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High pressure and thermal Diels–Alder reaction of 2-vinyl-benzo[*b*]furan and 2-vinyl-benzo[*b*]thiophene. Synthesis of new condensed heterocycles

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Abstract—A new preparation of 2-vinyl-benzo[*b*]furan and 2-vinyl-benzo[*b*]thiophene is described. Diels–Alder reactions of these dienes with 3-nitro-2-cyclohexen-1-one and 2-inden-1-one was examined under thermal and high pressure conditions. The reaction products have been converted to multi-ring heteroaromatic compounds.

1. Introduction

Polycyclic heterocycles are compounds of biological interest and the development of new synthetic approaches is a challenge for synthetic organic chemists. The Diels–Alder reaction[1] which provides a valuable method for the regioselective and stereoselective synthesis of polycyclic compounds, has been successfully applied to the synthesis of heterocycles using both heterodienes and/or heterodienophiles[2] and cycloaddition of vinylheterocycles.[3] The Diels–Alder reactions of vinylbenzofurans, vinylbenzothiophenes and indoles with very reactive dienophiles have been investigated and new routes to the synthesis of dibenzofurans, dibenzothiophenes and carbazoles[3] have been found.

Cycloaddition reactions of vinylaromatic carbocycles have been extensively studied in our laboratory with a range of dienophiles under different conditions (thermal, Lewis acid catalysis, high pressure) and new synthetic approaches to helicenes[4] and polycyclic aromatic compounds[5] have been developed.

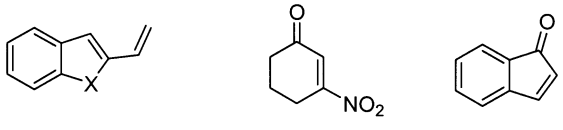
We were interested in the possibility of accessing new structurally diverse multi-ring heterocyclic systems and we now report the results of a study on the Diels–Alder reactions of 2-vinyl-benzo[*b*]furan **1a** and 2-vinyl-benzo[*b*]thiophene **1b** with 3-nitro-2-cyclohexen-1-one **2** and 2-inden-1-one **3**. It was expected that 3-nitro-2-cyclohexen-1-one **2** would not only be more reactive than 2-cyclohexen-1-one due to the presence of the strong electron withdrawing nitro-group at the β-olefinic carbon but also that the cycloadditions would be followed by HNO_2 elimination from the cycloadducts to afford a convenient and direct route to naphtho- and fluoreno-benzofurans and benzothiophenes. Compounds containing two five-membered rings, a five-membered heteroaromatic and a carbocyclic ring, might be readily prepared by Diels–Alder reactions with 2-inden-1-one **3** (Fig. 1).

2. Results and discussion

2.1. Synthesis of reagents

Both dienes **1** have been described in the literature[3a,6,7] but their synthesis was unsatisfactory. Therefore, we decided to revise and improve the synthesis. The commercially available 1-(benzo[*b*]furan-2-yl)ethanone **4a** and the readily accessible 1-(benzo[*b*]thiophen-2-yl)ethanone **4b**[8] were chosen as starting materials. The desired dienes **1** were attained by a short, new, facile procedure: reduction of the ketonic carbonyl function of **4** followed by dehydration of the alcohols **5** (Scheme 1).

3-Nitro-2-cyclohexen-1-one **2** was prepared according to the procedure reported in the literature[9] but in our hands



1 a: X=O
b: X=S

2 **3**

Figure 1.

Keywords: benzofurans; benzothiophenes; Diels–Alder reactions; polycyclic heterocyclic compounds.
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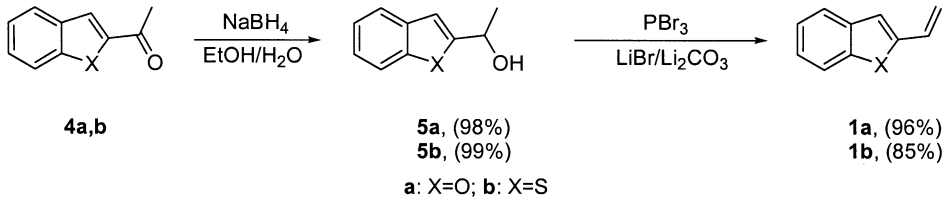


Scheme 1.

the deprotection of the ketonic carbonyl function requires heating at 35°C for 3 h, rather than at room temperature for 30 min.

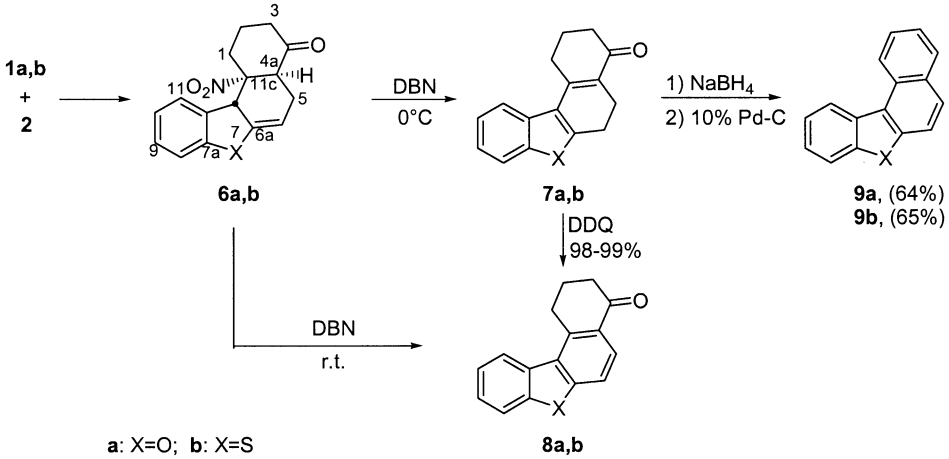
2.2. Diels–Alder reactions of 3-nitro-2-cyclohexen-1-one 2

When 2-vinyl-benzo[*b*]furan **1a** interacted with ketone **2** under thermal conditions (entry 2—Table 1) cycloadduct **6a** alone was obtained regioselectively and *exo* diastereoselectively (Scheme 2). The regiochemistry is the reverse of that usually observed in the cycloadditions of arylethenes and cycloalkenones; the strong electron withdrawing nitro group acts as regiodirector and controls the orientation of the reaction. The product was, however, unstable and partly decomposed on column chromatography. Treatment[9c] of the crude reaction mixture with DBN at 0°C led to unsaturated ketone **7a** in 15% overall yield. Carrying out the cycloaddition reaction under high pressure conditions[10] (9 kbar), strongly accelerated the reaction and increased the yield. A 43% overall yield of the cycloaddition–elimination sequence was obtained (entry 1—Table 1). Ketone **7a** was then oxidized by DDQ to the tetracyclic ketone **8a**. We also observed that if crude cycloadduct **6a** was treated with an excess of DBN at room temperature, rather than at 0°C (Scheme 2), it was directly converted to **8a**. Clearly the application of high pressure markedly promoted the Diels–Alder reaction and allowed much better results to be

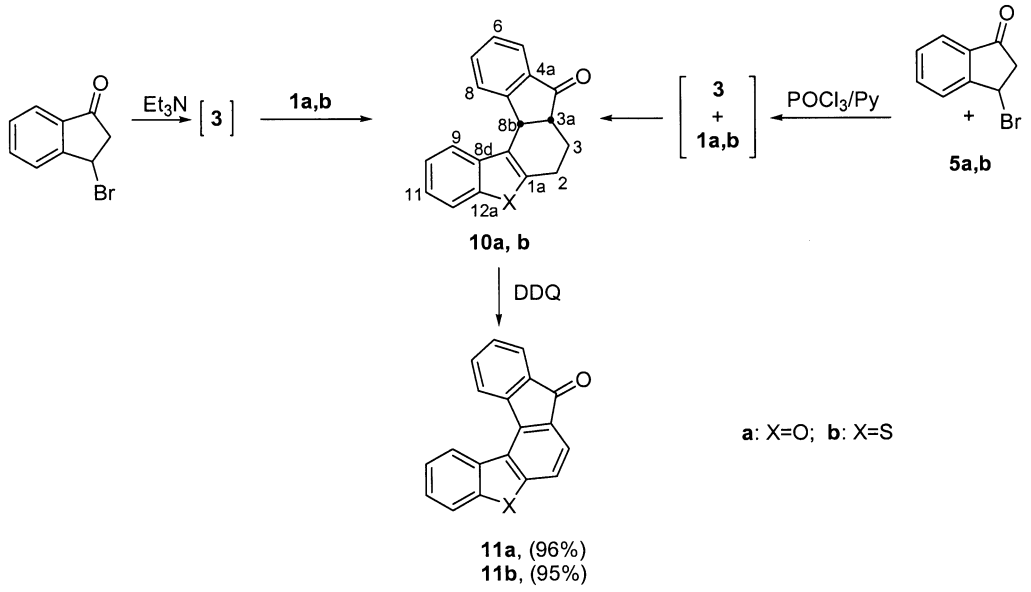
Table 1. Reaction conditions of the Diels–Alder reactions of dienes **1** with dienophiles **2** and **3**

Entry	Reactants	Diene/ketone (equiv.)	Solvent	Conditions	Product	Yield (%)
1	**1a**–**2**	1.5	CH_2Cl_2	9 kbar, 50°C, 16 h	**7a**[a] (**8a**)[a]	43[b] (42)[b,d]
2		1.2	Toluene	Reflux, 6d	**7a**[a]	15[c]
3	**1b**–**2**	1.5	CH_2Cl_2	9 kbar, 50°C, 16 h	**7b**[a] (**8b**)[a]	37[b] (37)[b,d]
4		1.2	Toluene	Reflux, 6d	**7b**[a]	10[c]
5	**1a**–**3**[e]	0.6	CH_2Cl_2	Et_3N, 10 kbar, 50°C, 3d	**10a**	80[c]
6		0.3	CCl_4	Et_3N, reflux, 3d	**10a**	68[c]
7	**1b**–**3**[e]	0.6	CH_2Cl_2	Et_3N, 10 kbar, 50°C, 3d	**10b**	26[c]
8		0.3	CCl_4	Et_3N, reflux, 3d	**10b**	48[c]
9	**5a**[f]–**3**[e]	0.3[d]	Toluene	$POCl_3$/Py, reflux, 48 h	**10a**	69[b]
10	**5b**[f]–**3**[e]	0.3[d]	Toluene	$POCl_3$/Py, reflux, 48 h	**10b**	47[b]

[a] Produced after treatment of initial adduct with DBN.
[b] Isolated yields.
[d] Yield of **8**.
[c] GC-based yields.
[e] 3-Bromoindan-1-one was used as a precursor of **3**.
[f] Alcohol **5** was used as a precursor of **1**.



Scheme 2.



Scheme 3.

obtained. On the other hand, Lewis acid catalysis was precluded because of the sensitivity of dienes **1** to acidic conditions.

Diels–Alder reaction of 2-vinyl-benzo[*b*]thiophene **1b** with ketone **2** led regioselectively to the cycloadduct **6b** which was less stable than **6a**, and an analytical sample could not even be isolated. The reaction mixture was therefore treated with DBN as described above and afforded ketones **7b** or **8b** (entry 3—Table 1).

Polycyclic aromatic compounds **9** were obtained from compounds **7** by a dehydration–aromatization procedure. Sodium borohydride reduction of **7** followed by treating the alcoholic mixture with 10% Pd–C in triglyme at reflux temperature, gave **9a** and **9b** in 64 and 65% yield, respectively.

2.3. Diels–Alder reactions of 2-inden-1-one 3

Since 2-inden-1-one **3** is an oil which polymerises very easily we chose, in our laboratory, to generate it in situ from its precursor 3-bromoindan-1-one and trap it with dienes **1**. When a carbon tetrachloride solution of crude 3-bromoindan-1-one and dienes **1** (Scheme 3) was heated at reflux temperature and triethylamine was added dropwise, 2-inden-1-one **3** was generated and allowed to react with dienes **1** to afford, regioselectively, products **10** in 68% (X=O) and 48% (X=S) yield (entries 6, 8—Table 1). When the Diels–Alder reactions were carried out under high pressure conditions, the yield of the cycloaddition with 2-vinyl-benzo[*b*]furan **1a** increases (80%) but that with 2-vinyl-benzo[*b*]thiophene **1b** decreases (26%) (entries 5, 7—Table 1).

Treatment of ketones **10** with DDQ led to polycyclic aromatic compounds **11**. In order to facilitate the cycloaddition process we modified the Diels–Alder reaction by directly using the crude mixture of alcohols **5** in order to also generate in situ the dienes **1**.

When a toluene solution of the crude alcohols **5** and 3-bromoindan-1-one was heated in the presence of a small amount of $POCl_3$/Py, the dienes **1** and 2-inden-1-one **3** were both generated in situ and reacted to afford products **10** in 69% (X=O) and 47% (X=S) yield, respectively (Scheme 3).

No reaction occurred when the mixture of alcohols **5** and

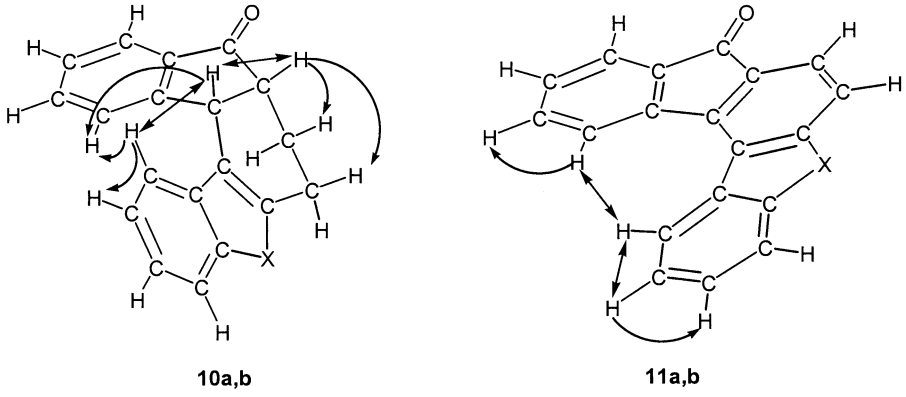


Figure 2. Minimized energy conformations of **10** and **11**; the arrows indicate observed NOEs.

3-bromoindan-1-one in the presence of $POCl_3$/Py was submitted to high pressure.

2.4. Structure analysis

2.4.1. Tetracyclic ketones 6–8. The regiochemical assignment of the carbonyl function at C(4) of all tetracyclic ketones follows from the examination of $^1H-^1H$ and $^1H-^{13}C$ connectivities (COSY spectra) and is confirmed by the NOE effects observed between H(1) and H(11) protons for all ketones. Furthermore, in the case of cycloadduct **6a**, no mutual enhancement was observed for resonances of H(4a) and H(11b), thus indicating the *trans*-relationship of H(4a) with H(11b).

2.4.2. Pentacyclic ketones 10 and 11. The regiochemical assignment of the carbonyl function for **10** and **11**, as well as the stereochemical relationship of H(3a) and H(8b) of ketones **10**, were inferred from a series of selective NOE experiments (Fig. 2). Irradiation of the resonance due to H(8b) proton in compounds **10** resulted in signal enhancements of resonance attributed to H(3a), H(8) and H(9) signals, suggesting a *cis* spatial relationship between H(3a) and H(8b). Furthermore, mutual dipolar contacts for compounds **10** were observed between H(9) and H(8), H(8b), H(10) protons, as well as between H(3a) and H(2), H(3) and H(8b) also indicating the regiochemical assignment of the carbonyl function at C(4). Further support was also given by the NOE effects observed between H(9), H(8) and H(10) in ketones **11**.

3. Conclusions

The Diels–Alder reactions of 2-vinyl-benzo[*b*]furan **1a** and 2-vinyl-benzo[*b*]thiophene **1b** with cycloalkenones were examined under thermal and high pressure conditions. The application of pressure was essential for carrying out the cycloadditions with 3-nitro-2-cyclohexen-1-one **2**. A new synthetic route to multi-ring heterocyclic systems has been developed.

4. Experimental

4.1. General

Melting points were determined on a Büchi 510 melting point apparatus and are uncorrected. IR spectra were recorded in $CHCl_3$ solution on a Perkin–Elmer Paragon 500 FT-IR. NMR spectra were run in $CDCl_3$ at room temperature on a Varian Associates VXR-400 multinuclear instrument (400 and 100.6 MHz for ^1H and ^{13}C, respectively). Chemical shifts are expressed in ppm downfield from internal TMS for ^1H and ^{13}C. The structures of the reaction products were assigned by analysis of ^1H and ^{13}C NMR spectra. Proton and carbon shift assignments were based on COSY, $^1H-\{^1H\}$NOE and HETCOR experiments; quaternary carbons were assigned by 2D long-range heterocorrelated experiments. GC analyses were performed on a Hewlett Packard 6890 chromatograph. Absorption chromatography was carried out on Merck silica gel (0.040–0.063 mm, 230–400 mesh ASTM). Mass spectra were observed on a Hewlett Packard 5970 GC-MS instrument (70 eV). 1-(Benzo[*b*]furan-2-yl)ethanone **4a** was purchased from Aldrich Chemical Company.

4.1.1. 2-Vinyl-benzo[*b*]furan (1a). Sodium borohydride (4.6 g, 121.0 mmol) dissolved in water (48 mL) was added to a refluxing solution of 1-(benzo[*b*]furan-2-yl)ethanone **4a** (2.0 g, 12.5 mmol) in ethanol (150 mL). The reaction mixture was refluxed for 1.5 h, then cooled to room temperature and extracted with $CHCl_3$. The combined extracts were washed with brine, dried (Na_2SO_4) and evaporated in vacuo to afford 1-(benzo[*b*]furan-2-yl)-ethanol **5a**[11] (2.0 g, 98%) as a white solid, which was used for the next step without purification.

A solution of PBr_3 (1 mL) in dry CH_2Cl_2 (12 mL) was added dropwise to a solution of **5a** (2 g, 12.3 mmol) in anhydrous DMF (40 mL) at −10°C under nitrogen. The reaction mixture was stirred at 0°C for 3 h. Then LiBr (3.4 g) and Li_2CO_3 (3.9 g) were added and the reaction mixture was heated for 3 h under nitrogen and stirring. It was cooled, poured into ice-water and extracted with ether. The combined extracts were washed with brine, dried (Na_2SO_4) and filtered. Evaporation of the solvent gave the title compound **1a** (1.7 g, 96%) as a pale yellow oil, having ^1H NMR spectroscopic data identical to those reported in the literature.[6]

4.1.2. 2-Vinyl-benzo[*b*]thiophene (1b). 1-(Benzo[*b*]thiophen-2-yl)ethanone **4b**[8] (3.5 g, 19.9 mmol) in 245 mL of ethanol was treated with sodium borohydride (7.3 g) in water (76 mL) as described above for the synthesis of **1a**. Usual work up afforded pure 1-(benzo[*b*]thiophen-2-yl)-ethanol **5b**[12] (3.5 g, 99%) as a white solid, which was used directly for the next step.

A solution of alcohol **5b** in DMF (38 mL) was treated with PBr_3 (1.6 mL) in CH_2Cl_2 (19 mL) and then with LiBr (5.4 g) and Li_2CO_3 (6.2 g) following the procedure reported above for compound **1a**. The title compound **1b** was obtained (2.9 g) as a yellow solid, which was pure enough for the subsequent transformations. For analytical purposes a sample was purified by flash chromatography (SiO_2, hexane) to give **1b** (85%) as a white solid, mp 65–66°C (lit.[7] 65–66°C); ^1H NMR data were identical to those reported in the literature.[7]

4.1.3. Diels–Alder reactions of dienes 1 with 3-nitro-2-cyclohexen-1-one (2). The cycloadditions were accomplished at atmospheric pressure (entries 2, 4) and under high pressure conditions (entries 1, 3) (see Table 1).

(*Entries* 2, 4). A solution of **1** (0.7 mmol) and **2** (0.6 mmol) in toluene (3 mL) was heated in an oil bath at reflux temperature for six days and then cooled to room temperature. Toluene was evaporated in vacuo and the residue chromatographed on silica gel.

(*Entries* 1, 3). A solution of **1** (4.2 mmol) and **2** (2.8 mmol) in 15 mL of CH_2Cl_2 in the presence of a small amount of hydroquinone was kept under high pressure according to the previously described procedure.[13] After depressurising, the solvent was evaporated in vacuo and the residue chromatographed on silica gel.

4.1.4. 11c-Nitro-2,3,4a,5,11b,11c-hexahydronaphtho[2,1-*b*]benzo[*b*]furan-4(1*H*)-one (6a). It was obtained (35% yield) by column chromatography (SiO_2, 4:1 hexane/ethyl acetate) from the crude reaction mixture of the cycloaddition between **1a** and **2** performed under high pressure (entry 1—Table 1); white microcrystalline solid, mp 125°C (dec.) (2:1 hexane/ethyl acetate); (found: C, 67.6; H, 5.3; N, 4.8. $C_{16}H_{15}NO_4$ requires C, 67.36; H, 5.30; N, 4.91%); IR 1722 (s, C=O), 1546 (s, $-NO_2$) cm^{-1}; ^1H NMR δ 2.06 (m, 1H, H-2), 2.32 (ddd, 1H, J=18.0, 7.8, 3.4 Hz, H-5), 2.38 (m, 1H, H-2), 2.56 (ddd, 1H, J=14.3, 7.8, 1.2 Hz, H-3), 2.70 (m, 1H, H-3), 2.73 (m, 1H, H-1), 3.05 (m, 1H, H-1), 3.09 (ddd, 1H, J=18.0, 3.2, 1.0 Hz, H-5), 3.65 (dt, 1H, J=7.8, 1.0 Hz, H-4a), 4.08 (dt, 1H, J=3.0, 1.0 Hz, H-11b), 5.11 (ddd, 1H, J=3.4, 3.2, 3.0 Hz, H-6), 6.94 (ddd, 1H, J=7.6, 7.5, 0.9 Hz, H-10), 7.23 (m, 1H, H-11), 7.26 (m, 1H, H-9); ^{13}C NMR δ 19.2 (C-5), 21.3 (C-2), 33.8 (C-1), 40.0 (C-3), 42.3 (C-11b), 52.8 (C-4a), 93.1 (C-11c), 94.3 (C-6), 110.3 (C-8), 122.1 (C-10), 123.5 (C-11a), 123.8 (C-11), 129.0 (C-9), 150.7 (C-7a), 157.6 (C-6a), 205.1 (C-4).

4.1.5. 2,3,5,6-Tetrahydronaphtho[2,1-*b*]benzo[*b*]furan-4(1*H*)-one (7a). The crude reaction mixture obtained by cycloaddition reaction of **1a** and **2** (entry 1—Table 1) dissolved in dry THF (6 mL) was treated with DBN (0.28 mL) for 0.5 h at 0°C, then poured into H_2O and extracted with ether. The organic layer was washed with brine, dried (Na_2SO_4) and evaporated in vacuo. Chromatography on silica gel of the crude product and elution with 4:1 hexane/ethyl acetate gave pure **7a** (43% overall yield) as a white microcrystalline solid, mp 142–143°C (2:1 hexane/ethyl acetate); (found: C, 80.5; H, 6.0. $C_{16}H_{14}O_2$ requires C, 80.65; H, 5.92%); IR 1642 (s, C=O) cm^{-1}; ^1H NMR δ 2.16 (m, 2H, Hs-2), 2.53 (dd, 2H, J=7.1, 6.6 Hz, Hs-3), 2.86 (m, 2H, Hs-5), 2.95 (m, 2H, Hs-6), 2.99 (m, 2H, Hs-1), 7.27 (m, 2H, H-9, H-10), 7.50 (m, 1H, H-8), 7.67 (m, 1H, H-11); ^{13}C NMR δ 20.8 (C-5), 21.9 (C-6), 22.4 (C-2), 27.5 (C-1), 37.5 (C-3), 111.8 (C-8); 114.4 (C-11a), 119.9 (C-11), 123.6 (C-10), 123.9 (C-9), 125.3 (C-11b), 125.8 (C-4a), 49.1 (C-11c), 155.5 (C7a), 160.6 (C-6a), 197.5 (C-4); MS *m/e* (rel. int.) 76 (16), 152 (30), 181 (86), 208 (45), 221 (27), 238 (M^+, 100).

4.1.6. 2,3-Dihydronaphtho[2,1-*b*]benzo[*b*]furan-4(1*H*)-one (8a). When the mixture obtained from the cycloaddition reaction between **1a** and **2** (entry 1—Table 1) was treated with DBN (0.42 mL) in dry THF (9 mL) for 36 h at room temperature, crude **8a** was obtained. It was chromatographed (SiO_2, hexane/ethyl acetate 4:1) to afford the title compoud **8a** (42% overall yield) as a pale yellow microcrystalline solid, mp 100–101°C (4:1 hexane/ethyl acetate); (found: C, 81.2; H, 5.1. $C_{16}H_{12}O_2$ requires C, 81.34; H, 5.12%); IR 1676 (s, C=O) cm^{-1}; ^1H NMR δ 2.35 (m, 2H, Hs-2), 2.77 (dd, 2H, J=6.5, 6.3 Hz, Hs-3), 3.50 (t, 2H, J=6.2 Hz, Hs-1), 7.41 (ddd, 1H, J=7.8, 7.3, 1.0 Hz, H-10), 7.50 (d, 1H, J=8.7 Hz, H-6), 7.51 (ddd, 1H, J=8.3, 7.3, 1.4 Hz, H-9), 7.62 (dd, 1H, J=8.3, 1.0 Hz, H-8), 8.06 (dd, 1H, J=7.8, 1.4 Hz, H-11), 8.24 (d, 1H, J=8.7 Hz, H-5); ^{13}C NMR δ 22.9 (C-2), 27.2 (C-1), 38.6 (C-3), 110.3 (C-6), 112.0 (C-8), 122.0 (C-11b), 122.4 (C-11), 123.4 (C-10), 124.2 (C-11a), 127.2 (C-9), 127.3 (C-5); 128.3 (C-4a), 140.9 (C-11c), 156.7 (C-7a), 158.9 (C-6a), 197.4 (C-4); MS *m/e* (rel. int.) 76 (27), 104 (13), 152 (34), 180 (82), 208 (99), 236 (M^+, 100).

4.1.7. 2,3,5,6-Tetrahydronaphtho[2,1-*b*]benzo[*b*]thiophen-4(1*H*)-one (7b). The reaction mixture obtained by the cycloaddition reaction between **1b** and **2** performed under high pressure (entry 3—Table 1) was treated with DBN as described above for the synthesis of **7a**. Usual work up and chromatography on silica gel (eluent: 4:1 hexane/ethyl acetate) afforded pure **7b** (37% overall yield) as white crystalline solid, mp 162–163°C (methanol); (found: C, 75.7; H, 5.6. $C_{16}H_{14}OS$ requires C, 75.55; H, 5.55%); IR 1642 (s, C=O) cm^{-1}; ^1H NMR δ 2.17 (m, 2H, Hs-2), 2.56 (dd, 2H, J=7.0, 6.3 Hz, Hs-3), 2.70 (dd, 2H, J=9.2, 8.2 Hz, Hs-5), 2.92 (dd, 2H, J=9.2, 8.2 Hz, Hs-6), 3.12 (dd, 2H, J=6.3, 6.2 Hz, Hs-1), 7.31 (ddd, 1H, J=7.9, 7.2, 1.2 Hz, H-9), 7.38 (ddd, 1H, J=7.8, 7.2, 1.2 Hz, H-10), 7.82 (dd, 1H, J=7.9, 1.2 Hz, H-8), 7.98 (dd, 1H, J=7.8, 1.2 Hz, H-11); ^{13}C NMR δ 20.8 (C-5), 21.9 (C-6), 22.4 (C-2), 27.5 (C-1), 37.5 (C-3), 111.8 (C-8), 114.4 (C-11a), 119.9 (C-11), 123.6 (C-10), 123.9 (C-9), 125.3 (C-11b), 125.8 (C-4a), 149.1 (C-11c), 155.5 (C-7a), 160.6 (C-6a), 197.5 (C-4); MS *m/e* (rel. int.) 99 (12), 152 (15), 165 (19), 184 (22), 197 (74), 211 (33), 226 (78), 254 (M^+, 100).

4.1.8. 2,3-Dihydronaphtho[2,1-*b*]benzo[*b*]thiophen-4(1*H*)-one (8b). The **1b**–**2** reaction mixture obtained, according to entry 3—Table 1, was treated with DBN as described above for the synthesis of **8a**. Usual work up and column chromatography of the residue (4:1 hexane/ethyl acetate) gave pure **8b** (37% overall yield) as a pale yellow solid, mp 140–141°C (ethanol); (found: C, 76.3; H, 4.8. $C_{16}H_{12}OS$ requires C, 76.16; H, 4.79%); IR 1675 (s, C=O) cm^{-1}; ^1H NMR δ 2.34 (m, 2H, Hs-2), 2.77 (dd, 2H, J=6.9, 6.5 Hz, Hs-3), 3.63 (t, 2H, J=6.2 Hz, Hs-1), 7.53 (m, 2H, H-9, H-10), 7.81 (d, 1H, J=8.5 Hz, H-6), 7.92 (m, 1H, H-8), 8.22 (d, 1H, J=8.5 Hz, H-5), 8.40 (m, 1H, H-11); ^{13}C NMR δ 23.3 (C-2), 29.4 (C-1), 38.8 (C-3), 121.6 (C-6), 123.8 (C-8), 125.4 (C-10), 125.8 (C-5), 126.0 (C-11), 127.0 (C-9), 130.6 (C-6a), 133.7 (C-7a), 136.7 (C-11b), 140.6 (C-11a), 142.4 (C-4a), 146.1 (C-11c), 198.7 (C-4); MS *m/e* (rel. int.) 76 (8), 98 (16), 152 (25), 196 (60), 224 (63), 252 (M^+, 100).

4.1.9. DDQ oxidation of compounds 7. A benzene solution (3 mL) of ketone **7a** or **7b** (1.2 mmol), and DDQ (0.6 g), was heated at reflux temperature for 1 h under nitrogen. After cooling, the reaction mixture was diluted with benzene (10 mL), washed with 10% aqueous $Na_2S_2O_4$ solution, 10% aqueous KOH solution and saturated brine.

Drying (Na_2SO_4), filtration and concentration in vacuo of the solvent afforded a residue which was chromatographed on silica gel. Elution with 95:5 hexane/ethyl acetate gave pure **8a** (98%) or **8b** (99%).

4.1.10. Tetracyclic hydrocarbons 9. A 1:1 methanol–dichloromethane solution (20 mL) of ketone **7a** or **7b** (1.3 mmol) and $NaBH_4$ (0.31 g) was stirred for 2 h at room temperature. The reaction mixture was then worked up as usual and the crude product was dissolved in triglyme (10 mL) and treated with 10% Pd–C catalyst (0.3 g) at reflux temperature for 24 h. Usual work up afforded a

residue which was purified by column chromatography. Elution with hexane gave pure **9a** (64%) or pure **9b** (65%), whose mp and spectroscopic data were identical to those reported in the literature.[14,15]

4.1.11. Diels–Alder reactions of 2-inden-1-one (3). The reactions were accomplished at atmospheric pressure (entries 6, 8–10—Table 1) and under high pressure conditions (entries 5, 7—Table 1) using 3-bromoindan-1-one as a precursor of 2-inden-1-one **3**.

(*Entries* 6, 8). Triethylamine (0.34 mL) and a small amount of hydroquinone were added to a solution of 3-bromoindan-1-one (2.3 mmol) and dienes **1** (0.7 mmol) in CCl_4 (5 mL) under nitrogen and stirring. The mixture was allowed to react at the indicated temperature, then worked up as usual[4a] and chromatographed on silica gel.

(*Entries* 9, 10). A solution of $POCl_3$ (0.25 mL) in dry pyridine (1 mL) was added to a solution of alcohols **5** (1.3 mmol) in anhydrous toluene (25 mL). The resulting solution was refluxed under nitrogen until the dehydration reactions to dienes **1** were complete (GLC analyses) (12 h for **1a**, 8 h for **1b**). Then 3-bromoindan-1-one (1.4 mmol) was added and the reflux continued for 36 h, during which time two further 1.4 mmol portions of 3-bromoindan-1-one were added. The reaction mixture was then cooled to room temperature, poured into ice-cooled 5% aqueous H_2SO_4 and extracted with $CHCl_3$. The combined extracts were washed with saturated aqueous $NaHCO_3$ solution and brine. Drying (Na_2SO_4), filtration and evaporation in vacuo of the solvent afforded a residue which was chromatographed on silica gel.

(*Entries* 5, 7). Triethylamine (0.05 mL) and a small amount of hydroquinone were added to a solution of 3-bromoindan-1-one (0.5 mmol) and **1** (0.3 mmol) in CH_2Cl_2 (3 mL). The mixture was allowed to react at the indicated pressure, then was worked up as usual[4a] and chromatographed on silica gel.

Column chromatography of the crude reaction mixtures eluting with 95:5 hexane/ethyl acetate gave pure pentacyclic ketones **10**.

4.1.12. 2,3,3a,8b-Tetrahydro-4*H*-fluoreno[3,4-*b*]benzo[*b*]-furan-4-one (10a). It was prepared according to entry 9—Table 1; white microcrystalline solid, mp 128–129°C (hexane/ethyl acetate); (found: C, 83.3; H, 5.1. $C_{19}H_{14}O_2$ requires C, 83.19; H, 5.14%); IR 1703 (s, C=O) cm^{-1}; ^1H NMR δ 2.10 (m, 1H, H-3), 2.55 (m, 1H, H-3), 2.66 (m, 1H, H-2), 2.77 (m, 1H, H-2), 3.22 (ddd, 1H, *J*=7.3, 5.2, 5.0 Hz, H-3a), 4.80 (d, 1H, *J*=7.3 Hz, H-8b), 7.25 (ddd, 1H, *J*=8.0, 7.3, 1.4 Hz, H-11), 7.31 (dd, 1H, *J*=7.6, 7.3 Hz, H-10), 7.37 (ddd, 1H, *J*=7.6, 7.4, 1.1 Hz, H-6), 7.41 (dd, 1H, *J*=8.0, 1.2 Hz, H-12), 7.55 (ddd, 1H, *J*=7.8, 7.4, 1.3 Hz, H-7), 7.77 (dd, *J*=7.6, 1.3 Hz, H-5), 7.83 (dd, 1H, *J*=7.6, 1.4 Hz, H-9), 7.87 (dd, 1H, *J*=7.8, 1.1 Hz, H-8); ^{13}C NMR δ 21.0 (C-2), 23.1 (C-3), 37.4 (C-8b), 48.2 (C-3a), 111.3 (C-12), 113.45 (C-8c), 118.9 (C-9), 122.6 (C-10), 123.6 (C-11), 124.1 (C-5), 126.6 (C-8), 127.7 (C-8d), 127.9 (C-6), 134.9 (C-7), 135.2 (C-4a), 153.9 (C-1a), 154.4 (C-12a), 156.1 (C-8a), 206.7 (C-4); MS *m/e* (rel. int.) 144 (16), 245 (14), 259 (64), 274 (M^+, 100).

4.1.13. 2,3,3a,8b-Tetrahydro-4*H*-fluoreno[3,4-*b*]benzo[*b*]-thiophen-4-one (10b). It was prepared according to entry 10—Table 1; pale yellow solid, mp 147–148°C (hexane–ethyl acetate); (found: C, 78.7; H, 4.9. $C_{19}H_{14}OS$ requires C, 78.59; H, 4.86%); IR 1706 (s, C=O) cm^{-1}; ^1H NMR δ 2.03 (m, 1H, H-2), 2.53 (m, 1H, H-3), 2.56 (m, 1H, H-2), 2.80 (m, 1H, H-3), 3.25 (ddd, 1H, *J*=7.2, 6.0, 4.2 Hz, H-3a), 5.02 (d, 1H, *J*=7.2 Hz, H-8b), 7.35 (ddd, 1H, *J*=8.0, 7.0, 1.3 Hz, H-11), 7.36 (ddd, 1H, *J*=7.5, 7.3, 0.9 Hz, H-6), 7.48 (ddd, 1H, *J*=7.8, 7.3, 1.2 Hz, H-7), 7.49 (ddd, 1H, *J*=8.1, 7.0, 1.1 Hz, H-10), 7.73 (ddd, 1H, *J*=7.8, 0.9, 0.7 Hz, H-8), 7.80 (dd, 1H, *J*=8.0, 1.1 Hz, H-12), 7.81 (dd, 1H, *J*=7.5, 1.2 Hz, H-5), 8.08 (dd, 1H, *J*=8.1, 1.3 Hz, H-9); ^{13}C NMR δ 23.5 (C-3), 26.2 (C-2), 38.5 (C-8b), 47.2 (C-3a), 121.2 (C-9), 122.8 (C-5), 123.8 (C-11), 123.9 (C-12), 124.2 (C-10), 126.6 (C-8), 127.9 (C-6), 129.1 (C-8c), 135.2 (C-7), 135.6 (C-4a), 138.8, 138.9, 139.1 (C-12a, C-1a, C-8d), 156.2 (C-8a), 208.2 (C-12); MS *m/e* (rel. int.) 160 (11), 134 (11), 261 (11), 275 (38), 290 (M^+, 100).

4.1.14. 4-Fluoreno[3,4-*b*]benzo[*b*]furan-4-one (11a). A benzene solution (10 mL) of ketone **10a** (0.15 g, 0.5 mmol) and DDQ (0.30 g, 1.2 mmol) was heated at reflux temperature for 4 h under nitrogen. After cooling, the reaction mixture was diluted with benzene (10 mL), washed with 10% aqueous $Na_2S_2O_4$ solution, 10% aqueous KOH solution and saturated brine. Drying (Na_2SO_4), filtration and concentration in vacuo of the solvent afforded the title compound **11a** (0.13 g, 96%) as a white solid, mp 187–188°C (ethyl acetate); (found: C, 84.3; H, 3.7. $C_{19}H_{10}O_2$ requires C, 84.43; H, 3.73%); IR 1708 (s, C=O) cm^{-1}; ^1H NMR δ 7.36 (dd, 1H, *J*=7.6, 7.4 Hz, H-6), 7.41 (d, 1H, *J*=8.1 Hz, H-2), 7.45 (ddd, 1H, *J*=8.0, 7.1, 1.2 Hz, H-10), 7.55 (ddd, 1H, *J*=8.2, 7.1, 1.3 Hz, H-11), 7.59 (ddd, 1H, *J*=7.6, 7.6, 1.3 Hz, H-7), 7.61 (dd, 1H, *J*=8.2, 1.2 Hz, H-12), 7.72 (dd, 1H, *J*=7.4, 1.3 Hz, H-5), 7.79 (d, 1H, *J*=8.1 Hz, H-3), 8.04 (d, 1H, *J*=7.6 Hz, H-8), 8.31 (dd, 1H, *J*=8.0, 1.3 Hz, H-9); ^{13}C NMR δ 111.4 (C-2), 112.1 (C-12), 120.3 (C-8d), 122.5 (C-8c), 123.3 (C-10), 123.4 (C-3), 123.6 (C-9), 123.7 (C-5, C-8), 128.4 (C-11), 129.4 (C-6), 129.8 (C-3a), 134.5 (C-7), 135.2 (C-4a), 140.8 (C-8b), 143.6 (C-8a), 157.3 (C-12a), 161.2 (C-1a), 193.0 (C-12); MS *m/e* (rel. int.) 187 (7), 213 (25), 242 (9), 270 (M^+, 100).

4.1.15. 4-Fluoreno[3,4-*b*]benzo[*b*]thiophen-4-one (11b). A solution of ketone **10b** (0.12 g, 0.4 mmol) in benzene (7 mL) was treated with 0.25 g (1.1 mmol) of DDQ at reflux temperature for 7 h. The reaction mixture was then worked up as described above for the synthesis of **11a** to give the title compound **11b** (0.11 g, 95%) as a pale yellow microcrystalline solid, mp 202–203°C (ethyl acetate); (found: C, 79.8; H, 3.5. $C_{19}H_{10}OS$ requires C, 79.69; H, 3.52%); IR 1709 (s, C=O) cm^{-1}; ^1H NMR δ 7.37 (ddd, 1H, *J*=7.6, 7.3, 0.9 Hz, H-6), 7.50–7.55 (m, 2H, H-10, H-11), 7.57 (ddd, 1H, *J*=7.7, 7.3, 1.4 Hz, H-7), 7.73 (d, 1H, *J*=7.9 Hz, H-3), 7.76 (d, 1H, *J*=7.9 Hz, H-2), 7.77 (dd, 1H, *J*=7.6, 1.4 Hz, H-5), 7.84 (m, 1H, H-12), 8.28 (dd, 1H, *J*=7.7, 0.9 Hz, H-8), 8.76 (m, 1H, H-9); ^{13}C NMR δ 121.5 (C-2 or C-3), 122.9 (C-5), 123.2 (C-12), 124.0 (C-8), 124.4 (C-2 or C-3), 124.7 (C-10 or C-13), 125.0 (C-9), 127.5 (C-10 or C-13), 129.3 (C-6), 131.6 (C-8c), 132.6 (C-8d), 134.3 (C-7), 134.4 (C-3a), 135.1 (C-4a), 140.2 (C-12a), 141.5 (C-8b),

144.9 (C-8a), 147.9 (C-1a), 193.3 (C-4); MS *m/e* (rel. int.) 129 (29), 213 (20), 258 (59), 286 (M^+, 100).

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