Cycloaddition Reactions of 2*H*-Benzo[*b*]thiete and Conjugated Cyclic Dienes

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2*H*-Benzo[*b*]thiete **1** reacts with cyclopentadiene **3** in consecutive [8π + 2π]cycloadditions yielding the condensed heterocycles **6-8**. Tetracyclone **9** on the other hand gives only the monoadduct **10**. An [8π + 8π]cycloaddition can be observed for **1** and diphenylisobenzofuran **11**. The related π system **13** shows again consecutive [47π + 27π]processes (**1** + **13** → **14**, **15**).

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2*H*-Benzo[*b*]thiete **1** proved to be a very versatile reagent for the synthesis of sulfur heterocycles [1,2]. The facile thermal or photochemical opening of the 4-membered ring generates the *o*-thiobenzoquinonemethide **1'**, a highly reactive 8π electron system. In the absence of reaction partners or in the presence of weakly reactive partners a cyclodimerization to 6*H*,12*H*-dibenzo[*b*,*f*][1,5]dithiocin **2** can occur [3]. A variety of dienophiles and heterodienophiles react with **1'** in [8π + 2π]cycloadditions yielding benzo-condensed 6-membered ring systems with sulfur atoms and possibly further hetero atoms. This result prompted us to investigate the behavior of **1** and conjugated dienes.

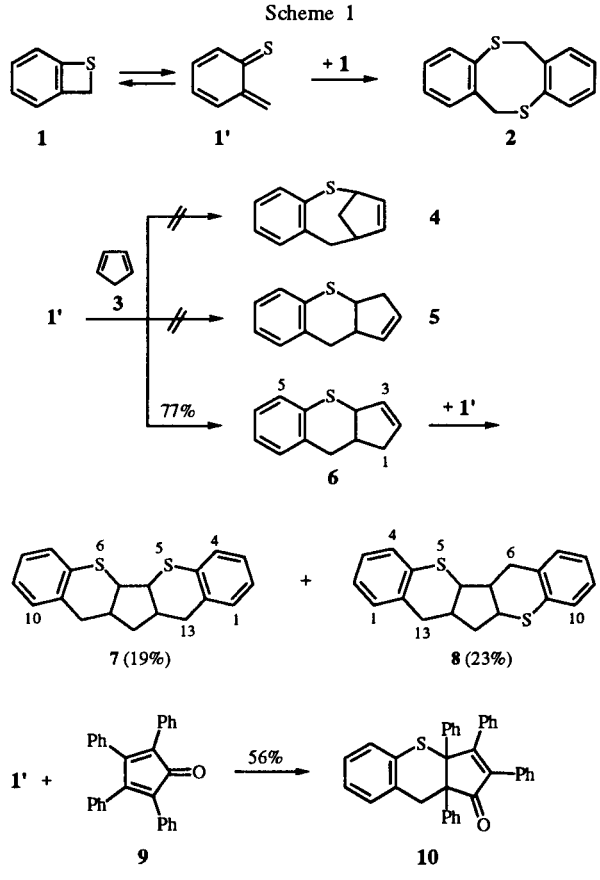
We examined first the reaction of **1** with cyclopentadiene **3** which led to the monoadduct **6**. An [8π + 4π] process **1** + **3** → **4** could be excluded. Additionally, the observed [8π + 2π]reaction turned out to be highly regioselective; compound **5**, a regioisomer of **6** could not be detected.

The discrimination between the structures **5** and **6** was performed by double resonance experiments in the ^{1}H nmr spectroscopy, especially by the ^{3}J coupling between the olefinic proton 3-H and the tertiary proton 3a-H. Isolated **6** and **1** reacted to the twofold adducts **7** and **8** which were separated by hplc [4]. The regioselective formation of **6** is in accordance with the FMO theory if one assumes that the interaction LUMO (**1'**)-HOMO (**3**) is decisive [1]. A significant regioselectivity of the second step cannot be expected.

Another interesting aspect concerns the stereochemistry. The *cis* fused monoadduct **6** could principally lead to *syn* and/or *anti* anellated bisadducts **7** and **8**, but only one stereoisomer was obtained in each case. The symmetric system **7** permits an easy destinction. The protons of the methylene group in the central 5-membered ring are homotopic, *i.e.* a .C_2 axis is present. Double resonance, INDOR and NOE experiments were performed in the ^{1}H nmr spectroscopy of the asymmetrical compound **8**. Additionally, a ^{1}H,^{13}C shift correlated 2D-spectrum was measured. It turned out that all three ^{3}J couplings between the tertiary protons in the central 5-membered ring are equal, namely 9.3 Hz; nevertheless, the *trans* fusion was established here as well as in **7**. A quantitative determination of the NOE showed that the effect is about six times bigger for vicinal protons in *cis* position than for those in *trans* position.

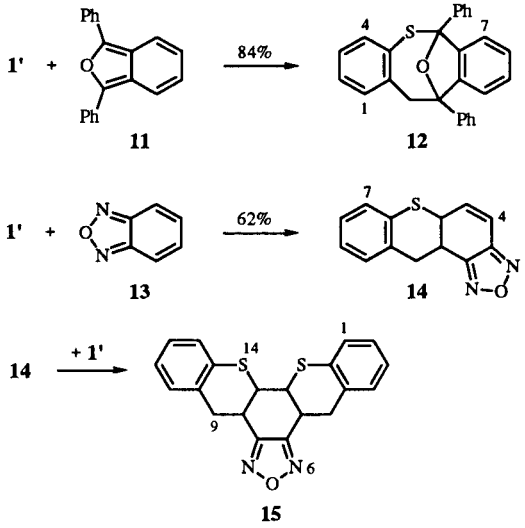
Moreover, Scheme 1 contains the cycloaddition of **1/1'** and tetraphenylcyclopentadienone **9**, an electron-deficient diene. Cycloadditions of **1'** with a reverse electron demand, that means with a predominant interaction HOMO (**1'**)-LUMO (2π component) are known [5]. Nevertheless, the reaction **1** + **9** stopped after the first step. Steric reasons in the crowded primary adduct **10** are certainly responsible for this result.

Scheme 1



Contrary to the dienes **3** and **9**, diphenylisobenzofuran **11** reacted as an 8π (or 4π) component. Thus the oxygen-bridged dibenzothiocin **12** was obtained. Although 2,1,3-benzoxadiazole **13** (benzofurazan) seems to be a π system, which is closely related to **11**, its reactivity towards **1/1'** is totally different. Instead of an 8π component **13** reacts twice as a 2π component in the benzene ring. Both steps are highly regioselective; besides monoadduct **14** and bisadduct **15** no other products were found. The stereochemistry of **15** is again characterized by the *cis* fusion. The stereochemistry of **15** was not determined. Due to steric reasons and in analogy to **7** and **8** an *anti* anellation can be assumed for the central 6-membered ring.

Scheme 2



The cycloaddition reactions discussed here are always accompanied by some dimerization (**1' + 1 → 2**). Whereas this competitive process is important for the reaction of **6**, it plays only a marginal role in the other cases.

Summarizing the reaction behavior of 2*H*-benzo[*b*]thiete **1** towards 4π or 8π electron systems, we noticed the formation of 6-membered ring systems **6-8, 10, 14, 15** as well as 8-membered ring systems **2,12**. Chemo-, regio- and stereoselectivities have to be determined individually.

EXPERIMENTAL

The ^1H and ^{13}C nmr spectra were recorded on Bruker WM-200 and AM-400 spectrometers using tetramethylsilane as internal standard. The EI mass spectra were measured on a Varian MAT 7A spectrometer at 70 eV. The infrared spectra were recorded on a Beckman IR Accu Lab 4 spectrophotometer. Melting points were determined on a Buchi SMP 20 apparatus and are not corrected. Merck silica gel (grain size: 0.063-0.200 mm) was used for column chromatography. A Gilson Abimed system and a column Si 60 were used for hplc.

1,3a,9,9a-Tetrahydrocyclopenta[*b*][1]benzothiopyran **6**.

2*H*-Benzo[b]thiete **1** (244 mg, 2.0 mmoles) and cyclopentadiene **3** (660 mg, 10.0 mmoles) were refluxed in 10 ml of toluene for 5 hours. After cooling to room temperature, the volatile parts were evaporated. The residue was purified by column chromatography (silica gel, toluene/ethyl acetate, 10/1). Product **6** was obtained as colorless crystals (270 mg, 77%) which melted at 40° and had ^1H nmr (400 MHz, deuteriochloroform): δ 2.11 (m, 1H, 1-H), 2.61 (m, 1H, 1-H), 2.66 (dd, ^2J = -13.5 Hz, ^3J = 5.6 Hz, 1H, 9-H), 2.89 (dd, ^2J = -13.5 Hz, ^3J = 5.2 Hz, 1H, 9-H), 3.20 (m, 1H, 9a-H), 4.34 (m, 1H, 3a-H), 5.58 (m, 2H, 2-,3-H), 7.10-7.37 (m, 4H, aromatic H); ^{13}C nmr (100 MHz, deuteriochloroform): δ 37.3, 38.5 (C-1, 9), 39.0 (C-9a), 53.1 (C-3a), 126.2, 126.6, 128.7, 129.9, 131.6, 131.9 (C-2,3,5,6,7,8), 135.4, 139.6 (C-4a,8a); ms: m/z (%) 188 (100, M^+), 173 (25), 147 (20), 134 (56), 123 (50), 122 (18), 121 (41); ir: ν 3060, 2920, 2850, 1465, 1440, 1070, 750 cm^{-1}.

Anal. Calcd. for $C_{12}H_{12}S$ (188.29): C, 76.55; H, 6.42; S, 17.03. Found: C, 76.50; H, 6.50.

5a,5b,11a,12,12a,13-Hexahydro-11*H*-cyclopenta[2,1-*b*:3,4-*b'*]dibenzothiopyran **7** and 5b,6,11a,12,12a,13-Hexahydro-5a*H*-cyclopenta[1,2-*b*:4,3-*b'*]dibenzothiopyran **8**.

2*H*-1-Benzo[*b*]thiete **1** (244 mg, 2.0 mmoles) and **6** (200 mg, 1.06 mmoles) were refluxed in 10 ml of toluene for 4 hours. Another portion of **1** (122 mg, 1.0 mmole) was added and the heating continued for 2 hours. The solvent was evaporated under reduced pressure and the residue chromatographed (silica gel, toluene/ethyl acetate, 10/1) to give **2** (250 mg), **6** (120 mg) and a mixture of **7/8**. The separation of **7** and **8** by hplc (eluent: hexane/ethyl acetate 10/1) yielded 25 mg (8%) **7** and 30 mg (9%) **8** as colorless oils. Related to the turnover the yields of **7** and **8** amount to 19 and 23%, respectively.

Compound **7** was characterized by the following data: ^1H nmr (400 MHz, deuteriochloroform): δ 1.70 (t, ^3J = 6.7 Hz, 2H, 12-H), 2.54 (dd, ^2J = -14.1 Hz, ^3J = 7.4 Hz, 2H, 11-, 13-H), 2.65 (m, 2H, 11a-, 12a-H), 2.74 (dd, ^2J = -14.1 Hz, ^3J = 4.5 Hz, 2H, 11-, 13-H), 3.43 (m, 2H, 5a-, 5b-H), 7.04-7.26 (m, 8H, aromatic H); ^{13}C nmr (100 MHz, deuteriochloroform):δ 34.8, 36.2, 38.4 (C-11,11a,12,12a,13), 53.1 (C-5a,5b), 125.4, 126.8, 128.1, 129.3 (aromatic CH), 133.9, 136.9 (C_q); ms: m/z (%) 310 (43, M^+), 187 (100), 147 (62), 134 (21), 128 (19), 121 (24); ir: ν 3060, 2940, 1470, 1445, 1070, 1040 cm^{-1}.

Anal. Calcd. for $C_{19}H_{18}S_2$ (310.48): C, 73.50; H, 5.84. Found: C, 73.45; H, 5.88.

Compound **8** was characterized by the following data: ^1H nmr (400 MHz, deuteriochloroform) δ 1.84 (m, 1H, 12-H), 1.94 (m, 1H, 12-H), 2.41 (m, 1H, 5b-H), 2.53 (dd, ^2J = -14.1 Hz, ^3J = 6.5 Hz, 1H, 13-H), 2.75 (dd, ^2J = -14.1 Hz, ^3J = 5.3 Hz, 1H, 13-H), 2.89 (dd, 2H, 6-H), 2.95 (m, 1H, 12a-H), 3.16 (t, 1H, 5a-H), 3.65 (m, 1H, 11a-H), 7.01-7.30 (m, 8H, aromatic H); ^{13}C nmr (100 MHz, deuteriochloroform): δ 32.0 (C-6), 35.0 (C-13), 39.3 (C-12), 39.5 (C-12a), 43.7 (C-11a), 47.7 (C-5b), 47.9 (C-5a), 125.0, 125.9, 126.8, 126.8, 127.2, 129.0, 129.2, 130.1 (aromatic CH), 132.2, 134.4, 138.8, 138.8 (C_q); ms: m/z (%) 310 (86, M^+), 187 (100), 162 (20), 147 (91), 128 (23), 121 (34), 115 (21); ir: ν 3060, 2940, 1470, 1445, 1070, 1040 cm^{-1}.

Anal. Calcd. for $C_{19}H_{18}S_2$ (310.48): C, 73.50; H, 5.84. Found: C, 73.39; H, 5.91.

1,3a,9,9a-Tetrahydro-2,3,3a,9a-tetraphenylcyclopenta[*b*][1]benzothiopyran-1-one **10**.

2*H*-Benzo[*b*]thiete **1** (244 mg, 2.0 mmoles) and tetraphenylcyclopentadienone **9** (768 mg, 2.0 mmoles) were refluxed in 10 ml of toluene for 5 hours. After cooling to room temperature the mixture was evaporated and the residue purified by column chromatography (silica gel, toluene). Product **10** was obtained as colorless crystals (565 mg, 56%) which melted at 253° and had ^{1}H nmr (400 MHz, deuteriochloroform): δ 3.46 (d, ^{2}J = -13.1 Hz, 1H, 9-H), 3.83 (d, ^{2}J = -13.1 Hz, 1H, 9-H), 6.55 (d, 2H, aromatic H), 6.93-7.37 (m, 22H, aromatic H); ^{13}C nmr (100 MHz, deuteriochloroform): δ 46.1 (C-9), 69.6, 73.3 (C-3a, 9a), 126.4, 127.2, 127.3, 127.5, 127.8, 128.0, 128.1, 128.2, 128.3, 128.5, 129.0, 129.2,129.6, 130.1, 131.2 (aromatic CH) [6], 133.7, 134.0, 138.1, 138.7, 138.7, 140.6, 143.7 (C-2 and aromatic C_q), 169.0 (C-3), 206.7 (C-1); ms: m/z (%) 506 (93, M^+), 478 (43), 384 (45), 296 (25), 267 (31), 211 (100), 178 (91); ir: ν 3060, 1690, 1485, 1440, 1340, 1150, 1030, 750, 695 cm^{-1}.

Anal. Calcd. for $C_{36}H_{26}OS$ (506.67): C, 85.34; H, 5.17. Found: C, 85.31; H, 5.23.

11,12-Dihydro-6,11-diphenyl- 6,11-epoxy- 6*H*-dibenzo[*b,f*]-thiocin **12**.

2*H*-Benzo[*b*]thiete **1** (244 mg, 2.0 mmoles) and diphenylisobenzofuran **11** (540 mg, 2.0 mmoles) were refluxed in 10 ml toluene for 5 hours. The mixture was cooled to room temperature, and evaporated. The residue was purified by column chromatography (silica gel, toluene/ethyl acetate, 10/1). Product **12** was obtained as colorless crystals (640 mg, 84%) which melted at 151° and had ^{1}H nmr (400 MHz, deuteriochloroform): δ 3.72 (d, ^{2}J = -15.2 Hz, 1H, 12-H), 4.32 (d, ^{2}J = -15.2 Hz, 1H, 12-H), 6.93-8.08 (m, 18H, aromatic H); ^{13}C nmr (100 MHz, deuteriochloroform): δ 50.6 (C-12), 88.5, 98.6 (C-6, 11), 121.3, 121.7, 126.3, 126.5, 126.6, 126.6, 127.0, 127.9, 128.0, 128.4, 128.6, 128.6, 128.6, 131.8, 133.1 (aromatic CH), 134.8, 140.4, 141.3, 142.6, 142.8, 144.6 (aromatic C_q); ms: m/z (%) 392 (58, M^+), 374 (30), 297 (18), 271 (22), 270 (100); ir: ν 3020, 1450, 1440, 1010, 1000, 755, 740, 700 cm^{-1}.

Anal. Calcd. for $C_{27}H_{20}OS$ (392.52): C, 82.62; H, 5.14. Found: C, 82.71; H, 5.20.

11,11a-Dihydro-5a*H*-2,1,3-oxadiazolo[4,5-*a*]thioxanthene **14**.

2*H*-Benzo[*b*]thiete **1** (244 mg, 2.0 mmoles) and benzofurazan **13** (240 mg, 2.0 mmoles) were refluxed in 10 ml toluene for 6 hours. After cooling to room temperature, the mixture was evaporated and the residue purified by column chromatography (silica gel, toluene/ethyl acetate, 10/1). Product **14** was obtained as yellow crystals (300 mg, 62 %) which melted at 79° and had ^{1}H nmr (200 MHz, deuteriochloroform): δ 3.35 (d, ^{3}J = 6.1 Hz, 2H, 11-H) [7], 3.91 (dt, 1H, 11a-H), 4.23 (dd, 1H, 5a-H), 6.43 (dd, ^{3}J = 4.9 Hz, ^{3}J = 9.8 Hz, 1H, 5-H), 6.77 (d, ^{3}J = 9.8 Hz, 1H, 4-H), 7.08-7.24 (m, 4H, aromatic H); ^{13}C nmr (50 MHz, deuteriochloroform): δ 32.4 (C-11a), 33.3 (C-11), 41.7 (C-5a), 115.6, 126.5, 127.0, 128.0, 129.5, 137.3 (C-4,5,7,8,9,10), 133.8, 134.5, (C-6a,10a) 148.2, 152.6 (C-3a,11b); ms: m/z (%) 242 (56, M^+), 122 (100), 121 (47); 78 (14); ir: ν 3050, 2930, 1480, 1440, 1060, 990, 860, 800, 755 cm^{-1}.

Anal. Calcd. for $C_{13}H_{10}N$:S (242.3): C, 64.44; H, 4.16; N, 11.56. Found: C, 64.31; H, 4.27; N, 11.56.

5,5a,8b,9,14a,14b-Hexahydrobenzothiopyrano[3,2-*c*]-[2,1,3]oxadiazolo[4,5-*a*]thioxanthene **15**.

2*H*-Benzo[*b*lthiete **1** (134 mg, 1.1 mmoles) and **14** (242 mg, 1.0 mmole) were refluxed in 10 ml toluene. After 4 hours **1** (122 mg, 1.0 mmole) was added and the heating continued. The mixture was evaporated and the residue was purified by column chromatography (silica gel, toluene). Product **15** was obtained as pale yellow crystals (250 mg, 69%) which melted at 79° and had ^{1}H nmr (400 MHz, deuteriochloroform): δ 3.16 (dd, ^{2}J = -15.5 Hz, ^{3}J = 4.1 Hz, 2H, 5-, 9-H), 3.50 (dd, ^{2}J = -15.5 Hz, ^{3}J = 4.6 Hz, 2H, 5-, 9-H), 4.08 (m, 2H, 5a-, 8b-H), 4.20 (m, 2H, 14a-, 14b-H), 6.96-7.23 (m, 8H aromatic H); ^{13}C nmr (100 MHz, deuteriochloroform): δ 28.0 (C-5a, 8b), 33.4 (C-5, 9), 44.8 (C-14a, 14b), 125.7, 126.6, 127.3, 130.1 (aromatic CH), 131.4, 132.1 (C-4a,9a,13a,15a), 151.7 (C-5b,8a); ms: m/z (%) 364 (80, M^+), 241 (39), 172 (23), 147 (82), 134 (51), 121 (100), 115 (29); ir ν: 3060, 2900, 1470, 1450, 1070, 1040 cm^{-1}.

Anal. Calcd. for $C_{20}H_{16}N_2OS_2$ (364.49): C, 65.91; H, 4.42; N, 7.69. Found: C, 65.80; H, 4.51; N, 7.69.

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[3] W. J. M. van Tilborg and R. Plomp, *Recl. Trav. Chim. Pays-Bas*, **96**, 282 (1977).

[4] In principal **8** could be generated by a subsequent reaction of **5** and **1**. Since the third possible bisadduct was not obtained, this would implicate that the second step is regioselective, whereas the first step is not. However, the failure to detect **5** in the course of the reaction and the fact, that **7** and **8** were formed by introducing **6** as precursor, making the latter alternative unlikely.

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[6] The signals are strongly superimposed.

[7] The geminal protons are accidentally isochronous.