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Synthesis and Photochemistry of 4-Methylene-2-protoadamantanone

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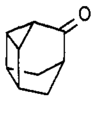
It is known that β,γ-unsaturated ketones undergo various photochemical reactions depending on the orbital interactions and the geometry of the β,γ-unsaturated carbonyl moiety.[2] Oxa-di-π-methano rearrangement of the β,γ-unsaturated ketones have been used in the synthesis of A-nor-$5_{\alpha},10_{\alpha}$-steroids[3] as well as in the planned construction of new polycyclic systems such as 2,8-didehydro-9-noradamantanone (**1**)[4] and 8,9-didehydro-2-adamantanone (**2**).[5]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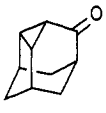
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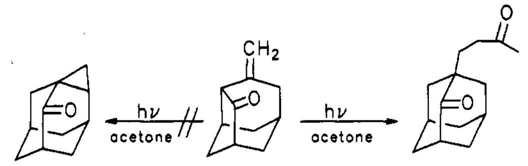

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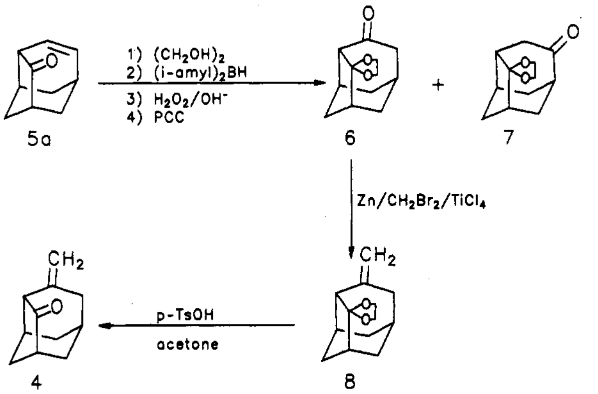
As a part of a program designed to survey the synthetic potential of the oxa-di-π-methano rearrangement of β,γ-unsaturated ketones, it was of interest to examine the behavior of 4-methylene-2-protoadamantanone (**4**) in direct and acetone-sensitized photolysis. This molecule was chosen for study due to the close proximity of the olefinic π-bond and the π-bond of the carbonyl group that might make them amenable to oxa-di-π-methano rearrangement[6,7] and the construction of the hitherto unknown 3,4-methano-2-adamantanone (**3**).

Scheme I



We report here the synthesis of the desired methylene ketone **4** and the attempted synthesis of **3**. The synthesis of 4-methylene-2-protoadamantanone (**4**) originated with 2-protoadamantanenone (**5a**)[8] (Scheme I). Unsaturated ketone **5a** was converted into 2-ethylenedioxa-4-protoadamantene (**5b**) by treatment with ethylene glycol. Hydroboration of **5b** with disiamylborane followed by oxidations with H_2O_2/OH^- and PCC furnished a 71% yield of a 9:1 mixture of 2-ethylenedioxa-4-protoadamantanone (**6**) and 2-ethylenedioxa-5-protoadamantanone (**7**), respectively. 4-Methylene-2-protoadamantanone (**4**) was readily prepared from **6** by the Wittig-type carbonyl methylenation by means of the electrophilic reagent Zn/$CH_2Br_2/TiCl_4$, followed by hydrolysis under acidic conditions. The spectral data are consistent with the assigned structures (see Experimental Section).

The photochemical reactions were studied under direct and acetone-sensitized irradiation. Irradiations were carried out in benzene and acetone solutions using a high pressure mercury lamp fitted with a Pyrex filter. Under direct irradiation in benzene **4** undergoes a rapid photodecomposition to the tarry polymeric material. No low molecular weight products were found. However, irradiation of a nitrogen-purged 0.05 M solution of **4** (λ_{max}(EtOH) 300 nm, $\epsilon = 142$) in acetone proceeds smoothly to give **9** in ca. 95% yield at 97% of conversion of the starting ketone. Besides **9**, three other products were obtained (<2% of each, by GC). The major product was isolated by column chromatography on silica gel in 64% yield and was readily identified as 1-(3-oxobutyl)-2-adamantanone (**9**) by its spectral data. According to the ^{1}H NMR spectrum of the crude mixture, the desired **3** was not observed.[9]

Mechanistically, we propose that the formation of the major product, **9**, occurs via a photoinitiated anti-Markovnikov addition of acetonyl radical[10] to the double bond

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[2] For a review of the photochemical reactions of β,γ-unsaturated carbonyl compounds, see: (a) Demuth, M.; Mikhail, G. *Synthesis* **1989**, 145. (b) Houk, K. N. *Chem. Rev.* **1976**, *76*, 1. (c) Hixon, S. S.; Mariano, P. S.; Zimmerman, H. E. *Chem. Rev.* **1973**, *73*, 531.

[3] Williams, R.; Ziffer, H. *J. Chem. Soc., Chem. Commun.* **1967**, 469.

[4] Šindler-Kulyk, M.; Majerski, Z.; Pavlović, D.; Mlinarić-Majerski, K. *Tetrahedron Lett.* **1989**, *30*, 3577.

[5] Murray, R. K., Jr.; Morgan, K., Jr.; Babiak, K. A. *J. Org. Chem.* **1975**, *40*, 1079.

[6] It is known that the relative orientation of the two chromophoric groups plays a significant role in triplet- and singlet-state photochemistry, and the geometry that yields ODPM rearrangements is that in which the CO–C_α σ-bond and the C_β=C_γ π-bond are aligned for maximum overlap (θ = 0° and 180°).[7] Examination of molecular model of **4** shows that the p orbitals of C_2 and C_4 are directed toward one another. Also, the UV spectrum of the unsaturated ketone **4** revealed enhanced n π^* absorption (λ_{max} (ETOH) 300 nm, $\epsilon = 142$) toward 2-protoadamantanone (λ_{max} (EtOH) 295 nm, $\epsilon = 26$) that suggests an interaction between the two chromophores.[2b]

[7] Coffin, R. L.; Cox, W. W.; Carlson, R. G.; Givens, R. S. *J. Am. Chem. Soc.* **1979**, *101*, 3261.

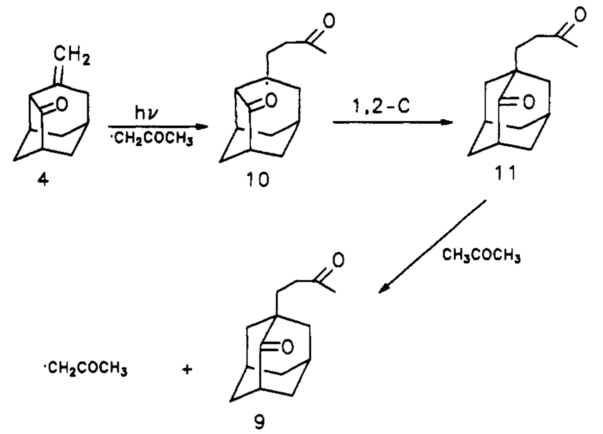
[8] Majerski, Z.; Žuanić, M. *J. Org. Chem.* **1983**, *48*, 898. Cupas, C. A.; Schumann, W.; Heyd, W. E. *J. Am. Chem. Soc.* **1970**, *92*, 3237.

[9] We were unable to completely separate and identify the minor products. However, the ^{1}H NMR spectrum of the enriched mixture of two minor products showed doublets at 4.82 and 4.03 (J = 6.5 Hz), 4.96 and 4.42 (J = 6.2 Hz), and singlets at 1.41, 1.38, 1.18, and 1.13 ppm, which most likely correspond to the oxetane ring protons and methyls of the products arising from a Paterno–Büchi reaction of acetone addition to the double bond of **4**. For comparison, see: Barltrop, J. A.; Carless, A. J. *J. Am. Chem. Soc.* **1972**, *94*, 8761.

[10] Numerous examples of the photoinitiated addition of acetone and of other ketones to olefins have appeared in the literature. For leading references, see: (a) deMayo, P. *Advances in Organic Chemistry*; Interscience: New York, 1960; Vol. II, p 367. (b) Elad, D. In *Organic Photochemistry*; Chapman, O., Ed.; Marcel Dekker: New York, 1969; Vol. II, p. 190. (c) Bartlett, P. D.; Roof, A. A. M.; Winter, W. J. *J. Am. Chem. Soc.* **1981**, *103*, 6520. (d) Reusch, W. *J. Org. Chem.* **1962**, *27*, 1882.

0022-3263/93/1958-0252$04.00/0

Scheme II



of β,γ-unsaturated ketone **4** (Scheme II) and by the formation of the 4-protoadamantyl radical **10** which rearranges to adamantyl radical **11**.[11] Acetone could serve as a hydrogen atom source which would permit the conversion of **11** into **9** with regeneration of the acetonyl radical. It thus appears that the photoinitiated addition of acetone reported here proceeds by chain addition of acetonyl radical. The radical nature of the addition can be seen also, from the increased yield of **9** after 15% of conversion of **4**. Figure 1 shows a plot of disappearance of **4** vs appearance of products. Two different slopes are observed for the conversion of **4** into **9**. At about 15% of the conversion of **4** the yield of **9** increases much more than the yield of the other three products.[12]

In conclusion, a hitherto unknown 4-methylene-2-protoadamantanone (**4**) has been prepared in a 50% overall yield, and its photochemical reactions have been studied under direct and acetone-sensitized irradiation. Although the geometry of two chromophores is well suited for ODPM rearrangement, the reaction proceeds instead by photoinitiated anti-Markovnikov addition of acetonyl radical.

Experimental Section

The purity of all compounds was controlled by GC. ^{1}H and ^{13}C NMR spectra were taken on JEOL FX 90Q and VARIAN GEMINI 300 spectrometers. IR spectra were recorded with a Perkin-Elmer 297 spectrophotometer, and UV spectra were taken on a Pye Unicam SP8-100 spectrophotometer. Mass spectra were recorded on EXTREL FTMS 2001, Varian CH-7, and SHIMADZU GC-MS QP-1000 spectrometers. GC analyses were carried out on Varian Aerograph 1800 and Varian 3300 gas chromatographs. Melting points were determined in sealed capillary tubes completely immersed in oil by using a Thiele apparatus and are uncorrected.

2-Protoadamantenone,[8] pyridinium chlorochromate (PCC),[13] and Lombardo reagent[14] were prepared according to published procedures. Preparative chromatography was performed on Merck kieselgel 60. The light source for photochemistry was a 450-W high-pressure Hg lamp.

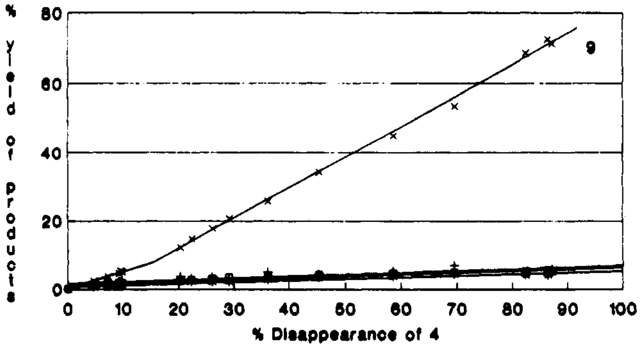


Figure 1.

2-Ethylenedioxa-4-protoadamantene (5b). To a solution of 3.0 g (20.3 mmol) of **5a** in 40 mL of benzene were added 2 mL (32.3 mmol) of ethylene glycol and 200 mg of *p*-toluenesulfonic acid. The reaction mixture was stirred at 90 °C for 5 h. After cooling, the mixture was diluted with water (50 mL) and extracted with ether (3 × 100 mL). The ether extracts were combined, washed with saturated aqueous sodium chloride, and dried over anhydrous magnesium sulfate. The solvent was evaporated and the residue was chromatographed on silica gel with (0 → 10%) ether in pentane as the eluent to give 3.5 g (90% yield) of 2-ethylenedioxa-4-protoadamantene (**5b**) as a colorless oil, more than 98% pure (GC, SE-30, 170 °C). **5b**: MS *m/e* (rel intensity) 192 (M^+, 100), 151 (17), 149 (15), 137 (13), 113 (38), 112 (39), 99 (44), 91 (19), 79 (75); IR (KBr film) ν 3040 (w), 2940 (s), 2880 (s), 1470 (w), 1175 (m), 1120 (m), 1105 (m), 820 (m), 700 (s) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 6.45 (dd, 1 H), 5.88 (dd, 1 H), 3.96–3.79 (m, 4 H), 2.74–1.35 (m, 10 H); ^{13}C NMR (CDCl$_3$) δ 139.6 (d), 127.7 (d), 116.2 (s), 64.6 (t), 63.5 (t), 44.9 (d, 2C), 38.3 (t), 37.9 (t), 32.3 (d), 31.5 (d), 30.4 (t). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.77; H, 8.19.

2-Ethylenedioxa-4-protoadamantanone (6). To a solution of 2-methyl-2-butene (5.4 mL, 52 mmol) in dry tetrahydrofuran (20 mL) was added a 2 M solution of borane–tetrahydrofuran complex (13 mL) under a nitrogen atmosphere, and the resulting mixture was stirred for 30 min. Then 2.5 g (13 mmol) of **5b** in dry tetrahydrofuran (20 mL) was added and the reaction mixture was stirred for 3 h at room temperature. After the solution was cooled to 0 °C, water (5 mL) was added, followed by aqueous 3 M sodium hydroxide (15 mL) and 30% hydrogen peroxide (15 mL). The reaction mixture was stirred for 2 h at room temperature, poured into 50 mL of water, and extracted with ether (2 × 100 mL). The organic extracts were washed with saturated aqueous sodium chloride and dried over anhydrous magnesium sulfate. After filtration and evaporation of solvent, the residue (2.5 g) was dissolved in methylene chloride (20 mL), PCC (5.1 g) was added in small portions, and the reaction mixture was stirred for 3 h at room temperature. Filtration through a Florisil column afforded 2.3 g of a mixture of keto ketals **6** and **7** in a 9:1 ratio (GC, SE-30, 170 °C). Chromatography on silica gel with (0 → 30%) ether in pentane as eluent gave 1.75 g (64%) of ketal **6** and 190 mg (7%) of **7**.

6: MS *m/e* (rel intensity) 208 (M^+, 100), 180 ($M^+ - CO$, 13), 165 (16), 152 (45), 138 (45), 113 (55), 99 (61); IR (KBr film) ν 2940 (s), 1715 (s), 1475 (m), 1180 (m), 1110 (m), 900 (m), 805 (m) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 4.0 – 3.8 (m, 4 H), 2.8–1.4 (m, 12 H); ^{13}C NMR (CDCl$_3$) δ 211.0 (s), 117.3 (s), 64.5 (t), 62.9 (t), 60.7 (d), 45.9 (t), 43.2 (d), 37.5 (t), 35.0 (d), 33.6 (t), 32.3 (t), 27.8 (d).

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.08; H, 7.81.

7: MS *m/e* (rel intensity) 208 (M^+, 100), 180 (41), 165 (8), 137 (20), 113 (40), 99 (81); IR (KBr film) ν 2940 (s), 2890 (s), 1730 (s), 1125 (m), 1030 (m), 860 (m), cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 4.0–3.8 (m, 4 H), 2.6–1.3 (m, 12 H); ^{13}C NMR (CDCl$_3$) δ 215.5 (s), 117.4 (s), 64.5 (t), 63.4 (t), 45.4 (d), 41.0 (d), 39.5 (d), 36.0 (t), 35.0 (t), 30.9 (t), 29.9 (t, 2 C).

2-Ethylenedioxa-4-methyleneprotoadamantane (8). To a stirred solution of 1.6 g (7.7 mmol) of keto ketal **6** in 40 mL of methylene chloride at 0 °C was added 100 mL (42 mmol) of a freshly prepared solution of Lombardo[14] reagent. The reaction

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[11] The rearrangement of **10** to **11** is based on the well-known rearrangement of the protoadamantane ring system to the thermodynamycally more stable adamantane nucleus. See, for example: (a) Lenoir, D.; Glaser, R.; Mison, P.; Schleyer, P.v.R. *J. Org. Chem.* **1971**, *36*, 1821. (b) Cuddy, B. D.; Grant, D.; McKervey, M. A. *J. Chem. Soc., Chem. Commun.* **1971**, 27.

[12] Even the irradiation was interrupted after 15% of conversion of **4** and the resulting reaction mixture left in the dark the reaction continued and the yield of **9** increased. The conversion of **4** and formation of products was followed by capillary GC (DB-210, 150 °C). The experiment of the acetone addition of **4** by use of free radical initiator also supports the free radical process (see Experimental Section).

[13] Corey, E.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

[14] Lombardo, L. *Tetrahedron Lett.* **1982**, 4293.

mixture was stirred at 0 °C for 2 h and then poured into 100 mL of saturated aqueous sodium bicarbonate, extracted with ether, and dried over anhydrous magnesium sulfate. The solvent was evaporated to afford 1.43 g (90%) of 8 as a colorless oil. GC analysis (SE-30, 170 °C) showed a single component. 8: MS *m/e* (rel intensity) 206 (M$^+$, 100), 163 (97), 135 (41), 111 (88), 99 (47), 91 (53), 79 (38); IR (KBr film) ν 3060 (w), 2930 (s), 1645 (w), 1115 (m), 1030 (m), 880 (m) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 4.8–4.7 (m, 2 H), 4.0–3.8 (m, 4 H), 2.8–1.3 (m, 12 H); ^{13}C NMR (CDCl$_3$) δ 145.7 (s), 118.1 (s), 109.7 (t), 64.6 (t), 62.6 (t), 54.1 (d), 41.9 (d), 38.5 (t), 36.7 (t), 35.2 (d), 33.2 (t), 32.7 (t), 28.0 (d).

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.48; H, 8.84.

4-Methylene-2-protoadamantanone (4). A solution of 1.35 g (6.6 mmol) of 8 in 40 mL of 40% aqueous acetone and 290 mg of *p*-toluenesulfonic acid monohydrate was stirred at room temperature for 50 h. Then 50 mL of saturated aqueous sodium chloride was added and the reaction mixture was extracted with ether (3 × 50 mL). The combined ether extracts were washed with 10% aqueous sodium bicarbonate (2 × 50 mL) and dried over anhydrous magnesium sulfate, and the solvent was evaporated to give crude methylene ketone 4. Column chromatography on silica gel with (0 → 10%) ether in pentane as eluent, followed by sublimination (90 °C, 14 mm) provided 950 mg (90% yield) of 4 as white crystals: mp 40–42 °C; MS *m/e* (rel intensity) 162 (M$^+$, 48), 134 (M$^+$, – CO, 23), 119 (17), 105 (18), 93 (43), 92 (100), 91 (55), 79 (41); IR (KBr) ν 3060 (w), 2940 (s), 2860 (m), 1730 (s), 1640 (m), 1440 (m), 1130 (m), 1080 (m), 910 (s), 900 (s), 800 (m), 690 (m) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 4.9–4.8 (m, 2 H), 3.0–1.5 (m, 12 H); ^{13}C NMR (CDCl$_3$) δ 219.0 (s), 141.0 (s), 111.2 (t), 55.9 (d), 46.7 (d), 37.7 (t), 35.2 (t), 35.1 (t), 33.7 (d), 30.9 (t), 27.9 (d).

Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.69. Found: C, 81.43; H, 8.55.

Photochemistry of 4-Methylene-2-protoadamantanone. A solution of 180 mg (1.11 mmol) of 4 in 20 mL of dry acetone was placed in a Pyrex vessel, bubbled with nitrogen for 10 min, and irradiated with a high-pressure Hg lamp at ambient temperature. The reaction was followed by GC (FS-101, 230 °C, or DB-210, 150 °C). The starting methylene ketone was consumed within 4 h to give a mixture of four components in a ratio of 48:1.5:0.5:1. The major product was isolated by column chromatography on silica gel using (10 → 40%) ether in pentane as eluent, yielding 155 mg (64% yield) of 9 as a colorless oil: >98% pure by GC (FS-101, 230 °C); MS *m/e* (rel intensity) 220 (M$^+$, 100), 205 (15), 177 (M$^+$ – CH$_3$CO, 62), 163 (M$^+$ – CH$_3$COCH$_2$, 22), 150 (47), 149 (26), 108 (19), 107 (19), 91 (25), 79 (25); IR (KBr film) ν 2910 (s), 2850 (s), 1710 (s), 1450 (m), 1360 (m), 1165 (m), 1065 (m) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 2.6–2.4 (m, 3 H), 2.16 (s, 3 H), 2.1–1.8 (m, 12 H), 1.62 (dd, 2 H); ^{13}C NMR (CDCl$_3$) δ 217.7 (s), 209.1 (s), 48.8 (s), 47.1 (d), 44.3 (t, 2 C), 39.2 (t, 2 C), 38.2 (t), 35.8 (t), 30.2 (t), 29.8 (q), 27.9 (d, 2 C).

Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.21; H, 9.42.

Free Radical Addition of Acetone to 4-Methylene-2-adamantanone. To a stirred solution of 70 mg (0.4 mmol) of methylene ketone 4 in 10 mL of dry acetone was added 25 mg (0.1 mmol) of dibenzoyl peroxide, and the mixture was stirred at reflux overnight. GC analysis (DB-210; 150–170 °C), showed a single product (98.7%, based on starting ketone). The acetone was evaporated and the residue was chromatographed on silica gel using (20 → 40%) ether in pentane as the eluent, yielding 56 mg of 1-(3-oxobutyl)-2-adamantanone (**9**) (71% yield, based on reacted ketone).

Acknowledgment. This work was supported by the Ministry of Science and Technology of the Republic of Croatia and the US Joint Fund for Scientific and Technical Cooperation with the NSF (grant PN-832).

Registry No. 4, 56933-52-9; **5a**, 28673-75-8; **5b**, 144436-27-1; 6, 144466-25-1; 7, 144436-28-2; 8, 144436-29-3; 9, 144436-30-6.