A New Synthetic Route to Electrophilic Cyclopropane Derivatives from Olefins

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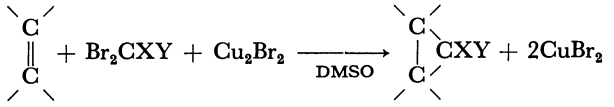
Synopsis. 1,1-Bis(alkoxycarbonyl)-, 1-alkoxycarbonyl-1-cyano-, and 1,1-dicyanocyclopropane derivatives were obtained in 10—99% yields by the reaction of $Br_2C(COOR)_2$, $Br_2C(CN)(COOR)$, and $KBr[Br_2C(CN)_2]_4$, respectively, with olefins and Cu_2Br_2 in dimethyl sulfoxide (DMSO).

Recently cyclopropane derivatives activated by two electron-withdrawing substituents such as COOR, COR, and CN at geminal position were found to be useful intermediates in organic synthesis.[1] A number of methods exist for the preparation of these electrophilic cyclopropanes.[2] This paper describes a new synthetic route to electrophilic cyclopropane derivatives from olefins by the reaction with organic *gem*-dihalide and Cu_2Br_2 in dimethyl sulfoxide (DMSO).

The reaction of $Br_2C(COOEt)_2$, $Br_2C(CN)(COOEt)$, and $KBr[Br_2C(CN)_2]_4$ with Cu_2Br_2 in the presence of olefins gave the corresponding 1,1-bis(ethoxycarbonyl)-, 1-cyano-1-ethoxycarbonyl-, and 1,1-dicyanocyclopropane derivatives, respectively, in good yields. Some experimental results are given in Table 1. All products were identified by comparison of their ^1H NMR and IR spectra with those of authentic samples, or showed satisfactory analytical data and expected spectra. GLC analysis of the reaction mixture showed that no isomeric olefins were formed.



(X, Y=COOEt, CN)

During the course of reaction Cu_2Br_2 was converted into $CuBr_2$, which was isolated as a coordinated complex with two molecules of DMSO, and identified by comparison of its spectral data with those of an authentic

TABLE 1. SYNTHESIS OF ELECTROPHILIC CYCLOPROPANE DERIVATIVES FROM OLEFINS BY THE REACTION WITH ORGANIC *gem*-DIHALIDE AND Cu_2Br_2 IN DMSO

Olefin	Halide	Temp °C	Product	Yield[a] %
Styrene	$Br_2C(COOEt)_2$[b]	28	1,1-Bis(ethoxycarbonyl)-2-phenylcyclopropane	71
		75		68
p-Chlorostyrene		60	1-(*p*-Chlorophenyl)-2,2-bis(ethoxycarbonyl)cyclopropane	77
		30		48
m-Chlorostyrene		60	1-(*m*-Chlorophenyl)-2,2-bis(ethoxycarbonyl)cyclopropane	79
		30		54
m-Trifluoromethylstyrene		60	1,1-Bis(ethoxycarbonyl)-2-(*m*-trifluoromethylphenyl)cyclopropane	71
		30		64
p-Methylstyrene		60	1,1-Bis(ethoxycarbonyl)-2-(*p*-methylphenyl)cyclopropane	24
cis-β-Methylstyrene		75	1,1-Bis(ethoxycarbonyl)-2-methyl-3-phenylcyclopropane	10[c]
trans-β-Methylstyrene		75		9[d]
1-Octene		75	1,1-Bis(ethoxycarbonyl)-2-hexylcyclopropane	32
cis-Cyclooctene		75	9,9-Bis(ethoxycarbonyl)bicyclo[6.1.0]nonane	10
Acrylonitrile		60	2-Cyano-1,1-bis(ethoxycarbonyl)cyclopropane	39
Ethyl acrylate		70	1,1,2-Tris(ethoxycarbonyl)cyclopropane	17
Styrene	$Br_2C(CN)(COOEt)$[e]	25	1-Cyano-1-ethoxycarbonyl-2-phenylcyclopropane	99[f]
Acrylonitrile		28	1,2-Dicyano-1-ethoxycarbonylcyclopropane	71[g]
cis-Cyclooctene	$Br_2C(CN)(COOEt)$[h]	100	9-Cyano-9-ethoxycarbonylbicyclo[6.1.0]nonane	47
1-Octene		80	1-Cyano-1-ethoxycarbonyl-2-hexylcyclopropane	20
Styrene	$KBr[Br_2C(CN)_2]_4$[i]	22	1,1-Dicyano-2-phenylcyclopropane	67
p-Methylstyrene		30	1,1-Dicyano-2-(*p*-methylphenyl)cyclopropane	39[j]
p-Chlorostyrene		30	1,1-Dicyano-2-(*p*-chlorophenyl)cyclopropane	34[j]
cis-Cyclooctene		50	9,9-Dicyanobicyclo[6.1.0]nonane	21

a) Determined by GLC analysis of the reaction mixture, based on the olefin. b) Reactions were carried out with 4.0 mmol of olefin, 8.0 mmol of $Br_2C(COOEt)_2$, and 9.0 mmol of Cu_2Br_2 in 6.0 ml of DMSO for 2 h. c) A 10 : 90 mixture of *cis* and *trans* isomers obtained. d) A 8 : 92 mixture of *cis* and *trans* isomers obtained. e) Reactions were carried out with 1.0 mmol of olefin, 2.0 mmol of $Br_2C(CN)(COOEt)$, and 2.0 mmol of Cu_2Br_2 in 1.5 ml of DMSO for 2 h. f) A 92 : 8 mixture of E and Z isomers obtained. g) A 60 : 40 mixture of E and Z isomers obtained. h) Reactions were carried out with 0.5 mmol of olefin, 1.0 mmol of $Br_2C(CN)(COOEt)$, and 1.0 mmol of Cu_2Br_2 in 1.0 ml of DMSO for 2 h. i) Reactions were carried out with 0.5 mmol of olefin, 0.25 mmol of $KBr[Br_2C(CN)_2]_4$, and 1.0 mmol of Cu_2Br_2 in 1.0 ml of DMSO for 2 h. j) Determined by isolation using column chromatography, based on the olefin.

material.[3]

The new reaction is useful for the synthesis of electrophilic cyclopropane derivatives from olefins (Table 1). The reaction with $Br_2C(COOEt)_2$ gave cyclopropane derivatives in a non-stereospecific way. A *ca.* 1 : 9 mixture of cis and trans isomers of the corresponding cyclopropane derivatives was obtained from both *cis*- and *trans*-β-methylstyrene. No isomerization of *cis*- and *trans*-β-methylstyrene or of *cis*- and *trans*-1,1-bis-(ethoxycarbonyl)-2-methyl-3-phenylcyclopropane was observed under the experimental conditions. The relative reactivity of substituted styrenes in the reaction with $Br_2C(COOEt)_2$ gave a Hammett ρ-value of −0.1. Thus the reaction was concluded to be weakly electrophilic.

In the reaction with $Br_2C(CN)(COOEt)$, two stereoisomers of the cyclopropane derivatives were obtained from styrene and acrylonitrile, the *E* to *Z* isomer ratio being 92 : 8 and 60 : 40, respectively. The relative configuration was determined on the basis of their ^1H NMR spectra. The *E* : *Z* isomer ratios seemed to reflect the thermodynamic stability of the product. However, GLC analysis of the reaction mixture showed only one peak in the cases with cyclooctene and 1-octene. ^1H NMR spectra of the isolated cyclopropane derivatives did not clearly indicate the presence of stereoisomers.

Experimental

Microanalyses were performed at the Elementary Analyses Center of Kyoto University. ^1H NMR spectra were recorded on a Varian Model T-60A spectrometer in CCl_4 or $CDCl_3$ using Me_4Si as an internal standard. IR spectra were recorded on a Hitachi Model 215 grating spectrophtometer, or a Japan Spectroscopic Co. Model DS-402G spectrophotometer. Mass spectra were obtained on a Hitachi Model RMU-6 mass spectrometer, or on a Japan Electron Optics Lab. Model JMS D-300 mass spectrometer at an ionization potential of 24 eV. GLC analyses were carried out on a Shimadzu GC-4B or GC-4C gas chromatograph.

Materials. $Br_2C(COOEt)_2$,[4] $Br_2C(CN)(COOEt)$,[5] and $KBr[Br_2C(CN)_2]_4$[6] were prepared according to the methods reported. *cis*- and *trans*-β-Methylstyrene, *p*-methylstyrene, *p*-chlorostyrene were prepared as reported.[2] DMSO was purified by distillation under reduced pressure.

Procedure. Olefin, organic *gem*-dihalide and Cu_2Br_2 were allowed to react in DMSO at the prescribed temperature with stirring for 2 h. After the reaction, the organic materials were extracted by hexane, benzene, or ethyl acetate from the reaction mixture. Yields were determined by GLC analysis of the organic layer, and the products were isolated by collection from the organic layer by GLC and analyzed. Some 1,1-dicyanocyclopropane derivatives were thermally unstable. In these cases, products were isolated by column chromatography, yields being determined by means of isolation. Results are given in Table 1.

1,1-Bis(ethoxycarbonyl)cyclopropane derivatives were identified by comparison of their spectral data with those of authentic samples.[2] Spectral data of (*E*)- and (*Z*)-1-cyano-1-ethoxycarbonyl-2-phenylcyclopropane were identical with those of authentic substances.[7] Spectral data of 1,1-dicyano-2-phenylcyclopropane were identical with those of an authentic sample.[8,9] Spectral and elementary analyses of the other electrophilic cyclopropane derivatives are given below.

1,2-Dicyano-1-(ethoxycarbonyl)cyclopropane. n_D^{30} 1.4644. Found: C, 58.37; H, 4.87; N, 16.81%. Calcd for $C_8H_8N_2O_2$: C, 58.53; H, 4.91; N, 17.06%. The *E* isomer: NMR ($CDCl_3$) δ 1.37 (t, J=7.2 Hz, 3H), 1.9—2.2 (m, 2H), 2.54 (d of d, J_{cis} =9.8 Hz and J_{trans}=7.2 Hz, 1H), 4.30 (q, J=7.2 Hz, 2H); $\nu_{C\equiv N}$ (liquid film) 2259 cm^{-1}; $\nu_{C=O}$ (liquid film) 1728 cm^{-1}. The *Z* isomer: NMR ($CDCl_3$) δ 1.38 (t, J=7.2 Hz, 3H), 1.9—2.3 (m, 2H), 2.53 (d of d, J_{cis}=9.8 Hz and J_{trans}=7.2 Hz, 1H), 4.36 (q, J=7.2 Hz, 2H); $\nu_{C\equiv N}$ (liquid film) 2255 cm^{-1}; $\nu_{C=O}$ (liquid film) 1730 cm^{-1}.

9-Cyano-9-(ethoxycarbonyl)bicyclo[6.1.0]nonane. n_D^{30} 1.4879; NMR (CCl_4) δ 1.37 (t, J=7.2 Hz, 3H), 1.0—2.3 (m, 14H), 4.20 (q, J=7.2 Hz, 2H); $\nu_{C\equiv N}$ (liquid film) 2248 cm^{-1}; $\nu_{C=O}$ (liquid film) 1727 cm^{-1}. Found: C, 70.66; H, 8.71; N, 6.16%. Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33%.

1-Cyano-1-ethoxycarbonyl-2-hexylcyclopropane. n_D^{30} 1.4472; NMR (CCl_4) δ 0.91 (t, J=6.0 Hz, 3H), 1.1—1.8 (m, 13H), 1.37 (t, J=6.8 Hz, 3H), 4.23 (q, J=6.8 Hz, 2H); $\nu_{C\equiv N}$ (liquid film) 2238 cm^{-1}; $\nu_{C=O}$ (liquid film) 1728 cm^{-1}. Found: C, 70.03; H, 9.60; N, 6.36%. Calcd for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27%.

9,9-Dicyanobicyclo[6.1.0]nonane. Mp 74—75 °C; NMR ($CDCl_3$) δ 0.9—2.4 (m, 14H); $\nu_{C\equiv N}$ (KBr disk) 2250 cm^{-1}. Found: C, 76.01; H, 8.21; N, 16.15%. Calcd for $C_{11}H_{14}N_2$: C, 75.82; H, 8.10; N, 16.08%.

1,1-Dicyano-2-(p-methylphenyl)cyclopropane. n_D^{30} 1.5429; NMR ($CDCl_3$) δ 2.17 (d, J=9.0 Hz, 2H), 2.33 (s, 3H), 3.22 (t, J=9.0 Hz, 1H), 7.11 (s, 4H); $\nu_{C\equiv N}$ (liquid film) 2252 cm^{-1}. Found: C, 79.22; H, 5.49; N, 15.21%. Calcd for $C_{12}H_{10}N_2$: C, 79.10; H, 5.53; N, 15.37%.

1,1-Dicyano-2-(p-chlorophenyl)cyclopropane. Mp 123—125 °C; NMR ($CDCl_3$) δ 2.21 (d, J=9.0 Hz, 2H), 3.24 (t, J= 9.0 Hz, 1H), 7.1—7.4 (m, 4H); $\nu_{C\equiv N}$ (KBr disk) 2256 cm^{-1}. Found: C, 65.09; H, 3.65; N, 13.53; Cl, 17.78%. Calcd for $C_{11}H_7N_2Cl$: C, 65.20; H, 3.48; N, 13.82; Cl, 17.50%.

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