

Generation of Ketocarbenoid by α -Elimination of ω,ω -Dibromoacetophenone with Copper, and Trapping by Cycloaddition to Olefins

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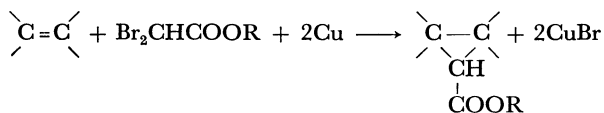
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Ketocarbenoid was generated by the reaction of ω,ω -dibromoacetophenone with copper in aromatic hydrocarbon, and was trapped by cycloaddition to olefins. This is the first example of cyclopropanation of olefins by formally divalent carbon intermediate without use of diazoketones.

Thermal, photochemical, and catalytic decomposition of diazoketones have been the source of ketocarbenes and carbenoids.¹⁾ The most useful reaction of carbene and carbenoid in synthesis is the cycloaddition to olefins to give the corresponding cyclopropane derivatives. However, in the reaction of the above ketocarbenes and carbenoids with olefins, the yields of acylcyclopropane derivatives are low due to Wolff rearrangement²⁾ and other side reactions.

On the other hand, α -elimination reaction provides a good route to most classes of carbenes and carbenoids.¹⁾ The metal α -haloenolates of α -haloketones have served as intermediates in a number of synthetically useful reactions such as Darzens condensation and related reactions, but these enolates usually do not decompose to ketocarbenes.³⁾ Even the addition of copper(I) compounds does not promote their decomposition to ketocarbenes.³⁾ Charpentier-Morize and Sansoulet⁴⁾ reported the formation of 1,2,3-tripivaloylcyclopropane and 1,2,3,4,5,6-hexapivaloylcyclohexane by the reaction of dichloromethyl *t*-butyl ketone with zinc-copper couple in ether. Furukawa and coworkers⁵⁾ reported that the reaction of ω,ω -dibromoacetophenone with zerovalent transition metal complexes gave *trans*-1,2,3-tribenzoylcyclopropane, or *trans*-1,2-dibenzoyl ethylene. Ketocarbenes or carbenoids seem to be included as an intermediate of these reactions, but it was not trapped by cycloaddition to olefins. Scott and Cotton⁶⁾ reported the formation of ketocarbenoid by α -elimination of α,α -dibromoketone with zinc dust or diethylzinc. The ketocarbenoid was trapped by an intramolecular carbon-hydrogen insertion reaction, but not by the cycloaddition to olefins. The reaction of the ketocarbenoid with olefin was reported to give a substituted dihydrofuran, which represents the product of formal 1,3-dipolar addition of the ketocarbenoid to olefin.⁷⁾

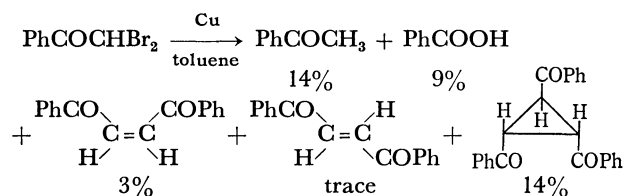


Recently, we found that the reaction of dibromoacetic esters with copper powder in the presence of olefins gave the corresponding alkoxy carbonylcyclopropane derivatives.⁸⁾ As an extension of this work, we have investigated the α -elimination of α,α -dihaloketones with copper powder, and found that ketocarbenoid was generated by the reaction and was trapped by cycloaddition to olefins. This is the first example of acylcyclopropanation of olefins by formally divalent carbon

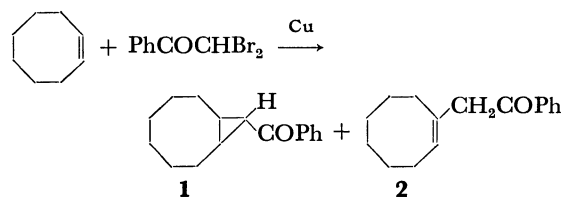
intermediate without use of diazoketones.

Results and Discussion

The reaction of ω,ω -dibromoacetophenone with copper powder in toluene at 100 °C for 93 h was found to give acetophenone, benzoic acid, *cis*- and *trans*-1,2-dibenzoyl ethylene, and *trans*-1,2,3-tribenzoylcyclopropane. In addition, a large amount of unidentified tar was obtained. Most of ω,ω -dibromoacetophenone was consumed under the conditions. This result suggests that the reaction involves ketocarbenes or carbenoid intermediate. In order to ascertain the nature of the intermediate, we attempted to trap it by the cycloaddition to olefins.



Treatment of *cis*-cyclooctene, ω,ω -dibromoacetophenone, and copper powder in toluene at 100 °C for 93 h gave *exo*-9-benzoyl-*cis*-bicyclo[6.1.0]nonane (**1**) together with ω -1-cycloocten-1-ylacetophenone (**2**) in 12 and 3% yields, respectively, based on the olefin.



Assignment of the *exo* stereochemistry of **1** rests on NMR coupling constant arguments. That is, with the aid of a shift reagent, the absorption of the cyclopropane ring proton in the geminal position to the benzoyl group was shown to exhibit a triplet ($J=3.5$ Hz). The coupling constant is consistent with the *exo* structure. The *cis* and *trans* coupling constants of the cyclopropane ring protons were reported to be 4—9 and 3—5 Hz, respectively.⁹⁾ The coupling constant 3.5 Hz of **1** agrees well with the corresponding coupling constants in the structurally similar cyclopropane derivatives. The absorption of the ring proton in the geminal position to the methoxycarbonyl group of *exo*-9-methoxycarbonyl-*cis*-bicyclo[6.1.0]nonane, *exo*-8-methoxycarbonylbicyclo[5.1.0]octane, and *exo*-7-methoxycarbonylbicyclo[4.1.0]heptane appeared as triplets with the coupling constants of 4.2, 3.9, and 4.2 Hz, respectively.⁸⁾ The coupling constants of the corresponding *endo* isomers were 8.6,

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8.3, and 9.4 Hz, respectively.⁸⁾

The endo isomer of **1** was not detected in the reaction mixture. Presumably the steric repulsion between the benzoyl group and the cyclooctane ring is significant.

Treatment of styrene, ω,ω -dibromoacetophenone, and copper powder in ethylbenzene at 100 °C for 120 h gave a 1:1.6 mixture of *cis*- and *trans*-1-phenyl-2-benzoylcyclopropane in 2% yield based on the olefin. In this case, most of styrene polymerized during the course of the reaction.

Since organocopper intermediates rather than free carbenes are probable intermediates in the reaction of copper powder with diiodomethane, chlorodiiodomethane, and dibromoacetic esters,⁸⁾ reaction of ω,ω -dibromoacetophenone with copper powder would also proceed *via* organocopper intermediate (ketocarbenoid of copper) rather than free ketocarbene.

Experimental

Elementary analyses were performed at the Elementary Analysis Center of Kyoto University. IR spectra were recorded on a Hitachi Model 215 grating spectrometer or Japan Spectroscopic Co. Model 402G grating spectrometer. NMR spectra were obtained with a Varian T-60-A spectrometer using tetramethylsilane as an internal standard. Mass spectra were obtained on a Hitachi Model RMU-6 mass spectrometer. Gas chromatographic analysis was carried out on a Shimadzu GC-4A or GC-4B gas chromatograph.

Materials. ω,ω -Dibromoacetophenone was prepared according to the procedure of Taylor.¹⁰⁾ The ordinary commercial grade of copper powder provided by Nakarai Chemicals Ltd., Kyoto, was used without further purification. Olefins and solvents were purified by distillation.

Reaction of ω,ω -Dibromoacetophenone with Copper Powder.

Copper powder (11.4 g, 180 mmol) was treated with 0.5 g (2 mmol) of iodine in 50 ml of toluene at room temperature with stirring. After the brown color of iodine disappeared, ω,ω -dibromoacetophenone (22.2 g, 80 mmol) was added, and the mixture was heated at 100 °C for 93 h. After the reaction, the inorganic materials were separated by filtration. Weight of the inorganic materials was 23.7 g after drying, suggesting that most of copper powder was converted to copper(I) bromide under the reaction condition. Solvent and other volatile materials were removed from the organic layer by heating under a reduced pressure, and the residue was dissolved in benzene. Addition of light petroleum ether to this benzene solution gave 1.29 g (14%) of *trans*-1,2,3-tribenzoylcyclopropane as a crystalline solid, which was purified by washing with carbon tetrachloride followed by recrystallization from benzene. It was identified by comparing its IR and NMR spectra with those of an authentic sample.¹¹⁾ When solvents were removed from the filtrate, 7.26 g of unidentified tar was obtained.

In another run of experiment which was carried out under the same reaction condition, the organic layer was analyzed by gas chromatography. The analysis showed the formation of acetophenone and benzoic acid in 14 and 9% yields, respectively, which were identified by comparing spectral data with those of authentic samples, and the presence of only 1.3% of unchanged ω,ω -dibromoacetophenone in the reaction mixture. The analysis also showed the presence of two minor reaction products in 3% and trace yields,

respectively. Spectral data of these products were identical with *cis*- and *trans*-1,2-dibenzoyl ethylene, respectively.

*Reaction of ω,ω -Dibromoacetophenone with Copper Powder in the Presence of *cis*-Cyclooctene.*

Copper powder (1.14 g, 18.0 mmol), iodine (0.05 g, 0.2 mmol), ω,ω -dibromoacetophenone (2.22 g, 8.0 mmol), and *cis*-cyclooctene (0.44 g, 4.0 mmol) were treated in a similar manner in 3.0 ml of toluene at 100 °C for 93 h, and **1** and **2** were obtained in 12 and 3% yields, respectively, based on the olefin. The yields were determined by gas chromatographic analysis of the reaction mixture. A sample of **1** collected by gas chromatography was analyzed. n_D^{20} = 1.5546; IR (neat) 1660 cm⁻¹ ($\nu_{C=O}$); NMR (CCl₄) τ 2.1 (2H, m), 2.6 (3H, m), 8.0 (3H, m), 8.42 (12 H, m). With aid of a shift reagent, tris(dipivaloylmethanato)europium (Eu(dpm)₃), the absorption of the cyclopropane ring proton in the geminal position to the benzoyl group was shown to exhibit a triplet (J = 3.5 Hz). Found: C, 84.31; H, 9.01%. Calcd for C₁₆H₂₀O: C, 84.16; H, 8.83%. A sample of **2** collected similarly from the reaction mixture was also analyzed. NMR (CCl₄) τ 2.1 (2H, m), 2.6 (3H, m), 4.5 (1H, m), 7.04 (2H, s), 7.9 (2H, m), 8.40 (10H, m); IR (neat) 1681 cm⁻¹ ($\nu_{C=O}$); MS m/e (rel intensity) 228 (7, M⁺), 120 (28), 108 (15), 105 (100), 77 (39), 67 (13), 44 (47), 40 (22).

Reaction of ω,ω -Dibromoacetophenone with Copper Powder in the Presence of Styrene.

Copper powder (11.4 g, 180 mmol), iodine (0.5 g, 2 mmol), ω,ω -dibromoacetophenone (22.2 g, 80 mmol) and styrene (4.2 g, 40 mmol) were treated in a similar manner in 30 ml of ethylbenzene at 100 °C for 120 h. Gas chromatographic analysis of the reaction mixture showed the presence of two reaction products in a ratio of 1:1.6 in 2% yield based on the olefin. Spectral data of these two products were consistent with *cis*- and *trans*-1-phenyl-2-benzoylcyclopropane, respectively. A sample of the *cis* isomer collected from the reaction mixture by gas chromatography was analyzed. NMR (CCl₄) τ 2.1 (2H, m), 2.6 (2H, m), 2.8 (1H, m), 2.91 (5H, narrow m), 7.2 (2H, m), 7.9 (1H, m), 8.7 (1H, m); IR (CCl₄) 1675 cm⁻¹ ($\nu_{C=O}$). A sample of the *trans* isomer collected similarly was also analyzed. NMR (CCl₄) τ 2.1 (2H, m), 2.6 (2H, m), 2.8 (1H, m), 2.83 (5H, narrow m), 7.3 (2H, m), 7.8–9.2 (2H, m); IR (CCl₄) 1670 cm⁻¹ ($\nu_{C=O}$).

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