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One-pot Formation of Functionalized Cyclopentenone Derivatives via Retro-Benzilic Acid Rearrangement of the Proto-Photocycloadducts of Methyl 2,4-Dioxopentanoate to Methylenecycloalkanes

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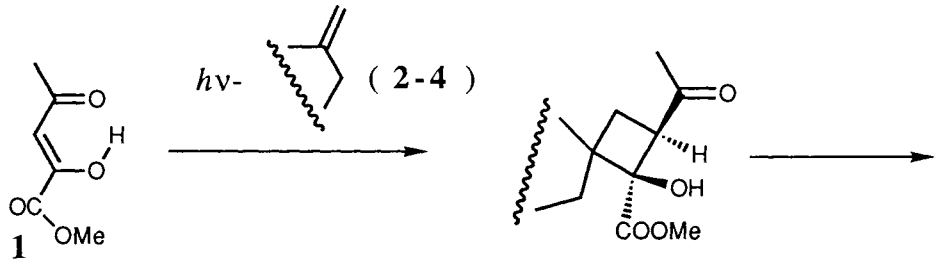
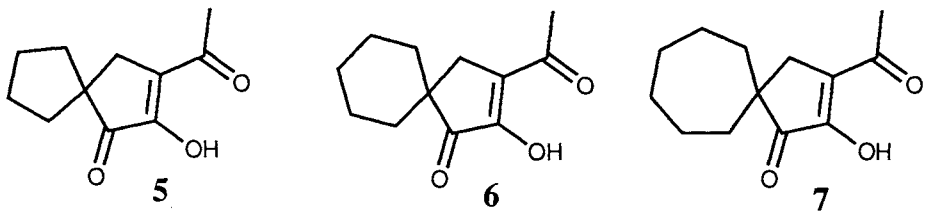
The *proto*-Photocycloadducts of methyl 2,4-dioxopentanoate to several methylenecycloalkanes and -alkenes spontaneously caused *retro*-benzilic acid rearrangement, exclusively. The reaction proceeded quite cleanly, and a simple work-up without chromatographic separation allowed to isolate the products directly in very good material balance.

Photocycloaddition reactions leading to cyclopentane derivatives are quite rare.[1] The recently-reported formation of 3-acetyl-2-hydroxycyclopentenone derivatives from the *proto*-[2+2] cycloadducts of methyl 2,4-dioxopentanoate (**1**) to olefins presents a unique example, which involves unprecedented rearrangement designated as "*retro*-benzilic acid rearrangement".[2] This was initially found upon heating of the *proto*-cycloadducts from sterically-hindered olefins, which are usually quite unreactive, and its application to organic syntheses is therefore limited.[3] However, since conformationally rigid bicycloolefins such as camphene exclusively gave the rearrangement products without pyrolytic work up, though in an inferior yield,[4] it is desirable to extend the study to conformationally rigid, but sterically less hindered olefins.





Herein, we report an exclusive and quantitative occurrence of the *retro*-benzilic rearrangement in the *proto*-photocycloadducts obtained from **1** and methylenecycloalkanes (**2-4**), together with the results obtained from the related derivatives.

The solution of **1** and methylenecyclopentane (**2**), methylenecyclohexane (**3**) or methylenecycloheptane (**4**) in AcOEt was respectively irradiated by means of a 400-W high-pressure Hg-lamp through a Pyrex-glass filter at 15-20 °C. The each product (**5**-**7**) was directly isolated; neither pyrolytic work-up nor chromatography of the methylated compound was required.

All colorless crystalline products, **5** (mp 100.5-102 °C), **6** (mp 197-200 °C), and **7** (mp 141-141.5 °C), revealed characteristic ^{1}H NMR features[4] for the rearrangement products; e.g., the low-field-shifted Ac signals at δ ca. 2.4.[3,5] The ^{13}C NMR spectra of these meso compounds, **5** [δ 25.4(2C), 28.2, 38.7(2C), 38.8, 53.4, 128.9, 158.6, 201.4, and 208.1], **6** [δ 22.5 (2C), 25.0, 28.3, 33.4(2C), 34.8, 46.8, 129.0, 158.0, 201.6, and 208.3], and **7** [δ 23.7 (2C), 28.2, 29.0(3C), 36.9(2C), 49.2, 128.3, 157.4, 201.6, and 209.0], were consistent to the structures depicted.

Other than those described above, the methylenecycloalkanes, 1-methyl-2-methylenecyclohexane (**8**) and 4-isopropyl-1-methyl-3-methylenecyclohexane (**9**), the methylenecycloalkenes, 3-methylene-1-cyclopentene (**10**), 3-methylene-1-cyclohexene (**11**), 5-isopropenyl-2-methyl-3-methylene-1-cyclohexene (**12**), and *endo*-3-methylenetricyclo[5.2.1.0^{2,6}]deca-4,8-diene (**13**), exclusively gave the *retro*-benzilic acid rearrangement products (**14a** and **14b**, **15a** and **15b**, **16**, **17**, **18a** and **18b**, and **19**) as shown in Chart 1. From all these semicyclic olefins, the products were formed in quantitative or excellent yields.[5]

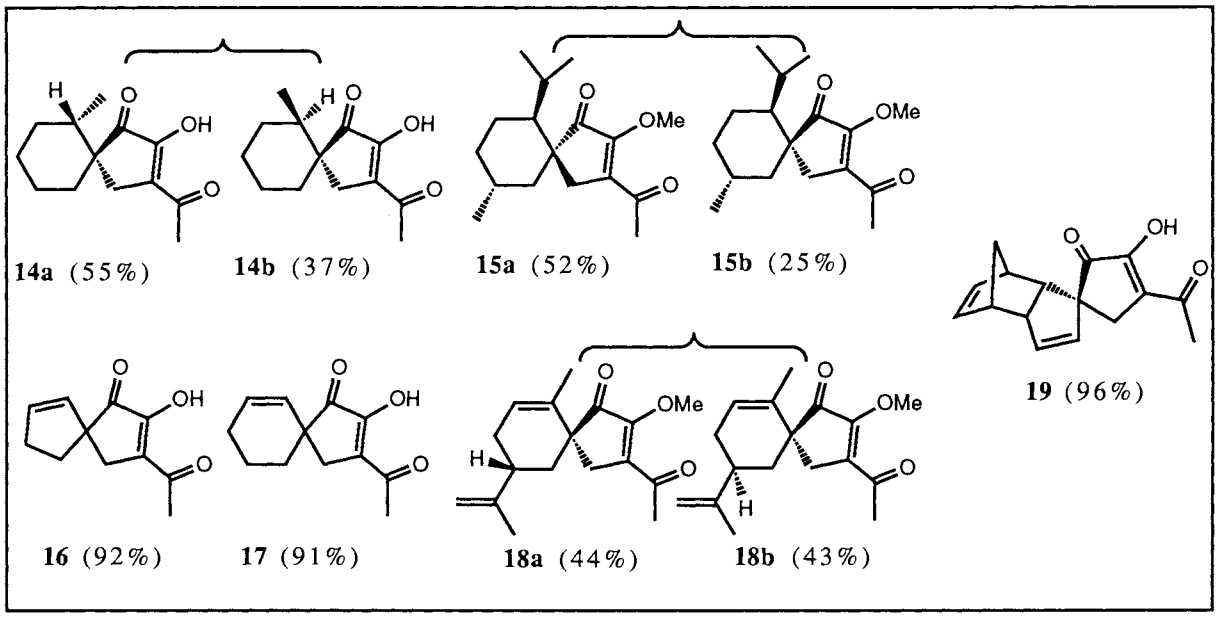


Chart 1. Yields of *retro*-benzilic acid rearrangement products of methylenecycloalkanes and methylenecycloalkenes.

As has been stated, the *proto*-photocycloadducts derived from α,α-disubstituted acyclic olefins such as isoprene and 2-methylpropene caused the rearrangement as only a minor process.[2] In addition, camphene, a methylene derivative of bicyclic cage compound, formed a pair of the *retro*-benzilic acid rearrangement products without pyrolytic work-up. However, the yields were still not satisfactory due to the diminished reactivity of

1.[3] In this regard, the nearly quantitative formations of **5**, **6**, and **7** from less hindered reactive olefins, **2**, **3**, and **4**, should be of interest from synthetic point of view. The driving force of the rearrangement is a release of the internal strain of the cyclobutanol system.

In conclusion, the methylenecycloalkanes, which have not been examined as reactants for the photocycloaddition, have been shown to take an entirely different course from the ordinary photoreaction with **1**,[6] and the reaction of **1** to methylenecycloalkanes and -alkenes thus provides a novel entry to functionalized spiro[4.n]alkenones, which should be suitable precursors for spirocyclic compounds to enhance the utility of enolized β-diketones in organic photochemistry.

References

1) It should be mentioned that an intramolecular version of the de Mayo reaction with appropriate substrates esults in, via the *retro*-aldol opening of the cyclobutanol ring, the construction of cyclopentane derivatives. Indeed, we have employed this strategy for synthesis of a triquinane, silphinene, from methyl 8-methyl-2,4-dioxo-7-nonenoate. See H. Takeshita, A. Mori, and T. Kubota, *Kyushu Daigaku Seisan Kagaku Kenkyusho Hokoku*, **81**, 1 (1986).

2) T. Hatsui, C. Nojima, and H. Takeshita, *Bull. Chem. Soc. Jpn.*, **62**, 2932 (1989); *Kyushu Daigaku Sogo Rikogaku Kenkyuka Hokoku,* **11**, 291 (1989); *Bull. Chem. Soc. Jpn.*, **63**, 1611 (1990).

3) T. Hatsui, S. Ikeda, and H. Takeshita, *Chem. Express*, **6**, 845 (1991).

4) New compounds revealed following ^{1}H NMR (270 MHz) spectral data in $CDCl_3$:
5: δ 1.55-2.00(8H, m), 2.39(3H, s), 2.61(2H, s), and 9.87(1H, O*H*). **6**: δ 1.30-1.86(10H, m), 2.42(3H, s), 2.57(2H, s), and 9.93(1H, O*H*). **7**: δ 1.45-1.85(12H, m), 2.40(3H, s), 2.57(2H, s), and 9.73(1H, O*H*). **14a**: δ 0.63(3H, d, *J*=7.0 Hz), 1.30-1.90(9H, m), 2.37(1H, d, *J*=16.8 Hz), 2.45(3H, s), 2.58(1H, d, *J*= 16.8 Hz), and 9.72(1H, O*H*). **14b**: δ 0.79(3H, d, *J*=6.6 Hz), 1.30-1.90(9H, m), 2.38(1H, d, *J*=16.8 Hz), 2.41(3H, s), 2.65(1H, d, *J*=16.8 Hz), and 9.61(1H, O*H*). **15a**: δ 0.75(3H, d, *J*=7.0 Hz), 0.81(3H, d, *J*= 7.0 Hz), 0.86(3H, d, *J*=7.0 Hz), 1.30-1.90(9H, m), 2.17 (1H, d, *J*=18.0 Hz), 2.49(3H, s), 2.56(1H, d, *J*= 18.0 Hz), and 4.16(3H, s). **15b**: δ 0.65(3H, d, *J*=7.0 Hz), 0.85(3H, d, *J*=7.0 Hz), 0.89(3H, d, *J*=7.0 Hz), 1.30-1.90(9H, m), 2.36 (1H, d, *J*=18.0 Hz), 2.50(3H, s), 2.62(1H, d, *J*=18.0 Hz), and 4.19(3H, s). **16**: δ 1.30-2.20(4H, m), 2.43(3H, s), 2.44(1H, d, *J*=16.0 Hz), 2.49(1H, d, 16.0 Hz), 5.48(1H, m), 5.63 (1H, m), and 10.05(1H, O*H*). **17**: δ 1.52-2.20(6H, m), 2.40(3H, s), 2.65(1H, d, *J*=16.5 Hz), 2.67(1H, d, *J*=16.5 Hz), 5.34 (1H, dm, *J*=9.9 Hz), 5.99(1H, dt, *J*=9.9, 4.0 Hz), and 9.80(1H, O*H*). **18a**: δ 1.44(3H, m), 1.71(3H, br s), 2.33(1H, d, *J*=18.0 Hz), 2.51(3H,s), 2.88(1H, d, *J*=18.0 Hz), 4.19 (3H, s), 4.72(1H, m), and 5.77(1H, m). **18b**: δ 1.49(3H, m), 1.71(3H, br s), 2.51(3H, s), 2.56(1H, d, *J*=19.0 Hz), 2.58 (1H, d, *J*=19.0 Hz), 4.16 (3H, s), 4.72(1H, m), and 5.63(1H, m). **19**: δ 1.42(1H, d, *J*=8.1 Hz), 1.59(1H, d, *J*=8.1 Hz), 2.42(3H, s), 2.45(1H, m), 2.49(1H, d, *J*=16.5 Hz), 2.76(1H, d, *J*=16.5 Hz), 2.87(1H, br s), 2.95(1H, br s), 3.62(1H, m), 5.10(1H, dd, *J*=5.5, 1.8 Hz), 5.68 (1H, dd, *J*=5.5, 2.2 Hz), 5.87(1H, dd, *J*= 5.8, 3.3 Hz), 5.99(1H, dd, *J*=5.8, 2.9 Hz), and 9.73(1H, O*H*).

5) The stereostructures of **14a** and **14b** and **15a** and **15b** were assigned by assuming preferred attack of **1** to the cycloaddends from the convex side of the molecules, i.e., the major products, **14a** and **15a**, should have trans relationship between the oxo-carbons of cyclopentenone rings and the alkyl groups. This could not be applied to **18a** and **18b**; however, their stereostructures were distinguished by the chemical shift differences (Δδ) between the *gem*-protons on the γ-positions of the α,β-unsaturated keto group. Namely, the Δδ of **16**

and **17**, unsubstituted methylenecycloalkene adducts, are very small, 0.05 and 0.02, which appeared ca. δ 2.5. This was also the case for **18b**, Δδ 0.02, but **18a** showed a large Δδ, 0.55, with δ 2.33 and 2.88. Thus, the isopropenyl side chain and the methylene hydrogens of **18a** are suggested to be in the cis relationship.

6) It is not surprising that a molecular mechanics calculation (Chem 3D Plus program with the Version 3.0, licensed from Cambridge Science Computing Inc.) carried out with most of these *proto*-cycloadducts revealed almost the same results as obtained from camphene adduct;[3] i.e., the π-axis of the ester carbonyl double bond is nearly parallel to the *exo*-C(1)-C(2) bond to be migrated in the cyclobutanol moiety. These results, which strongly support our view, will be reported in a full paper. At the same time, we like to mention that the original, hydrogen-bonded conformation of the *proto*-photocycloadducts is stereoelectronically unfavorable for the *retro*-aldol process.[2]

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