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Stereochemical Behavior of 1-Methoxycyclopropyl Radical in Hunsdiecker Reaction[1)]

Teiichi ANDO,* Takashi ISHIHARA, Akira YAMASHITA, and Masahiro MATSUMOTO
Department of Industrial Chemistry, Faculty of Engineering, Kyoto University, Sakyo-ku, Kyoto 606

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Synopsis. The Hunsdiecker reaction of Ag (*E*)- and (*Z*)-2,2-dichloro-1-methoxy-3-methylcyclopropanecarboxylates with bromine in CCl_4 at 0 and 77 °C occurs with substantial inversion of configuration, suggesting that the 1-methoxycyclopropyl radical is configurationally less stable than the 1-fluorocyclopropyl or the 1-methoxyvinyl radical.

Recent studies[2)] have established that the configurational stability, or the energy barrier for inversion, of 1-substituted cyclopropyl radicals is strongly affected by the nature of the 1-substituent; best known is the effect of 1-fluorine stabilizing the pyramidal configuration of the cyclopropyl radical, which is much more powerful than that of 1-chlorine.

As compared with the configurational stability of 1-halo radicals, that of the 1-methoxy radical has only scarcely been investigated, probably because of the difficulty of its generation. In fact, no reports on this subject have appeared so far in the literature except the one by Walborsky *et al.*[2b,c)]

The stereochemistry of the Hunsdiecker reaction of Ag salts of some 1-methoxy- and 1-fluorocyclopropanecarboxylic acids has now been examined to learn the effect of the 1-methoxyl substituent on the stereochemical stability of cyclopropyl radicals.

Results and Discussion

The Hunsdiecker reaction of Ag salts of (*Z*)-2,2-dichloro-1-methoxy- (**1a**), (*E*)-2,2-dichloro-1-methoxy- (**2a**), and (*Z*)-2,2-dichloro-1-fluoro-3-methylcyclopropanecarboxylic acids (**1b**) was effected in the presence of bromine in CCl_4, to give the corresponding bromocyclopropane as an isomeric mixture (Scheme and Table 1). The structures of these bromocyclopropanes were determined from their ^1H[3)] and/or ^{13}C NMR spectra.[4)]

The reaction of methoxy acids **1a** and **2a** occurred with substantial inversion of configuration even at 0 °C. The stereospecificity was completely lost at 77 °C; the isomer ratios of the product are equal irrespective of the stereochemistry of the starting acid. This indicates that isomeric 1-methoxycyclopropyl radicals are configurationally rather unstable, inverting their configuration at a rate comparable to their bromine abstraction at 0 °C and at a rate faster than the latter at 77 °C.

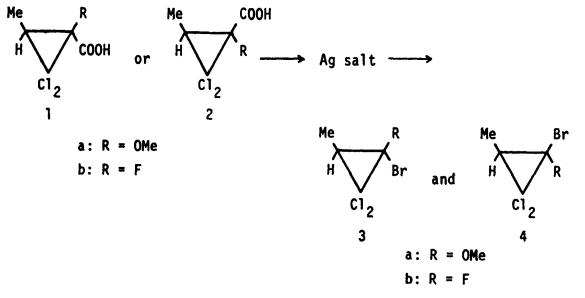

TABLE 1. HUNSDIECKER REACTION OF ACIDS **1** AND **2**

Acid	Temp °C	Time h	Yield %	Isomer ratio retn : invn
1a	0	1.5	54	58 : 42
	0	2.0	76	56 : 44
	77	1.5	53	41 : 59
	77	2.0	59	39 : 61
2a	0	2.0	—	68 : 32
	0	3.0	71	69 : 31
	77	0.5	—	61 : 39
	77	1.0	62	62 : 38
1b	20	1.5	—	90 : 10
	20	2.5	59	91 : 9
	77	2.0	69	81 : 19
	77	3.0	—	82 : 18

In discussing the effect of the 1-methoxyl substituent from the above facts, the presence of two 2-chlorine atoms in this system must be taken into account, because they can more or less destabilize the pyramidal configuration of cyclopropyl radicals. Such an effect of electronegative 2-substituents was suggested theoretically by Dewar *et al.*[6)] and demonstrated experimentally in our previous work.[7)]

The Hunsdiecker reaction of Ag salt of **1b** was conducted in this connection; the reaction took place with high (but not complete) stereospecificity at room temperature, and the degree of inversion increased at 77 °C (Table 1). Evidently, the configurational stability of the 1-fluorocyclopropyl radical is lowered to such an extent that its inversion of configuration competes with its bromine abstraction, in spite of the presence of 1-fluorine.

These findings, as combined with the extremely high configurational stability of 2-hetero-unsubstituted 1-fluorocyclopropyl radicals observed in the previous work,[2)] strongly suggest the existence of the 2-chlorine effect in the 1-methoxy radicals as well as in the 1-fluoro radical.[8)] The data in Table 1 also show that the 1-methoxy radical is configurationally less stable than the 1-fluoro radical, *i.e.*, that the 1-methoxyl substituent is less powerful than the 1-fluoro in stabilizing the pyramidal configuration of cyclopropyl radicals.

The behavior of 1-methoxycyclopropyl radicals described herein is in sharp contrast with that of (*E*)- and (*Z*)-1-methoxy-1-propenyl radicals.[9)] This difference can be explained in terms of the difference in *s*-character of the odd-electron orbital between the cyclopropyl and the vinyl systems, though the above-cited 2-chlorine effect may play a minor role. It is to be noted that similar differences have been observed between the 1-chlorocyclopropyl[2)] and the 1-chlorovinyl radicals.[10)]

Experimental[11]

Methyl (E)-2-Methoxy-2-butenoate. Methyl *trans*-2-methylglycidate was treated with *p*-toluenesulfonic acid to form 2-hydroxy-3-(*p*-tolylsulfonyloxy)butanoate (100%), which was then methylated with methyl iodide/Ag$_2$O (97%). Treatment of the resulting 2-methoxy-3-(*p*-tolylsulfonyloxy)-butanoate with KOH in methanol, followed by acidification, gave an isomeric mixture of (*E*)- and (*Z*)-2-methoxy-2-butenoic acid (*E*/*Z*=85/15). Recrystallization from hexane gave pure (*E*)-acid, mp 44.5—45.5 °C (65%), which was converted to the methyl ester by the usual method (82%), bp 62—63 °C/16 mmHg. IR (film) 1724, 1644, 1207, 1164, 1105, 1026 cm^{-1}; ^{1}H NMR δ 1.93 (d, $J=7.4$ Hz, 3H), 3.50 (s, 3H), 3.70 (s, 3H), 5.14 (q, $J=7.4$ Hz, 1H); MS *m/e* (%) 130 (M$^+$, 68), 55 (100).

Methyl (Z)-2-Methoxy- and (Z)-2-Fluoro-2-butenoates were prepared according to the method of Owen[12] and of Bergmann *et al.*,[13] respectively. Attempts to prepare the (*E*)-fluoro acid or its ester in our hands were unsuccessful.

*1-Substituted 2,2-Dichloro-3-methylcyclopropanecarboxylic Acids (**1a**, **2a**, and **1b**)* were prepared by addition of dichlorocarbene to the corresponding methyl 2-substituted-2-butenoate followed by hydrolysis. The reaction conditions were similar to those described in our previous paper.[14]

1a: 37% yield; mp 75—76 °C; IR (KBr) 3000, 1708, 1292, 1258, 1040 cm^{-1}; ^{1}H NMR δ 1.29 (d, $J=6.6$ Hz, 3H), 2.43 (q, $J=6.6$ Hz, 1H), 3.76 (s, 3H), 12.24 (s, 1H); ^{13}C NMR δ 7.9 (Me on ring).

Found: C, 36.30; H, 4.11; Cl, 35.47%.

2a: 37% yield; mp 52.5—53.5 °C; IR (KBr) 3030, 1706, 1301, 1158, 1075 cm^{-1}; ^{1}H NMR δ 1.43 (d, $J=6.6$ Hz, 3H), 2.03 (q, $J=6.6$ Hz, 1H), 3.61 (s, 3H), 12.14 (s, 1H); ^{13}C NMR δ 9.7 (Me on ring).

Found: C, 36.29; H, 4.22%. Calcd for $C_6H_8O_3Cl_2$: C, 36.21; H, 4.05; Cl, 35.63%.

1b: 33% yield; mp 42—43 °C; IR (KBr) 3000, 1720, 1250, 1180, 1000 cm^{-1}; ^{1}H NMR δ 1.37 (d, $J=6.6$ Hz, 3H), 2.53 (dq, $J=6.6$ and 7.8 Hz, 1H), 11.16 (s, 1H); ^{13}C NMR δ 7.4 ($J_{CF}=6.0$ Hz, Me on ring).

Found: C, 31.82; H, 2.57; Cl, 38.04; F, 10.16%. Calcd for $C_5H_5O_2Cl_2F$: C, 32.11; H, 2.70; Cl, 37.92; F. 10.16%.

*Hunsdiecker Reaction of **1a**, **2a**, and **1b**.* To a suspension, which had been maintained at a specified temperature, of Ag salt (5 mmol) in dry CCl$_4$ (10 ml) was rapidly added 1.2 equiv. of bromine in dry CCl$_4$ (10 ml). After a specified period, inorganic silver salt was removed by filtration and was washed with a small amount of CCl$_4$. The filtrate was concentrated below 30 °C. The isomer ratios in the products were measured by GLC before distillation.

3a** and **4a: Bp 78—79 °C/15 mmHg; IR (film) 2960, 1043, 780, 765 cm^{-1}; ^{1}H NMR **3a**: δ 1.30 (d, $J=6.6$ Hz, 3H), 2.12 (q, $J=6.6$ Hz, 1H), 3.54 (s, 3H), **4a**: δ 1.25 (d, $J=6.6$ Hz, 3H), 1.84 (q, $J=6.6$ Hz, 1H), 3.54 (s, 3H); ^{13}C NMR **3a**: δ 8.1 (Me on ring), **4a**: δ 13.3 (Me on ring); MS *m/e* (%) 232 (M$^+$, 1), 199 (100).

3b** and **4b: Bp 52—53 °C/23 mmHg; IR (film) 2940, 1096, 996, 898, 862 cm^{-1}; ^{1}H NMR **3b**: δ 1.35 (d, $J=6.6$ Hz, 3H), 2.03 (dq, $J=6.6$ and 7.2 Hz, 1H), **4b**: δ 1.33 (dd, $J=6.6$ and 1.6 Hz, 3H), 2.06 (dq, $J=6.6$ and 19.8 Hz, 1H); ^{13}C NMR **3b**: δ 7.9 ($J_{CF}=5.2$ Hz, Me on ring), **4b**: δ 12.7 ($J_{CF}=0$ Hz, Me on ring); MS *m/e* (%) no parent to 220, 141 (100).

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