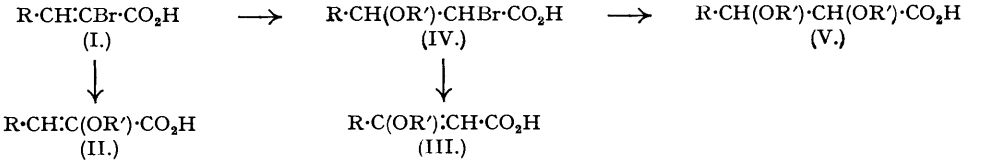
57. *Olefinic Acids. Part III.* iso*Propylidene*–iso*Propenyl Isomerisation in the Reaction of α-Bromo-ββ-dimethylacrylic Acid with Alkoxides.*

By L. N. Owen.

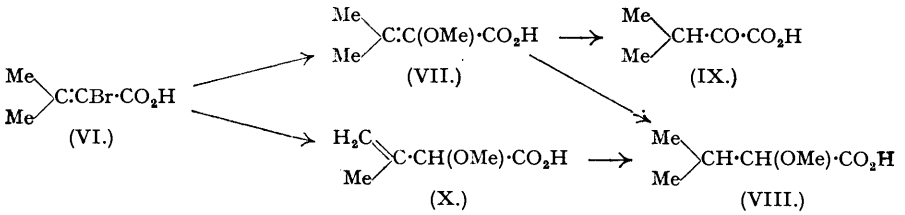
With methanolic alkali, α-bromo-ββ-dimethylacrylic acid gives mainly *α-methoxy-β-methylenebutyric acid* (X), together with a small amount of *α-methoxy-ββ-dimethylacrylic acid* (VII); similarly, with sodium ethoxide the corresponding *ethoxy*-derivatives are obtained. *α-Methoxy-* and *α-ethoxy*-iso*valeric acids* are formed by hydrogenation of these products. There is no evidence of any addition of alkoxide to the double bond.

In Part I (Owen, *J.*, **1945**, 385; cf. Pfister, Robinson, and Tishler, *J. Amer. Chem. Soc.*, **1945**, **67**, 2269) it was shown that by treatment with the appropriate alkoxide the halogen atom in α-bromocrotonic acid (I; R = Me) could be replaced by an alkoxy-group to give the α-alkoxycrotonic acid (II; R = Me). The β-alkoxy-compound (III; R = Me) was also formed, probably through the intermediate α-bromo-β-alkoxybutyric acid (IV; R = Me); the proportion of this isomer increased as the higher alkoxides were used, indicating that the addition of alkoxide to the double bond is less affected by increasing size of the entering group than is the substitution reaction. In Part II (Owen and Somade, *J.*, **1947**, 1030), similar reactions were carried out on α-bromoacrylic acid (I; R = H), and were shown to give the β-alkoxy-derivatives (III; R = H), together with the αβ-dialkoxypropionic acid (V; R = H), both formed through the intermediate α-bromo-β-alkoxypropionic acid (IV; R = H); the

α-alkoxy-compounds (II; R = H) were not encountered, because the much greater reactivity of the double bond in the acrylic series resulted in addition, rather than direct substitution of the halogen atom.



These experiments have now been extended to α-bromo-ββ-dimethylacrylic acid (VI), since the presence of the additional methyl group in the β-position was expected to reduce the tendency towards addition at the double bond. The formation of α-bromo-β-alkoxy- or αβ-dialkoxy-*iso*valeric acids was thus unlikely (no β-alkoxy-olefinic acid, is, of course, possible), and it was thought that the product would be the α-alkoxy-ββ-dimethylacrylic acid. When the bromo-acid was refluxed with potassium hydroxide in methanol, an unsaturated oil was formed, analysis of which suggested that it was the expected α-methoxy-compound (VII). This was

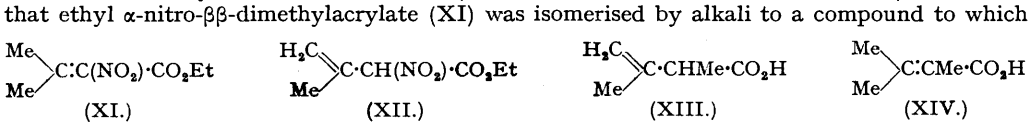


supported by the observation that on hydrogenation it took up the theoretical amount of hydrogen to give α-*methoxy*iso*valeric* acid (VIII) (p-*phenylphenacyl* ester), identical with a sample synthesised from α-bromo*iso*valeric acid. Its light absorption, however, was anomalous; although it showed the expected maximum, at 2290 A., the intensity (ε 3500) was low. Furthermore, when it was warmed with dilute sulphuric acid only a small yield of α-keto*iso*valeric acid (IX) was obtained, most of the material being recovered unchanged, and unaffected by further treatment with dilute sulphuric acid; it then showed no light absorption in the ultra-violet.

The most likely explanation of these observations appeared to be that the product consisted largely of α-methoxy-β-methylenebutyric acid (X), which, although giving the same hydrogenation product (VIII), would differ from the αβ-unsaturated isomer (VII) in showing no absorption band at 2290 A., and being stable to acid hydrolysis. This was readily confirmed by the production of formaldehyde on ozonolysis. After being kept for several weeks, the remainder of the original reaction product deposited a small amount of crystalline material; this proved to be the pure αβ-isomer, *α-methoxy-ββ-dimethylacrylic acid* (VII), m. p. 70°, which showed normal light absorption ($\lambda_{max.}$ 2290 A., ε 10,000) and gave α-keto*iso*valeric acid (IX) with dilute sulphuric acid.

Similar results were obtained when α-bromo-ββ-dimethylacrylic acid was treated with sodium ethoxide. The unsaturated product, which on hydrogenation gave *α-ethoxy*iso*valeric acid*, was again a mixture. It deposited a small amount of *α-ethoxy-ββ-dimethylacrylic acid*, but consisted mainly of *α-ethoxy-β-methylenebutyric acid*, which was purified by treatment with dilute sulphuric acid.

The only published instance of isomeric change in a simple α-substituted ββ-dimethylacrylic acid is recorded by Bouveault and Wahl (*Bull. Soc. chim.*, 1901, **25**, 801, 814, 918) who found that ethyl α-nitro-ββ-dimethylacrylate (XI) was isomerised by alkali to a compound to which



they assigned the formula (XII). One example is also known of the reverse change; Kon and Speight (*J.*, 1926, 2727) observed that the acid (XIII) on being heated with alkali was largely converted into the αβ-unsaturated isomer (XIV).

In their extended studies of the equilibria of αβ- and βγ-unsaturated acids, Kon and Linstead (*J.*, 1925, **127**, 616) have shown that ββ-dimethylacrylic acid cannot be isomerised by alkali

into β-methylenebutyric acid, and the isomerisation to the βγ-form now observed in the reactions of α-bromo-ββ-dimethylacrylic acid with alkoxides appears at first sight to indicate that an alkoxy-group in the α-position facilitates the αβ ⟶ βγ transformation; alternatively, however, the isomerisation may occur within the bromo-acid, before substitution takes place. The yields of crystalline α-methoxy- and α-ethoxy-ββ-dimethylacrylic acids were unfortunately too small for a satisfactory investigation to be made of their behaviour towards alkali, but it may be possible later to present further experimental evidence, and to discuss the mechanism of the isomerisation in more detail.

Murfitt and Roberts (*J.*, 1944, 371), by the action of dimethylamine or piperidine on ethyl α-bromo-ββ-dimethylacrylate, have obtained products which they describe as ethyl α-dimethylamino- and ethyl α-piperidino-ββ-dimethylacrylate, respectively, although the structures were not proved. It is possible, in view of the present results, that these compounds were actually the βγ-unsaturated isomers.

Experimental.

α-Bromo-ββ-dimethylacrylic acid was prepared from ββ-dimethylacrylic acid, *via* αβ-dibromo*iso*valeric acid, by the method of Staudinger and Ott (*Ber.*, 1911, **44**, 1635).

Action of Methanolic Potassium Hydroxide on α-Bromo-ββ-dimethylacrylic Acid.—The acid (18 g.), dissolved in methanol (10 c.c.), was treated with potassium hydroxide in methanol (70 c.c., 3·76N) and refluxed for 12 hours. The solution was then neutralised to phenolphthalein with aqueous N-hydrochloric acid, concentrated under reduced pressure to remove the alcohol, and finally acidified at 0° with concentrated hydrochloric acid (10 c.c.) and rapidly extracted with ether. Evaporation of the dried ($CaCl_2$) extracts, followed by distillation of the residue, gave an unsaturated oil (8·4 g.), b. p. 114—116°/15 mm., $n_D^{18°}$ 1·4520; light absorption : $\lambda_{max.}$ 2290 A., ϵ 3500 (Found : equiv., 130·5. Calc. for $C_6H_{10}O_3$: equiv., 130·1).

Hydrogenation. A portion (2·0 g.) of the oil, in water (30 c.c.), was shaken with hydrogen at ordinary temperature and pressure in the presence of a 10% palladium–charcoal catalyst (0·3 g.). Absorption of hydrogen (0·96 mol.) was complete after 5 hours, and the product on distillation furnished α-*methoxy*isovaleric acid (1·3 g.), b. p. 104°/16 mm., $n_D^{15°}$ 1·4290 (Found : C, 54·5; H, 9·3. $C_6H_{12}O_3$ requires C, 54·5; H, 9·2%), which gave a p-*phenylphenacyl* ester, crystallising from ethanol in plates (Found : C, 73·3; H, 6·6. $C_{20}H_{22}O_4$ requires C, 73·6; H, 6·8%). This derivative had an initial m. p. 58°, but immediately after re-solidification it had m. p. 63°; after standing for a few hours, however, the original m. p. 58° was again shown. This cycle could be repeated several times with the same melting-point specimen. The derivative of the synthetic acid (see below) behaved in the same way.

Acid hydrolysis. Another portion (2·2 g.) of the oil, in 2N-sulphuric acid (3 c.c.), was heated on the steam-bath for 8 hours. The solution was extracted thrice with ether, and the extracts were washed once with water and then dried ($CaCl_2$) and distilled to give (i) 0·1 g., b. p. 75—115°/15 mm., $n_D^{15°}$ 1·4340; and (ii) 1·7 g., b. p. 115—116°/15 mm., $n_D^{15°}$ 1·4500. Fraction (i) was mainly α-keto*iso*valeric acid; it gave the 2 : 4-dinitrophenylhydrazone, yellow needles from methanol, m. p. 194° (lit. 195°) (Found : C, 45·0; H, 4·1. Calc. for $C_{11}H_{12}O_6N_4$: C, 44·6; H, 4·1%). Fraction (ii) was α-*methoxy-β-methylenebutyric acid*, which showed no light-absorption maximum in the ultra-violet and was recovered unchanged (b. p. 113°/15 mm., $n_D^{15°}$ 1·4502) after further treatment with 2N-sulphuric acid (Found : C, 55·3; H, 7·7. $C_6H_{10}O_3$ requires C, 55·35; H, 7·75%); it gave a p-*phenylphenacyl* ester, needles from methanol, m. p. 61° (Found : C, 74·0; H, 6·2. $C_{20}H_{20}O_4$ requires C, 74·0; H, 6·2%).

Ozonisation. A third portion (1·0 g.) of the oil was ozonised in carbon tetrachloride (15 c.c.), the issuing gases being passed through water. After completion of the reaction (2 hours), addition of dimedon reagent to the wash water gave a copious precipitate of the formaldehyde derivative, m. p. 190°. Removal of the carbon tetrachloride gave an oily residue which evolved more formaldehyde on being boiled with water; evaporation of this solution to dryness gave a small residue (30 mg.) of oxalic acid, indicating the presence of the αβ-isomer in the original oil.

*Synthesis of α-Methoxy*isovaleric *Acid.*—α-Bromo*iso*valeric acid (2·5 g.) was refluxed with 3N-methanolic sodium methoxide (20 c.c.) for 6 hours. Water (40 c.c.) was then added, the alcohol distilled off under reduced pressure, and the solution strongly acidified with hydrochloric acid. Ether extraction gave a semi-solid product, from which ββ-dimethylacrylic acid (1·2 g.), m. p. and mixed m. p. 70°, was separated. The oily residue was then freed from any remaining unsaturated acid by treatment in sodium carbonate solution at 10° with excess of 2% potassium permanganate solution. After the solution had been cleared with sulphur dioxide, it was made alkaline with sodium carbonate, concentrated to small bulk, acidified with sulphuric acid, and extracted with ether to give α-methoxy*iso*valeric acid (0·35 g.), b. p. 100°/12 mm., $n_D^{20°}$ 1·4240, the *p*-phenylphenacyl ester of which showed the same two m. p.s, 58° and 63°, referred to above, unchanged on admixture with the previous derivative.

α-Methoxy-ββ-dimethylacrylic Acid.—The remainder of the original reaction product from α-bromo-ββ-dimethylacrylic acid and methanolic alkali was found, after 3 weeks, to contain a small amount of solid. This *α-methoxy-ββ-dimethylacrylic acid* was collected and dried on porous tile; it recrystallised from light petroleum (b. p. 60—80°) in long needles (0·4 g.), m. p. 70° (Found : C, 55·35; H, 7·7. $C_6H_{10}O_3$ requires C, 55·35; H, 7·75%). Light absorption : $\lambda_{max.}$ 2290 A., ϵ 10,000. On treatment with 2 : 4-dinitrophenylhydrazine in dilute sulphuric acid it gave the 2 : 4-dinitrophenylhydrazone of α-keto*iso*valeric acid, m. p. and mixed m. p. 197°.

Action of Sodium Ethoxide on α-Bromo-ββ-dimethylacrylic Acid.—The acid (18 g.) was refluxed with 2·5N-ethanolic sodium ethoxide (120 c.c.) for 12 hours and then worked up as for the methoxy-compound. The unsaturated product (10·5 g.) had b. p. 114°/14 mm., $n_D^{18°}$ 1·4462 (Found : equiv., 144·4. Calc. for $C_7H_{12}O_3$: equiv., 144·1).

Hydrogenation. A portion (2 g.) of the oil was hydrogenated in water (30 c.c.) in the presence of a

10% palladium–charcoal catalyst (0·3 g.). Absorption of hydrogen (1·01 mol.) ceased after 4 hours, and the resulting *α-ethoxyisovaleric* acid (1·2 g.) had b. p. 108—109°/16 mm., $n_D^{15°}$ 1·4255 (Found: C, 57·2; H, 9·6. $C_7H_{14}O_3$ requires C, 57·5; H, 9·7%). It gave a p-*phenylphenacyl* ester, crystallising from aqueous ethanol in leaflets, m. p. 73° (Found: C, 73·7; H, 6·9. $C_{21}H_{24}O_4$ requires C, 74·1; H, 7·1%).

Acid hydrolysis. A second portion of the oil (2 g.) was treated with 2N-sulphuric acid (3 c.c.) under the same conditions as for the methoxy-compounds. Distillation of the product gave a first fraction (0·3 g.), b. p. 70—120°/15 mm., $n_D^{20°}$ 1·4305, consisting mainly of α-keto*iso*valeric acid (2 : 4-dinitrophenylhydrazone, m. p. 196°); the main fraction (1·4 g.) consisted of *α-ethoxy-β-methylenebutyric acid*, b. p. 120°/15 mm., $n_D^{20°}$ 1·4470 (Found: C, 57·9; H, 8·5. $C_7H_{12}O_3$ requires C, 58·3; H, 8·4%).

α-Ethoxy-ββ-dimethylacrylic Acid.—On standing, the remainder of the oil deposited a solid, which on crystallisation from water gave needles of *α-ethoxy-ββ-dimethylacrylic acid* (0·3 g.), m. p. 55° (Found: C, 57·9; H, 8·2. $C_7H_{12}O_3$ requires C, 58·3; H, 8·4%). Light absorption: $\lambda_{max.}$ 2280 A., ϵ 12,400. With 2 : 4-dinitrophenylhydrazine in dilute sulphuric acid it gave the 2 : 4-dinitrophenylhydrazone of α-keto*iso*valeric acid, m. p. 196°.

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IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W. 7.

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