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The Reaction of 2-Chlorotropone with Methyl Methacrylate

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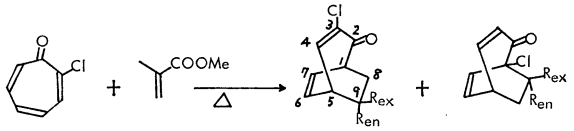
The Diels-Alder reaction of troponoids with cyclic dienophiles including maleic anhydride is known to give only respective *endo*-adducts[1] with exception for tropolones[2-4] which yielded two stereoisomers. Our recent study[5] has disclosed even in the last case that the *endo*-adduct was initially formed but it underwent an acyloin rearrangement to the *exo*-isomer at the later stage. Contrary to the reactions with cyclic dienophiles, troponoids formed four regio- and stereoisomeric adducts in concerted fashion when an acyclic dienophile, acrylonitrile, was used.[6] We have extended our study to the reaction using 2-chlorotropone with methyl methacrylate, another acyclic dienophile for the generalization of the reaction.



III: R_{ex}=Me, R_{en}=COOMe V: R_{ex}=COOMe, R_{en}=Me
IV: R_{ex}=COOMe, R_{en}=Me VI: R_{ex}=Me, R_{en}=COOMe

Results and Discussion

When 2-chlorotropone (I) was heated with methyl methacrylate (II) at 135—140 °C for 48 hr, four 1 : 1

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1) For a general reference, see T. Nozoe, *et al.*, "Comprehensive Organic Chemistry", Vol. 13, Asakura Shoten, Tokyo (1960), p. 148.
2) E. Sebe and Y. Osako, *Proc. Japan Acad.*, **28**, 282 (1952).
3) E. Sebe and Y. Itsuno, *ibid.*, **29**, 110 (1953).
4) S. Itô, H. Takeshita, Y. Shoji, Y. Toyooka, and T. Nozoe, *Tetrahedron Lett.*, **1969** 3215.
5) S. Itô, A. Mori, Y. Shoji, and H. Takeshita, *ibid.*, **1972** 2685.
6) S. Itô, H. Takeshita, and Y. Shoji, *ibid.*, **1969** 1815.

Table 1. NMR parameters of the adducts, III—VI (Solvent: CCl_4)

Compounds	III	IV	V	VI
Positions of hydrogens	Chemical shifts (in δ)			
1	3.70	3.67		
3			5.80	5.83
4	7.10	7.15	6.88	7.05
5	3.58	3.47	3.22	3.42
6	6.52	6.53	6.50	6.50
7	6.05	6.19	5.92	6.03
8 *ex*	1.62	2.67		
8 *en*	2.95	1.72		
9 *ex*			2.73	1.87
9 *en*			1.77	2.39
Me	1.35	1.29	1.47	1.27
MeO	3.62	3.69	3.60	3.63
*J*s between	Coupling constants (in Hz)			
1—7	7.5	7.0		
1—8 *ex*	0	0		
1—8 *en*	7.7	7.0		
3—4			11.0	11.0
3—5			1.0	0.5
4—5	9.5	9.3	8.7	8.5
5—6	6.8	6.8	7.7	7.5
5—7	1.0	1.0	1.0	0.5
5—9 *ex*			1.0	0.5
5—9 *en*			5.0	4.7
6—7	8.7	9.0	8.5	9.0
6—9 *ex*			1.0	1.0
7—8 *ex*	0.5	0		
8 *ex*—8 *en*	14.5	14.3		
9 *ex*—9 *en*			13.3	13.5

adducts, III (19), IV (23), V (2), and VI (2.3%), were produced. The structures of these adducts were deduced by spectroscopic analyses. Thus, all the compounds have α,β-unsaturated carbonyl chromophore in IR and UV spectra showing them to be normal $_{\pi}4+_{\pi}2$ adducts, bicyclo[3.2.2]nona-3,6-dien-2-one derivatives. The presence of the absorption maximum around 260 nm for III and IV revealed them to be 3-chloro-derivatives,[7] and the absence of this particular absorption in the other two (V and VI) is therefore discernible as 1-chloro-derivatives. The methylene proton signals, in NMR spectra of all the four (III—VI) appears as AB patterns of ABX systems. Therefore, the methyl and methoxycarbonyl groups in V and VI can be located at C-8 position (Otherwise the signal should appear primarily as AB type). In order to confirm the poistion of these groups in III and IV the corresponding deuterio-derivatives were prepared using 2-chlorotropone-3,5,7-d_3 (I-d_3) and the major products, III-d_3 and IV-d_3, were isolated. The NMR signals of the methylene protons appeared as the AB type both in III-d_3 and IV-d_3, establishing the position of the substituents at C-9. The orientation of the substituents in III and IV was again deduced from the differences in chemical shifts of the methylene protons, which should suffer the magnetic anisotropy from the adjacent carbonyl group of the substituent. The *exo*-protons, having smaller coupling constants with bridge head protons and long-range couplings with one of olefinic protons in III and VI appeared in considerably higher field than those in IV and V, revealing the formers (III and VI) to have *exo*-methyl and *endo*-methoxycarbonyl groups and the latters (IV and V) the opposite orientations.

All of the adducts are the primary products of the reaction of I and II because each adduct was quantitatively recovered after being heated in the presence of II at 140 °C for 48 hr.

Table 2. Relative yield of Diels-Alder adducts of 2-chlorotropone

Dienophiles	Sites of the reaction[a]					
	[4,7]		[5,2]		[7,4]	
	exo	*endo*	*exo*	*endo*	*exo*	*endo*
II			4.3	5.0	49.7	41.0
Acrylonitrile	8.6	11.1	39.5			40.8

a) [*m*,*n*] denotes the positions of I which formed a bond between β- and α-positions of dienophiles, respectively.

Thus, the dienophile reacted rather regiospecifically but nonstereospecifically. As summarized in Table 2, this is quite a contrast with the reaction of I and acrylonitrile[6] which afforded the adducts with stereospecificity but without regiospecificity. In the present reaction, the polar effect due to electron-releasing chlorine atom and electron-withdrawal ester group appears to be reinforced with steric repulsion between chlorine and the substituents at α-carbon atom of II to exhibit the high regiospecificity. The lack of stereospecificity may come from the stabilization of transition state by the methyl group as well as the methoxycarbonyl group.[8,9]

Experimental

Reaction of 2-Chlorotropone (I) and Methyl Methacrylate (II). I (2 g) and II (9 ml) were heated at 135—140 °C for 48 hr in a sealed glass tubing. After the removal of the excess of II, the residual oil was distilled under reduced pressure to give faintly yellow liquid (1.95 g) which was chromatographed through silica gel (40 g) with chloroform–pet. ether (4: 1). From the least polar fractions, the adduct III was separated out as colorless crystals whose recrystallization from cyclohexane yielded colorless prisms, mp 98—99 °C (320 mg).

Found: C, 60.27; H, 5.59%. Calcd for $C_{12}H_{13}O_3Cl$: C, 59.88; H, 5.44%. λ_{max}^{MeOH} 241 (ε=6020), 262 (sh), 320 nm (ε=100). ν^{KBr}: 1738, 1685 cm^{-1} (C=O), 1632, 1598 cm^{-1} (C=C, strong). Following fractions yielded the adduct IV which was distilled on a cold finger to give colorless liquid, bp 130 °C/1.5 mmHg (bath temp.) (190 mg) with a distinct single spot on thin layer chromatograms. Found: C, 60.12;

7) S. Itô, H. Takeshita, Y. Shoji, Y. Toyooka, and T. Nozoe, *Tetrahedron Lett.*, **1969**, 443.

8) Y. Kobuke, T. Fueno, and J. Furukawa, *J. Amer. Chem. Soc.*, **92**, 6548 (1970).

9) However, there is an experiment which shows a contravention to this explanation. *cf.* K. N. Houk and L. J. Luskus, *ibid.*, **93**, 4606 (1971).

H, 5.63%. λ_{max}^{MeOH} 240.5 (ε=6000), 262 (sh), 323 nm (ε=100). ν^{liq}: 1735, 1685 cm^{-1} (C=O), 1631, 1598 cm^{-1} (C=C, strong). Subsequent fractions contained the adduct V and a few mg of recovered I which was removed by brief extraction with concd hydrochloric acid. Analytical specimen of V was obtained by cold finger distillation to give 76 mg of colorless liquid, bp 130 °C/1.5 mmHg (bath temp.). Found: C, 59.79; H, 5.75%. λ_{max}^{MeOH} 225 (ε=8050), 330 nm (ε=200), ν^{liq}: 1736, 1680 cm^{-1} (C=O), 1630, 1600 cm^{-1} (C=C, weak). The most polar fraction afforded the adduct VI (80 mg) as colorless plates, mp 110.5—112 °C (fr. cyclohexane). Found: C, 60.12; H, 5.74%. λ_{max}^{MeOH} 225 (ε=8000), 330 nm (ε=180). ν^{KBr}: 1735, 1680 cm^{-1} (C=O), 1630, 1598 cm^{-1} (C=C, weak). Repeated chromatography of intermediary fractions further afforded some amounts of the adducts, III to VI, but the absence of their isomer was confirmed by NMR spectral analysis of every fraction of the chromatography. Final yields of the products were estimated by NMR analysis as 19 (III), 23 (IV), 2 (V), and 2.3% (VI), respectively.

Reaction of 2-Chlorotropone-3,5,7-d_3*(I-*d_3*) and II.* I-d_3 (200 mg) and II (1 g) were heated in a sealed glass tubing at 135—145 °C for 60 hr. A similar work up with the above afforded III-d_3, mp 98—99 °C (20 mg) and IV-d_3, colorless liquid (30 mg). The other two compounds were not isolated.

Heating of the Adducts (III, IV, V, and VI) with II. Each adduct (10—20 mg) was mixed with II (1—2 ml) in a sealed tube and heated at 140±5 °C for 48 hr. After the evaporation of II, whole residue was analyzed by NMR spectral determination. Only the starting compound was shown to be presented in each reaction.