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Three-Membered Ring-formation Reactions. V. The Cyclopropane Derivative Obtained from the α-Halogenoacrylic Ester by Means of Zinc Alkyl-Active Methylene Chelate Compounds

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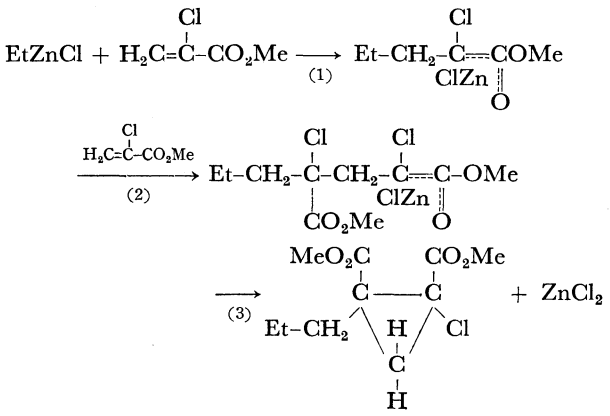
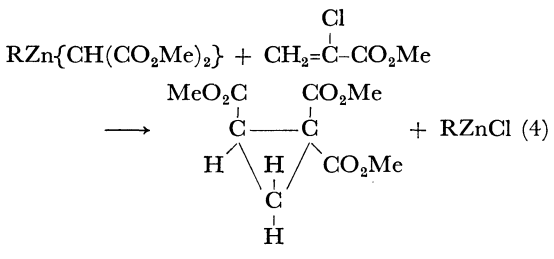
It was previously reported that two molecules of methyl α-chloroacrylate undergo a ring-formation reaction with ethylzinc chloride to produce dimethyl 1-chloro-2-propyl-*cis*-1,2-cyclopropanedicarboxylate (I).[1-3] The reaction was considered to proceed according to a step-by-step mechanism:



(I)

Diethylzinc, instead of ethylzinc chloride, was also effective in the ring-formation reaction.[4] It was further confirmed that the zinc alkyl–active methylene chelate compound[5] behaved in a different fashion from ethylzinc chloride or diethylzinc,[3] as is exemplified by Reaction (4):



(II)

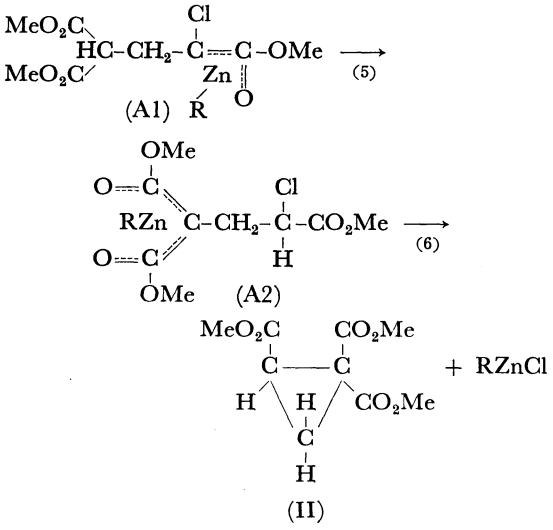
Only one molecule of methyl α-chloroacrylate participates in Reaction (4). Since it was considered that the second active hydrogen atom in the intermediate (A1) may play an essential role as is shown below (Reaction (5)) in the ring-formation reaction (4), we

1) Y. Kawakami and T. Tsuruta, *Tetrahedron Lett.*, **1971**, 1173.
2) Y. Kawakami and T. Tsuruta, *ibid.*, **1971**, 1959.
3) T. Tsuruta and Y. Kawakami, *Tetrahedron*, in press.
4) T. Tsuruta Y. Kawakami, and R. Tsushima, *Makromol. Chem.*, **149**, 135 (1971).
5) Y. Kawakami and T. Tsuruta, This Bulletin, **44**, 247 (1971).

Table 1. Reaction of methyl α-halogenoacrylate with metal alkyl–active methylene chelate compounds[a)]

Acrylate[b)]	Chelate compound	Product yield (%)				
		II	III	IV	V	VI
MCA	n-BuZn{$CH(CO_2Me)_2$}	60.0	—	—	—	—
MBA	n-BuZn{$CH(CO_2Me)_2$}	75.2	—	—	—	—
MCA	EtClAl{$CH(CO_2Me)_2$}	13.0	—	—	—	—
MCA	n-BuZn{$C(CH_3)(CO_2Me)_2$}	—	—	22.6	21.5	—
MCA	n-BuZn{$C(Br)(CO_2Me)_2$}	—	—	—	—	15.0
MA	n-BuZn{$C(Br)(CO_2Me)_2$}	22.2	—	—	—	—
MCA	n-BuZn{$CH_3COCHCO_2Me$}	—	16.0[c)]	—	—	—

a) Reaction for 2 hr in benzene at 70 °C.
b) MCA, MBA, and MA are methyl α-chloroacrylate, methyl α-bromoacrylate, and methyl acrylate, respectively.
c) The yield was calculated based on 1/2 [MCA].



have undertaken a study of the reactions of methyl α-chloroacrylate with metal alkyl–active methylene chelate compounds, which have substituents on the α-carbon of the active methylene component.

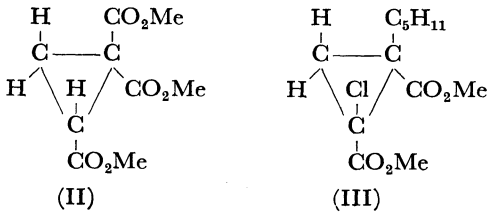
Experimental

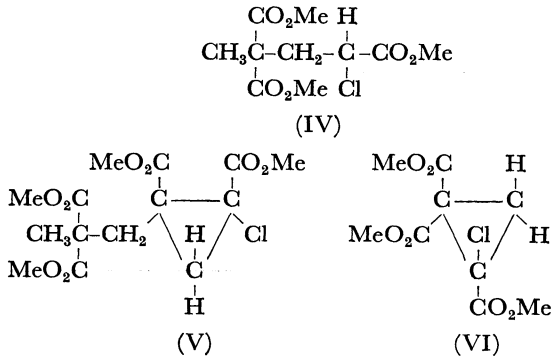
The NMR spectra were recorded at 100 MHz in benzene, TMS being used as the internal standard.

The metal alkyl-active methylene chelate compounds were prepared by a method reported before.[5)] Methyl α-chloroacrylate and methyl α-bromoacrylate were prepared according to the literature.[6)]

To a benzene solution of methyl α-chloroacrylate, equimoles of metal alkyl–active methylene chelate compounds were added at 70 °C. After a given time interval, the reaction was stopped by pouring the reaction system into water containing a small amount of hydrochloric acid. The organic layer was then separated and distilled. The results obtained are shown in Table 1.

The structures of the products in Table 1 were established to be as follows:





Compounds II (n_D^{20} 1.4518, d_4^{20} 1.17, bp 108 °C/1 mmHg) and III (n_D^{20} 1.4618, d_4^{20} 1.08, bp 90 °C/2 mmHg) were identified by comparing their NMR spectra with those reported previously.[1,4)] Compounds IV and V were obtained in 22.5 and 21.5% yields respectively from n-butyl(dimethylmethylmalonato)zinc and methyl α-chloroacrylate. Moreover, Compound VI was obtained in a 15% yield from n-butyl(dimethyl bromomalonato)zinc and methyl α-chloroacrylate.

IV: n_D^{20} 1.4577, d_4^{20} 1.22, bp 115.5 °C/1 mmHg; NMR: δ 4.50 (1H, t, >CH), δ 3.38, 3.37, 3.32 (9H, s, $-CO_2CH_3$), δ 2.76, 2.47 (2H, q, $-CH_2-$), δ 1.29 (3H, s, CH_3-).

Found: C, 45.36; H, 5.97; Cl, 13.14%. Calcd for $C_{10}H_{15}ClO_6$: C, 45.02; H, 5.67; Cl, 13.30%.

V: n_D^{20} 1.4838, d_4^{20} 1.26, bp 165 °C/1 mmHg.

Found: C, 48.25; H, 5.76; Cl, 9.74%. Calcd for $C_{14}H_{19}ClO_8$: C, 47.92; H, 5.46; Cl, 10.11%.

VI: n_D^{20} 1.4638, bp 116 °C/1 mmHg; NMR: δ 3.28, 3.20 (9H, s, $-CO_2CH_3$), δ 2.09 (2H, q, >CH_2).

Found: C, 43.22; H, 4.77; Cl, 14.03%. Calcd for $C_9H_{11}ClO_6$: C, 43.11; H, 4.43; Cl, 14.15%.

Results and Discussion

When dimethyl methylmalonate was used as an active methylene component in the reaction with methyl α-chloroacrylate, the first-step addition product, IV, of dimethyl methylmalonate to methyl α-chloroacrylate was isolated from the reaction mixture along with V. Thus, a close similarity in the mode of formation can be seen between I and V. The results can be reasonably explained in terms of the lack of the exchange reaction (5), because no active hydrogen

6) C. S. Marvel, J. Dec, H. G. Cooke, and J. C. Cowan, *J. Amer. Chem. Soc.*, **62**, 3495 (1940).

atom exists in the intermediate formed by the addition reaction of *n*-butyl(dimethyl methylmalonato)zinc to the acrylate.

When dimethyl α-bromomalonate was used as the active methylene component, an elimination reaction of bromine atom predominate to form VI, because the bromine atom is a good leaving group. In conformity with this, dimethyl α-bromomalonate could undergo a ring-formation reaction, even with methyl acrylate (Table 1, No. 6). In the reaction of *n*-butyl(methyl acetoacetato)zinc with methyl α-chloroacrylate, methyl acetoacetate component did not act as an addendum, but *n*-butyl group underwent the addition reaction, giving dimethyl 1-chloro-2-amyl-*cis*-1,2-cyclopropanedicarboxylate.[4] These results may be ascribed to the chelate ring of methyl acetoacetate being much more stable than that of dimethyl malonate.

Some results on the asymmetric synthesis by zinc alkylactive methylene chelate compounds in the presence of Et_2Zn-*l*-menthol are shown in Table 2.

The rather small value of the optical rotation in II should be ascribed to an exchange reaction (for example, Reaction (5)) between RZn and H groups, which may also be a cause of the racemization around the chiral center in II.

From the results presented above, it seems reasonable to conclude that the mode of the ring-formation reaction of α-halogenoacrylate with alkylzinc–active methylene chelate compounds is strongly influenced by the nature of substituents at the α-carbon atom of an active methylene component, and also by the stability of the chelating systems.

Table 2. Asymmetric synthesis by zinc alkyl–active methylene chelate compounds in the presence of Et_2Zn–*l*-menthol (1.0 : 1.2) system[a)]

$[\alpha]_D^{20}$ in benzene	Chelate	Product
−6.6°	*n*-BuZn{$CH(CO_2Me)_2$}	II
−8.0°	*n*-BuZn{$CH_3COCHCO_2Me$}	III

a) One to one mole ratio of the chelate compound to Et_2Zn was used.
Et_2Zn–*l*-menthol system was prepared as reported.[2,7)]

7) a) J. M. Bruce and D. W. Farren, *Polymer*, **6**, 509 (1965). b) M. Ishimori, T. Tomoshige, and T. Tsuruta, *Makromol. Chem.*, **120**, 161 (1968).