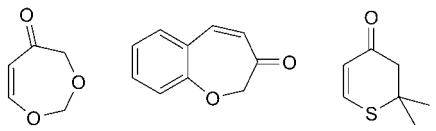
Photocyclodimers of '*Made-to-Measure*' Seven- and Six-Membered Cyclic Enones

by **Kerstin Schmidt** and **Paul Margaretha***

Department of Chemistry, University of Hamburg, Martin-Luther-King Platz 6, D-20146 Hamburg (phone: +49-40-428384316; fax: +49-40-428385592; e-mail: Paul.Margaretha@chemie.uni-hamburg.de)

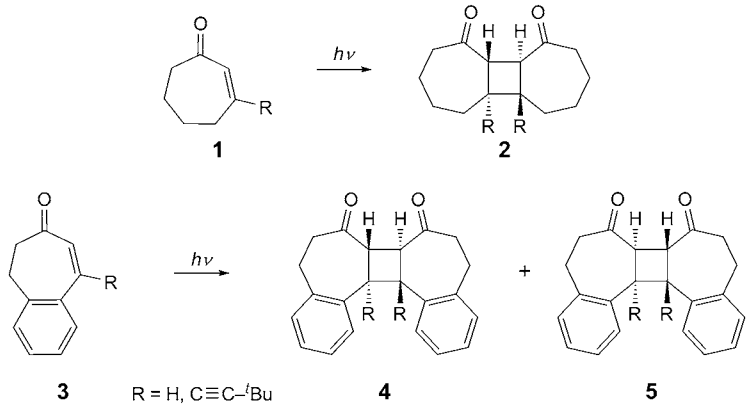
On irradiation (350 nm) in benzene as solvent, dioxepinone **6** and benzoxepinone **7** afford quantitatively mixtures of two diastereoisomeric *head-to-head* dimers, respectively. In both cases, on contact with SiO_2 the minor dimer containing *trans*-ring fusions undergoes spontaneous isomerization to the (major) *cis-transoid-cis* diastereoisomer. In contrast, thiopyranone **8** is converted selectively, but in very low yield, to dimer **13**.

Introduction. – Synthetic applications and mechanistic details of both photocyclodimerization and photocycloaddition to alkenes have been thoroughly investigated for five- and six-membered cyclic enones [1–3]. In contrast, information on the corresponding behavior of cyclohept-2-enones is restricted to the finding that such seven-membered cyclic enones **1** on irradiation afford predominantly doubly *trans*-fused dimers **2**, the formation of which has been proposed to occur *via* (*Z*/*E*)-isomerization of the excited enone, followed by thermal $[_2\pi_s + _2\pi_a]$ cycloaddition to a second ground-state enone [4–6]. Benzocyclohepten-7-ones **3** behave similarly to give diastereoisomer mixtures of dimers **4** and **5** [6][7] (*Scheme 1*). We have recently reported that dioxepinone **6** and benzoxepinone **7** undergo [2+2] photocycloaddition to 1,3-dienes, *e.g.*, 2,3-dimethylbuta-1,3-diene [8] without any or very little interference of photodimer formation. Whereas photocycloaddition to 1,3-dienes is atypical for cyclopentenones and cyclohexenones due to very efficient energy transfer from the excited enone to the diene, more flexible six-membered ring enones, *e.g.*, thiopyranone **8**, have been found to give cyclobutanes almost quantitatively under these conditions [9]. For all these heterocyclic enones, the *a*) a shorter C–O bond, or *b*) a longer C–S bond as compared to a standard C–C bond seems to control the rigidity of the ring to prevent the above mentioned typical (*Z*/*E*)-isomerization of cycloheptenones. Here, we report on the photocyclodimerization of these oxa- and thia-enones.



6 **7** **8**

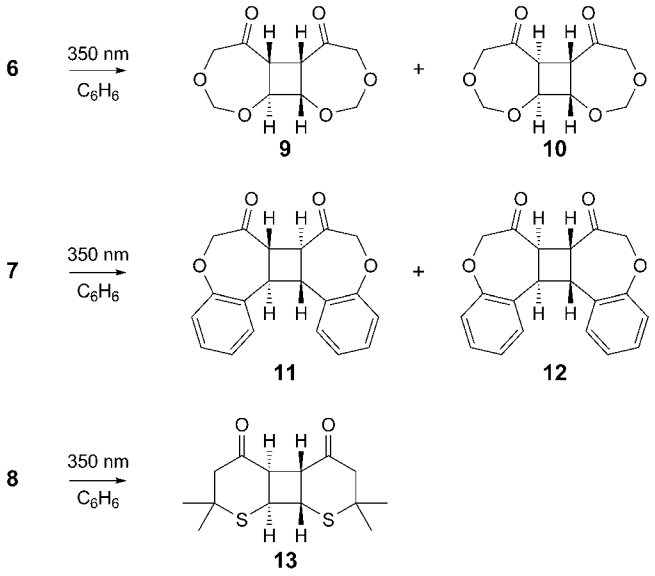
Scheme 1



Results. – Irradiation (350 nm) of a 1M solution of 1,3-dioxepin-5(4*H*)-one (**6**) in benzene for 24 h afforded a 2 : 3 mixture of dimers **9** and **10**, as monitored by ^{1}H-NMR. On standing in $CDCl_3$ or on treatment with SiO_2 in CH_2Cl_2, dimer **9** underwent isomerization quantitatively to **10**. Similarly, irradiation of a 1M solution of 1-benzoxepin-3(2*H*)-one (**7**) for 24 h led to a 2 : 3 mixture of dimers **11** and **12**; the minor product **11** again isomerized quantitatively to **12** in the presence of acids. The structures of dimers **10** and **12** were established by X-ray crystal-structure determination. In contrast, the photodimerization of 2,3-dihydro-2,2-dimethyl-4*H*-thiopyran-4-one (**8**) required much longer irradiation times (80 – 90 h for *ca.* 20% conversion) to give dimer **13** selectively (*Scheme 2*).

Discussion. – By assuming that *trans-anti-trans*-dimers, *e.g.* **2** or **4**, were formed solely *via* the sequence *a*) photoisomerization of the (excited) (*Z*)-cycloheptenone to the (ground state) (*E*)-diastereoisomer, followed by *b*) thermal $[_2\pi_s + _2\pi_a]$ cycloaddition to a second ground-state enone, the behavior of benzoxepinone **7** parallels that of benzocycloheptenones **3**. The effect of the shorter C–O–C bonds in **11** as compared to the carbocyclic dimer **4** is reflected in the spontaneous isomerization of the former to **12** in contact with SiO_2, while the latter is apparently stable under these conditions. In contrast, a comparison of the results on the photodimerization of dioxepinone **6** with those of cycloheptenones **1** indicates, that (*Z*/*E*)-isomerization of the excited dioxaenone was inhibited, as no doubly *trans*-fused tricyclic dimer was formed at all. Indeed, the behavior of **6** rather corresponds to that of six-membered cyclic oxa-enones, *e.g.*, 2,3-dihydro-2,2-dimethyl-4*H*-pyran-4-one [10]. Here, the *twisted* excited enone is trapped by a second ground-state enone molecule to yield a mixture of a *trans-anti-cis*-dimer **9**, wherein (only) one of the external rings is *trans*-fused to the (central) cyclobutane ring, in addition to the (conventional) *cis-anti-cis*-dimer **10**. In this context, the inefficiency observed in the photodimerization of thiopyranone **8** is difficult to rationalize. Thus, in contrast to their carbocyclic counterparts, 1,3-dioxepin-5(4*H*)-ones can be regarded as '*made-to-measure*' seven-membered ring enones. Due to the shorter

Scheme 2



C–O bond length (*vs.* C–C), the rigidity of the ring system is increased, thereby preventing the (typical) (*Z*/*E*)-photoisomerization of cyclohept-2-enones.

Experimental Part

1. *General.* Photolyses were performed in a *Rayonet RPR-100* photoreactor equipped with (16) 350-nm lamps using solvents of spectrophotometric grade. Column chromatography (CC) was performed on silica gel (*Merck* grade *60*; 230–400 mesh). ^{1}H- and ^{13}C-NMR spectra (including 2D plots): *Bruker WM-500* at 500.13 and 125.8 MHz, resp.; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. X-Ray analyses: *Bruker SMART APEX II* three-circle diffractometer at 153 K with MoK_α radiation (λ 0.71073 Å).

2. *Starting Materials.* Compounds **6** [11], **7** [12], and **8** [13] were synthesized according to the literature procedures.

3. *Photocyclodimerizations.* Ar degassed $5 \cdot 10^{-1}$ M solns. of **6**, **7**, or **8** in benzene were irradiated for the time indicated up to the degree of conversion determined by ^{1}H-NMR monitoring. Workup of the crude product mixtures as described below.

Irradiation of **6**. A soln. of 114 mg of **6** in benzene (2 ml) was irradiated for 18 h up to total conversion. After filtering from polymeric material, subsequent evaporation of the solvent afforded 80 mg of a 2:3 mixture of dimers **9** and **10** (^{1}H-NMR).

rac-*(5a*R,*5b*S,*10a*S,*10b*S*)-Tetrahydrocyclobuta[1,2*-d*:4,3*-d′*]bis[1,3]dioxepine-5,6(4*H,*7*H*)-dione* (**9**). ^{1}H-NMR ($CDCl_3$; from the mixture **9**/**10**)): 5.50, 4.68 (*AB*, *J* = 7.3, CH_2(9)); 5.07, 4.93 (*AB*, *J* = 5.3, CH_2(2)); 4.65 (*dd*, *J* = 4.1, 6.5, H–C(5b)); 4.54, 4.20 (*AB*, *J* = 18.3, CH_2(7)); 4.44, 4.08 (*AB*, *J* = 18.2, CH_2(4)); 4.33 (*dd*, *J* = 9.3, 9.8, H–C(10b)); 3.98 (*dd*, *J* = 6.5, 9.8, H–C(10a)); 3.37 (*dd*, *J* = 4.4, 9.3, H–C(5a)). ^{13}C-NMR ($CDCl_3$): 208.7 (*s*, C(5)); 206.4 (*s*, C(6)); 101.5 (*t*, C(9)); 97.1 (*t*, C(2)); 80.0 (*t*, C(7)); 75.1 (*t*, C(4)); 74.1 (*d*, C(5b)); 73.5 (*d*, C(10a)); 59.0 (*d*, C(10b)); 45.2 (*d*, C(5a)).

The crude residue was dissolved in CH_2Cl_2 (1 ml), added to a suspension of 50 mg of SiO_2 in CH_2Cl_2 (2 ml), and the mixture was stirred for 3 h at r.t. After filtering and evaporation of the solvent, recrystallization from hexane afforded 55 mg (48%) of **10**.

rac-*(5a*S*,5b*S*,10a*S*,10b*S*)-Tetrahydrocyclobuta[1,2*-d*:4,3*-d′*]bis[1,3]dioxepine-5,6(4*H*,7*H*)-dione* (**10**). M.p. 208–210°. ^{1}H-NMR ($CDCl_3$): 4.97, 4.80 (*AB*, $J = 5.3$, $CH_2(2)$, $CH_2(9)$); 4.34, 3.98 (*AB*, $J = 17.8$, $CH_2(4)$, $CH_2(6)$); 4.32, 4.13 (*AA′XX′*, $J_{AX} = 8.1$, $J_{AA'} = 5.7$, $J_{XX'} = 3.0$, $J_{AX'} = 0.5$, H–C(5a), H–C(5b), H–C(10a), H–C(10b)). ^{13}C-NMR ($CDCl_3$): 209.6 (*s*, C(5), C(6)); 96.1 (*t*, C(2), C(9)); 76.1 (*t*, C(4), C(7)); 74.2 (*d*, C(5a), C(5b)); 47.5 (*d*, C(10a), C(10b)).

X-Ray Crystal-Structure Determination of **10**[1]). $C_{10}H_{12}O_6$, orthorhombic, space group $P2_12_12_1$, $a =$ 6.5219(2), $b = 8.5138$ (2), $c = 17.3353(5)$ Å.

Irradiation of **7**. A soln. of 160 mg of **7** in benzene (2 ml) was irradiated for 18 h up to total conversion. After filtering from polymeric material, subsequent evaporation of the solvent afforded 120 mg of a 2:3 mixture of dimers **11** and **12** (^{1}H-NMR).

rac-*(7a*S*,7b*S*,14b*R*,14c*R*)-7a,7b,14b,14c-Tetrahydrodibenzo[*b,b′*]cyclobuta[1,4-*d*:2,3-*d′*]bisoxepine-7,8(6*H*,9*H*)-dione* (**11**). ^{1}H-NMR ($CDCl_3$; from the mixture **11**/**12**): 7.35–7.13 (8 arom. H); 4.68, 4.46 (*AB*, $J = 17.1$, $CH_2(6)$, $CH_2(9)$); 3.88, 3.80 (2*m*, H–C(7a), H–C(7b), H–C(14b), H–C(14c)). ^{13}C-NMR ($CDCl_3$): 206.2 (*s*, C(7), C(8)); 158.9 (*s*, C(4a), C(10a)); 133.5 (*s*, C(14a), C(14d)); 129.2, 128.8, 127.5, 126.9 (4*d*, 8 arom. CH); 49.2 (*d*, C(7a), C(7b)); 43.1 (*d*, C(14b), C(14c)).

The crude residue was dissolved in CH_2Cl_2 (1 ml), added to a suspension of 50 mg SiO_2 in CH_2Cl_2 (2 ml), and the mixture was stirred for 3 h at r.t. After filtering and evaporation of the solvent, recrystallization from hexane/benzene 2:1 afforded **12** (85 mg, 52%).

rac-*(7a*R*,7b*R*,14b*R*,14c*R*)-7a,7b,14b,14c-Tetrahydrodibenzo[*b,b′*]cyclobuta[1,4-*d*:2,3-*d′*]bisoxepine-7,8(6*H*,9*H*)-dione* (**12**). M.p. 245–247°. ^{1}H-NMR ($CDCl_3$): 7.40–7.15 (8 arom. H); 4.74, 4.28 (*AB*, $J = 16.4$, $CH_2(6)$, $CH_2(9)$); 4.58, 4.38 (*AA′XX′*, $J_{AX} = 11$, $J_{AA'} = 9$, $J_{XX'} = 4$, $J_{AX'} = 1$, H–C(7a), H–C(7b), H–C(14b), H–C(14c)). ^{13}C-NMR ($CDCl_3$): 209.1 (*s*, C(7), C(8)); 158.2 (*s*, C(4a), C(10a)); 133.4 (*s*, C(14a), C(14d)); 129.2, 128.8, 127.5, 126.9 (4*d*, 8 arom. CH); 46.0 (*d*, C(14b), C(14c)); 42.2 (*d*, C(7a), C(7b)).

X-Ray Crystal-Structure Determination of **12**[1]). $C_{20}H_{16}O_4$, orthorhombic, space group *P212121*, $a =$ 5.216(2), $b = 10.846(4)$, $c = 26.570(10)$ Å.

Irradiation of **8**. A soln. of 142 mg of **8** in benzene (2 ml) was irradiated for 90 h, After filtering from polymeric material, evaporation of the solvent afforded a 4:1 mixture of **8** and dimer **13** (^{1}H-NMR). CC (SiO_2; pentane/Et_2O 3:2) afforded first **8**, followed by **13** (15 mg, 10%).

rac-*(4a*R*,4b*R*,8a*S*,8b*S*)-2,2,7,7-Tetramethyloctahydrocyclobuta[1,2-*b*:4,3-*b′*]bisthiopyran-4,5-dione* (**13**). M.p. 120–121°. ^{1}H-NMR ($CDCl_3$): 3.95, 3.72 (*AA′XX′*, $J_{AX} = 8.6$, $J_{AA'} = 6.9$, $J_{XX'} = 5.2$, $J_{AX'} = 0.4$, H–C(4a), H–C(4b), H–C(8a), H–C(8b)); 2.67, 2.63 (*AB*, $J = 14.3$, $CH_2(3)$, $CH_2(6)$); 1.41, 1.33 (2*s*, 4 Me). ^{13}C-NMR ($CDCl_3$): 208.1 (*s*, C(4), C(5)); 56.2 (*t*, C(3), C(6)); 48.3 (*d*, C(4a), C(4b)); 47.2 (*d*, C(8a), C(8b)); 44.8 (*s*, C(2), C(7)); 31.1, 30.2 (2*q*, 4 Me).

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[1]) CCDC-840649 and -840650 contain the supplementary crystallographic data for **12** and **10**, respectively. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/data_request/cif.

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