR (DMSO-d_6, δ): 4.27 (s, 2H, H-11), 7.52 (d, J=2.4 Hz, 1H), 7.57 (s, 1H), 7.59 (d, J=2.4 Hz, 2H), 7.62 (s, 1H), 8.12 (s, 1H), 11.67 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, δ): 29.0, 102.3, 105.7, 110.4, 124.2, 126.9, 127.7, 128.9, 129.0, 135.3, 137.7, 142.5, 148.1, 151.2. Anal. Calcd for $C_{15}H_8Cl_2N_2O_3$: C, 53.76; H, 2.41; N, 8.36. Found: C, 53.56; H, 2.49; N, 8.67. IR (ν_{max}, KBr): 3424, 1528, 1448, 1352, 1336.

4.2.5. Preparation of N-tosyl-11-alkoxy-2,11-dihydrobenz[6,7]-oxepino[4,3,2-cd]indoles ***7*** *(general procedure)*

To a suspension of **2a** (4 mmol) in $CHCl_3$ (10 mL), Br_2 (0.64 g, 4 mmol) was added dropwise for 15 min under stirring. The reaction mixture was stirred for a further 10 min, then Et_3N (0.40 g, 4 mmol) was added to the resulting solution, and stirring was continued for 5 min. The reaction mixture was filtered, the filtrate evaporated to dryness, and the residual oily bromide **6** was

dissolved in MeOH or EtOH (10 mL), refluxed for 30 min, and the solvent was evaporated. The residue was crystallized from MeCN.

4.2.5.1. 11-Bromo-4-nitro-2-(p-toluenesulphonyl)-2,11-dihydrobenz-[6,7]oxepino[4,3,2-cd]indole ***6***. Yield of the crude product 94%. Brown oil. ^{1}H NMR ($CDCl_3$, δ): 2.38 (s, 3H), 6.19 (s, 1H), 7.16 (t, J=7.8 Hz, 1H), 7.30–7.40 (m, 5H), 7.80 (s, 1H), 7.84 (d, J=8.3 Hz, 2H), 7.98 (s, 1H), 8.57 (s, 1H).

4.2.5.2. 11-Methoxy-4-nitro-2-(p-toluenesulphonyl)-2,11-dihydrobenz-[6,7]oxepino[4,3,2-cd]indole ***7a***. Yield 83%. Mp 115–120 °C (benzene). ^{1}H NMR (DMSO-d_6, δ): 2.32 (s, 3H, Ts), 3.22 (s, 3H), 5.40 (s, 1H, H-11), 7.23 (t, J=7.9 Hz, 1H), 7.36–7.40 (m, 2H), 7.43 (d, J=8.3 Hz, 2H, Ts), 7.48 (d, J=8.1 Hz, 1H), 7.89 (s, 1H), 7.94 (d, J=8.3 Hz, 2H, Ts), 8.24 (s, 1H), 8.45 (s, 1H, H-3). ^{13}C NMR (DMSO-d_6, δ): 21.1, 55.8, 75.8, 104.9, 107.7, 119.3, 122.9, 125.4, 125.8, 126.9 (2CH), 128.3, 130.5, 130.6, 130.7 (2CH), 132.0, 133.5, 134.3, 145.8, 146.5, 150.0, 155.5. EIMS (70 eV) (*m*/*z*, *I*, %): 450 [M^+, 25], 419 [48], 155 [58], 91 [100]. Anal. Calcd for $C_{23}H_{18}N_2O_6S$: C, 61.32; H, 4.03; N, 6.22; S, 7.12. Found: C, 61.05; H, 3.84; N, 5.90; S, 7.17. IR (ν_{max}, KBr): 1528, 1340, 1192, 1180, 1088, 672.

4.2.5.3. 11-Ethoxy-4-nitro-2-(p-toluenesulphonyl)-2,11-dihydrobenz-[6,7]oxepino[4,3,2-cd]indole ***7b***. Yield 81%. Mp 185–186 °C (benzene). ^{1}H NMR (DMSO-d_6, δ): 1.07 (t, J=7.3 Hz, 3H), 2.32 (s, 3H, Ts), 3.44 (q, J=7.3 Hz, 2H), 5.56 (s, 1H, H-11), 7.22–7.25 (m, 1H), 7.34–7.39 (m, 2H), 7.43 (d, J=8.3 Hz, 2H, Ts), 7.47 (d, J=8.2 Hz, 1H), 7.89 (s, 1H), 7.93 (d, J=8.3 Hz, 2H, Ts), 8.17 (s, 1H), 8.45 (s, 1H, H-3). Anal. Calcd for $C_{24}H_{20}N_2O_6S$: C, 62.06; H, 4.34; N, 6.03; S, 6.90. Found: C, 61.92; H, 4.45; N, 5.70; S, 7.12. IR (ν_{max}, KBr): 1528, 1380, 1340, 1180, 1100, 672.

Acknowledgements

We are grateful to Chemical Block Ltd. Company (www.chem-block.com) for financial support of this research.

References and notes

1. (a) Gribble, G. W. Pyrroles and their Benzo Derivatives: Applications. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F., Eds.; Pergamon: New York, NY, 1996; Vol. 2, p 207; (b) Sundberg, R. J. Pyrroles and their Benzo Derivatives: (iii) Synthesis and Applications. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 4, p 313.
2. Brown, L. E.; Konopelski, J. P. *Org. Prep. Proced. Int.* **2008**, *40*, 411.
3. (a) May, J. A.; Stoltz, B. *Tetrahedron* **2006**, *62*, 5262; (b) Yamada, F.; Makita, Y.; Suzuki, T.; Somei, M. *Chem. Pharm. Bull.* **1985**, *33*, 2162; (c) Kozlovskii, A. G.; Soloveva, T. F.; Sakharovskii, V. G.; Adanin, V. M. *Dokl. Akad. Nauk SSSR* **1981**, *260*, 230.
4. (a) Ku, J.; Jeong, B.; Jew, S.; Park, H. *J. Org. Chem.* **2007**, *72*, 8115; (b) Yokoyama, Y.; Hikawa, H.; Mitsuhashi, M.; Uyama, A.; Hiroki, Y.; Murakami, Y. *Eur. J. Org. Chem.* **2004**, *6*, 1244; (c) Kozikowski, A. P.; Greco, M. N. *J. Org. Chem.* **1984**, *49*, 2310.
5. Yamskov, A. N.; Samet, A. V.; Semenov, V. V. *Mendeleev Commun.* **2008**, *18*, 320.
6. Samet, A. V.; Kislyi, K. A.; Marshalkin, V. N.; Strelenko, Y. A.; Raihstat, M. M.; Nelyubina, Y. V.; Semenov, V. V. *Tetrahedron* **2008**, *64*, 11763.
7. Kislyi, K. A.; Samet, A. V.; Strelenko, Y. A.; Semenov, V. V. *J. Org. Chem.* **2008**, *73*, 2285.
8. (a) Samet, A. V.; Marshalkin, V. N.; Kislyi, K. A.; Chernysheva, N. B.; Strelenko, Y. A.; Semenov, V. V. *J. Org. Chem.* **2005**, *70*, 9371; (b) Samet, A. V.; Kislyi, K. A.; Marshalkin, V. N.; Strelenko, Y. A.; Nelyubina, Yu. V.; Lyssenko, K. A.; Semenov, V. V. *Russ. Chem. Bull.* **2007**, *56*, 2089.
9. Zlotin, S. G.; Kislitsin, P. G.; Samet, A. V.; Serebryakov, E. A.; Konyushkin, L. D.; Semenov, V. V.; Buchanan, A. C., III; Gakh, A. A. *J. Org. Chem.* **2000**, *65*, 8430.
10. Samet, A. V.; Zakharov, E. P.; Semenov, V. V.; Gakh, A. A.; Buchanan, A. C., III. *Synth. Commun.* **2001**, *31*, 1441.
11. Compound **1** has already been used for the preparation of biologically active indoles: Pullagurla, M.; Siripurapu, U.; Kolanos, R.; Bondarev, M. L.; Dukat, M.; Setola, V.; Roth, B. L.; Glennon, R. A. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 5298.
12. Some alternative approaches to peri-annulated heterocyclic systems starting from polynitroaromatic compounds are described in: (a) Bastrakov, M. A.; Starosotnikov, A. M.; Kachala, V. V.; Nesterova, E. N.; Shevelev, S. A. *Russ. Chem. Bull.* **2007**, *56*, 1603; (b) Zlotin, S. G.; Kislitsin, P. G.; Kucherov, F. A.; Gakh, A. A. *Heterocycles* **2006**, *68*, 1109; (c) Kozikowski, A. P.; Greco, M. N.; Springer, J. P. *J. Am. Chem. Soc.* **1982**, *104*, 7622.
13. Yamskov, A. N.; Samet, A. V.; Semenov, V. V. *Russ. Chem. Bull.* **2003**, *52*, 759.
14. For a similar reaction of 2,3-dihydro-2-methyl-4,6-dinitrobenzo[*b*]furan, see: TNT itself reacts with 2-hydroxybenzaldehydes in a similar way to afford 1,3-dinitrodibenz[*b*,*f*]oxepines: Hoyer, H.; Vogel, M. *Monatsh. Chem.* **1962**, *93*, 766; Yamskov, A. N.; Samet, A. V.; Semenov, V. V. *Chem. Heterocycl. Compd.* **2005**, *41*, 796.
15. (a) Murphy, J. A.; Khan, T. A.; Zhou, S.-Z.; Thomson, D. W.; Mahesh, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1356; (b) Bergman, J.; Janosik, T.; Koch, E.; Pelcman, B. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2615; (c) Tietze, L. F.; Grote, T. *J. Org. Chem.* **1994**, *59*, 192.
16. (a) Suarez-Castillo, O. R.; Contreras-Martinez, Y. M. A.; Beiza-Granados, L.; Melendez-Rodriguez, M.; Villagomez-Ibarra, J. R.; Torres-Valencia, J. M.; Morales-Rios, M. S.; Joseph-Nathan, P. *Tetrahedron* **2005**, *61*, 8809; (b) Kawasaki, T.; Nonaka, Y.; Watanabe, K.; Ogawa, A.; Higuchi, K.; Terashima, R.; Masuda, K.; Sakamoto, M. *J. Org. Chem.* **2001**, *66*, 1200; (c) Morales-Rios, M. S.; Bucio, M. A.; Joseph-Nathan, P. *Tetrahedron* **1996**, *52*, 5339.
17. Tidwell, J. H.; Peat, A. J.; Buchwald, S. L. *J. Org. Chem.* **1994**, *59*, 7164.
18. Jones, R. A. Pyrroles and their Benzo Derivatives: (ii) Reactivity. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 4, p 201.
19. For a large-scale synthesis with TNT, see: *Organic Syntheses*; Wiley & Sons: New York, NY, 1941; Collect. Vol. I, p. 543 (no special safety precautions were recommended by the submitters or checkers of this procedure). Moreover, TNT was successfully used for industrial production of phloroglucinol: Castens, M. L.; Kaplan, J. F. *Ind. Eng. Chem.* **1950**, *42*, 402.