

Photocycloaddition of 4-(Alk-1-ynyl)-Substituted Coumarins and Thiocoumarins to 2,3-Dimethylbuta-1,3-diene

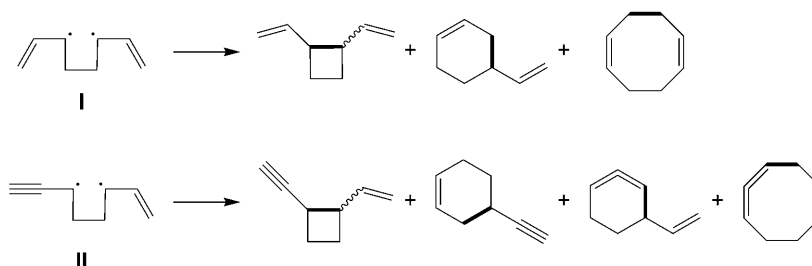
by Inga Inhülsen, Karin Chin, Maren Göwert, and Paul Margaretha*

Department of Chemistry, University of Hamburg, Martin-Luther-King Platz 6, D-20146 Hamburg
(phone: + 4940-428384316; fax: + 4940-428385592; e-mail: Paul.Margaretha@chemie.uni-hamburg.de)

On irradiation (350 nm) in the presence of 2,3-dimethylbuta-1,3-diene (**8**), 4-(alk-1-ynyl)coumarins **1** afford mixtures of cyclobuta- and cycloocta-annulated products **9** and **10**, respectively. In contrast, the corresponding thiocoumarins **2** react with the same diene chemoselectively to give cyclohexa-annulated products **11**.

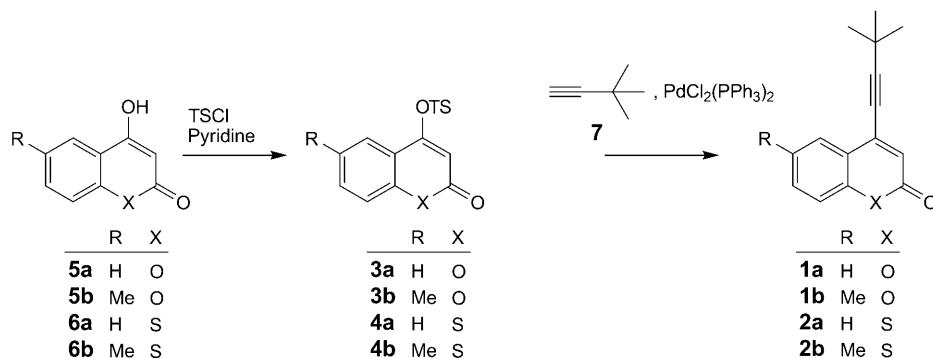
Introduction. – The thermal isomerization of 1,2-divinylcyclobutanes to either of their diastereoisomers, to vinylcyclohexenes, or to cycloocta-1,5-dienes has been intensively studied, and hypothetical octa-1,7-diene-3,6-diyl radicals (**I**) proposed as common intermediates for the three possible cyclization modes [1][2]. In contrast, the much less [3][4] investigated oct-1-en-7-yne-3,6-diyl biradicals (**II**) can formally undergo four modes of cyclization, *i.e.*, one 1,4-, two 1,6-, and one 1,8-cyclization, to afford cyclobutanes, 4-alkynylcyclohexenes and 4-vinylcyclohexa-1,2-dienes, and cyclo-octa-1,2,5-trienes, respectively (*Scheme 1*).

Scheme 1



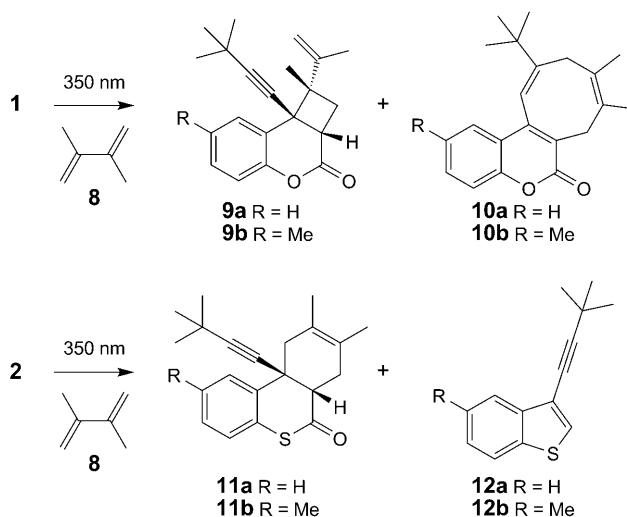
We have recently observed competitive 1,4- vs. 1,8-cyclization of intermediates of type **II** in photocycloadditions of 3-(alk-1-ynyl)cyclohept-2-enones to dienes, and proposed that additional benzylic stabilization of the propargyl radical moiety of the bis-delocalized 1,4-biradical would favor ‘*end-to-end*’, *i.e.*, 1,8-cyclization [5]. We have now extended these studies to alkynyl-substituted coumarins **1** and thiocoumarins **2**, readily available by Pd-mediated coupling of the corresponding 4-tosyloxy (TsO) derivatives **3** and **4** (obtained from the 4-OH precursors **5** and **6**, resp.) with 3,3-dimethylbut-1-yne (**7**) (*Scheme 2*). Here, we report the results of these reactions.

Scheme 2



Results. – Irradiation (350 nm) of coumarin (=2*H*-1-benzopyran) **1a** in the presence of a 20-fold molar excess of 2,3-dimethylbuta-1,3-diene (**8**) afforded a 2:1 mixture of products **9a** and **10a**. Similarly, irradiation of coumarin **1b** gave a 2:1 mixture of **9b** and **10b**. In contrast, both thiocoumarins (=2*H*-1-benzothiopyrans) **2a** and **2b** afforded dibenzothiopyrans **11a** and **11b**, respectively, as main products, together with minor amounts of benzothiophenes **12a** and **12b**, respectively, resulting from photodecarbonylation (Scheme 3). All products were separated and purified by column chromatography, and fully characterized by 1D- and 2D-NMR spectroscopy.

Scheme 3



Discussion. – The essential point regarding the results presented above is certainly the dissimilar behavior of excited heterocycles **1** and **2** towards diene **8**, as reflected in

the formation of cycloadducts **9** and **10** (from **1**), and **11** (from **2**), respectively. On one hand, the behavior of excited 4-alkynylcoumarins **13** parallels that of 5-alkynylbenzocyclohept-5-en-7-ones [5] in the reaction with **8** affording two products resulting from either 1,4- or 1,8-cyclization of biradical **14**. On the other hand, there appear two differences: *a*) here, the intermediate cyclic allene **15** is not observed; and *b*) again here, the 1,3-H shift originates in the α -position to the CO group. Whereas, for benzocycloheptenones, the cyclooctatriene adduct represented the major (2:1) product, it is now not surprising that the less flexible six-membered lactone ring gives a relatively higher amount (2:1) of cyclobuta-annulated product. Nevertheless, from this point of view, we expected that thiocoumarins **2** would again afford cycloocta-annulated products preferentially due to the – now longer – C–S bonds in the thiolactone ring. Our answer to the question ‘why do thiocoumarins **2** behave differently?’ is for the moment purely speculative. It is well-known that organic molecules containing (bivalent) S-atoms react with alkyl radicals to afford sulfuranyl radicals, *i.e.*, intermediates involving an expansion of the sulfur valence octet [6][7]. Similarly, intramolecular addition/elimination sequences proceeding *via* sulfuranyl-alkyl biradicals have been proposed in light-induced rearrangements of S-heterocycles [8]. If both benzo adducts **11** and benzothiophenes **12** are formed *via* a common intermediate stemming from excited thiocoumarins **16**, then sulfuranyl-alkyl biradicals **17** are indeed highly plausible candidates, as addition to diene **8** would now occur *via* the benzylic radical center with formation of biradical **18**, whereas concomitant decarbonylation would afford benzothiophenes **12**. Finally, the selective 1,6-cyclization of **17** to **11** is thermodynamically controlled, reflecting the higher strain in vinyl-cyclobutanes as compared to that in cyclohexenes [9] (*Scheme 4*).

Experimental Part

1. *General*. Photolyses were conducted in a *Rayonet RPR-100* photoreactor, equipped with 350-nm lamps, and with solvents of spectrophotometric grade. Column chromatography (CC): silica gel 60 (SiO₂; *Merck*; 230–400 mesh). ¹H- and ¹³C-NMR spectra (including 2D plots): *Bruker WM-500*; at 500.13 and 125.8 MHz, resp.; δ in ppm rel. to Me₄Si as internal standard, *J* in Hz. GC/EL-MS: *Varian MAT-311A* at 70 eV.

2. *Starting Materials*. The syntheses of compounds **1a** and **2a** have been reported in [10]. The 4-hydroxy-substituted heterocycles **5b** and **6b** were synthesized according to [11], and converted into **1b** and **2b**, resp., *via* the 4-TsO derivatives **3b** and **4b**, resp., according to [12].

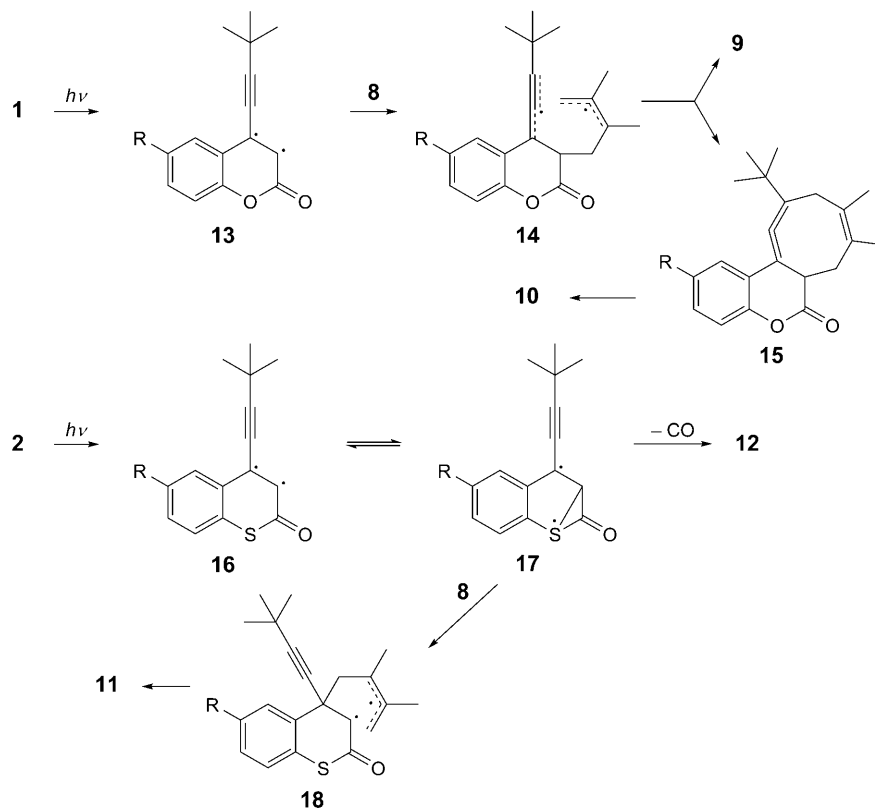
4-(3,3-Dimethylbut-1-yn-1-yl)-6-methyl-2H-1-benzopyran (**1b**). Light-yellow solid. M.p. 103–105°. ¹H-NMR (CDCl₃): 7.57 (s, 1 H); 7.34 (d, *J* = 7.2, 1 H); 7.20 (d, *J* = 7.2, 1 H); 6.45 (s, 1 H); 2.43 (s, 3 H); 1.41 (s, 9 H). ¹³C-NMR (CDCl₃): 159.7 (s); 149.9 (s); 136.7 (q); 133.1 (s); 131.0 (d); 130.2 (d); 126.7 (d); 126.1 (s); 117.3 (d); 111.2 (s); 74.2 (s); 30.5 (s); 30.4 (q); 21.2 (q). MS: 240 (100, *M*⁺).

4-(3,3-Dimethylbut-1-yn-1-yl)-6-methyl-2H-1-benzothiopyran-2-one (**2b**). Light-yellow solid. M.p. 110–112°. ¹H-NMR (CDCl₃): 8.00 (s, 1 H); 7.33 (s, 2 H); 6.72 (s, 1 H); 2.46 (s, 3 H); 1.41 (s, 9 H). ¹³C-NMR (CDCl₃): 184.3 (s); 148.3 (s); 136.7 (s); 133.1 (s); 131.0 (d); 130.2 (d); 126.7 (d); 126.1 (s); 125.6 (d); 111.2 (s); 76.2 (s); 30.8 (s); 30.5 (q); 21.4 (q). MS: 256 (32, *M*⁺), 213 (100).

3. *Photocycloadditions to 2,3-Dimethylbuta-1,3-diene*. Ar-Degassed solns. of **1** or **2** (1 mmol) and **8** (20 mmol) in benzene (10 ml) were irradiated for 12–14 h up to 80–90% conversion (as monitored by GC). After evaporation of the solvent and excess diene, the residue was subjected to CC.

3.1. *Photocycloaddition of 1a*. CC (pentane/Et₂O 5:1) afforded first 139 mg (45%) of (*1S,2aS,8bR*)-8b-(3,3-dimethylbut-1-yn-1-yl)-1,2,2a,8b-tetrahydro-1-methyl-1-(prop-1-en-2-yl)-3H-cyclobuta[c]chromen-3-one (**9a**; *R_f* 0.35). Colorless oil. ¹H-NMR (CDCl₃): 7.11–6.98 (m, 4 H); 4.71 (s, 1 H); 4.50 (s, 1 H);

Scheme 4



3.54 (*dd*, $J = 9.3, 9.3$, 1 H); 2.53 (*dd*, $J = 9.3, 11.3$, 1 H); 2.10 (*dd*, $J = 9.3, 11.3$, 1 H); 1.59 (*s*, 3 H); 1.55 (*s*, 3 H); 1.22 (*s*, 9 H). $^{13}\text{C-NMR}$ (CDCl_3): 162.1 (*s*); 150.1 (*s*); 146.2 (*s*); 130.3 (*d*); 128.9 (*d*); 125.5 (*d*); 124.1 (*d*); 121.7 (*s*); 117.0 (*d*); 112.8 (*t*); 94.6 (*s*); 80.3 (*s*); 53.1 (*s*); 43.2 (*s*); 39.1 (*d*); 32.8 (*t*); 30.1 (*s*); 29.8 (*q*); 24.1 (*q*); 20.5 (*q*). EI-MS: 308 (41, M^+); 226 (100).

The second fraction consisted of 77 mg (25%) of 11-(*tert*-butyl)-8,9-dimethyl-6H-cycloocta[*c*]chromen-6-one (**10a**; R_f 0.24). Viscous yellow oil. $^1\text{H-NMR}$ (CDCl_3): 7.48–7.43 (*m*, 2 H); 7.32 (*d*, $J = 8.2$, 1 H); 6.54 (*s*, 1 H); 3.27 (*s*, 2 H); 2.67 (*s*, 2 H); 1.93 (*s*, 3 H); 1.79 (*s*, 3 H); 1.20 (*s*, 9 H). $^{13}\text{C-NMR}$ (CDCl_3): 160.9 (*s*); 152.5 (*s*); 151.0 (*s*); 147.6 (*s*); 129.4 (*d*); 124.8 (*s*); 124.5 (*d*); 122.8 (*d*); 119.4 (*s*); 118.3 (*s*); 130.4 (*s*); 116.7 (*d*); 115.6 (*d*); 36.2 (*t*); 35.3 (*t*); 32.9 (*s*); 28.7 (*q*); 22.3 (*q*); 22.1 (*q*). EI-MS: 308 (11, M^+), 224 (100).

3.2. Photocycloaddition of 1b. CC (pentane/Et₂O/toluene 25:2:2) afforded first 138 mg (43%) of (1*S*,2*aS*,8*bR*)-8*b*-(3,3-dimethylbut-1-yn-1-yl)-1,2,2*a*,8*b*-tetrahydro-1,7-dimethyl-1-(*prop*-1-en-2-yl)-3H-cyclobuta[*c*]chromen-3-one (**9b**; R_f 0.27). Colorless oil. $^1\text{H-NMR}$ (CDCl_3): 7.05 (*s*, 1 H); 7.02 (*d*, $J = 8.2$, 1 H); 6.68 (*d*, $J = 8.2$, 1 H); 4.71 (*s*, 1 H); 4.50 (*s*, 1 H); 3.51 (*dd*, $J = 9.3, 9.3$, 1 H); 2.52 (*dd*, $J = 9.3, 11.1$, 1 H); 2.29 (*s*, 3 H); 2.08 (*dd*, $J = 9.3, 11.1$, 1 H); 1.58 (*s*, 3 H); 1.54 (*s*, 3 H); 1.23 (*s*, 9 H). $^{13}\text{C-NMR}$ (CDCl_3): 165.7 (*s*); 148.1 (*s*); 146.3 (*s*); 133.3 (*s*); 130.3 (*d*); 129.3 (*d*); 121.1 (*s*); 116.5 (*d*); 112.8 (*t*); 94.5 (*s*); 78.9 (*s*); 53.0 (*s*); 45.5 (*s*); 38.9 (*d*); 32.8 (*t*); 30.9 (*q*); 29.6 (*s*); 23.8 (*q*); 20.6 (*q*); 20.1 (*q*). EI-MS: 322 (23, M^+); 240 (100).

The second fraction consisted of 81 mg (25%) of 11-(tert-butyl)-3,8,9-trimethyl-6H-cycloocta[c]-chromen-6-one (**10b**; R_f 0.11). Viscous yellow oil. $^1\text{H-NMR}$ (CDCl_3): 7.29–7.19 (m, 2 H); 7.21 (s, 1 H); 6.52 (s, 1 H); 3.26 (s, 2 H); 2.66 (s, 2 H); 2.40 (s, 3 H); 1.93 (s, 3 H); 1.78 (s, 3 H); 1.21 (s, 9 H). $^{13}\text{C-NMR}$ (CDCl_3): 162.1 (s); 153.5 (s); 149.9 (s); 148.6 (s); 134.5 (s); 133.2 (s); 131.3 (d); 125.5 (s); 125.3 (s); 124.9 (d); 120.2 (s); 117.0 (d); 116.3 (d); 39.7 (t); 36.2 (t); 31.1 (s); 29.5 (q); 23.2 (q); 22.9 (q); 20.6 (q). EI-MS: 322 (18, M^+), 238 (100).

3.3. Photocycloaddition of **2a**. CC (pentane/Et₂O/toluene 20:2:1) afforded first 43 mg (20%) of 3-(3,3-dimethylbut-1-yn-1-yl)-1-benzothiophene (**12a**; R_f 0.7). Colorless oil. $^1\text{H-NMR}$ (CDCl_3): 7.90 (d, $J = 7.3$, 1 H); 7.82 (d, $J = 7.5$, 1 H); 7.48 (s, 1 H); 7.43 (dd, $J = 7.3$, $J = 7.5$, 1 H); 7.37 (dd, $J = 7.3$, $J = 7.5$, 1 H); 1.39 (s, 9 H). $^{13}\text{C-NMR}$ (CDCl_3): 139.3 (s); 139.0 (s); 128.0 (d); 124.9 (d); 124.4 (d); 122.6 (d); 122.4 (d); 119.1 (s); 101.1 (s); 79.1 (s); 31.1 (s); 28.0 (q). EI-MS: 214 (60, M^+), 199 (100).

The second fraction consisted of 120 mg (37%) of (6a*S*,10a*R*)-10a-(3,3-Dimethylbut-1-yn-1-yl)-6a,7,10,10a-tetrahydro-8,9-dimethyl-6H-benzo[c][1]benzothiopyran-6-one (**11a**; R_f 0.5). Yellow oil. $^1\text{H-NMR}$ (CDCl_3): 7.26–7.20 (m, 2 H); 7.17–7.14 (m, 2 H); 2.95 (dd, $J = 5.8$, 5.8, 1 H); 2.78 (d, $J = 17.3$, 1 H); 2.35–2.27 (m, 2 H); 2.19 (d, $J = 17.3$, 1 H); 1.62 (s, 3 H); 1.59 (s, 3 H); 1.19 (s, 9 H). $^{13}\text{C-NMR}$ (CDCl_3): 199.1 (s); 135.8 (s); 130.4 (s); 127.8 (d); 127.1 (d); 126.5 (d); 126.1 (d); 124.1 (s); 122.6 (s); 94.5 (s); 80.3 (s); 52.9 (d); 40.6 (s); 40.3 (t); 30.9 (q); 30.3 (t); 27.3 (s); 18.9 (q); 18.3 (q). EI-MS: 324 (40, M^+), 214 (100).

3.4. Photocycloaddition of **2b**. CC (pentane/Et₂O/toluene 12:2:1) afforded first 13 mg (6%) of 3-(3,3-dimethylbut-1-yn-1-yl)-5-methyl-1-benzothiophene (**12b**; R_f 0.27). Colorless oil. $^1\text{H-NMR}$ (CDCl_3): 7.70 (d, $J = 8.3$, 1 H); 7.65 (d, $J = 8.3$, 1 H); 7.54 (s, 1 H); 7.32 (s, 1 H); 2.51 (s, 3 H); 1.40 (s, 9 H). $^{13}\text{C-NMR}$ (CDCl_3): 139.8 (s); 137.6 (s); 134.3 (s); 133.6 (s); 126.3 (d); 125.6 (d); 122.5 (d); 121.8 (d); 111.3 (s); 86.4 (s); 31.2 (q); 30.9 (q); 20.9 (q). EI-MS: 228 (56, M^+), 213 (100).

The second fraction consisted of 125 mg (37%) of (6a*S*,10a*R*)-10a-(3,3-Dimethylbut-1-yn-1-yl)-6a,7,10,10a-tetrahydro-2,8,9-trimethyl-6H-benzo[c][1]benzothiopyran-6-one (**11b**; R_f 0.11). Yellow oil. $^1\text{H-NMR}$ (CDCl_3): 7.07 (d, $J = 8.0$, 1 H); 7.06–7.03 (m, 2 H); 2.92 (dd, $J = 5.7$, 5.7, 1 H); 2.77 (d, $J = 17.4$, 1 H); 2.42–2.32 (m, 2 H); 2.36 (s, 3 H); 2.15 (d, $J = 17.3$, 1 H); 1.62 (s, 3 H); 1.60 (s, 3 H); 1.20 (s, 9 H). $^{13}\text{C-NMR}$ (CDCl_3): 199.4 (s); 136.8 (s); 135.7 (s); 130.5 (s); 128.3 (d); 128.0 (d); 126.4 (d); 123.9 (s); 122.6 (s); 92.6 (s); 80.5 (s); 52.5 (d); 40.4 (s); 40.3 (t); 30.6 (s); 29.9 (t); 27.4 (q); 20.9 (q); 18.3 (q); 17.6 (q). EI-MS: 338 (32, M^+), 228 (100).

REFERENCES

- [1] P. Caramella, P. Quadrelli, L. Toma, S. Romano, K. S. Khuong, B. Northrop, K. N. Houk, *J. Org. Chem.* **2005**, 70, 2994.
- [2] J. A. Berson, P. B. Dervan, *J. Am. Chem. Soc.* **1973**, 95, 267.
- [3] W. R. Roth, T. Bastigkeit, *Liebigs Ann.* **1996**, 2171.
- [4] H. Siegel, L. Eisenhuth, H. Hopf, *Chem. Ber.* **1985**, 118, 597.
- [5] M. R. J. Vallée, I. Inhülsen, P. Margaretha, *Helv. Chim. Acta* **2010**, 93, 17.
- [6] P. Margaretha, in 'The Chemistry of Sulfur Radicals', Ed. Z. B. Alfassi, John Wiley & Sons, Chichester, 1999, p. 278.
- [7] E. Anklam, P. Margaretha, *Res. Chem. Intermed.* **1989**, 11, 127.
- [8] E. Er, P. Margaretha, *Helv. Chim. Acta* **1992**, 75, 2265.
- [9] B. Northrop, K. N. Houk, *J. Org. Chem.* **2006**, 71, 3.
- [10] M. Soltan, M. Göwert, P. Margaretha, *Org. Lett.* **2005**, 7, 5159.
- [11] W.-T. Gao, W.-D. Hou, M.-R. Zheng, *Chin. J. Org. Chem.* **2008**, 28, 2011.
- [12] J. Wu, Y. Liao, Z. Yang, *J. Org. Chem.* **2001**, 66, 3642.

Received March 15, 2011