Revista de la Sociedad Química de México, Vol. **47***, Núm. 3 (2003) 227-229*

Investigación

Photochemistry of 7-Alcoxy and Thioalcoxy-3,3-dimethoxybicyclo[2.2.2] oct-5-en-2-one. Sequence 1,3-acyl shift-decarbonylation reaction

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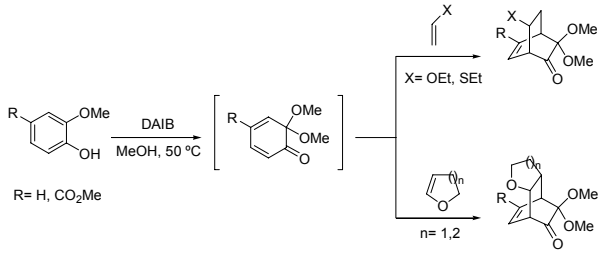
Recibido el 30 de junio del 2003; aceptado el 3 de septiembre del 2003

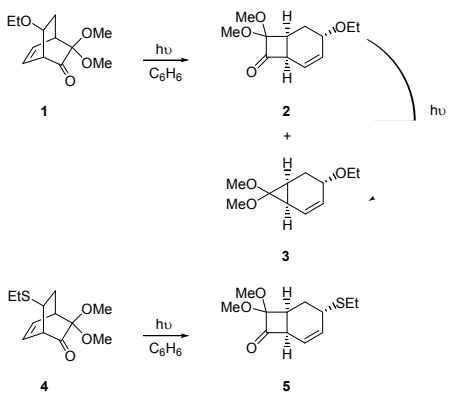
Abstract. The photochemical behavior of the title compounds under direct irradiation has been studied. A sequence of 1,3-acyl shift-decarbonylation reactions was observed in the cases studied.
Keywords: Bicyclo[2.2.2]octenones, acyl shift, photochemistry.

Resumen. Se ha estudiado el comportamiento fotoquímico de algunos compuestos bajo irradiación directa. Una secuencia de reacciones de migración 1,3 de acilo-descarbonilación fue observada en los casos estudiados.
Palabras clave: Biciclo[2.2.2]octenones, migración de acilo, fotoquímica.

Bicyclo[2.2.2]octenones with an embedded β,γ-unsaturated carbonyl group are known to undergo a variety of photochemical reactions useful on the synthetic point of view [1]. Thus, reactions such as decarbonylation [2], photoreduction [3] and 1,3-acyl shift [1,4] and 1,2-acyl shift [1,2] (oxa-di-π-methane rearrangement) have been described [5]. In a previous paper [6] we described for the first time the synthesis of 7-alcoxy and thioalcoxy-3,3-dimethoxybicyclo[2.2.2]oct-5-en-2-one by the inverse electronic demand Diels-Alder reactions of *in situ* generated masked *o*-benzoquinones [7] with enol and thioenol ethers (Scheme 1).



Due to the interesting photochemical reactivity of bicyclo[2.2.2]octenones, we decided to study the behavior of these compounds when they were submitted to direct irradiation. In this way, a solution of **1** in dry benzene was irradiated with a mercury vapor lamp (400 W) for 15 min. After removal of the solvent followed by chromatography, the bicyclic compound **2** was obtained in moderate yield (51 %), together the cyclopropane **3** (22 %). This compound was generated from **2** by photochemical decarbonylation, as was confirmed by independent irradiation of **2** under the same conditions. Under identical conditions, compound **4** gave only cyclobutenone **5** in 45 % isolated yield. It should be pointed out that this reaction conditions are not optimized and in all cases unreacted starting material was recovered (Scheme 2).

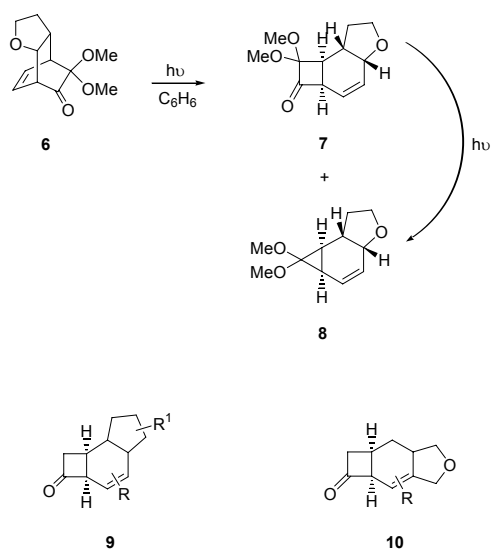


Tricyclic compounds show analogous behavior. Thus, irradiation of **6** in benzene furnished both 1,3-acyl shift product **7** (60 %) and cyclopropane **8** (30 %). Also in this case compound **7** was transformed in **8** by irradiation under the same conditions. It should be pointed out that compound **7** constitutes an structural analogue of the protoilludanes **9** [8] and oxa-sterpurane framework **10** [9] is present in different types of terpenoids (Scheme 3).

In summary, in this paper we have described the photochemical sequence 1,3 acyl shift-decarbonylation reactions in 7-alcoxy and thioalcoxy-3,3-dimethoxybicyclo[2.2.2]oct-5-en-2-one. Starting from the appropriate tricyclic derivative new analogous of protoilludanes and oxasterpurane systems were obtained.

Experimental part

All starting materials were commercially available research-grade chemicals and used without further purification.



6 **7** + **8** **9** **10**

Laboratory solvents were purified and pre-dried before use according to standard procedures. Silica gel 60 F_{254} was used for TLC, and the spots were detected with UV or basic solution of $KMnO_4$. Flash column chromatography was carried out on silica gel 60. IR spectra have been recorded as $CHCl_3$ solutions. ^1H and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz respectively, in $CDCl_3$ solution with TMS as internal reference.

Synthesis of the 7-alcoxy and thioalcoxy-3,3-dimethoxybicyclo[2.2.2]oct-5-en-2-ones 1,4 and 6. General procedure
A mixture of 0.4 mmol of guacaiol and 10 mmol of dienophile in 1.2 mL of MeOH was warmed to 50 ºC. When this temperature was reached, 1.2 mmol of (diacetoxy)iodobenzene in 3.6 ml of MeOH was added via a syringe pump over 1.5 h. The reaction mixture was stirred for 10 min and then the solvent was eliminated in vacuo. The residue was purified by chromatography (hexane : EtOAc = 10 : 1).

(1*R, 4*R**, 7*R**)-7-ethoxy-3,3-dimethoxybicyclo[2.2.2]oct-5-en-2-one (1).** Pale yellow oil (48 %): IR ($CHCl_3$) ν_{max} 2876, 1740, 1348 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.17 (t, 3 H, *J* = 7.1 Hz, Me), 1.31 (dt, 1 H, *J* = 3.6, 13.4 Hz, H 8), 2.41 (ddd, 1 H, *J* = 2.9, 8.3, 13.7 Hz, H-8), 3.07 (dtd, 1 H, *J*= 1.5, 2.9, 6.8 Hz, H-4), 3.30 (s, 3 H, OMe), 3.31 (s, 3 H, OMe), 3.46 (q, 2 H, *J* = 7.1, CH2O), 3.55 (ddd, 1 H, *J* = 1.2, 2.7, 7.1 Hz, H-1), 3.98 (dddd, 1 H, *J* = 1.0, 2.7, 3.7, 8.3 Hz, H-7), 6.07 (ddt, 1 H, *J* = 1.2, 6.6, 7.8 Hz, H-6), 6.52 (ddd, 1 H, *J* = 1.5, 6.8, 8.1 Hz, H-5); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 15.3, 30.1, 37.9, 49.6, 50.3, 53.7, 64.2, 74.1, 93.7, 124.7, 134.4, 201.6; *Anal.* C, 63.61 % , H, 8.10 %, calcd for $C_{12}H_{18}O_4$: C, 63.72 %; H, 7.96 %.

(1*R, 4*R**, 7*R**)-7-ethylsulfenyl-3,3-dimethoxybicyclo[2.2.2]oct-5-en-2-one (4).** Pale yellow oil (82 %): IR ($CHCl_3$) ν_{max} 2837, 1736, 1508, 1362 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.11 (ddd, 1 H, *J* = 2.9, 5.6, 13.4 Hz, H-8), 1.23 (t, 3 H, *J* = 7.6 Hz, Me), 2.42-2.58 (m, 2 H, H-7 y H-8), 2.53 (q, 2 H, *J* = 7.6 Hz, CH_2S), 3.06 (ddd, 1 H, *J* = 1.2, 2.9, 8.3 Hz, H-4), 3.24 (dddd, 1 H, *J* = 1.0, 2.0, 5.8, 9.3 Hz, H-1), 3.30 (s, 3 H, OMe), 3.31 (s, 3 H, OMe), 6.15 (td, 1 H, J= 1.0, 7.8 Hz, H-6), 6.46 (td, 1 H, J= 1.0, 7.8 Hz, H-5). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 11.4, 22.6, 26.1, 26.3, 35.4, 35.6, 47.2, 50.0, 90.7, 122.9, 131.7, 198.3; Anal. C, 59.62 % , H, 7.38 %, calcd for $C_{12}H_{18}O_3S$: C, 59.50 %; H, 7.44 %.

(1*R, 2*R**, 6*R**, 7*S**)-8,8-dimethoxy-3-oxatricyclo [5.2.2.0^{2,6}]undec-10-en-9-one (6).** Pale yellow oil (40 %): IR ($CHCl_3$) ν_{max} 2839, 1740, 1508, 1034 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.57-1.69 (m, 1 H, H-5), 2.02-2.14 (m, 1 H, H-5), 2.92 (qd, 1 H, *J* = 2.9, 7.8 Hz, H-6), 3.20 (dq, 1 H, *J* = 1.5, 7.8 Hz, H-7), 3.31 (s, 3 H, OMe), 3.36 (s, 3 H, OMe), 3.61-3.53 (m, 2 H, H-1 y H-4), 3.87-3.93 (m, 1 H, H-4), 4.36 (dd, 1 H, *J* = 2.9, 8.3 Hz, H-2), 6.14 (t, 1 H, *J* = 7.8 Hz, H-10), 6.40 (t, 1 H, *J* = 7.8 Hz, H-11); ^{13}C NMR ($CDCl_3$, 75 MHz): 30.7, 38.5, 42.3, 49.7, 50.2, 55.0, 69.1, 78.9, 89.5, 127.0, 132.6, 205.7; *Anal*. C, 64.14% , H, 7.03 %, calcd for $C_{12}H_{16}O_4$: C, 64.28 %; H, 7.14 %.

Direct irradiation of bicyclo[2.2.2]octenones 1,4 and 6. General procedure. A solution of 0.2 mmol of the bicyclo[2.2.2]octenone in 180 ml of benzene was irradiated in a Pyrex inmersion well under argon for 15 min. The solvent was removed under reduced pressure and the residue was purified by chromatography (hexane : EtOAc = 5:1).

(1*S, 3*S**, 6*R**)-3-ethoxy-8,8-dimethoxybicyclo[4.2.0]oct-4-en-7-one (2).** Pale yellow oil (51 %): IR ($CHCl_3$) ν_{max} 2928, 2854, 1709 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.23 (t, 3 H, *J* = 7.3 Hz, Me), 1.89-1.96 (m, 2 H, 2 H-2), 2.94 (dt, 1 H, *J* = 7.3, 10.3 Hz, H-1), 3.35 (s, 3 H, OMe), 3.39 (s, 3 H, OMe), 3.57 (qd, 2 H, *J* = 3.4, 7.3 Hz, CH_2O), 3.74 (ddd, 1 H, *J* = 1.1, 4.9, 10.3 Hz, H-6), 3.98 (q, 1 H, *J* = 4.9 Hz, H 3), 5.86 (ddd, 1 H, *J* = 3.9, 4.9, 9.8 Hz, H-5), 6.06 (ddd, 1 H, *J* = 2.4, 3.9, 9.8 Hz, H-4); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 15.6, 25.1, 33.6, 50.9, 51.5, 52.5, 64.0, 69.3, 112.2, 122.4, 131.1, 203.2; *Anal.* C, 63.66 % , H, 7.84 %, calcd for $C_{12}H_{18}O_4$: C, 63.72 %; H, 7.96 %.

(1*R, 4*S**, 6*S**)-4-ethoxy-7,7-dimethoxybicyclo[4.1.0]hept-2-ene (3).** Pale yellow oil (22 %): IR ($CHCl_3$) ν_{max} 2930, 2854, 1522 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.22 (t, 3 H, *J* = 7.3 Hz, Me), 1.33-1.43 (m, 1 H, H-5), 1.51 1.57 (m, 1 H, H-6), 1.72 (dd, 1 H, *J* = 6.3, 9.8 Hz, H-1), 2.41 (dd, 1 H, *J* = 8.8, 13.2 Hz, H-5), 3.26 (s, 3 H, OMe), 3.35 (s, 3 H, OMe), 3.58 (q, 2 H, *J* = 7.3 Hz, CH2O), 3.85 (t, 1 H, *J* = 8.3 Hz, H 4), 5.67 (d, 1 H, *J* = 9.8 Hz, H-2), 5.90-5.95 (m, 1 H, H-3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 15.7, 21.0, 22.5, 23.0, 53.1, 54.1, 64.0, 71.5, 95.8, 121.8, 128.7; *Anal.* C, 66.54 % , H, 8.99 %, calcd for $C_{11}H_{18}O_3$: C, 66.67 %; H, 9.09 %.

(1*S, 3*S**, 6*R**)-3-ethylsulfenyl-8,8-dimethoxybicyclo[4.2.0]oct-4-en-7-one (5).** Pale yellow oil (45 %): IR

($CHCl_3$) ν_{max} 2930, 2839, 1711 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.29 (t, 3 H, *J* = 7.3 Hz, Me), 1.86-2.12 (m, 2 H, 2 H-2), 2.60 (q, 2 H, = 7.3 Hz, CH2S), 3.02 (dt, 1 H, *J* = 7.1, 10.2 Hz, H-1), 3.36 (s, 3 H, OMe), 3.39 (s, 3 H, OMe), 3.47 (q, 1 H, *J* = 5.1 Hz, H-3), 3.73 (ddd, 1 H, *J* = 2.2, 4.4, 9.5 Hz, H-6), 5.82 (ddd, 1 H, *J* = 1.0, 4.4, 9.8 Hz, H-5), 6.01 (ddd, 1 H, *J* = 2.2, 5.1, 9.8 Hz, H-4); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.9, 25.5, 25.5, 33.7, 36.9, 51.4, 51.4, 52.2, 112.8, 121.6, 130.3, 202.7; *Anal.* C, 59.61 %, H, 7.30 %, calcd for $C_{12}H_{18}O_3S$: C, 59.50 %; H, 7.44 %.

(2a*R, 4a*R**, 7a*S**, 7b*S**)-1,1-dimethoxy-2a,4a,6,7,7a,7b-hexahydro-1*H*-5-oxacyclobuta[*e*]inden-2-one (7).** Pale yellow oil (60 %): IR ($CHCl_3$) ν_{max} 2930, 2854, 1736 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.59-1.70 (m, 1 H, H-7), 2.07-2.13 (m, 1 H, H-7), 2.73 (q, 1 H, *J* = 7.8 Hz, H-7a), 2.91-2.96 (m, 1 H, H 7b), 3.35 (s, 3 H, OMe), 3.35 (s, 3 H, OMe), 3.53-3.61 (m, 1 H, H-6), 3.76-3.93 (m, 2 H, H-2a and H-6), 4.58 (d, 1 H, *J* = 7.3 Hz, H-4a), 5.68-5.79 (m, 2 H, H-3 y H-4); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 29.7, 31.3, 33.2, 38.2, 50.8, 52.2, 65.9, 72.2, 111.4, 119.7, 130.8, 201.3; *Anal.* C, 64.40 % , H, 7.11 %, calcd for $C_{12}H_{16}O_4$: C, 64.27 %; H, 7.19 %.

(1a*R, 3a*R**, 6a*S**, 6b*S**)-1,1-dimethoxy-1a,3a,5,6,6a,6b-hexahydro-1*H*-4-oxacyclopropan[*e*]indene (8).** Pale yellow oil (30 %): IR ($CHCl_3$) ν_{max} 2960, 2928, 2854, 1443 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.56-1.65 (m, 2 H, H-6 y H-6b), 1.72 (dd, 1 H, *J* = 5.6, 9.3 Hz, H-1a), 1.98-2.13 (m, 1 H, H-6), 2.65 (q, 1 H, *J* = 9.0 Hz, H-6a), 3.28 (s, 3 H, OMe), 3.36 (s, 3 H, OMe), 3.71-3.92 (m, 2 H, 2 H-5), 4.33 (d, 1 H, *J* = 8.5 Hz, H-3a), 5.41 (dd, 1 H, *J* = 1.9, 10.2 Hz, H-3), 5.84 (ddd, 1 H, *J* = 2.0, 5.6, 10.2 Hz, H-2); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.7, 29.7, 30.8, 32.0, 53.3, 54.0, 66.5, 74.1, 95.4, 121.2, 127.6; *Anal.* C, 67.26 % , H, 8.16 %, calcd for $C_{11}H_{16}O_3$: C, 67.35 %; H, 8.16 %.

Acknowledgements

Ministerio de Ciencia y Tecnología of Spain (Project BQU 2000-0653) is gratefully thanked for financial support.

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