Pergamon

Tetrahedron Letters, Vol. 35, No. 47, pp. 8829-8832, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 \$7.00+0.00

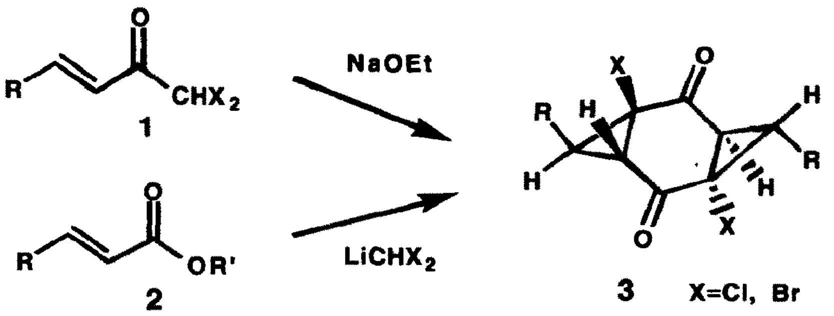
0040-4039(94)01870-7

A Novel Synthesis of Tricyclo[5.1.0.0^{3,5}]octane-2,6-dione Derivatives via Double Michael Addition-Induced Cyclopropanation Reactions

Sadao Tsuboi,* Takashige Ono, Katsushi Kunito, Mikio Kageyama, Takashi Sakai, and Masanori Utaka

Department of Applied Chemistry, Faculty of Engineering, Okayama University, Tsushima, Okayama 700, Japan

Michael additon is an important reaction in organic synthesis for making carbon-carbon bonds. Recently, a number of tandem reactions via Michael additions, which are useful for the construction of carbon skeletons, have been reported.[1] This paper communicates a new and novel synthesis of tricyclo[5.1.0.0^{3,5}]octane-2,6-dione derivatives **3** via double Michael addition-induced cyclopropanation reactions from 1,1-dichloro-3-alken-2-ones **1** and α,β-unsaturated esters **2**, as shown below.



Various dichloroketones **1**[2] were treated with an equimolar amount of sodium ethoxide in dry ether at low temperature (-78- -60 °C for ca. 10 h, and 0 °C for a few days) under an atmosphere of nitrogen and quenched with cold water to afford tricyclooctanes **3** in 50-67% yields as white crystals. All of **3** are good crystals and scarcely soluble in almost of organic solvents. Yields of **3**, and some of physical properties are tabulated in Table 1. Characteristic signals of the IR and NMR data were identical with those of the samples which were previously reported and whose stereochemistry was absolutely verified by X-ray crystallographic analysis.[3]

The mechanism of the present reaction can be obviously explained by a novel base-catalyzed cyclization reaction of **1** via double Michael additions between two molecules of the enolate anion **4** following double cyclopropanation reactions, as shown below.

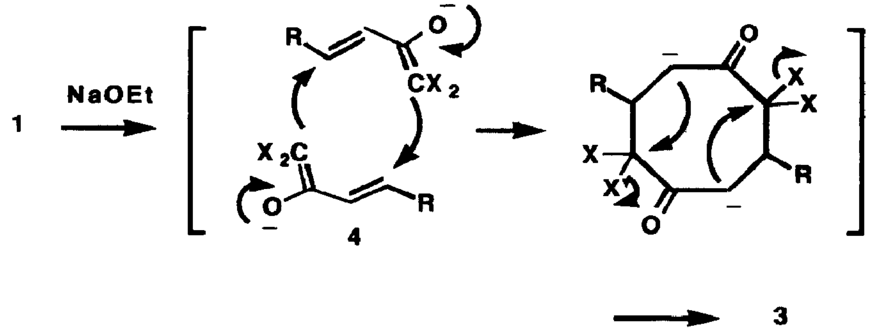


Table 1. Yields and Physical Properties of Compound 3

No.	R	X	Yield (%)[a]	M. P. (°C)	IR (KBr) (C=O)	NMR (CDCl$_3$) (ring H)
a	CH_3	Cl	52.9	228[b]	1685	2.00, 2.21
b	$CH_3(CH_2)_2$	Cl	56.9	105	1700	1.86, 2.24
c	$CH_3CH{=}CH$	Cl	67.4	153[b]	1700	2.50, 2.60
d	n-C_6H_{13}	Cl	53.4	105[b]	1690	1.84, 2.23
e	C_6H_5	Cl	50.2	223[b]	1700	3.09, 3.33
f		Cl	60.7	171[b]	1690	2.96, 3.22

[a] Isolated yield. [b] Decomposed.

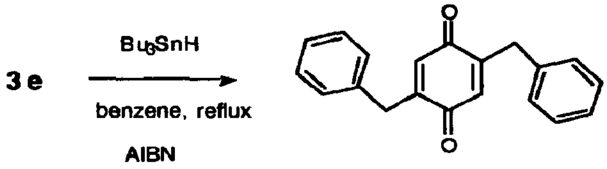
Surprisingly, compound 3 was also obtained by the reaction of α,β-unsaturated esters with lithiodihalomethanes. Several esters were allowed to react with an equivalent of lithiodichloromethane (BuLi + CH_2Cl_2) in anhydrous THF at -95 °C (20 min) under an atmosphere of nitrogen, and quenched with water to give 3 as crystals in moderate yields. Reactions of esters with 2.2 equivalent of lithiodibromomethane ($LiN(SiMe_3)_2$ + CH_2Br_2) in anhydrous THF was also carried out at -78 °C (10 min) and then at -78 °C ~ room temperature (30 min). The yields and physical properties are tabulated in Table 2. The reaction with aromatic esters gave 3 in moderate yields. On the other hand, the reaction of lithiodichloromethane with aliphatic esters afforded 3 in low yields along with bisdichloromethyl-substituted carbinols, which were derived from the further reaction of an initially formed ketone 1 with lithiodichloromethane. It is obvious that the reaction proceeded via the enolate 4 produced from the reaction between esters 2 and lithiodihalomethanes, as shown above.

Table 2. Synthesis of **3** by the Reaction of α,β-Unsaturated Esters **2** with Lithiodihalomethane

R	X	Yield (%)
CH_3	Cl	33
C_2H_5	Cl	31
C_6H_5	Cl	71
C_6H_5	Br	64
p-Cl-C_6H_4	Cl	56
p-CH_3O-C_6H_4	Br	51

Some papers concerning with the reaction of lithiodihalomethanes with carbonyl compounds have been reported.[4-10] Normant *et al.*[9] report the reaction of lithiodichloromethane with ethyl crotonate, leading the formation of 1,1-dichloro-3-penten-2-one (**5**). However, they have not detected the compound **3**. This discrepancy to our results may be due to the different reaction conditions.[11] The reaction in the less polar solvent (THF/ether, 3/2)[9] will decrease the nucleophilicity of the enolate **4** to give the ketone **5** after being quenched.

Reduction of **3e** with tributyltin hydride proceeded via the cleavage of a tricyclooctane skeleton, giving 2,5-bisbenzyl-1,4-benzoquinone (**6**) in 50.2% yield. This will be useful for the synthesis of 2,5-disubstituted 1,4-benzoquinones, which are found in natural products[12] and exhibit anti-cancer activity.[13]



6

Although *anti*-tricyclo[5.1.0.0^{3,5}]octane-2,6-dione is known as bishomochinone and prepared by the dehydrobromination of brominated cyclooctane-1,5-dione,[14-16] the synthesis by the present type reaction has never been reported. To our knowledge, one pot synthesis of tricyclooctane derivatives **3** from dichloroketones **1** and α,β-unsaturated esters **2** is unprecedented and the present reaction is synthetically useful and mechanistically interesting. Current investigations are directed toward the generalization of this reaction to other α,β-unsaturated ketones and lithiomethanes substituted with electron-withdrawing groups.

Acknowledgement. We thank Emeritus Professor Akira Takeda for providing us the opportunity of this work. We are grateful to the SC-NMR Laboratory of Okayama University for high-field NMR measurements.

References

(1) For example, see: Ho, T.-L. *Tandem Organic Reactions*; John Wiley & Sons: New York, 1992.

(2) Compound **1** was prepared in good yields by the oxidation of 1,1-dichloro-3-alken-2-ols, which were obtained by the reaction of α,β-unsaturated aldehydes with lithiodichloromethane (see ref 4), with electrolytic manganese dioxide: Tsuboi, S.; Ishii, N.; Sakai, T.; Tari, I.; Utaka, M. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1888.

(3) Tsuboi, S.; Furutani, H.; Takeda, A.; Kawazoe, K.; Sato, S. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 2475.

(4) Köbrich, G.; Flory, K.; Drischel, W. *Angew. Chem.* **1964**, *76*, 536.

(5) Taguchi, H.; Yamamoto, H.; Nozaki, H. *Tetrahedron Lett.* **1972**, 4661.

(6) Kowalski, C. J.; Haque, M. S.; Fields, K. W. *J. Am. Chem. Soc.* **1985**, *107*, 1429.

(7) Kowalski, C. J.; Reddy, R. E. *J. Org. Chem.* **1992**, *57*, 7194.

(8) Ward, H. D.; Teager, D. S.; Murray, Jr., R. K. *J. Org. Chem.* **1992**, *57*, 1926.

(9) Bacquet, C.; Villieras, J.; Normant, J.-F. *Compt. Rend. (C)* **1974**, *278*, 929.

(10) Villieras, J.; Bacquet, C.; Normant, J.-F. *Bull. Soc. Chem. Fr.* **1975**, 1797.

(11) In the literature (ref 9), two equivalents of lithiodichloromethane to ethyl crotonate and mixed solvent (THF/ether, 3/2) have been used, and the experiment has been carried out in larger scale (10~50 times) than ours. Following the procedure of this reaction in ref 9, we got a mixture of **3a** (11%), (*E*)-1,1-dichloro-2-dichloromethyl-3-penten-2-ol (ca. 30%), and unreacted ethyl crotonate besides **5** (ca. 30%).

(12) Dougan, J.; Robinson, J. M.; Sumar, S.; Howard, G. E.; Coursey, D. G. *J. Sci. Food Agric.* **1983**, *34*, 874.

(13) Holiat, S. M.; Smith, W. E.; Hubert, D. D.; Davis, S. *Cancer Treat. Rep.* **1981**, *65*, 1113.

(14) Heller, J.; Yogev, A.; Dreiding, A. S. *Helv. Chim. Acta* **1972**, *55*, 1003.

(15) Chapleo, C. B.; Dreiding, A. S.; Dyllick-Brenzinger, R. A.; Oth, J. F. M. *Helv. Chim. Acta* **1976**, *59*, 1311.

(16) Prakash, G. K. S.; Fung, A. P.; Rawdah, T. N.; Olah, G. A. *J. Am. Chem. Soc.* **1985**, *107*, 2920.

(*Received in Japan* 25 *July* 1994)