

Studies on the Kolbe Electrolysis

X.¹ Generation of Optically Active Radicals from Monoethyl (+)-Ethylmethylmalonate and Their Fate in a Mixed Coupling Reaction

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The mixed Kolbe coupling of monoethyl (+)-ethylmethylmalonate and isovaleric acid at a platinum anode in methanol has been found to give a product which is racemized to an extent of at least 99.98 %.

The problem of free *vs.* adsorbed radicals, $R\cdot$, as intermediates in the Kolbe electrochemical oxidation of carboxylates, $RCOO^-$, has been under lively discussion during recent years.²⁻⁵ The overwhelming part of the evidence from electrochemical studies seems to indicate that formation of the coupling product, $R-R$, takes place *via* adsorbed radicals;⁵ on the other hand, there is no real need for this postulate in order to account for the product distributions observed.^{4,6,7} In particular, it has been suggested⁴ that the formation of racemized coupling products from the anodic oxidation of optically active carboxylates having an asymmetric α carbon atom^{8,9} must be due to the intervention of free radicals, since a mechanism involving adsorbed radicals would be expected to give coupling products with at least partial retention of configuration. On the other hand, it has been claimed that the microscopic roughness of the anode surface might as well provide the necessary racemization mechanism.⁵

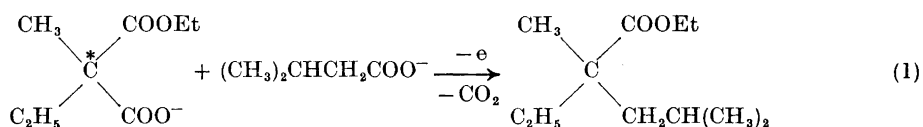
While the nature of the racemization step must still be a matter for speculation, the stereochemical studies referred to above^{8,9} are not entirely satisfactory for the distinction between different mechanisms. Even a small degree of retention of configuration in the coupling product would constitute significant evidence in favor of the postulate of adsorbed radicals as intermediates, and hence it is important to know the exact extent of racemization. The two studies reported^{8,9} do not give exact data on this point, and we there-

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fore decided to undertake a study of a more suitable system. This paper is a report of the stereochemistry of the mixed Kolbe coupling of a mixture of monoethyl (+)-ethylmethylmalonate and isovaleric acid. The mixed coupling product, ethyl ethylisobutylmethylacetate, is racemic to an extent of 99.98 %.

RESULTS AND DISCUSSION

The system studied, mixed coupling between monoethyl ethylmethylmalonate and isovaleric acid (eqn. 1), was chosen because of the relatively good yields of coupling product that are obtained in mixed couplings of



substituted malonates and alkanolic acids¹⁰ and the fact that the optical properties of the product are well known.¹¹ It is especially important to note that ethylisobutylmethylacetic acid has a relatively high specific rotation allowing for a high precision in measuring the degree of racemization. For the same reason, a mixed coupling process was preferred in order to avoid dilution by the *meso* isomer that always accompanies the *dl* isomer in a symmetrical coupling process.^{12,13}

Monoethyl ethylmethylmalonate was completely resolved,¹⁴ and then electrolyzed together with isovaleric acid in a 1 : 3 ratio in methanolic solution at a platinum anode, the acid mixture being neutralized with potassium hydroxide to an extent of 1 %. The reaction mixture was worked up as described previously,¹⁰ giving 99 % pure (GLC) ethyl ethylisobutylmethylacetate in 23 % yield. After preparative GLC to remove the last traces of impurities, $[\alpha]_{589}^{25}$ of a neat sample was $0.004 = 0.002^\circ$, showing that racemization had taken place to an extent of at least 99.98 %. A sample of ethyl ethylisobutylmethylacetate of 62.7 % optical activity ($[\alpha]_{589}^{25} \pm 13.44^\circ$; neat) was prepared from the optically active acid¹² by treatment of its chloride with ethanol and used as a reference compound.

Thus, in the above coupling process racemization takes place to a very high extent, indicating that a very efficient racemization step must be included in the mechanism. At present, we do not wish to discuss the nature of this step in any length, but it is obvious that a mechanism involving discharge of adsorbed carboxylate ions with formation of free radicals, as previously suggested,^{2,4} provides a satisfactory racemization process. This is, however, in conflict with results from electrochemical studies⁵ showing that adsorbed radicals must be involved. Recent studies¹⁵ on the competition between 2e-(acetamidation) and 1e-oxidation (coupling) of carboxylates at the carbon anode in acetonitrile as a function of the chain-length of the carboxylate indicate that readsorption of initially formed free radicals might play an important role. For short-chain carboxylates, readsorption of radicals is favored (and leads to further oxidation to carbonium ions in the particular case of carbon anodes), whereas for long-chain radicals a stacking or layering effect prevents

the radicals from diffusing toward the anode surface, coupling thus becoming the favored process. Similar conclusions were reached in a study of the competition between 2e- (methoxylation) and 1e-oxidation (coupling) in the electrolysis of phenylacetate ions.¹⁶

EXPERIMENTAL

Resolution of monoethyl ethylmethylmalonate. This resolution was made according to the procedure described by Kenyon and Ross,¹⁴ $[\alpha]_{589}^{22}$ (Perkin-Elmer 141 polarimeter) for the completely resolved compound being $+3.38^\circ$ ($c=9.3$, chloroform); reported¹⁴ $[\alpha]_{589}^{18}=3.38^\circ$ ($c=15.0$, chloroform).

(+)-*Ethylisobutylmethylacetic acid.* The acid was prepared as described previously¹⁰ and was partially resolved by recrystallization of its brucine salt.¹¹ The distilled optically active acid had $[\alpha]_{589}^{24}=+13.44^\circ$ ($c=9.5$, 95% ethanol), corresponding to a degree of resolution of 62.7%.¹¹

Ethyl (+)-ethylisobutylmethylacetate. Optically active ethylisobutylmethylacetic acid (2.0 g) from above was treated with thionyl chloride (5 ml) in ether (5 ml) overnight at room temperature and then the solution was refluxed for 3 h. After evaporation of the volatile components, the residue was refluxed with absolute ethanol (5 ml) for 48 h, whereafter the ethanol was distilled off. Distillation then gave the ethyl ester (2.0 g), b.p. 75–76°/11 mm. The last traces of impurities were removed by preparative GLC on a 9 mm × 4 m Apiezon L column at 150° (Autoprep gas chromatograph), $[\alpha]_{589}^{25}=13.44^\circ$ (neat).

Mixed coupling of monoethyl (+)-ethylmethylmalonate and isovaleric acid. This reaction was carried out as described previously,^{10,12} with fully resolved monoethyl (+)-ethylmethylmalonate (12.0 g) and isovaleric acid (21.3 g), partly neutralized with potassium hydroxide (0.16 g), in methanol (200 ml). The product was distilled and a fraction (3.5 g) with b.p. 79–80°/15 mm was collected. After preparative GLC on the same column as above the sample showed $[\alpha]_{589}^{25}=0.004 \pm 0.002^\circ$ (neat).

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