ANODIC SYNTHESES WITH CARBOXYLIC ACIDS

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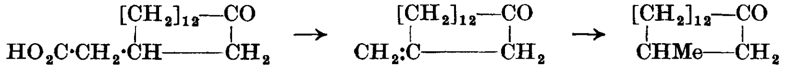
ALTHOUGH the formation of hydrocarbons on electrolysis of acetate solutions was reported by M. Faraday [1] in 1834, the classical work of H. Kolbe, started about 15 years later,[2] constitutes the first detailed study of the anodic reactions of carboxylic acids ; he showed that on electrolysis of an aqueous solution of an alkali-metal carboxylate (I), carbon dioxide and a hydrocarbon (II) are formed :

$$\text{(I)}\quad 2C_nH_{2n+1}\cdot CO_2' \xrightarrow{-2\varepsilon} 2CO_2 + C_{2n}\cdot H_{4n+2}\quad \text{(II)}$$

This reaction, known by the name of its discoverer, has since been the subject of extensive investigations and has been found to constitute a valuable, and remarkably simple, method for the synthesis of many organic compounds. Other anodic reactions of carboxylic acids have received comparatively little attention and accordingly it is with coupling reactions of the Kolbe type that this review is mainly concerned.

The Kolbe reaction is known to be accompanied by a number of side reactions, the extent to which these occur being governed both by the experimental conditions and by the structure of the acid itself.

Experimental Factors and Techniques.—Detailed studies have been made of the optimum conditions for the formation of ethane from acetic acid,[3] and there is little doubt that the conclusions drawn from these investigations are equally applicable to most other examples of the Kolbe reaction. For electrolyses in aqueous solutions the nature of the anode is of great importance, coupling occurring to an appreciable extent only with a smooth platinum (or iridium) anode. The Kolbe reaction is also favoured by using a high anode current density ($> 0{\cdot}25$ amp./cm.^{2}), an acid medium kept at a low temperature ($< 50°$), and a high concentration ($>$ N) of alkali carboxylate. Low anode current densities promote the formation of olefins, C_nH_{2n}, and paraffins, C_nH_{2n+2},[4] possessing only half the carbon atoms of the Kolbe product. Electrolysis (in methanol) at low current density, followed by hydrogenation of the resulting mixture, has in fact been utilised to convert an acetic acid side chain ($\cdot CH_2\cdot CO_2H$) into a methyl group in, *e.g.*, a synthesis of ($\pm$)-muscone [5] (III) :



(III)

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[1] *Pogg. Ann.*, 1834, **33**, 438.

[2] *Annalen*, 1849, **69**, 257.

[3] For references, see S. Glasstone and A. Hickling, *Trans. Electrochem. Soc.*, 1939, **75**, 333 ; A. Hickling, *Quart. Reviews*, 1949, **3**, 121.

[4] S. N. Shukla and O. J. Walker, *Trans. Faraday Soc.*, 1931, **27**, 35.

[5] L. Ruzicka and M. Stoll, *Helv. Chim. Acta*, 1934, **17**, 1308.

Another side reaction frequently encountered is the formation of alcohols, $C_nH_{2n+1}\cdot OH$.[6, 7] This is usually referred to as the Hofer–Moest reaction, and is favoured by the use of alkaline solutions and by the addition of various inorganic salts, in particular perchlorates, sulphates, and bicarbonates, to the electrolyte. Under suitable conditions high yields (70%) of methanol can be isolated from the electrolysis of acetic acid, but much lower yields are obtained with longer-chain acids.[6] Little is known about the formation of alcohols in the electrolysis of carboxylic acids, although it has been shown that the reaction can involve attack at positions α, β, and even γ to the eliminated carboxyl group.[8, 9] Other by-products which have been reported include esters [2, 10] of the starting acid with the alcohol(s) $C_nH_{2n+1}\cdot OH$, and ketones by anodic oxidation of the latter.

The use of various non-aqueous solvents for the Kolbe reaction has been examined. Electrolyses of solutions of fatty acid salts in the corresponding anhydrous fatty acids yield results which are qualitatively similar to those obtained with aqueous solutions.[11] Of the non-aqueous solvents, methanol is especially suitable, the yields of coupled products being usually higher, and the conditions for optimum yields less critical, than in aqueous media. Thus the nature of the anode, and variations of current density, concentration, and temperature have relatively little effect on the yield of coupled materials.[3, 12] For these reasons methanolic solutions have been employed in most synthetical applications of the Kolbe reaction of recent years. In practice, it is found that the addition of traces of water to the electrolyte improves the conductivity without causing any appreciable diminution in yield of the Kolbe product.

Electrolysis of fused acetates of alkali and alkaline-earth metals gives methane and ethane.[13]

Much ingenuity has been displayed in the design of cells for carrying out electrolytic reactions. Diaphragms, to enable the anodic and cathodic products to be collected separately, rotating anodes, flowing-mercury cathodes, and other devices all have their special uses. It is, however, not generally appreciated that for normal synthetical purposes a very simple apparatus is quite sufficient. Electrolyses, including those in methanol, can conveniently be conducted in beakers [14] or large boiling-tubes,[15] two

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[6] H. Hofer and M. Moest, *Annalen*, 1902, **323**, 285 ; F. Fichter and W. Siegrist, *Helv. Chim. Acta*, 1932, **15**, 698.

[7] S. Glasstone and A. Hickling, *J.*, 1934, 1878.

[8] F. Fichter and A. Bürgin, *Helv. Chim. Acta*, 1931, **14**, 90 ; F. Fichter and F. Metz, *ibid.*, 1936, **19**, 880 ; F. Fichter and R. Ruegg, *ibid.*, 1937, **20**, 1578 ; F. Fichter and O. Leupin, *ibid.*, 1938, **21**, 616.

[9] A. Kruis and W. Schanzer, *Z. physikal. Chem.*, 1942, **191**, *A*, 301.

[10] J. Petersen, *ibid.*, 1900, **33**, 116.

[11] K. Hopfgartner, *Monatsh.*, 1911, **32**, 523.

[12] J. Salauze, *Bull. Soc. chim.*, 1925, **37**, 522.

[13] E. Berl, *Ber.*, 1904, **37**, 325 ; J. Petersen, *Z. Elektrochem.*, 1914, **20**, 328 ; G. B. Moorhouse, *Trans. Faraday Soc.*, 1932, **28**, 766.

[14] L. Ruzicka, M. Stoll, and H. Schinz, *Helv. Chim. Acta*, 1928, **11**, 1174.

[15] W. S. Greaves, R. P. Linstead, B. R. Shephard, S. L. S. Thomas, and B. C. L. Weedon, *J.*, 1950, 3326.

parallel pieces of platinum foil being used as electrodes. By a suitable modification in apparatus, comparatively large runs can be handled on the laboratory scale, involving batches of a total of 200—300 g. of reagents,[15] and a semitechnical apparatus has been developed [16] for continuous electrolysis.

Influence of Structure on Anodic Behaviour

Following Kolbe's synthesis of hydrocarbons from simple fatty acids, electrolyses of a wide range of carboxylic acids were examined, primarily to determine the scope of the anodic coupling reaction. It soon became apparent that the extent to which coupling occurs is determined, not only by the experimental factors summarised above, but also, to a marked degree, by the structure of the acid electrolysed. The account given below is not intended to be complete, but merely to furnish a broad outline of the variation of anodic behaviour with structure of carboxylic acids. Unless stated otherwise, the results quoted relate to electrolyses of the sodium or potassium salts of the carboxylic acids, usually in the presence of the free acid. For detailed information on the products of electrolysis of individual acids the reader is referred to earlier reviews and bibliographies of the subject.[17-19]

Straight-chain Fatty Acids.—Good yields of Kolbe products are obtained on electrolysis of fatty acids possessing six or more carbon atoms (Table 1). The lower members of the series, with the exception of acetic acid, give rather poorer yields and larger amounts of olefins, esters, and other by-

TABLE 1. *Kolbe reaction with straight-chain fatty acids,* $CH_3\cdot[CH_2]_n\cdot CO_2H$

n	Solvent	Yield (%)	Ref.	n	Solvent	Yield (%)	Ref.
0	H_2O	90*	20	14	H_2O–EtOH	89	23
,,	MeOH	93*	20	,,	,,	60	24
1	H_2O	40	19	16	,,	88	23
2	,,	60	21	,,	,,	60	24
4	,,	89	22	18	,,	73	23
10	H_2O–EtOH	90	23				

* Current yield.

[16] B.I.O.S. Final Report No. 1472, Item No. 22, p. 13; C.I.O.S. XXXIII—50, p. 728.

[17] C. J. Brockman, "Electro-Organic Chemistry", New York, 1926.

[18] S. Swann, *Trans. Electrochem. Soc.*, 1936, **69**, 289, 339; 1940, **77**, 460; 1945, **88**, 104.

[19] F. Fichter, "Organische Elektrochemie," Dresden and Leipzig, 1942.

[20] F. Fichter and R. E. Meyer, *Helv. Chim. Acta*, 1933, **16**, 1408.

[21] E. Denina, *Gazzetta*, 1938, **68**, 443.

[22] J. Petersen, *Z. physikal. Chem.*, 1900, **33**, 294.

[23] *Idem*, *Z. Elektrochem.*, 1906, **12**, 141.

[24] A. W. Schmidt, V. Schoeller, and K. Eberlein, *Ber.*, 1941, **74**, 1313.

products. These side reactions can, however, be suppressed to an appreciable extent by using high concentrations of the alkali carboxylates.

Owing to the occurrence of side reactions and the evolution of oxygen, the current efficiencies of the Kolbe reaction are sometimes rather low. The proportion of the total current used in various anodic processes on electrolysis in aqueous solutions of a series of acids under comparable conditions is given in Table 2.[17]

TABLE 2. *Current efficiencies of anodic reactions of fatty acids,* $CH_3\cdot[CH_2]_n\cdot CO_2H$

n	Percentage of current used in formation of:			n	Percentage of current used in formation of:		
	Kolbe product	Olefin	Ester		Kolbe product	Olefin	Ester
0	85	2*	2	10	45	—	—
1	8	66	5	12	33·7	—	—
2	14·5	53	10	14	30	—	—
3	50	18	4	16	27·6	—	—
6	75	7	1·5				

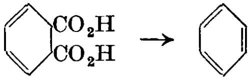
* Ethylene.

Dibasic Acids and Half Esters.—Dibasic acids (from malonic to sebacic) do not undergo reactions of the Kolbe type at the anode. The products formed include olefins and alcohols, containing two carbon atoms less than the starting material, and both saturated and unsaturated acids by loss of only one carbon atom.[25] All attempts to isolate *cyclo*alkanes have been unsuccessful. Even with $\beta\beta$-dimethylglutaric acid (IV) electrolysis leads to 2-methylbutene (V), with rearrangement of the carbon chain, and not to dimethyl*cyclo*propane or tetramethyl*cyclo*hexane:[26]

$$\underset{(IV)}{HO_2C\cdot CH_2\cdot CMe_2\cdot CH_2\cdot CO_2H} \longrightarrow \underset{(V)}{CH_2{:}CMe\cdot CH_2\cdot CH_3}$$

A special example of olefin formation on electrolysis of a diacid is the preparation of benzene (70% yield) from *trans*-1 : 2-dihydrophthalic acid (VI):[27]

(VI)



In contrast to the aliphatic dicarboxylic acids themselves, the corresponding half esters (VII) readily undergo the Kolbe reaction, giving high yields of the diesters (VIII) (see Table 3):[28]

$$(VII)\quad RO_2C\cdot[CH_2]_n\cdot CO_2H \longrightarrow RO_2C\cdot[CH_2]_{2n}\cdot CO_2R\quad (VIII)$$

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[25] B. L. Vanzetti, *Atti R. Accad. Lincei*, 1898, **17,** 331; 1904, **13,** 112; 1906, **15,** 574; 1907, **16,** 79, 139.

[26] J. Walker and J. K. Wood, *J.*, 1906, **89,** 598.

[27] E. A. Pasquinelli, *Anal. Asoc. Quim. Argentina*, 1943, **31,** 181.

[28] A. C. Brown and J. Walker, *Annalen*, 1891, **261,** 107; *Trans. Roy. Soc. Edin.*, 1891, **36,** 291.

TABLE 3. *Kolbe reaction with straight-chain half esters,* $RO_2C\cdot[CH_2]_n\cdot CO_2H$

Half ester:		Solvent	Yield (%)	Ref.	Half ester:		Solvent	Yield (%)	Ref.
R	*n*				R	*n*			
Et	1	H_2O	60	28	Et	8	H_2O	40–55	32
Et	2	,,	50	29	Me	8	MeOH	66	15
Me	2	MeOH	76	30	Me	11	,,	60	33
Me	4	,,	90–95	16	Me	14	,,	68	14
Et	7	,,	45	31	Et	16	H_2O–EtOH	60	34

This route to diesters, which represents one of the most valuable extensions of the Kolbe reaction, is sometimes referred to as the Brown–Walker synthesis. Since, however, a detailed study of the electrolysis of ethyl hydrogen malonate [3, 35] has shown the reaction to be strictly analogous to that with acetic acid, no such distinction is made in the present article : the term Kolbe reaction is used to denote anodic couplings which occur on electrolysis of both carboxylic acids and half esters.

Branched-chain Acids and Half Esters.—Most α-alkyl substituted acids and *cyclo*alkyl acids give a small, or even negligible, yield of coupled product on electrolysis.[23, 36] This fact imposes one of the most important restrictions on the choice of starting materials for synthetical applications of the Kolbe reaction. However, alkyl substituents further removed from the carboxyl group than the α-position do not in general exert a similar adverse effect. Numerous examples have been reported recently of anodic couplings in high yield with β-mono- and -di-alkyl acids and half esters, and the Kolbe reaction with γ-methyl acids was utilised with great success in the synthesis of perhydrobixin (IX) [37] and perhydrocrocetin.[38]

$$EtO_2C\cdot CH_2\cdot CH_2\cdot CHMe\cdot CH_2\cdot CH_2\cdot CH_2\cdot CHMe\cdot CH_2\cdot CH_2\cdot CO_2H$$

$$\text{(i) electrolysis}\ \Big\downarrow\ \text{(ii) hydrolysis}$$

$$HO_2C\cdot[CH_2]_2\cdot CHMe\cdot[CH_2]_3\cdot CHMe\cdot[CH_2]_4\cdot CHMe\cdot[CH_2]_3\cdot CHMe\cdot[CH_2]_2\cdot CO_2H$$

(IX)

As will be apparent from Table 4, the Kolbe reaction constitutes a valuable route to branched-chain compounds, provided that the starting acids are not α-substituted. Branching of the chain in the α-position pro-

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[29] A. R. Murray and T. W. J. Taylor, *J.*, 1937, 1450.

[30] L. Bouveault, *Bull. Soc. chim.*, 1903, **29,** 1042, 1046.

[31] G. M. Bennett and H. Gudgeon, *J.*, 1938, 1679.

[32] S. Swann, R. Oehler, and P. S. Pinkey, *Org. Synth.*, 1941, **21,** 48.

[33] L. Ruzicka and M. Stoll, *Helv. Chim. Acta*, 1933, **16,** 493.

[34] D. A. Fairweather, *Proc. Roy. Soc. Edin.*, 1925, **45,** 283.

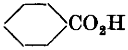
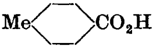
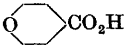
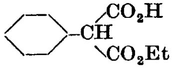
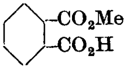
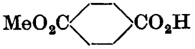
[35] A. Hickling and J. V. Westwood, *J.*, 1938, 1039.

[36] S. Swann, *Trans. Electrochem. Soc.*, 1929, **56,** 457.

[37] P. Karrer, F. Benz, R. Morf, H. Raudnitz, M. Stoll, and T. Takahashi, *Helv. Chim. Acta*, 1932, **15,** 1399.

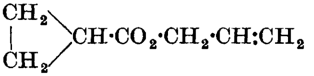
[38] P. Karrer, F. Benz, and M. Stoll, *ibid.*, 1933, **16,** 297.

TABLE 4. *Kolbe reaction with branched-chain acids and half esters*

	Acid	Solvent	Yield (%)	Ref.
α-Substituted acids	$CH_3{\cdot}[CH_2]_2{\cdot}CHMe{\cdot}CO_2H$	H_2O	0	36
	$CHEt_2{\cdot}CO_2H$	H_2O	5·5	39
		$MeOH–C_5H_5N$	14	40
		H_2O	0	41
		,,	20	42
	$MeO_2C{\cdot}CHMe{\cdot}CO_2H$	,,	40*	43
		,,	17	29
		H_2O or MeOH	0	52
		MeOH	32	44
	$EtO_2C{\cdot}CH_2{\cdot}CMe_2{\cdot}CO_2H$	$H_2O–MeOH$	5–8	45
	$CHMe_2{\cdot}CH_2{\cdot}CO_2H$	H_2O	28	22
	$CH_3{\cdot}[CH_2]_7{\cdot}CHMe{\cdot}[CH_2]_8{\cdot}CO_2H$	$H_2O–EtOH$	12	46
	$EtO_2C{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H$	$H_2O–MeOH$	30–35	45
	,,	MeOH	67	47
	$MeO_2C{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2H$	,,	80	48, 49
	$MeO_2C{\cdot}CH_2{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H$	MeOH–petrol	75	50
	$MeO_2C{\cdot}CH_2{\cdot}CHMe{\cdot}[CH_2]_2{\cdot}CO_2H$	MeOH	70	51
	$EtO_2C{\cdot}[CH_2]_2{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_2{\cdot}CO_2H$	,,	48	37
	$EtOCH_2{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_2{\cdot}CO_2H$	,,	70	38

* Product of unspecified purity.

motes the formation of olefins, alcohols, and esters by the side reactions mentioned earlier. An interesting example is the electrolysis of *cyclo*propanecarboxylic acid which is reported to give the allyl (X), and not the *cyclo*propyl, ester of the starting material.[52]



$$\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix}\!\!>CH{\cdot}CO_2{\cdot}CH_2{\cdot}CH{:}CH_2 \quad (X)$$

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[39] F. Fichter and M. Rudin; *ibid.*, 1941, **24**, 398E.

[40] F. Fichter and A. Petrovitch, *ibid.*, 1940, **23**, 806.

[41] F. Fichter and C. Simon, *ibid.*, 1934, **17**, 717.

[42] C. T. Blood, N. J. Cartwright, and R. P. Linstead, *J.*, 1952, 2268.

[43] A. C. Brown and J. Walker, *Annalen*, 1893, **274**, 42.

[44] F. Fichter and T. Holbro, *Helv. Chim. Acta*, 1938, **21**, 141.

[45] E. H. Farmer and J. Kracovski, *J.*, 1926, 2318.

[46] L. G. Ginger and R. J. Anderson, *J. Biol. Chem.*, 1945, **157**, 213.

[47] N. J. Leonard and P. M. Mader, *J. Amer. Chem. Soc.*, 1950, **72**, 5388.

[48] R. P. Linstead, J. C. Lunt, and B. C. L. Weedon, *J.*, 1950, 3333.

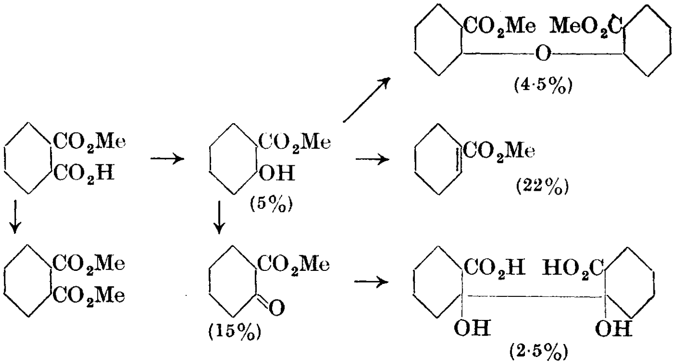
[49] S. Ställberg-Stenhagen, *Arkiv Kemi*, 1950, **2**, 95.

[50] S. F. Birch, V. E. Gripp, D. T. McAllan, and W. S. Nathan, *J.*, 1952, 1363.

[51] R. P. Linstead, J. C. Lunt, B. R. Shephard, and B. C. L. Weedon, *J.*, 1952, 3261.

[52] F. Fichter and H. Reeb, *Helv. Chim. Acta*, 1923, **6**, 450.

The anodic behaviour of methyl hydrogen *trans*-hexahydrophthalate[53] has been the subject of careful investigation and the results obtained are summarised below; no Kolbe product was isolated on using either aqueous or methanolic solutions:



Rather surprisingly, the isomeric methyl hydrogen *trans*-hexahydroterephthalate (XI) in methanol gives an appreciable yield (32%) of the Kolbe product (XII).[44]

(XI)  (XII)

The products of coupling (±)-forms of acids containing an asymmetric carbon atom are, of course, mixtures of racemic and *meso*-forms, produced by both symmetrical and unsymmetrical coupling of the enantiomorphs present in equal amounts in the starting material. Recently, attention has been directed to the electrolysis of optically active acids to develop a convenient route to stereoisomers, with known configurations, of the branched-chain products. Although complete loss of activity occurs during the preparation of 3 : 4-dimethylhexane from (+)- and (−)-α-methylbutyric acid,[54] racemisation of this kind is not unexpected because the asymmetric centre is directly attached to the carboxyl group eliminated in the reaction. If, for example, a free radical be involved in the process, this would mean a temporary planar distribution at the α-carbon and a loss of activity. However, it has been shown that activity involving an asymmetric carbon further removed from the carboxyl group is preserved during the Kolbe reaction. Thus the readily available stereoisomers of methyl hydrogen β-methylglutarate (XIII) give the methyl ββ′-dimethylsuberates (XIV) (in *ca.* 70% yield) with complete retention of optical activity.[48, 49]

$$\underset{\text{(XIII)}}{MeO_2C{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2H} \longrightarrow \underset{\text{(XIV)}}{MeO_2C{\cdot}CH_2{\cdot}CHMe{\cdot}[CH_2]_2{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2Me}$$

Unsaturated Acids.—A further important limitation of the Kolbe reaction is that neither αβ- nor βγ-unsaturated acids undergo anodic coupling. αβ-Unsaturated acids give small amounts of acetylenes[55, 56] but the

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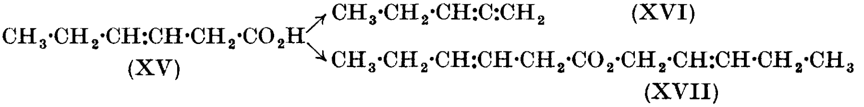
[53] F. Fichter and C. Simon, *ibid.*, 1934, **17**, 1218.

[54] E. S. Wallis and F. H. Adams, *J. Amer. Chem. Soc.*, 1933, **55**, 3838.

[55] J. Petersen, *Z. Elektrochem.*, 1912, **18**, 711.

method is of no preparative value. The half esters of fumaric and muconic acids do not yield products of the Kolbe type.[57]

Electrolysis of $\beta\gamma$-hexenoic acid (XV) in aqueous solution is reported to yield mainly the allene (XVI) together with some of the ester (XVII).[58] However, the allene is probably contaminated with hexenes and the method is again one which is unlikely to be of preparative value.



$$\underset{\text{(XV)}}{CH_3{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CO_2H} \begin{array}{l} \nearrow CH_3{\cdot}CH_2{\cdot}CH{:}C{:}CH_2 \qquad \text{(XVI)} \\ \searrow \underset{\text{(XVII)}}{CH_3{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CO_2{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH_3} \end{array}$$

$$CH_3{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH_3 \quad \text{(XVIII)}$$

$\gamma\delta$-Hexenoic acid, in contrast to its $\alpha\beta$- and $\beta\gamma$-isomers, does undergo the Kolbe reaction to an appreciable extent, giving (XVIII),[58] and normal coupling occurs (50%) on electrolysis of the half ester (XIX) to give the diester (XX).[51] The Kolbe reaction thus seems to be applicable to unsaturated acids provided that the double bond is separated from the carboxyl group to be eliminated by at least two carbon atoms. Unsaturated acids,

$$\underset{\text{(XIX)}}{EtO_2C{\cdot}CH{:}CMe{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H} \longrightarrow \underset{\text{(XX)}}{[EtO_2C{\cdot}CH{:}CMe{\cdot}CH_2{\cdot}CH_2]_2}$$

such as undec-10-enoic, oleic, petroselenic, erucic, and ricinoleic acids, in which the double bond is even further removed from the carboxyl group, have also been successfully employed,[55, 59, 60] although difficulty is frequently encountered in the electrolysis of ethylenic acids due to coating of the anode with insoluble polymers.

Unsaturated dicarboxylic acids such as maleic, fumaric,[61] citraconic,[62] mesaconic,[63] itaconic,[64] and glutaconic [65] give products containing allene and/or acetylenes on electrolysis.

Aromatic Acids.—Aromatic carboxylic acids ($Ar{\cdot}CO_2H$) also fail to undergo the Kolbe reaction to any appreciable extent. Benzoic acid on electrolysis in methanol yields benzene,[66] and the diethylamine salt in pyridine solution gives traces of diphenyl together with 4-phenylpyridine and 4-phenylbenzoic acid.[67]

[56] A. D. Petrov and D. A. Vyakhirev, *J. Gen. Chem., U.S.S.R.*, 1939, **9**, 513 (*Chem. Abstr.*, 1939, **33**, 9153).

[57] P. Karrer and M. Stoll, *Helv. Chim. Acta*, 1931, **14**, 1189.

[58] F. Fichter and T. Holbro, *ibid.*, 1937, **20**, 333.

[59] S. Kitaura, *Bull. Inst. Phys. Chem. Res., Tokyo*, 1937, **16**, 765 (*Chem. Abstr.*, 1938, **32**, 4523).

[60] S. Ueno and T. Tamura, *J. Soc. Chem. Ind., Japan*, 1943, **46**, 1213 (*Chem. Abstr.*, 1948, **42**, 6735).

[61] A. Kekulé, *Annalen*, 1864, **131**, 88 ; F. Fichter and A. Petrovitch, *Helv. Chim. Acta*, 1941, **24**, 549.

[62] G. Aarland, *J. pr. Chem.*, 1873, **7**, 142 ; F. Henrich and W. Schenk, *Ber.*, 1919, **52**, 2120.

[63] G. Aarland, *J. pr. Chem.*, 1873, **7**, 142.

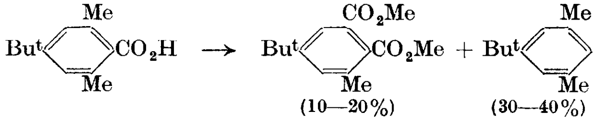
[64] *Idem, ibid.*, 1873, **6**, 256 ; A. Béhal, *Ann. Chim. Phys.*, 1887, **16**, 367.

[65] F. Henrich and A. Herzog, *Ber.*, 1919, **52**, 2128.

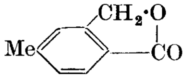
[66] F. Fichter and R. E. Meyer, *Helv. Chim. Acta*, 1934, **17**, 535.

[67] F. Fichter and H. Stenzl, *ibid.*, 1939, **22**, 971.

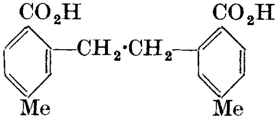
Oxidation of a methyl substituent on the aromatic ring was observed on electrolysis of 4-*tert.*-butyl-2 : 6-dimethylbenzoic acid (XXI) in methanol, the substituted phthalic ester (XXII) being obtained in addition to the aromatic hydrocarbon (XXIII).[66] Under similar conditions 2 : 4-dimethylbenzoic acid gave a mixture containing *m*-xylene, *m*-xylenol, 5-methylphthalide (XXIV), and a diacid, probably (XXV).[68] Both phenylacetic and β-phenylpropionic acids (XXVI ; $n = 1$ and 2) couple normally on electrolysis in pyridine and/or methanol : [67, 69]



(XXI) (XXII) (XXIII)



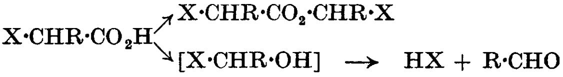
(XXIV)



(XXV)

$$\text{(XXVI)}\quad \text{Ph}\cdot[\text{CH}_2]_n\cdot\text{CO}_2\text{H} \longrightarrow \text{Ph}\cdot[\text{CH}_2]_{2n}\cdot\text{Ph}$$

Substituted Acids.—As would be expected, substituent groups exert the most pronounced influence on the anodic behaviour of fatty acids when in the α-position. Here they may result in the Kolbe reaction's being largely or totally suppressed. Thus, although normal coupling of the Kolbe type occurs with alkyl hydrogen malonates,[28] negligible coupling has been observed on electrolysis of α-phenyl-,[70] α-hydroxy-,[71] α-alkoxy-,[71, 72] α-halogeno-,[73] α-cyano-,[74] α-amino-,[75] and α-acylamino [75]-acids in aqueous solution. The products reported from these electrolyses suggest that the main reaction with the aliphatic acids is one of the Hofer–Moest type giving an ester and/or an unstable α-substituted alcohol which decomposes, yielding an aldehyde or ketone. With monosubstituted fatty acids these reactions may be represented as follows :



$$\text{X}\cdot\text{CHR}\cdot\text{CO}_2\text{H} \begin{cases} \nearrow \text{X}\cdot\text{CHR}\cdot\text{CO}_2\cdot\text{CHR}\cdot\text{X} \\ \searrow [\text{X}\cdot\text{CHR}\cdot\text{OH}] \longrightarrow \text{HX} + \text{R}\cdot\text{CHO} \end{cases}$$

where R is alkyl and X the substituent group. Thus, with the exception

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[68] F. Fichter, H. Stenzl, and E. Beglinger, *ibid.*, 1938, **21**, 375.

[69] R. P. Linstead, B. R. Shephard, and B. C. L. Weedon, *J.*, 1952, 3624.

[70] J. Petersen, *Bull. Acad. roy. Danemark*, 1897, 387.

[71] W. von Miller and H. Hofer, *Ber.*, 1894, **27**, 461.

[72] D. A. Fairweather, *Proc. Roy. Soc. Edin.*, 1925, **45**, 23.

[73] F. Kaufler and C. Herzog, *Ber.*, 1909, **42**, 3870 ; K. Elbs and K. Kratz, *J. pr. Chem.*, 1897, **55**, 502.

[74] F. Fichter and A. Schnider, *Helv. Chim. Acta*, 1930, **13**, 103.

[75] F. Fichter and M. Schmid, *ibid.*, 1920, **3**, 704.

of trifluoroacetic acid, which is reported[76] to yield hexafluoroethane by normal anodic coupling, α-halogeno-acids give esters, hydrogen halide, and halogen. With α-monohalogeno-acetic acids, formaldehyde and methylene halides are also formed. α-Amino-acids and their *N*-acyl- and -sulphonyl-derivatives are degraded to give ammonia and an aldehyde or ketone. Similarly, α-hydroxy- and α-alkoxy-acids yield among other products the aldehydes containing one carbon atom less than the parent acid. D-Glucuronic and melibionic acids for example are stated to yield D-arabinose (XXVII) and a C_{11}-reducing sugar respectively.[77]

$$CH_2(OH)\cdot[CH\cdot OH]_3\cdot CH(OH)\cdot CO_2H \longrightarrow CH_2(OH)\cdot[CH\cdot OH]_3\cdot CHO \qquad (XXVII)$$

In connection with the electrolyses of substituted fatty acids referred to above, it must be emphasised that the experimental conditions employed in much of the early work cannot now be regarded as the most suitable for the Kolbe reaction. More recent investigations using anhydrous methanol (or methanol–pyridine) solutions have shown that α-phenyl-,[67, 69] α-aryloxy-,[67, 68] and occasionally, to a much smaller extent,[79] α-acylamino-acids (see below) will undergo anodic coupling. The yields of Kolbe products that have been reported from electrolyses of various substituted acetic acids are summarised in Table 5.

TABLE 5. *Kolbe reaction with substituted acetic acids*

Acid	Solvent	Yield (%)	Ref.
$ClCH_2\cdot CO_2H$	H_2O	0	73
$EtO\cdot CH_2\cdot CO_2H$	,,	0	72
$NC\cdot CH_2\cdot CO_2H$	,,	1·4*	74
$PhO\cdot CH_2\cdot CO_2H$	$MeOH–C_5H_5N$	35	67
$Ph\cdot CH_2\cdot CO_2H$	,,	50	67, 69
$Ph_2CH\cdot CO_2H$	,,	9	80
$Ph_3C\cdot CO_2H$	MeOH	0	69, 81
$R\cdot CO\cdot NH\cdot CH_2\cdot CO_2H$	,,	<15	79
$EtO_2C\cdot CH_2\cdot CO_2H$	H_2O	60	28

*Current yield.

Many substituents which lead to a partial or complete inhibition of the Kolbe reaction when in the α-position exert only a minor influence when further removed from the carboxyl group. For instance, successful anodic couplings have been reported with hydroxy-,[59, 82] alkoxy-,[72, 83] keto-,[84]

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[76] F. Swartz, *Bull. Soc. chim. Belg.*, 1933, **42**, 102; *Bull. Acad. roy. Belg.*, 1931, **17**, 27.

[77] C. Neuberg, *Biochem. Z.*, 1908, **7**, 527.

[79] R. P. Linstead, B. R. Shephard, and B. C. L. Weedon, *J.*, 1951, 2854.

[80] A. J. van der Hoek and W. T. Nauta, *Rec. Trav. chim.*, 1942, **61**, 845.

[81] L. Riccoboni, *Gazzetta*, 1940, **70**, 748.

[82] D.R.-P. 624,331 (*Chem. Abs.*, 1936, **30**, 2504).

[83] A. A. Noyes, *Amer. Chem. J.*, 1897, **19**, 775; J. Hamonet, *Bull. Soc. chim.*, 1905, **33**, 513.

[84] H. Hofer, *Ber.*, 1900, **33**, 655; F. Fichter and S. Lurie, *Helv. Chim. Acta*, 1933, **16**, 885; R. Willstätter and A. Pfannenstiel, *Annalen*, 1921, **422**, 1.

cyano-,[85] amido-,[85] and acylamino-acids,[79, 86] also with acetals of aldehydo-acids,[87] other than those of the α-series.

Mixtures of Carboxylic Acids

The electrolysis of a mixture of two carboxylic acids ($R{\cdot}CO_2H$ and $R'{\cdot}CO_2H$) gives rise to products ($R{\cdot}R$, $R{\cdot}R'$, and $R'{\cdot}R'$) by both symmetrical and unsymmetrical (" crossed ") coupling. The process is of wide application and affords a valuable synthetical route to many unsymmetrical molecules. Generally, the relative proportions of the three products are those to be expected from the composition of the initial acid mixture. Thus an increase in the molar proportion of one component effects a marked improvement in the conversion of the other into the unsymmetrical product.[15, 88] A wide difference in size of the two coupling units can be tolerated, but, in general, those structural features which inhibit or prevent symmetrical coupling seem to exert a similar adverse effect on the crossing reactions. In a few instances, however, crossed coupling has been claimed even where one of the components is stated to give no product of the Kolbe type when electrolysed alone.[43, 89]

Mixtures of two monocarboxylic acids,[90] half esters,[91] and keto-acids [92] all yield the expected mixtures of hydrocarbons, diesters, and diketones severally.

Cross coupling of two dissimilar units has been achieved by using mixtures of a fatty acid with half esters,[15, 88, 89, 93] keto-acids,[84, 94] cyano-acids,[95] and phenyl-substituted acids,[96] also with mixtures of a half ester with an ω-acetamido-acid [85] and of a keto-acid with an alkoxy-acid.[97]

Of particular value is the coupling of a monocarboxylic acid with a half ester which has been developed into a general method for the synthesis of fatty acids (XXVIII) : [15]

$$R{\cdot}CO_2H + HO_2C{\cdot}[CH_2]_n{\cdot}CO_2Me \longrightarrow R{\cdot}R + MeO_2C{\cdot}[CH_2]_{2n}{\cdot}CO_2Me$$
$$+ R{\cdot}[CH_2]_n{\cdot}CO_2Me \longrightarrow R{\cdot}[CH_2]_n{\cdot}CO_2H \quad \text{(XXVIII)}$$

Although in all cases a mixture of three products (hydrocarbon, mono- and di-ester) is obtained, the separation of the required unsymmetrical product can in general be readily accomplished, by distillation either directly or

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[85] H. A. Offe, *Z. Naturforsch.*, 1947, **2b,** 185.

[86] *Idem, ibid.*, p. 182.

[87] A. Wohl and H. Schweitzer, *Ber.*, 1906, **39,** 890 ; M. Stoll and A. Rouvé, *Helv. Chim. Acta*, 1937, **20,** 525.

[88] W. von Miller and H. Hofer, *Ber.*, 1895, **28,** 2427.

[89] W. von Miller, *Z. Elektrochem.*, 1897, **4,** 55.

[90] A. Würtz, *Ann. Chim. Phys.*, 1855, **44,** 291.

[91] B. L. Vanzetti and A. Coppadora, *Gazzetta*, 1904, **34,** 1, 154 ; *Atti R. Accad. Lincei*, 1903, **12,** 209 ; M. Carmichael, *J.*, 1922, **121,** 2545.

[92] M. Stoll, *Helv. Chim. Acta*, 1951, **34,** 1817.

[93] M. Asano, Y. Kamdta, and T. Wada, *J. Pharm. Soc. Japan*, 1945, **65** (No. 7/8A), 5 ; M. Asano and J. Ota, *ibid.*, p. 10 (*Chem. Abstr.*, 1951, **45,** 5617, 4302).

[94] H. Hunsdiecker, *Ber.*, 1942, **75,** 447.

[95] M. Asano, Y. Kameda, and T. Wada, *J. Pharm. Soc. Japan*, 1944, **64** (No. 8A). 25 (*Chem. Abstr.*, 1951, **45,** 4302).

[96] *Idem, ibid.*, 1945, **65** (No. 4A), 15 (*Chem. Abstr.*, 1951, **45.** 4303)

[97] H. Hunsdiecker, *Ber.*, 1942, **75,** 460.

after hydrolysis. Stearic acid, for example, has been prepared by coupling myristic acid with adipic half ester, decanoic acid with sebacic half ester, and acetic acid with methyl hydrogen hexadecane-1 : 16-dicarboxylate.[15] In addition to its simplicity, the anodic synthesis of long-chain fatty acids has the great merit that, by suitable choice of starting materials, a product is obtained which is uncontaminated by substances of the same, or very similar, molecular weight. In consequence, acids may readily be prepared and isolated in a state of high purity. An interesting application of the method is to the preparation of trideuteropropionic acid (XXIX) from trideuteroacetic acid and ethyl hydrogen malonate : [98]

$$CD_3{\cdot}CO_2H + HO_2C{\cdot}CH_2{\cdot}CO_2Et \longrightarrow CD_3{\cdot}CH_2{\cdot}CO_2H \quad (XXIX)$$

Terminally unsaturated acids have been prepared from crossing reactions of half esters with oct-7-enoic [99] and undec-10-enoic acids.[100]

The isolation of branched-chain fatty acids from a number of natural sources,[101] and the recognition that some of them possess marked physiological activity,[102] has led in the last few years to a search for convenient and unambiguous methods for their synthesis. The electrolytic route has been found eminently suitable.[49, 93, 103, 104] The scope of the method is well illustrated by a new synthesis indicated below of (±)-3 : 13 : 19-trimethyltricosanoic acid (XXX) from 3-methylheptanoic acid (XXXI) : [105]

$$CH_3{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2H + HO_2C{\cdot}[CH_2]_3{\cdot}CO_2Me$$

$$(XXXI) \qquad \downarrow$$

$$CH_3{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_4{\cdot}CO_2H + HO_2C{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2Me \quad (XIII)$$

$$\downarrow$$

$$CH_3{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_5{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2H + HO_2C{\cdot}[CH_2]_7{\cdot}CO_2Me$$

$$\downarrow$$

$$CH_3{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_5{\cdot}CHMe{\cdot}[CH_2]_8{\cdot}CO_2H + (XIII)$$

$$\downarrow$$

$$CH_3{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_5{\cdot}CHMe{\cdot}[CH_2]_9{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2H \quad (XXX)$$

This acid is known to cause granulomatous lesions when injected intraperitoneally in guinea-pigs,[106] and was until recently believed to

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[98] Hölemann and K. Clusius, *Ber.*, 1937, **70,** 819.

[99] L. Ruzicka, M. Stoll, and H. Schinz, *Helv. Chim. Acta,* 1928, **11,** 670.

[100] L. Ruzicka, M. Stoll, W. Scherrer, H. Schinz, and C. F. Seidel, *ibid.*, 1932, **15,** 1459 ; G. Gustbée, and E. Stenhagen, *Sartryck ur Svensk Kemisk Tidskrift,* 1942, **54,** 243 (*Chem. Abstr.*, 1944, **38,** 3611).

[101] G. Weitzel, *Angew. Chem.*, 1948, **60,** *A*, 263 ; E. V. Truter, *Quart. Reviews,* 1951, **5,** 393, 394.

[102] G. Brownlee, *Ann. Reports,* 1948, **45,** 292.

[103] R. P. Linstead, J. C. Lunt, and B. C. L. Weedon, *J.*, 1950, 3331.

[104] T. Moroe, *J. Pharm. Soc. Japan,* 1950, **70,** 54 ; 1951, **71,** 123 (*Chem. Abstr.*, 1951, **45,** 2396, 8456).

[105] R. P. Linstead, J. C. Lunt, B. R. Shephard, and B. C. L. Weedon, forthcoming publication.

[106] S. David, N. Polgar, and Sir Robert Robinson, *J.*, 1949, 1541.

be a racemate of a biologically active material isolated from tubercle bacilli.[107]

In view of the frequent occurrence in Nature of compounds with a polyisoprenoid skeleton, it is noteworthy that the half ester (XXXII) undergoes normal cross coupling.[51] This fact opens up the possibility of extending the carbon chain of fatty acids, in successive stages, by one isoprene unit at a time :

$$\begin{array}{c} \mathrm{R{\cdot}[CH_2{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2]_{\mathit{n}}{\cdot}CO_2H + HO_2C{\cdot}CH_2{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2Et} \\ \downarrow \qquad\qquad \mathrm{(XXXII)} \\ \mathrm{R{\cdot}[CH_2{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2]_{\mathit{n}+1}{\cdot}CO_2Et} \end{array}$$

Since the naturally occurring branched-chain fatty acids are optically active, it is of particular interest that the anodic synthesis of fatty acids can be extended to the preparation of pure enantiomorphs. Thus (+)- and (−)- forms of 10-methyloctadecanoic (tuberculostearic) acid (XXXIII ; $n = 7$) [108] and 11-methylnonadecanoic acid (XXXIII ; $n = 8$) [109] have been prepared from the readily accessible enantiomorphs of methyl hydrogen β-methylglutarate (XIII) by processes involving only two stages :

$$\begin{array}{c} \mathrm{Me{\cdot}[CH_2]_6{\cdot}CO_2H + HO_2C{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2Me \quad (XIII)} \\ \downarrow \\ \mathrm{Me{\cdot}[CH_2]_7{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2H + HO_2C{\cdot}[CH_2]_{\mathit{n}}{\cdot}CO_2Me} \\ \downarrow \\ \mathrm{Me{\cdot}[CH_2]_7{\cdot}CHMe{\cdot}[CH_2]_{\mathit{n}+1}{\cdot}CO_2H \quad (XXXIII)} \end{array}$$

Clearly, substitution of the optically active forms of (XXXI) and (XIII) for the racemates in the synthesis of 3 : 13 : 19-trimethyltricosanoic acid (XXX), outlined above, would furnish stereoisomers of known configuration and enable a study to be undertaken of the relationship between optical and biological activity in this field.

Other syntheses of optically active acids reported include cross couplings of stearic acid with enantiomorphs of methyl hydrogen α'-ethyl-α'-methylsuccinate (XXXIV),[110] $\beta\beta'$-dimethyladipate (XXXV),[111] and $\beta\beta'$-dimethylsuberate (XXXVI).[112]

$$\mathrm{HO_2C{\cdot}CH_2{\cdot}CMeEt{\cdot}CO_2Me} \quad \mathrm{(XXXIV)}$$

$$\mathrm{HO_2C{\cdot}CH_2{\cdot}CHMe{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2Me} \quad \mathrm{(XXXV)}$$

$$\mathrm{HO_2C{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2Me} \quad \mathrm{(XXXVI)}$$

Among examples of the anodic synthesis of unsymmetrical compounds, reference must also be made to the preparation from (XIII) of the

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[107] N. Polgar and Sir Robert Robinson, *Chem. and Ind.*, 1951, 685 ; J. Cason and G. Sumrell, *J. Biol. Chem.*, 1951, **192,** 405 ; J. Cason, N. K. Freeman, and G. Sumrell, *ibid.*, p. 415.

[108] R. P. Linstead, J. C. Lunt, and B. C. L. Weedon, *J.*, 1951, 1130.

[109] R. Cavanna and S. Ställberg-Stenhagen, *Atti R. Accad. Lincei*, 1950, **3,** 31.

[110] S. Ställberg-Stenhagen, *Arkiv Kemi*, 1951, **3,** 273.

[111] *Idem, ibid.*, p. 244.

[112] *Idem, ibid.*, 1950, **2,** 431.

methoxy-acid (XXXVII), an important intermediate for the synthesis of (±)-muscone.[113] No doubt substitution in this synthesis of the appropriate enantiomorph of (XIII) would lead to natural (—)-muscone.

$$\mathrm{MeO{\cdot}[CH_2]_{10}{\cdot}CO_2H} + \text{(XIII)} \longrightarrow \underset{\text{(XXXVII)}}{\mathrm{MeO{\cdot}[CH_2]_{11}{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2H}}$$

Electrolyses of mixtures of salts of carboxylic acids and inorganic acids have also been examined in the expectation of obtaining interaction between organic and inorganic anions discharged simultaneously. Claims by early workers in this field to have effected anodic syntheses of alkyl halides and nitroalkanes, by electrolysis of mixtures of carboxylates and either inorganic halides or nitrites respectively, have not been substantiated in subsequent investigations.[19] Of these attempted crossing reactions those with salts of fatty acids and sodium nitrate have been studied most thoroughly (for review see ref. 114). A typical example is the electrolysis of a propionate–nitrate mixture which yields a variety of products including ethyl nitrate, *n*-butyl nitrate, and the dinitrates of ethylene glycol and butane-1 : 4-diol.[115] The formation of derivatives with the same number of carbon atoms as the Kolbe product is particularly noteworthy.

Anodic Alkoxylation, Acetoxylation, and Alkylation

A recent examination of the electrolysis of *N*-acylglycines and *N*-acyl-DL-α-alanines in alcoholic solutions revealed that *N*-alkoxymethyl- and *N*-1′-alkoxyethyl-amides respectively are formed in excellent yields (up to 90%).[79] These reactions, which afford facile routes to products difficult to prepare in other ways, may be generalised as follows:

$$\mathrm{X{\cdot}NH{\cdot}CHR{\cdot}CO_2H + R'OH \longrightarrow X{\cdot}NH{\cdot}CHR{\cdot}OR' + CO_2}$$

where X is acyl, R hydrogen or methyl, and R′ alkyl. In some instances small amounts of α-diamine derivatives, the products of normal coupling, are formed simultaneously.

Anodic alkoxylations, which are reminiscent of the Hofer–Moest reaction of fatty acids in aqueous solution, also occur on electrolysis of di- [80] and tri- [69] phenylacetic acids in methanolic solutions, methyl di- and tri-phenylmethyl ethers being formed (35 and 60% yields respectively). Under similar conditions, monophenylacetic acid gives (50%) dibenzyl by normal coupling.[67, 69]

Analogous to the alkoxylations are the acetoxylation reactions which take place on electrolysis of glacial acetic acid solutions of sodium acetate to which α-acylamino-acids [79] or mono-, di-, or tri-phenylacetic acids [69] have been added. Thus diphenylacetic acid is converted into diphenylmethyl acetate (XXXVIII) in good yield. Substitution of di- and triphenylmethane for the di- and tri-phenylacetic acids in these electrolyses

$$\mathrm{Ph_2CH{\cdot}CO_2H \longrightarrow Ph_2CH{\cdot}OAc} \quad \text{(XXXVIII)}$$

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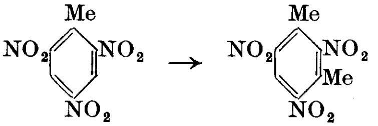
[113] H. Hunsdiecker, *Ber.*, 1942, **75**, 1197.

[114] F. Fichter, *Trans. Electrochem. Soc.*, 1939, **75**, 309; *Bull. Soc. chim.*, 1934, **1**, 1585.

[115] F. Fichter, W. Siegrist, and H. Buess, *Helv. Chim. Acta*, 1935, **18**, 18.

in glacial acetic acid results in attack of the aromatic hydrocarbon, but the reaction is complex and the isolation of pure products extremely difficult. However, under the same conditions, naphthalene is substituted and gives, after hydrolysis of the initial product, α-naphthol (25%) together with small amounts of the β-isomer.[69]

In addition to acetoxylation, electrolysis of sodium acetate in glacial acetic acid is capable of effecting methylation of other substances present. After the addition of trinitrotoluene to the electrolyte small amounts (9%) of trinitro-*m*-xylene (XXXIX) may be isolated.[116]

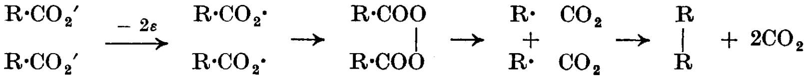


(XXXIX)

Mechanisms of the Anodic Reactions

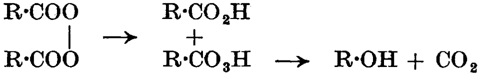
Of the mechanisms which have been proposed for the Kolbe reaction, in particular the formation of ethane at the anode on the electrolysis of acetate solutions, three have received serious consideration of recent years. These are summarised below.

Peroxide Theory.—The view originally expressed by C. Schall[117] that diacyl peroxides are intermediates in the electrolysis of carboxylic acids has since been developed by Fichter.[19, 114] On this theory, in its present form, at least three intermediates, *viz.*, discharged anions, diacyl peroxides, and alkyl radicals, are involved in the conversion of carboxylate ions into the final products of electrolysis. Thus the Kolbe reaction is represented in the following manner:



$$\begin{matrix}R\cdot CO_2' \\ \\ R\cdot CO_2'\end{matrix} \xrightarrow{-2\varepsilon} \begin{matrix}R\cdot CO_2\cdot \\ \\ R\cdot CO_2\cdot\end{matrix} \rightarrow \begin{matrix}R\cdot COO \\ | \\ R\cdot COO\end{matrix} \rightarrow \begin{matrix}R\cdot & CO_2 \\ + & \\ R\cdot & CO_2\end{matrix} \rightarrow \begin{matrix}R \\ | \\ R\end{matrix} + 2CO_2$$

To account for the by-products in the Kolbe rèaction, it is suggested that the intermediate peroxides also undergo hydrolysis, particularly in an alkaline electrolyte, to give per-acids which subsequently decompose to yield alcohols:



$$\begin{matrix}R\cdot COO \\ | \\ R\cdot COO\end{matrix} \rightarrow \begin{matrix}R\cdot CO_2H \\ + \\ R\cdot CO_3H\end{matrix} \begin{matrix} \\ \\ \rightarrow R\cdot OH + CO_2\end{matrix}$$

In acid solutions, according to Fichter, the alcohols formed in this way are readily dehydrated to olefins, or combine with free carboxylic acid at the anode to give esters. The formation of *iso*-alcohols and their esters is attributed to the addition of water and carboxylic acid respectively to the olefins. However, dehydrations of alcohols, and additions to olefins, seem rather unlikely under the conditions prevailing during electrolysis.

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[116] L. F. Fieser, R. C. Clapp, and W. H. Daudt, *J. Amer. Chem. Soc.*, 1942, **64**, 2052.

[117] *Z. Elektrochem.*, 1896, **3**, 83.

In support of the peroxide theory it has been claimed that, by using streaming solutions and low temperatures, the presence of diacyl peroxides and per-acids may be demonstrated during the electrolysis of fatty acids [118] and half esters.[119] However, the formation, under conditions different from those normally employed in the electrolysis of carboxylic acids, of small amounts of peroxides does not, of course, mean that the latter are necessarily intermediates in the Kolbe and other anodic reactions.

Considerable importance has been attached by advocates of the peroxide theory to the fact that many diacyl peroxides are known to decompose on heating, or on irradiation, to give a mixture of products closely resembling those obtained on electrolysis of the corresponding fatty acids.[19, 120] It is nevertheless extremely doubtful whether these analogies between the electrolytic and the non-electrolytic reactions have any other significance than that both proceed by a common intermediate, presumably an alkyl free radical.

Hydrogen Peroxide Theory.—A detailed study of the electrolysis of acetates in aqueous solution led S. Glasstone and A. Hickling [3, 7] to suggest that hydrogen peroxide is first formed at the anode by the irreversible union of discharged hydroxyl radicals, and that this, if present in sufficient concentration, reacts with acetate ions to give ethane and carbon dioxide :

$$\begin{aligned} 2OH' &\longrightarrow H_2O_2 + 2\varepsilon \\ H_2O_2 + 2CH_3{\cdot}CO_2' &\longrightarrow C_2H_6 + 2CO_2 + 2OH' \end{aligned}$$

These authors also envisage that acetate radicals are probably formed in an intermediate stage :

$$H_2O_2 + 2CH_3{\cdot}CO_2' \longrightarrow 2CH_3{\cdot}CO_2{\cdot} + 2OH'$$

and do not exclude the possibility that these may combine to give diacyl peroxides, the intermediates postulated by Fichter. If the hydrogen peroxide concentration is not sufficient to bring about the above series of reactions, or if the acetate-ion concentration at the anode is low, then the hydrogen peroxide is thought to react with the acetate ions, or with acetic acid, to form peracetic acid which decomposes yielding methanol and carbon dioxide :

$$H_2O_2 + CH_3{\cdot}CO_2H \longrightarrow H_2O + CH_3{\cdot}CO_3H \longrightarrow CH_3{\cdot}OH + CO_2$$

The Hofer–Moest reaction is thus regarded as occurring whenever the conditions are not favourable for the Kolbe synthesis.

The importance of the anode material, and the suppression of the Kolbe reaction in favour of the Hofer–Moest reaction which occurs on addition to acetate solutions of inorganic salts or catalysts for the decomposition of hydrogen peroxide, are readily accounted for on the present mechanism, but receive no adequate explanation on the basis of the diacyl peroxide theory.

An objection to those theories of the Kolbe reaction which postulate

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[118] F. Fichter and R. Zumbrunn, *Helv. Chim. Acta*, 1927, **10**, 869 ; G. Hallié, *Rec. Trav. chim.*, 1938, **57**, 152 ; E. Denina, *Gazzetta*, 1938, **68**, 443.

[119] F. Fichter and H. Buess, *Helv. Chim. Acta*, 1935, **18**, 445.

[120] F. Fichter, *ibid.*, 1930, **13**, 89 ; D. Swern, *Chem. Reviews*, 1949, **45**, 1.

an initial discharge at the anode of carboxylate ions from aqueous solution is apparent from a consideration of the potentials at this electrode. The Kolbe reaction is reported to occur only at an anode potential which is appreciably higher than those required at the same current density and pH either for the Hofer–Moest reaction or for oxygen evolution from solutions not containing acetate ions.[3, 35, 121] Nevertheless, ethane formation, under optimum conditions, is accompanied by very little oxygen evolution. Glasstone and Hickling account for the experimental observations by assuming that the anode potential is determined by the fate of the hydrogen peroxide which they believe to be formed irreversibly at the anode. If it decomposes readily, because of either the presence of catalysts or the absence of acetate ions with which to react, oxygen is liberated and the potential approximates to that for oxygen evolution in solutions of the same pH not containing acetate. When decomposition of the hydrogen peroxide is not catalysed and acetate ions are present in sufficient amount, acetate radicals are liberated instantaneously and since these, according to Glasstone and Hickling, are more electromotively active than oxygen, the electrode acquires a more positive potential.

The hydrogen peroxide theory, of course, requires that hydroxyl ions be present and hence applies only to electrolyses in aqueous solutions. In anhydrous solvents, as mentioned earlier, the Kolbe reaction is much less susceptible to changes in experimental conditions, and, although the formation in side reactions of traces of water cannot be definitely excluded, it is generally agreed that the initial anodic process is the discharge of carboxylate ions.[3] It is therefore noteworthy that the Kolbe reaction with acetates in anhydrous ethylene glycol requires an anode potential almost identical with that for aqueous solutions.[122] This is rather unexpected if different primary anodic processes are operative in the anhydrous and aqueous media.

The most important objection to the hydrogen peroxide theory is that all attempts to simulate the Kolbe reaction by the addition of concentrated hydrogen peroxide to acetate solutions have been unsuccessful, only very small amounts of hydrocarbons being obtained.[3, 7] These failures have been ascribed by Glasstone and Hickling to the fact that the conditions in these purely chemical experiments are very different from those at the anode. Moreover, it is known that oxidation of acetate solutions can be effected with either fluorine [123] or sodium persulphate [7, 35, 124] to give mixtures of products very similar to those obtained on electrolysis. In the presence of carbonates, the action of fluorine on acetates leads to products of the Hofer–Moest type,[125] whereas the addition of a catalyst for the decomposition of hydrogen peroxide to the acetate–persulphate mixture inhibits the formation of hydrocarbons, exactly as in the anodic process.[3, 7]

[121] S. N. Shukla and O. J. Walker, *Trans. Faraday Soc.*, 1931, **27**, 722.

[122] S. Glasstone and A. Hickling, *J.*, 1936, 820.

[123] F. Fichter and K. Humpert, *Helv. Chim. Acta*, 1926, **9**, 692.

[124] F. Fichter and J. Heer, *ibid.*, 1935, **18**, 704.

[125] F. Fichter and E. Brunner, *ibid.*, 1929, **12**, 573.

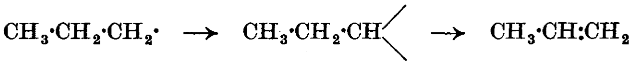
Radical Theory.—Insight into the mechanism of some of the side reactions of the Kolbe synthesis has been obtained by Clusius and his collaborators from electrolyses of fatty acids and deutero-fatty acids in light and heavy water. Electrolyses of acetates in water were found to give ethane and, at low current densities, methane, the compositions of both products depending only on the isotopic structure of the acetate ion, and not on that of the solvent.[126, 127] These results are consistent with the view that during electrolysis methyl free radicals are formed as intermediates and that these either dimerise to give ethane or alternatively, when present in low concentration, abstract hydrogen from a molecule of acetic acid or an acetate ion. Other organic compounds, such as methanol and ethanol, can act as proton donors, but only C–H, and not O–H bonds are attacked, the resulting dehydrogenation products being subsequently oxidised at the anode to carbon dioxide and water :

$$CH_3\cdot + CH_3\cdot CO_2H \longrightarrow CH_4 + \cdot CH_2\cdot CO_2H$$

The olefin produced as the main product on electrolysis of propionates and butyrates was shown [9, 98, 128] to arise from the intermediate alkyl free radicals by elimination of a hydrogen atom from the carbon atom originally β to the carboxyl group, *e.g.*,

$$CH_3\cdot CH_2\cdot CH_2\cdot \longrightarrow CH_3\cdot CH{:}CH_2$$

and not by an intramolecular hydrogen migration, *e.g.*,



The paraffin containing the same number of carbon atoms as the olefin, and formed simultaneously to the extent of *ca.* 5% of the olefin, is probably produced by disproportionation of the alkyl radical,[9, 128] *e.g.*,

$$2CH_3\cdot CH_2\cdot CH_2\cdot \longrightarrow CH_3\cdot CH{:}CH_2 + CH_3\cdot CH_2\cdot CH_3$$

(Far higher ratios of paraffin to olefin, up to 1 : 1, have been reported with electrolyses of other acids in methanol.[49, 108])

These studies have also provided [9] information concerning the formation of ethanol on electrolysis of propionates in acid solution. The hydroxyl group in the resulting alcohol is attached to carbon atoms which were originally both α and β to the carboxyl group. The β-attack, which predominates over α-, is attributed to β-oxidation of the alkyl radical, followed by hydrogen abstraction of the type envisaged in methane formation :

$$CH_3\cdot CH_2\cdot \longrightarrow HO\cdot CH_2\cdot CH_2\cdot \longrightarrow HO\cdot CH_2\cdot CH_3$$

Although, as indicated above, neither the diacyl peroxide nor the hydrogen peroxide theory is incompatible with the formation of alkyl free radicals, Clusius and his collaborators favour the view that carboxylate ions are first discharged at the anode, as suggested originally by Brown and Walker,[28]

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[126] P. Hölemann and K. Clusius, *Z. physikal. Chem.*, 1937, **35**, *B*, 261.
[127] K. Clusius and W. Schanzer, *ibid.*, 1943, **192**, *A.*, 273.
[128] W. Schanzer and K. Clusius, *ibid.*, 1941, **190**, *A*, 241.

and that the resulting carboxylate radicals yield alkyl radicals by loss of carbon dioxide:

$$C_nH_{2n+1}\cdot CO_2' \xrightarrow{-e} C_nH_{2n+1}\cdot CO_2\cdot \rightarrow C_nH_{2n+1}\cdot + CO_2$$

Other results which are readily explained on a free-radical mechanism are the formation during the electrolysis of benzoic acid in pyridine of 4-phenylpyridine and 4-phenylbenzoic acid,[67] and of oxidation products of diphenylmethyl when diphenylacetic acid is electrolysed in methanol–pyridine.[80] The failure of aryl carboxylic acids ($Ar\cdot CO_2H$) to undergo the Kolbe reaction to any significant extent is in accord with the known tendency of aryl radicals to attack solvent molecules and to give polymers rather than to dimerise.[129] Again, a strong case can be made for the intervention of free radicals in the anodic acetoxylations and methylations; analogous reactions can be effected by purely chemical means using lead tetra-acetate [69, 116, 130] which can furnish both acetoxy- and methyl free radicals.[130, 131]

The evidence cited will suffice to show that there is good reason for assuming that free radicals are involved in many, if not all, of the anodic reactions of carboxylic acids. If alkyl radicals are intermediates in the Kolbe reaction, then the extent to which they dimerise under these conditions is unusually high, but can possibly be attributed to the anode acting as a catalytic surface.

There seems little doubt that in non-aqueous media the sequence of radical reactions depicted above commences with the discharge of carboxylate ions. No conclusion can, however, be drawn as to the exact mechanism of formation of carboxylate radicals in aqueous solution in the absence of decisive physical evidence on the nature of the primary anodic process.

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[129] D. H. Hey, *Ann. Reports*, 1944, **41**, 181; 1948, **45**, 139.

[130] O. Süs, *Annalen*, 1949, **564**, 137.

[131] W. A. Waters, "The Chemistry of Free Radicals", Oxford, 1946.