

829. *Unsaturated Systems. Part II.* The Reactivity of α -Chlorocrotonic and α -Chloro- β -methylcrotonic Acid.*

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The difference in reactivity between α -chloro- and α -bromo-crotonic acid towards methanolic sodium methoxide is held to be mainly due to the lower solubility of sodium α -chlorocrotonate in the reaction medium. The behaviour of α -chloro- β -methylcrotonic acid towards methanolic sodium methoxide and aqueous sodium hydroxide is similar to that of α -bromo- β -methylcrotonic acid.

α -BROMOCROTONIC ACID with methanolic sodium methoxide gives α -methoxycrotonic acid.¹ However, it was reported by Owen and Sultanbawa² that the chlorine atom of α -chlorocrotonic acid is replaced if alkali of sufficient concentration is used, in contrast to earlier observations.³ α -Chlorocrotonic acid in an excess of *ca.* 2.5*N*-methanolic sodium methoxide formed a heterogeneous mixture which after refluxing for 24 hours gave α -methoxycrotonic acid in 58% yield, together with a small amount of oil. The oil could have been formed by the addition of methanol to α -methoxycrotonic acid, and when this acid was heated with 2.5*N*-sodium methoxide for 22 hours and the product purified by means of alkaline permanganate a liquid was obtained which on analytical evidence (carbon and hydrogen) may have contained some $\alpha\beta$ -dimethoxybutyric acid (cf. refs. 1 and 4).

* The paper by Alles and Sultanbawa, *J.*, 1956, 3472, is considered as Part I of the series.

¹ Owen, *J.*, 1945, 385.

² Owen and Sultanbawa, *J.*, 1949, 3089.

³ Sarnow, *Annalen*, 1872, 164, 96; Kahlbaum, *Ber.*, 1879, 12, 2338; Friedrich, *Annalen*, 1883, 219, 322.

⁴ Owen and Somade, *J.*, 1947, 1030.

In its reactions with the higher alkoxides, α -chloro- was similar to α -bromo-crotonic acid, but only the addition products β -ethoxy-, β -isopropoxy-, and β -*tert.*-butoxy-crotonic acid¹ could be characterised.

The difference in reactivity of the chloro- and the bromo-crotonic acid was not directly determined as the chloro-acid gave a heterogeneous reaction medium. However, it was found that sodium α -bromocrotonate was nearly 1.4 times more soluble in methanol and nearly 4 times more soluble in methanolic 3.5N-sodium methoxide (the approximate concentration at the start of the reaction) than sodium α -chlorocrotonate. The solubility difference may, therefore, in our opinion, be an important factor (cf. α -chloro- β -methylcrotonic acid below) in the different reactivities.

To extend the study, α -chloro- β -methylcrotonic-acid was prepared by adding chlorine to β -methylcrotonic acid with sulphuryl chloride⁵ as all attempts to add chlorine directly failed (crotonic acid failed to react) and converting the $\alpha\beta$ -dichloro- β -methylbutyric into α -chloro- β -methylcrotonic acid by treatment with ethanolic sodium ethoxide (cf. ref. 2). This acid gave a homogeneous solution with *ca.* 4N-methanolic sodium methoxide. Its reactivity and that of the corresponding bromo-acid towards sodium methoxide are shown in Table I. The reaction rates—the net effect of prototropy and replacement at an allylic centre—are almost equal. That the mechanisms of the two reactions are similar was shown by the isolation in 80% yield of an unsaturated acid mixture, the light absorption of which showed that it contained only 19% of α -methoxy- β -methylcrotonic acid but which was converted in 77% yield into α -methoxy- β -methylcrotonic acid by hot aqueous *ca.* 5N-sodium hydroxide in 24 hours.

The reaction of the α -chloro- β -methylcrotonic acid with aqueous sodium hydroxide was shown quantitatively to be very similar to that of the bromo-acid² (see Table 2). In keeping with this the chloro-acid, on treatment with aqueous 2N-sodium hydroxide gave both β -methyl- α -oxobutyric and γ -hydroxy- β -methylcrotonic acid, the formation of the latter, as in the bromo-series, indicating the occurrence of anionotropy as well as of prototropy.

EXPERIMENTAL

$\alpha\beta$ -Dichlorobutyric acid⁶ was converted into α -chlorocrotonic acid,⁷ m. p. 99.5°, by means of pyridine.

Reaction of α -Chlorocrotonic Acid with Sodium Methoxide.—The heterogeneous mixture of the acid (6.0 g.), methanol (50 c.c.), and methanolic 5.2N-sodium methoxide (75 c.c.) was refluxed for 24 hr. (preliminary experiments showed 98% reaction). After removal of the solvent, the residue was dissolved in water, cooled, acidified with 6N-hydrochloric acid, and extracted with ether. The extracts were dried (CaCl₂) and evaporated. The semisolid residue (3.3 g., 58%) was filtered off and a few drops of a liquid, n_D^{20} 1.4275, were collected. The solid was α -methoxycrotonic acid, m. p. and mixed m. p. 58° [S-benzylthiuronium salt, m. p. 168—169° (from ethanol) (Found: C, 55.2; H, 6.5; N, 9.8. C₁₃H₁₈O₃N₂S requires C, 55.3; H, 6.8; N, 9.7%)].

Reaction of α -Methoxycrotonic Acid with Sodium Methoxide.— α -Methoxycrotonic acid (5 g.) was heated on a water-bath for 22 hr. with methanolic 2.5N-sodium methoxide (105 c.c.) and worked up as above, giving a pale yellow mobile liquid (4.3 g.), λ_{\max} 218 m μ (ϵ 4700) in ethanol, *i.e.*, containing *ca.* 50% of $\alpha\beta$ -unsaturated acid. By fractionation were separated (a) α -methoxycrotonic acid (1.9 g.), (b) a liquid (1.8 g.), b. p. 59—62°/0.35 mm., n_D^{20} 1.4250—1.4380, λ_{\max} 219 m μ (ϵ 3000—3400) in ethanol.

The liquid (1.8 g.) in dilute aqueous sodium carbonate was treated with 3% aqueous potassium permanganate (10 c.c.) at 5° with stirring during 15 min.; the precipitate was filtered off and washed with water, and the filtrate was cooled, acidified, and extracted with ether. On removal of the ether from the dried extracts (CaCl₂), a colourless liquid (0.8 g.) was obtained, having λ_{\max} 218 m μ (ϵ 350) (*ca.* 4% of $\alpha\beta$ -unsaturated acid). It was distilled into

⁵ Kharasch and Brown, *J. Amer. Chem. Soc.*, 1939, **61**, 3432.

⁶ Michael and Bunge, *Ber.*, 1908, **41**, 2910.

⁷ Pfeiffer, *Ber.*, 1910, **43**, 3041.

fractions: (1) b. p. 90—94°/9 mm., n_D^{29} 1.4180 (0.1 g.); (2) b. p. 94—98°/9 mm., n_D^{29} 1.4310 (0.3 g.) [Found for fraction (1): C, 49.9; H, 8.1. For fraction (2): C, 49.7; H, 7.65. Calc. for $C_5H_8O_3$ (α -methoxycrotonic acid): C, 51.7; H, 6.9. Calc. for $C_6H_{12}O_4$ ($\alpha\beta$ -dimethoxybutyric acid): C, 48.6; H, 8.2%].

Reaction of α -Chlorocrotonic Acid with Sodium Ethoxide.—The heterogeneous mixture of the acid (6.0 g.) and ethanolic 2.6N-sodium ethoxide (250 c.c.) was heated on the steam-bath for 23 hr. (preliminary experiments showed 96% reaction). The product was isolated as a dark brown viscous oil (2.2 g.) which deposited some β -ethoxycrotonic acid (0.12 g.), m. p. 140° (from aqueous methanol), at 0°. Attempts to isolate other products failed.

Reaction of α -Chlorocrotonic Acid with Potassium isoPropoxide.—The acid (3.6 g.) was heated with a solution of potassium (10 g.) in propan-2-ol (100 c.c.) on a steam-bath for 24 hr. and the product worked up as above. A methanolic extract of the dark brown semisolid product (0.2 g.) gave a few crystals of β -isopropoxycrotonic acid, m. p. 105—106°.

Solubility of Sodium α -Chlorocrotonate and α -Bromocrotonate.—(A) *Methanol.* (1) Sodium α -chlorocrotonate was refluxed with methanol for 5 min. and the amount of salt dissolved in 15 c.c. of the solution determined. The solubility was found to be 92.3 g./l. (0.648 equiv./l.). (2) The solubility of sodium α -bromocrotonate was similarly found to be 166.5 g./l. (0.890 equiv./l.).

(B) *Methanolic 3.5N-sodium methoxide.* (1) Sodium α -chlorocrotonate was refluxed with 3.5N-sodium methoxide for 5 min., the undissolved salt was allowed to precipitate, 10 c.c. of the hot supernatant liquid were removed and heated under reflux for 24 hr. and the halide ion produced was estimated volumetrically. The solubility was thus found to be 9.16 g./l. (0.064 equiv./l.).

(2) A similar experiment gave the solubility of sodium α -bromocrotonate as 49.65 g./l. (0.266 equiv./l.).

*Addition of Chlorine to β -Methylcrotonic Acid with Sulphuryl Chloride.*⁵—Freshly crystallised β -methylcrotonic acid (100 g.) and benzoyl peroxide (0.2 g.) in carbon tetrachloride (200 c.c.) were refluxed and sulphuryl chloride (90 c.c., ca. 8% excess) in carbon tetrachloride (100 c.c.) was added during an hour. On removal of the solvent after a further 6 hours' refluxing, a colourless viscous oil was obtained having b. p. 78—80°/0.033 mm., n_D^{29} 1.4660—1.4698 (148 g., 78%). Some of the fractions on storage deposited $\alpha\beta$ -dichloro- β -methylbutyric acid, which crystallised from light petroleum (b. p. 40—60°) as prisms, m. p. 48—49° (Found: C, 35.4; H, 4.7; Cl, 41.4. $C_5H_8O_2Cl_2$ requires C, 35.1; H, 4.7; Cl, 41.5%) [*S-benzylthiuronium salt*, needles (from aqueous alcohol), m. p. 120° (decomp.) (Found: N, 8.3. $C_{13}H_{18}O_2Cl_2N_2S$ requires N, 8.65%)].

Under the above conditions or with 50% excess of sulphuryl chloride or refluxing for 24 hr. addition of chlorine to crotonic acid could not be effected.

Preparation of α -Chloro- β -methylcrotonic Acid.—To a cooled solution of $\alpha\beta$ -dichloro- β -methylbutyric acid (35 g.) in ethanol (100 c.c.) was added, with stirring, 4N-sodium ethoxide (100 c.c.) in 15 min., the temperature being kept below 5°. The mixture was kept at 0° for 10 hr., then heated on a water-bath for 30 min., and the solvent was removed. The residue was dissolved in water and extracted with ether. The aqueous solution was then acidified and extracted with ether, and the extracts dried (Na_2SO_4) and evaporated. The residue (18.5 g., 68%) of α -chloro- β -methylcrotonic acid crystallised in needles (from water), 85—86° (lit.,⁸ m. p. 85—86°).

Comparison of the Reactivities of α -Chloro- β -methylcrotonic and α -Bromo- β -methylcrotonic Acid.—(a) α -Chloro- β -methylcrotonic acid (1.350 g.) was dissolved in methanol and the solution made up to 50 c.c. Portions (4 c.c.) of this solution were run into Pyrex test tubes containing methanolic 3.7N-sodium methoxide (2 c.c.). The tubes were sealed and kept in a boiling-water bath. At intervals, the tubes were removed and the cooled contents poured into water and acidified with 4N-nitric acid, and any unchanged chloro-acid was extracted with ether. The chloride ion in the aqueous solution was determined volumetrically (Volhard's method). The results are given in Table 1.

(b) A similar determination with α -bromo- β -methylcrotonic acid (1.80 g.) in methanol (50 c.c.) is also shown in Table 1.

Reaction of α -Chloro- β -methylcrotonic Acid with Sodium Methoxide.—The acid (3.5 g.) in methanol (50 c.c.) was refluxed with methanolic 4.3N-sodium methoxide (120 c.c.) for 10 hr.

⁸ Prentice, *Annalen*, 1896, **292**, 275.

The product (10.2 g., 80%), worked up as in the case of the bromo-acid,² had b. p. 51—54°/3.6 × 10⁻³ mm., n_D^{29} 1.4465—1.4520, λ_{\max} . 228 m μ (ϵ 1460—2320) in EtOH, *i.e.*, it contained about 19% of α -methoxy- β -methylcrotonic acid, the rest being the $\beta\gamma$ -unsaturated isomer.

The mixed acids (1.0 g.) were heated with aqueous 4.9N-sodium hydroxide (10 c.c.) for 24 hr. on the steam-bath and worked up as above. α -Methoxy- β -methylcrotonic acid (0.77 g.), m. p. and mixed m. p. 70.5°, was obtained.

TABLE I.

	α -Chloro- β -methylcrotonic acid.						α -Bromo- β -methylcrotonic acid.						
Time (hr.) ...	0.5	1.0	3.0	5.5	9.0	11.0	0.5	1.5	2.5	4.0	6.0	8.5	10.0
Reaction (%)	18.0	34.1	72.5	88.2	97.0	98.6	21.5	51.0	65.3	83.0	94.5	98.5	99.2

Action of Aqueous Sodium Hydroxide on α -Chloro- β -methylcrotonic Acid.—(1) The chloro-acid (1.35 g.) was made up to 50 c.c. with aqueous 1.017N-sodium hydroxide and heated under reflux on a steam-bath. At intervals, 5 c.c. portions were removed and titrated against 0.1000N-hydrochloric acid. The results are given in Table 2.

TABLE 2.

Time (hr.)	1	2	4	6	8	10	12	24
1.017N-NaOH								
Cl ⁻ liberated (%)	—	33	48	61	72	79	81	85
Keto-acid formed (%)	—	1	2.5	4	5.5	7.5	10	20
2.03N-NaOH								
Cl ⁻ liberated (%)	59	80	92	98	102	102	—	—
Keto-acid formed (%)	—	5	10.5	17.5	21	25	27.5	34

The solution from each titration was treated with excess of 1% 2 : 4-dinitrophenylhydrazine in 4N-sulphuric acid (40 c.c.). The precipitated 2 : 4-dinitrophenylhydrazone of γ -methyl- α -oxobutyric acid was filtered off, dried, and weighed. The results are given in Table 2.

(2) A similar experiment to (1) with the chloro-acid (1.35 g.) in aqueous 2.034N-sodium hydroxide (made up to 50 c.c.) is also in Table 2.

Reaction of α -Chloro- β -methylcrotonic Acid with Aqueous Sodium Hydroxide.—The acid (5.0 g.) in aqueous 2N-sodium hydroxide (125 c.c.) was heated on a steam-bath for 9 hr. and the product (3.35 g., 78%) was worked up as for the bromo-acid.² The product on distillation gave β -methyl- α -oxobutyric acid, b. p. 72—75°/18 mm., n_D^{29} 1.4145 (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 194°). From the residue, by distillation in a retort, two fractions were collected at bath-temperature 110—130°/3.6 × 10⁻³ mm.: (1) 0.18 g., n_D^{29} 1.4535; (2) 0.55 g., n_D^{29} 1.4715. In the trap γ -methyl- α -oxobutyric acid (0.75 g.) was also collected. Fraction (2) at 0° deposited a small amount of γ -hydroxy- β -methylcrotonic acid, m. p. and mixed m. p. 112—113° (hot stage).

The authors thank Professor E. L. Fonseka for his interest and encouragement. One of them (M. U. S. S.) thanks the Council of the University of Ceylon for a research grant. Analyses were carried out by Dr. K. W. Zimmermann of the Australian Microanalytical Service.