Synthesis A. A. Hassan et al. Paper

Synthesis of Oxa-aza- and Bis-oxathiaaza[3.3.3]propellanes from Dicyanomethylene-1,3-indanedione and 2,5-Dithiobiureas

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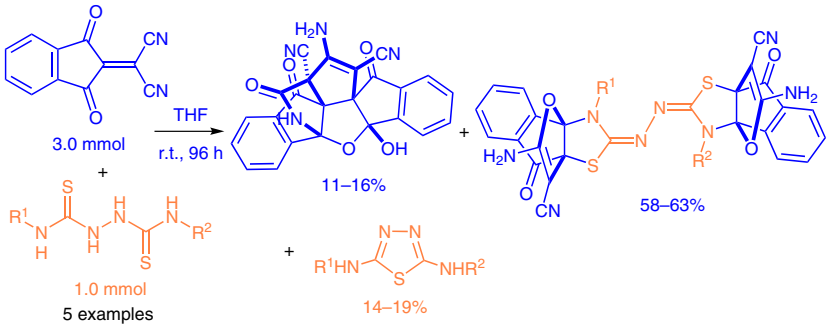

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Abstract An efficient route for the synthesis of oxa-aza- and bis-oxathiaaza[3.3.3]propellanes via reactions of symmetrical and unsymmetrical N^1,N^2-disubstituted hydrazine-1,2-dicarbothioamides (2,5-dithiobiureas) with (1,3-dioxo-2,3-dihydro-1*H*-inden-2-ylidene)propanedinitrile in tetrahydrofuran is described. The rationale behind these conversions involving nucleophilic addition on the dicyanomethylene carbon atom is presented. The structures of these unusual products are confirmed by X-ray crystal structure analysis.

Key words dicyanomethylene-1,3-indanedione, 2,5-dithiobiureas, oxa-aza[3.3.3]propellane, bis-oxathiaaza[3.3.3]propellanes, N^2,N^5-disubstituted 1,3,4-thiadiazoles

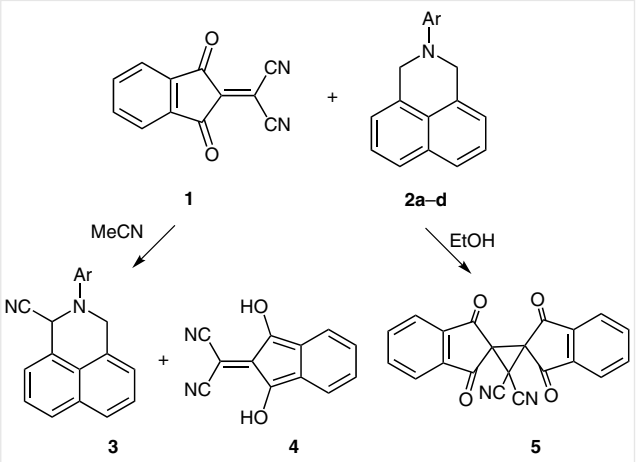
Molecules such as cubanes, prismanes and propellanes, which possess unusual shapes and inherent strain, have attracted the interest of many chemists as they are useful intermediates and target compounds in organic synthesis.[1–3] In addition, some of these molecules, for example those exhibiting propellane skeletons, are present in natural products.[4–9] Propellanes are unique compounds in which one common C–C single bond is shared by three different rings in the overall three-dimensional structure.[10]

Nitrogen- and oxygen-containing propellanes and their analogues have attracted attention due to their presence in biologically active natural products and pharmaceuticals such as periglaucine A, sinoacutine and hasubanan alkaloids.[11,12] Aza-propellanes can be used as synthons for natural products,[13–15] as ligands for transition-metal-mediated reactions and as building blocks for the cucurbiturils.[16] Although the strain present in propellane compounds may be the reason for their instability and makes their synthesis difficult, many derivatives of these compounds have been prepared.[17–23]

Recently, multicomponent reactions (MCRs) have been used for the synthesis of heteropropellanes. For example, the addition of ninhydrin and malononitrile to arylisothiocyanates and primary amines led to the formation of oxathiaaza[3.3.3]propellanes.[7] The reaction of trichloroacetamidine with the Knoevenagel condensation product of ninhydrin and malononitrile afforded trichloromethylated [3.3.3]propellanes.[24] Oxa-aza[3.3.3]propellanes have been synthesized via the multicomponent reaction of malononitrile and ninhydrin with ketene aminals,[25] arylisothiocyanates[26] or hydrazine derivatives with an electron-withdrawing group close to the $NHNH_2$ moiety.[27]

On the other hand, spiro-indenepyrazoles[28] and spiro-indenethiazines[29,30] have been isolated from the reactions of thiosemicarbazide or thiosemicarbazone derivatives with 2-(1,3-dioxo-2,3-dihydro-1*H*-inden-2-ylidene)propanedinitrile (**1**). Additionally, Döpp et al.[31] have reported that the known compounds: 1,3-dihydroxy-2*H*-inden-2-ylidenepropanedinitrile (**4**), benzo[*d*,*e*]isoquinoline-1-carbonitriles **3** and dispirocyclopropane derivative **5** (Scheme 1) were formed from compound **1** via reactions with *N*-aryl-2,3-dihydro-1*H*-benzo[*d*,*e*]isoquinolines **2a**–**d** in acetonitrile or ethanol.[31]

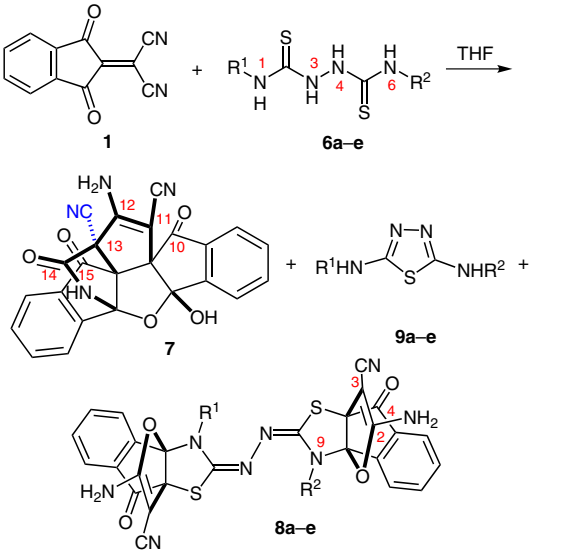
Herein, we describe the synthesis of new oxa-aza- and bis-oxathiaaza[3.3.3]propellanes **7** and **8a**–**e** (Table 1) via the reaction of compound **1** with symmetrical and unsymmetrical 1,6-disubstituted-2,5-dithiobiureas **6a**–**e** in the molar ratio of 3:1 in tetrahydrofuran. The reaction mixtures were stirred at room temperature (open to air) for 96 hours resulting in the formation of fine colorless precipitates of bis-oxathiaaza[3.3.3]propellane derivatives **8a**–**e**. The filtrate was separated by preparative thin-layer chromatography to give two zones; the fastest migrating zone contained thiadiazoles **9a**–**e** whilst the slower-moving zone consisted of the oxa-aza[3.3.3]propellane **7**.



Scheme 1 Previous work on the reactions of compound **1** with benzo[*d*,*e*]isoquinolines **2a–d**

The IR spectrum of product **7** clearly indicated the presence of OH, NH_2 and NH (3425–3209 cm^{-1}), CN (2210 cm^{-1}), C=O (1734, 1654 cm^{-1}) and C–O–C (1098 cm^{-1})[32] functional groups.

Table 1 Reactions of Compound **1** with 2,5-Dithiobiureas **6a–e**



Products, yields (%)						R^2	R^1	Substrate
19	**9a**	59	**8a**	11	**7**	Ph	Ph	**6a**
16	**9b**	63	**8b**	12	**7**	Bn	Bn	**6b**
14	**9c**	61	**8c**	15	**7**	allyl	allyl	**6c**
15	**9d**	58	**8d**	13	**7**	Bn	Ph	**6d**
14	**9e**	62	**8e**	16	**7**	allyl	Bn	**6e**

The ^1H NMR spectrum of compound **7** showed broad exchangeable (with D_2O) signals at 10.90, 8.38 and 7.62 ppm due to the amide NH, NH_2 and hydroxy groups. The eight aromatic hydrogens gave rise to characteristic signals in the aromatic region of the spectrum.

The decoupled ^{13}C NMR spectrum showed a signal at 96.5 ppm due to the aliphatic quaternary carbon atom bearing a hydroxy group. The C3 and C4 furan carbons resonated at 75.9 and 71.5 ppm, respectively, whereas C5 of the furan was evident as a downfield shifted signal at 145.4 ppm due to the adjacent NH and oxygen. The ^{13}C NMR spectrum of **7** supported the ^1H NMR spectroscopic data with the appearance of characteristic aromatic C–H carbon signals. The pyrrole C4 (C13) carbon and pyrrole C=O resonated at 56.8 and 169.9 ppm, respectively. In addition, the C11 and C12 carbons resonating at 51.7 and 164.2 ppm were in accord with the observed trends in chemical shift values for carbon atoms in push–pull alkenes.[33,34] The signals at 193.3 and 193.4 ppm were due to the carbonyl carbons of the indeno moiety. The mass spectrum of compound **7** displayed the molecular ion peak at *m*/*z* 436.

Aside from the ^1H and ^{13}C NMR spectra which demonstrate the presence of two oxoindenylidene units, two cyano groups, amide CO and other functional groups, it is very difficult to elucidate the three-dimensional structure of propellane **7**. However, the structure of **7** was unambiguously determined by single crystal X-ray structure analysis, which confirmed the presence of a propellane system (Figure 1, and Tables S1–S7 in the Supporting Information; note that the crystallographic numbering does not correspond with the symmetric IUPAC numbering rules).

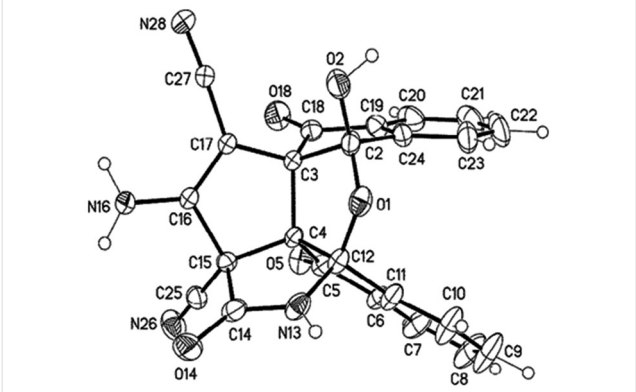


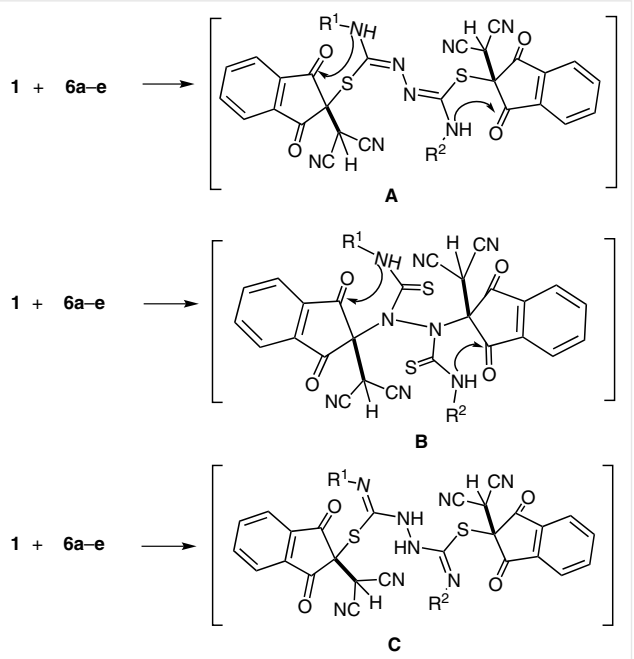
Figure 1 X-ray crystal structure of **7** (ORTEP plot; displacement parameters are drawn at the 30% probability level)

In addition to compound **7**, the results of combustion analysis and spectroscopic data suggested the presence of other novel compounds, which were regularly detected and identified as symmetrical and unsymmetrical bis-oxathia-aza[3.3.3]propellane derivatives **8a–e**.

The structures of **8a–e** were delineated from their spectroscopic properties. The salient features were the changes in the carbon–carbon double bond of **1** and the NH resonances of **6a–e** on reacting to give products **8a–e**. As a result of the formation of the propellane rings, new signals were observed in the ^{13}C NMR spectra.

The molecular formula of **8e**, as an example, was confirmed by mass spectrometry. The molecular ion was observed at m/z = 696 (23%), which was in agreement with the proposed structure and clearly indicated that the addition of one molecule of **6e** to two molecules of **1** had occurred without any associated elimination. The IR spectrum of **8e** showed absorptions at 3340 (NH_2), 2197 (CN), 1725 (CO), 1650 (C=N) and 1094 (C–O–C) cm^{-1}.

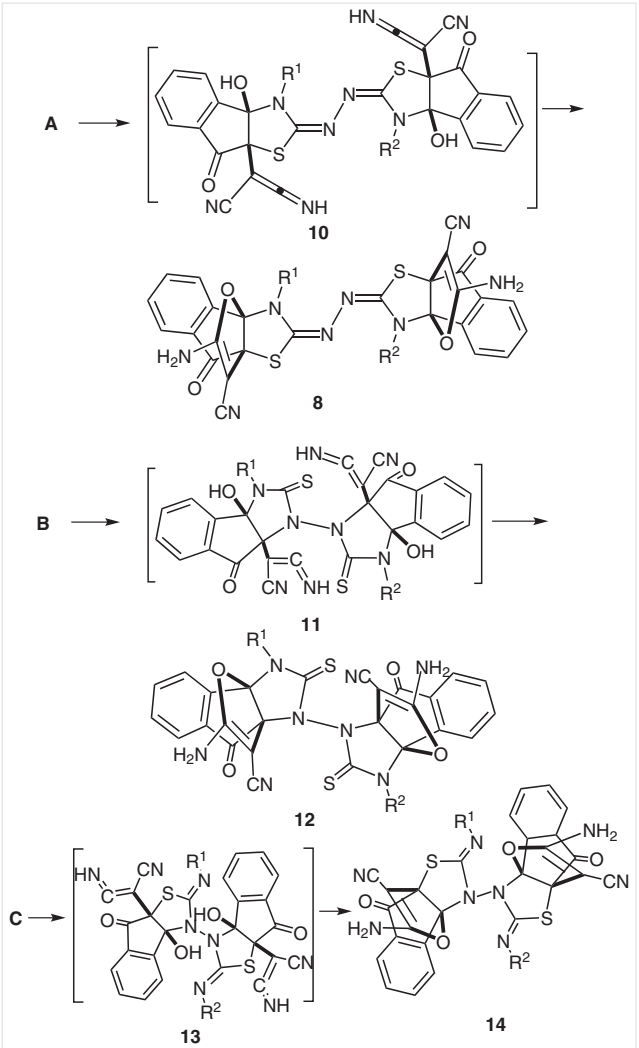
The ^1H NMR spectrum of **8e** displayed one broad singlet at 8.12 ppm (4 H) for the NH_2 protons. The downfield shift of the NH_2 group may be due to intermolecular H-bonding between the NH_2 and the oxygen of the carbonyl group of acetone (the solvent of crystallization). The allyl group resonated as three multiplets at 4.30–4.40 ($-CH_2N$), 5.10–5.18 ($H_2C=$) and 5.72–5.80 (–CH=) ppm, respectively. The presence of allyl and benzyl groups was evident from the ^{13}C NMR DEPT spectrum which exhibited positive signals at 136.3 ppm (–CH=) and negative signals at 46.2 ($-CH_2N$), 47.4 (CH_2Ph) and 117.9 ($H_2C=$) ppm. In the ^{13}C NMR spectrum of **8e**, the thiazole C4 and C-4 carbons resonated at 108.2 and 70.8 ppm, respectively. Additional diagnostic resonances occurred at 53.4 (furan-C3), 165.9 (furan-C2), 116.2 (CN), 158.1 (C=N) and 193.1 (indeno-CO).



Scheme 2 Possible adducts formed via reactions of **1** with **6a–e**

The analytical data of compounds **8** would also match with the other possible regioisomeric products **12** and **14**. Compounds **6a–e** may react via their sulfur atom, HN^3, HN^4 and HN^1, HN^6 as nucleophilic sites. It is probable that the observed products **8a–e** are formed from one of three labile 1:2 adducts (**A**–**C**) (Scheme 2).

The product would have structure **8** if the reaction took place through SH and HN^1, HN^6 via adduct **A** and intermediate **10** (Schemes 2 and 3). Product **12** would be isolated if the reaction involved the participation of HN^3, HN^4 and HN^1, HN^6 by way of adduct **B** and intermediate **11** (Schemes 2 and 3). If the SH group attacks the carbon–carbon double bond of **1**, adduct **C** would be observed followed by intramolecular nucleophilic attack of HN^3, HN^4 at the carbonyl group of **1**; this would lead to product **14** via intermediate **13** (Schemes 2 and 3).



Scheme 3 Structures of the possible alternative regioisomers **12** and **14**

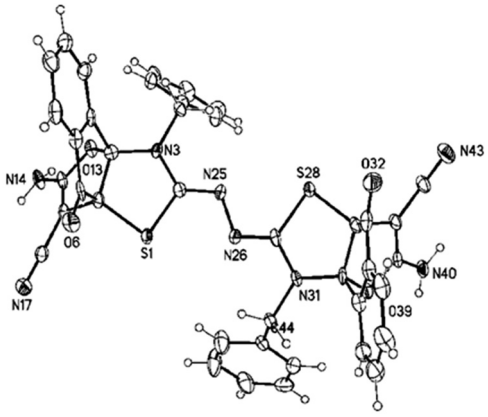


Figure 2 X-ray crystal structure of **8b** (ORTEP plot; one crystallographically independent molecule is shown)

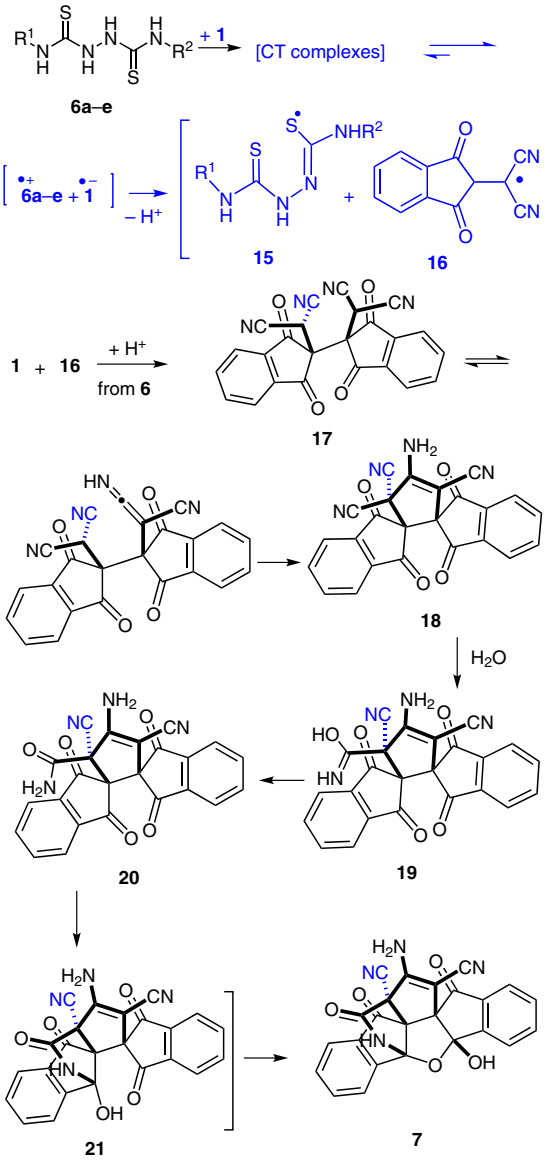
Structure **12** was excluded on the basis of ^{13}C NMR spectroscopy and by the absence of a C=S functional group in compound **8**. A comparison of the ^{1}H NMR or ^{13}C NMR chemical shifts of the possible isomers **8** and **14** does not serve as a useful supplementary tool in confirming the correct structure. Therefore, the propellane-type structure of compounds **8a**–**e** was determined by X-ray crystallographic analysis. The X-ray crystal structure of compound **8b** consists of three fused five-membered rings (Figure 2, and Tables S8–S10 in the Supporting Information).

Plausible mechanism for the formation of propellanes **7** and **8a**–**e** have been proposed based on previous results (Schemes 4 and 5).

In order to rationalize the formation of products **7**–**9**, the generation of cation **15** and anion **16** may be regarded as the initial event, whereby charge-transfer (CT) complexes may form (but not necessarily) during intermediate stages. The nucleophilic addition of **16** to the dicyanomethylene carbon atom of **1** in the presence of a proton (possibly originating from **6**) affords intermediate **18**. This subsequently undergoes addition of a molecule of water, and via intermediates **19**–**21** gives oxa-aza[3.3.3]propellane **7** (Scheme 4).

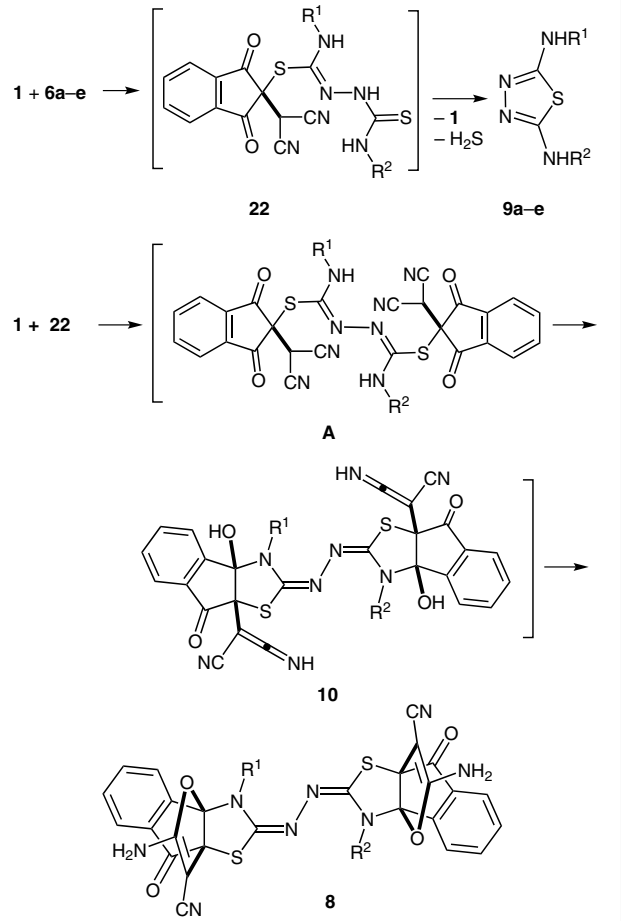
The nucleophilic attack of compound **6** on the carbon–carbon double bond of dinitrile **1** affords the intermediate **22**. Since the formation of compounds **9a**–**e** involves intramolecular nucleophilic attack of the hydrazine NH on the thiocarbonyl group, it is conceivable that **1** accelerates the process by functioning as a Lewis acid, through intermediate **22** (Scheme 5), activating the respective C=S bonds toward nucleophilic addition. After cyclization, dinitrile **1** is released and liberation of hydrogen sulfide (H_2S) occurs. On the other hand, the addition of **22** to another molecule of dinitrile **1** affords the bis-oxathiaaza[3.3.3]propellane **8** via intermediate **10**.

In conclusion, novel oxa-aza- and bis-oxathia-aza[3.3.3]propellanes have been synthesized from the nucleophilic addition reactions of 2,5-dithiobiureas on dicyanomethylene-1,3-indanedione **1**. The products were synthesized in good yields from readily accessible starting materials, using a simple experimental procedure and substrates that did not require any prior activation. In order to be reactive, the symmetrical and unsymmetrical 2,5-dithiobiureas required the availability of HN^1, HN^6 and HN^3, HN^4 as well as sulfur atoms as nucleophilic sites.



Scheme 4 A possible mechanism for the formation of compound **7**

Melting points (uncorrected) were determined using open glass capillaries on a Gallenkamp melting point apparatus. IR spectra were recorded on Shimadzu 408 or Bruker Alpha FT-IR instruments with samples prepared as potassium bromide pellets. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were obtained using a Bruker AM



Scheme 5 A possible mechanism for the formation of compounds **8a–e**

400 spectrometer with tetramethylsilane as an internal standard. The multiplicities are defined as follows: s = singlet, m = multiplet, br s = broad singlet. The ^{13}C NMR signals were assigned on the basis of DEPT 135/90 spectra. Chemical shifts (δ) are expressed in ppm. Mass spectra (70 eV, electron impact mode) were recorded on a Finnigan MAT instrument. Elemental analysis (C, H, N and S) was carried out at the Microanalytical Center, Cairo University, Egypt. Preparative thin-layer chromatography was accomplished using glass plates (48 cm wide and 20 cm tall) covered with a layer (1.0 mm thick) of air-dried silica gel (Merck Pf_{254}). 1,6-Disubstituted 2,5-dithiobiureas were prepared according to published procedures, as were *N*^{1},*N*^{2}-diphenylhydrazine-1,2-dicarbothioamide (**6a**),[35] *N*^{1},*N*^{2}-dibenzylhydrazine-1,2-dicarbothioamide (**6b**),[36] *N*^{1},*N*^{2}-diallylhydrazine-1,2-dicarbothioamide (**6c**),[37] *N*^{1}-benzyl-*N*^{2}-phenylhydrazine-1,2-dicarbothioamide (**6d**),[38] *N*^{1}-allyl-*N*^{2}-benzylhydrazine-1,2-dicarbothioamide (**6e**).[39] (1,3-Di-oxo-2,3-dihydro-1*H*-inden-2-ylidene)propanedinitrile (**1**) was prepared according to the method reported by Chatterjee.[40]

General Procedure

A solution of **6** (1.0 mmol) and **1** (624 mg, 3.0 mmol) in dry THF (50 mL) was stirred at r.t. for 96 hours, during which time the color changed from yellow to reddish brown and a fine colorless precipitate formed. The solid was collected and recrystallized from acetone to give colorless crystals of **8**. The mother liquor was subjected to preparative TLC using toluene–EtOAc (5:4) in the reactions of **1** with **6a**,**e**, toluene–EtOAc (1:1) in the reaction of **1** with **6b**, toluene–EtOAc (5:3) in the reaction of **1** with **6c**, and toluene–EtOAc (2:1) in the reaction of **1** with **6d**, resulting in numerous zones, the two most intense of which were removed and extracted. The fastest migrating zone contained N^2,N^5-disubstituted 1,3,4-thiadiazole-2,5-diamines **9**. The slowest migrating zone, which quenched all indicator fluorescence upon exposure to UV light (254 nm), contained product **7**.

12-Amino-5a-hydroxy-10,14,15-trioxo-5a,10,13,14-tetrahydro-4b,13-(epiminomethano)cyclopenta[*c*]diindeno[1,2-*b*:2′,1′-*d*]furan-11,13-dicarbonitrile (7)

Yield: 70 mg (16%); brown crystals (EtOH); mp 210–212 °C.

IR (KBr): 3425–3209 (OH, NH_2, NH), 2210 (CN), 1734–1654 (CO), 1604 (Ar-C=C), 1098 (C–O–C) cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 7.20–7.44 (m, 3 H, H_{Ar}), 7.58–7.60 (m, 2 H, H_{Ar}), 7.62 (br s, 1 H, OH), 7.72–7.80 (m, 3 H, H_{Ar}), 8.38 (br s, 2 H, NH_2), 10.90 (br s, 1 H, amide-NH).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 51.7 (C-11), 56.8 (C-13), 71.5 (furan-C4), 75.9 (furan-C3), 96.5 (quaternary-C-OH), 113.7, 116.0 (CN), 122.6, 123.2, 124.1, 124.3 (CH_{Ar}), 130.9, 133.5, 136.0, 137.6 (C_{Ar}), 145.4 (furan-C5), 164.2 (C-12) 169.9 (amide-CO), 193.3, 193.4 (indeno-CO).

MS (EI): *m*/*z* (%) = 436 (17) [M]$^+$, 410 (19), 382 (12), 370 (26), 104 (76), 76 (100), 66 (54).

Anal. Calcd for $C_{24}H_{12}N_4O_5$: C, 66.06; H, 2.77; N, 12.84. Found: C, 65.92; H, 2.66; N, 13.02.

(10*E*,10′*E*)-10,10′-(Hydrazine-1,2-diylidene)bis[2-amino-4-oxo-9-phenyl-4*H*-3a,8b-(epithiomethanoimino)indeno[1,2-*b*]furan-3-carbonitrile] (8a)

Yield: 424 mg (59%); colorless crystals (MeCN); mp 190–192 °C.

IR (KBr): 3409 (NH_2), 2187 (CN), 1716 (CO), 1636 (C=N), 1602 (Ar-C=C), 1093 (C–O–C) cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 7.12–7.21 (m, 4 H, H_{Ar}), 7.32–7.46 (m, 4 H, H_{Ar}), 7.55–7.64 (m, 2 H, H_{Ar}), 7.66–7.69 (m, 2 H, H_{Ar}), 7.72–7.75 (m, 2 H, H_{Ar}), 7.86–8.05 (m, 4 H, H_{Ar}), 8.16 (br s, 4 H, 2 × NH_2).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 53.7 (furan-C3), 71.1 (thiazolidine-C5), 108.2 (furan-C5), 116.4 (CN), 125.8, 126.7, 127.2, 129.1, 131.4, 132.5, 134.5 (CH_{Ar}), 136.9, 142.9, 143.9 (C_{Ar}), 158.9 (C=N), 165.5 (furan-C2), 192.9 (indeno-CO).

MS (EI): *m*/*z* (%) = 718 (12) [M]$^+$, 652 (17), 583 (44), 517 (9), 359 (12), 345 (10), 135 (66), 77 (100), 66 (41).

Anal. Calcd for $C_{38}H_{22}N_8O_4S_2$: C, 63.50; H, 3.09; N, 15.59; S, 8.92. Found: C, 63.34; H, 2.95; N, 15.76; S, 9.13.

(10*E*,10′*E*)-10,10′-(Hydrazine-1,2-diylidene)bis[2-amino-9-benzyl-4-oxo-4*H*-3a,8b-(epithiomethanoimino)indeno[1,2-*b*]furan-3-carbonitrile] (8b)

Yield: 470 mg (63%); colorless crystals (acetone); mp 234–236 °C.

IR (KBr): 3329 (NH_2), 2194 (CN), 1725 (CO), 1638 (C=N), 1597 (Ar-C=C), 1106 (C–O–C) cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 4.89 (s, 4 H, CH_2Ph), 7.00–7.05 (m, 2 H, H_{Ar}), 7.14–7.22 (m, 4 H, H_{Ar}), 7.36–7.44 (m, 4 H, H_{Ar}), 7.52–7.60 (m, 4 H, H_{Ar}), 7.65–7.74 (m, 2 H, H_{Ar}), 7.90–8.03 (m, 2 H, H_{Ar}), 8.10 (br s, 4 H, 2 × NH_2).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 47.9 (CH_2Ph), 53.5 (furan-C3), 70.9 (thiazolidine-C5), 107.9 (furan-C5), 116.5 (CN), 125.3, 125.9, 127.1, 128.6, 129.5, 132.5, 135.2 (CH_{Ar}), 137.2, 142.7, 143.7 (C_{Ar}), 158.6 (C=N), 165.7 (furan-C2), 193.0 (indeno-CO).

MS (EI): *m*/*z* (%) = 746 (22) [M]$^+$, 614 (19), 465 (12), 378 (11), 364 (22), 149 (76), 91 (100), 66 (42).

Anal. Calcd for $C_{40}H_{26}N_8O_4S_2$: C, 64.33; H, 3.51; N, 15.00; S, 8.59. Found: C, 64.51; H, 3.40; N, 14.87; S, 8.76.

(10*E*,10′*E*)-10,10′-(Hydrazine-1,2-diylidene)bis[9-allyl-2-amino-4-oxo-4*H*-3a,8b-(epithiomethanoimino)indeno[1,2-*b*]furan-3-carbonitrile] (8c)

Yield: 394 mg (61%); colorless crystals (MeCN); mp 268–270 °C.

IR (KBr): 3333 (NH_2), 2194 (CN), 1725 (CO), 1628 (C=N), 1598 (Ar-C=C), 1095 (C–O–C) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.35–4.37 (m, 4 H, allyl-CH_2N), 5.05–5.08 (m, 4 H, allyl-CH_2=), 5.81–5.83 (m, 2 H, allyl-CH=), 7.20–7.32 (m, 2 H, H_{Ar}), 7.63–7.71 (m, 6 H, H_{Ar}), 8.08 (br s, 4 H, 2 × NH_2).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 46.6 (allyl-CH_2N), 53.2 (furan-C3), 71.2 (thiazolidine-C5), 107.8 (furan-C5), 116.2 (CN), 118.0 (allyl-CH_2=), 125.7, 126.9, 128.3, 130.2 (CH_{Ar}), 135.9 (allyl-CH=), 143.8, 144.1 (C_{Ar}), 158.4 (C=N), 166.2 (furan-C2), 193.4 (indeno-CO).

MS (EI): *m*/*z* (%) = 646 (22) [M]$^+$, 592 (52), 564 (32), 464 (26), 297 (100), 91 (83).

Anal. Calcd for $C_{32}H_{22}N_8O_4S_2$: C, 59.43; H, 3.43; N, 17.33; S, 9.92. Found: C, 59.29; H, 3.51; N, 17.21; S, 10.08.

(*E*)-2-Amino-10-{[(*E*)-2-amino-3-cyano-4-oxo-9-phenyl-4*H*-3a,8b-(epithiomethanoimino)indeno-[1,2-*b*]furan-10-ylidene]hydrazone}-9-benzyl-4-oxo-4*H*-3a,8b-(epithiomethanoimino)indeno[1,2-*b*]furan-3-carbonitrile (8d)

Yield: 425 mg (58%); colorless crystals (MeCN); mp 230–232 °C.

IR (KBr): 3334 (NH_2), 2194 (CN), 1726 (CO), 1651 (C=N), 1584 (Ar-C=C), 1075 (C–O–C) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.92 (s, 2 H, CH_2Ph), 7.05–7.10 (m, 2 H, H_{Ar}), 7.20–7.40 (m, 4 H, H_{Ar}), 7.50–7.58 (m, 4 H, H_{Ar}), 7.62–7.70 (m, 2 H, H_{Ar}), 7.73–7.80 (m, 4 H, H_{Ar}), 7.82–8.00 (m, 2 H, H_{Ar}), 8.20 (br s, 4 H, 2 × NH_2).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 47.4 (CH_2Ph), 53.3 (furan-C3), 70.8 (thiazolidine-C5), 107.9 (furan-C5), 116.2 (CN), 124.5, 125.4, 125.5, 127.0, 128.1, 129.3, 129.4, 132.5, 132.6, 136.2 (CH_{Ar}), 137.9, 139.7, 143.8, 144.1 (C_{Ar}), 158.5, 159.5 (C=N), 165.9 (furan-C2), 192.9, 193.0 (indeno-CO).

MS (EI): *m*/*z* (%) = 732 (11) [M]$^+$, 615 (9), 597 (26), 583 (11), 359 (32), 149 (27), 135 (36), 91 (86), 77 (100), 66 (54).

Anal. Calcd for $C_{39}H_{24}N_8O_4S_2$: C, 63.92; H, 3.30; N, 15.29; S, 8.75. Found: C, 64.12; H, 3.22; N, 15.16; S, 8.91.

(*E*)-9-Allyl-2-amino-10-{[(*E*)-2-amino-9-benzyl-3-cyano-4-oxo-4*H*-3a,8b-(epithiomethanoimino)indeno[1,2-*b*]furan-10-ylidene]hydrazono}-4-oxo-4*H*-3a,8b-(epithiomethanoimino)indeno[1,2-*b*]furan-3-carbonitrile (8e)

Yield: 432 mg (62%); colorless crystals (MeCN); mp 218–220 °C.

IR (KBr): 3340 (NH_2), 2197 (CN), 1725 (CO), 1650 (C=N), 1598 (Ar-C=C), 1094 (C–O–C) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.30–4.40 (m, 2 H, allyl-CH_2N), 4.90 (s, 2 H, CH_2Ph), 5.10–5.18 (m, 2 H, allyl-CH_2=), 5.72–5.80 (m, 1 H, allyl-CH=), 7.00–7.22 (m, 4 H, H_{Ar}), 7.78–7.90 (m, 5 H, H_{Ar}), 7.92–8.05 (m, 4 H, H_{Ar}), 8.12 (br s, 4 H, 2 × NH_2).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 46.2 (allyl-CH_2N), 47.4 (CH_2Ph), 53.4 (furan-C3), 70.8 (thiazolidine-C5), 108.2 (furan-C5), 116.2 (CN), 117.9 (allyl-CH_2=), 125.4, 125.5, 126.9, 127.0, 128.0, 131.9, 132.4 (CH_{Ar}), 136.3 (allyl-CH=), 137.1, 143.9, 144.1 (C_{Ar}), 158.0, 158.1 (C=N), 165.9 (furan-C2), 193.0, 193.1 (indeno-CO).

MS (EI): *m*/*z* (%) = 696 (23) [M]$^+$, 506 (33), 478 (12), 456 (18), 149 (100), 135 (28), 91 (57), 41 (36).

Anal. Calcd for $C_{36}H_{24}N_8O_4S_2$: C, 62.06; H, 3.47; N, 16.08; S, 9.20. Found: C, 62.21; H, 3.61; N, 15.91; S, 9.36.

***N*^{2},*N*^{5}-Diphenyl-1,3,4-thiadiazole-2,5-diamine (9a)**[41]

Yield: 51 mg (19%); colorless crystals.

***N*^{2},*N*^{5}-Dibenzyl-1,3,4-thiadiazole-2,5-diamine (9b)**[42]

Yield: 47 mg (16%); colorless crystals.

***N*^{2},*N*^{5}-Diallyl-1,3,4-thiadiazole-2,5-diamine (9c)**[43]

Yield: 27 mg (14%); colorless crystals.

***N*^{2}-Benzyl-*N*^{5}-phenyl-1,3,4-thiadiazole-2,5-diamine (9d)**[44]

Yield: 42 mg (15%); colorless crystals.

***N*^{2}-Allyl-*N*^{5}-benzyl-1,3,4-thiadiazole-2,5-diamine (9e)**[45]

Yield: 34 mg (14%); colorless crystals.

Single Crystal X-ray Structure Determinations of 7 and 8b

Single crystal X-ray diffraction was carried out on an Agilent SuperNova diffractometer at 173 K (for **7**) using an EOS CCD-detector and MoKα radiation (λ = 0.71073 Å), and an Agilent SuperNova dual source diffractometer at 120 K (for **8b**) using an ATLAS CCD-detector and CuKα radiation (λ = 1.54178 Å). Dual space methods (for **7**, SHELXD)[46] and direct methods (for **8b**, SHELXS-98)[46] were used for structure solution. Refinement was carried out using SHELXL-2013 [46] (full-matrix least-squares on F^2). Hydrogen atoms were localized using a difference Fourier synthesis map and refined using a riding model [H(N)-free]. Semi-empirical absorption corrections were applied.[47]

Compound **7**: $C_{24}H_{12}N_4O_5{\cdot}C_2H_6O$, M_r = 482.44 g mol^{-1}, brown blocks, size = 0.22 × 0.18 × 0.12 mm, monoclinic $P2_1/n$ (no. 14), a = 11.2100(4) Å, b = 14.2407(3) Å, c = 15.8004(6) Å, β = 109.173(4)°, V = 2382.44(14) Å^3, Z = 4, D_{calcd} = 1.345 mg m^{-3}, F(000) = 1000, μ = 0.098 mm^{-1}, T = 173 K, 10196 measured reflections ($2\theta_{max}$ = 60.2°), 5985 independent reflections [R_{int} = 0.021], 337 parameters, 21 restraints, $R1$ [for 3967, $I > 2\sigma(I)$] = 0.076, $wR2$ (for all data) = 0.242, S = 1.04, largest diff. peak and hole = 0.913 eÅ^{-3} and –0.659 eÅ^{-3}.

Compound **8b**: $C_{40}H_{26}N_8O_4S_2{\cdot}C_3H_6O$, M_r = 804.88 g mol^{-1}, colorless plates, size = 0.16 × 0.12 × 0.06 mm, orthorhombic $Pca2_1$, a = 30.5182(7) Å, b = 8.2651(2) Å , c = 30.6114(5) Å, V = 7721.3(3) Å^3, Z = 8, D_{calcd} = 1.385 mg m^{-3}, F(000) = 3344, μ = 1.73 mm^{-1}, T = 120 K, 17226 measured reflections ($2\theta_{max}$ = 153°), 10507 independent reflections [R_{int} = 0.035], 1074 parameters, 9 restraints, $R1$ [for 9962, $I > 2\sigma(I)$] = 0.085, $wR2$ (for all data) = 0.207, S = 1.06, largest diff. peak and hole = 2.42 eÅ^{-3} and –0.47 eÅ^{-3}. The structure was refined as racemic twin [absolute structure parameter 0.40(3)]. Due to the poor quality of the crystal and unresolved high electron density, only the constitu-

tion and conformation of the structure could be determined (these data have not been included in the Supporting Information and have not been deposited at the Cambridge Crystallographic Data Centre).

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-34-1380447.

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(47) Crystallographic data (excluding structure factors) for the structure reported in this work have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1034843 (**7**). Copies of the data can be obtained free of charge on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk.