

Electron-transfer Processes: Oxidation of Arylacetic Acids by Peroxydisulphate in Acetic Acid

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The oxidation of arylacetic acids by peroxydisulphate in acetic acid media in the presence of potassium and copper(II) acetates leads to the corresponding benzylacetates. The mechanism of the reaction is rationalized by the occurrence of two pathways: the intermediate formation of aromatic radical cations or the direct decarboxylation of the arylacetate ion. The importance of acetic acid as a reaction medium is stressed.

THE heterogeneous system peroxydisulphate in acetic acid has recently been shown¹⁻⁴ to be a versatile reagent for the selective functionalization of the ring or side chain of aromatic compounds. The mechanism of the oxidation of aromatic compounds by peroxydisulphate is also matter of considerable interest.⁵

We now report that the oxidation of arylacetic acids by peroxydisulphate in acetic acid in the presence of potassium and copper(II) acetates provides arylmethyl acetates in moderate to quantitative yield [equation (1)]. Results of non-optimized experiments are in the

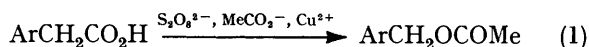


Table. With *p*-tolyl acetic acid the methyl group is also acetoxyated to some extent with formation of *p*-(acetoxymethyl)phenylacetic acid. The results in the

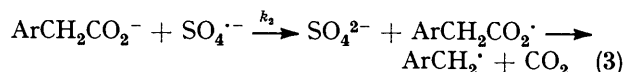
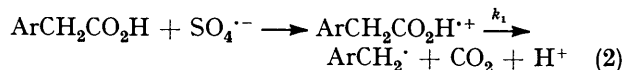
Oxidation of arylacetic acids (ArCH₂CO₂H) and 4-phenylbutanoic acid by potassium peroxydisulphate in the presence of potassium and copper(II) acetates

Ar	% Conversion	ArCH ₂ (OCOMe)		Reaction time/h	
		% Yield ^a	% Yield ^a		
Ph	60	80	3	4.5	
<i>p</i> -MeC ₆ H ₄ ^b	63	56	8	3	
<i>p</i> -Cl-Ph	65	54	3	3	
<i>p</i> -MeOC ₆ H ₄	90	95	—	2	
1-Naphthyl	96	100	—	2	
2-Naphthyl	93	95	—	2	
<i>p</i> -MeOC ₆ H ₄ ^c	55	54	4	12	
		(1)	(2)	(3)	
Ph[CH ₂] ₃ CO ₂ H	34	40	15	6	2

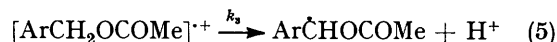
^a Yields are based on amount of ArCH₂CO₂H (or PhCH₂CO₂H) converted. ^b *p*-(AcOCH₂)C₆H₄CH₂CO₂H and *p*-(AcOCH₂)C₆H₄CH₂OAc were isolated in 11 and 8% yield respectively. ^c The reaction was performed without the copper salt. Potassium peroxydisulphate (35%) was recovered at the end of the reaction. *p*-MeOC₆H₄CHO (23%) and *p*-MeOC₆H₄CH(OAc)₂ (6%) were isolated from the reaction mixture.

Table indicate that in some cases the reaction is of synthetic interest, owing to the high selectivity of the oxidation, compared with the uncatalysed reaction of the same substrates.

Mechanism of the Reaction.—Two mechanisms can be envisaged for reaction (1): (i) formation of a radical cation [equation (2)], and (ii) direct oxidation of the carboxylate ion [equation (3)]. The oxidation of the



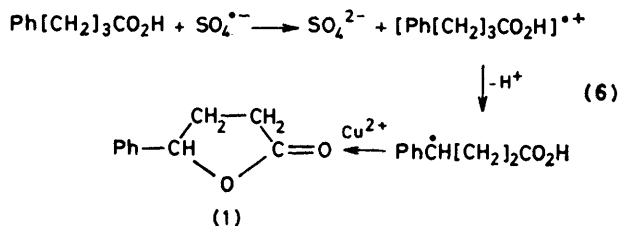
benzyl radicals by copper(II) acetate leads to the final products. Mechanisms (i) and (ii) are both well documented.⁶⁻⁸ It has been reported⁹ that carboxylate anions are oxidized by SO₄^{·-} more slowly than aromatic rings,¹⁰ so that on this basis mechanism (i) should be operative. However, this mechanism does not explain the results of the Table. Thus, the fact that 1-naphthylacetic acid gives rise to the acetoxymethyl derivative with almost quantitative conversion means that the starting acid is much more reactive (at least two orders of magnitude) than the ester which is formed; this is not consistent with the expected substituent effect on the formation of the corresponding aromatic radical cations and with the reported rate constants for mechanism (i) in substituted benzenes. Mechanism (i) would be reasonable only if the electron-transfer from the aromatic ring is reversible and the loss of CO₂ from the radical cation of arylacetic acid is much faster than the loss of a proton from the radical cation of the arylmethylacetates [equation (5)] (*k*₁ > *k*₃).



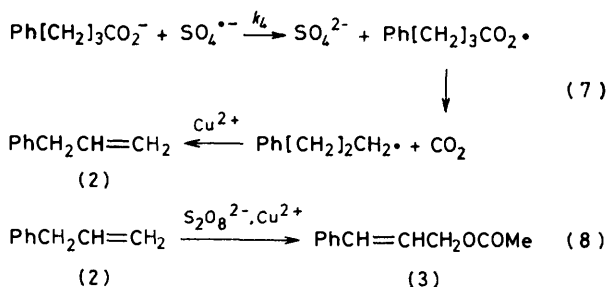
Mechanism (ii) is consistent with the results of the Table, but it assumes that the electron transfer from the carboxylate ion is faster than the electron transfer from the aromatic ring, in contrast with the reported rate constants. Our previous results on the acetoxymethylation of naphthalene and the formation of γ -lactones from isopropylbenzenes³ suggest that the oxidation of acetate ion by peroxydisulphate can compete with the electron transfer involving aromatic compounds with low ionization potentials, such as naphthalene and alkylbenzenes.

As the rate of decarboxylation is strictly related to the stability of the alkyl radical formed⁶ a considerably higher oxidation rate would be expected for the arylacetate ions which give rise to benzylic-type radicals.

In order to obtain other information concerning the reaction mechanism, the oxidation of 4-phenylbutanoic acid was investigated under the same conditions. The lactone (1) (40%), the olefins (2) (15%) and (3) (6%), and methyl acetate (8%) are formed together with other unidentified products. The formation of (1) can be



explained by the electron-transfer process of equation (6). In contrast, the olefin (2) arises from oxidative decarboxylation of 4-phenylbutanoate anion [equation (7)] and the acetate (3) arises from further oxidation of (2) [equation (8)]. The formation of methyl acetate is clear evidence that the acetate ion is also oxidized under the reaction conditions. It appears that both mechanisms of type (i) and (ii) are operative with 4-phenylbutanoic acid. However, the concentration of the 4-



phenylbutanoate anion must be rather low on the basis of the acidity constants of acetic and 4-phenylbutanoic acids and of the strong excess of acetic acid (a molar ratio of 44 : 1 was used); moreover, the rate constant k_2 must be considerably higher than k_4 favouring the process in the case of arylacetic acids. The competition between phenylacetic and 4-phenylbutanoic acids indicates that the former is about seven times more reactive than the latter, but the result has a limited meaning because we do not know sufficient about the acid-base equilibria of the two acids in acetic-acetate solution.

Further evidence that mechanism (ii) is operative with arylacetic acids arises from the behaviour of methyl phenylacetate and methyl 4-phenylbut-2-enoate.* Methyl phenylacetate appears to be less reactive than phenylacetic acid; under the same conditions phenylacetic acid was 60% converted, whereas methyl phenylacetate was 7% converted. The small amount of benzylacetate formed probably arises from the transesterification of phenylacetate with acetic acid. Moreover, competition between methyl phenylacetate and phenyl-

* These experiments were suggested by a referee.

and *p*-tolyl-acetic acids indicates that essentially only the free acids react leading to the benzylacetates in the Table; only traces of the ester reacts. Methyl 4-phenylbut-2-enoate appears to be more reactive than methyl phenylacetate in agreement with a mechanism characterized by electron-transfer from the aromatic ring; under conditions in which methyl phenylacetate was 7% converted, methyl 4-phenylbut-2-enoate was 40% converted. In this case the reaction is not clean; the lactone (1) comprised 40% of the reaction products, the benzylacetate was formed in 20% yield and g.l.c. revealed the presence of other two unidentified products [(2) and (3) were absent].

Thus it appears that the esters are oxidized by electron transfer from the aromatic ring and arylacetic acids by oxidation of the carboxylate group; moreover, the ester of phenylacetic acid is considerably deactivated towards the electron transfer from the ring.

In order to define more precisely the ratio of reactivity of the carboxylate ion and the aromatic ring, naphthalene (10 mmol), pivalic acid (40 mmol), and sodium acetate (45 mmol) were oxidized in the presence of quinoline (10 mmol) (a good trap for alkyl radicals¹¹) under the same conditions as those for the oxidation of arylacetic acids. 1-Acetoxy-naphthalene and 2-*t*-butylquinoline were formed in a 4 : 1 ratio; the former arises from the naphthalene radical cation, whereas *t*-butylquinoline arises from decarboxylation of pivalate ion followed by homolytic alkylation of quinoline.¹² This result clearly indicates that naphthalene and pivalate ion are simultaneously oxidized by peroxydisulphate; however, the ratio of naphthalene to pivalate ion in solution is in fact greater than 40 : 1 because of the relative concentrations of acetic and pivalic acids. This means that the oxidation of the pivalate ion by peroxydisulphate is faster than the oxidation of naphthalene under the reaction conditions. Since electron transfer from the aromatic ring of naphthalene is easier than from the aromatic ring of phenylacetic acid, and the oxidation of phenylacetate ion must be faster than that of pivalate ion because benzyl radicals are more stabilized than *t*-butyl radicals, it follows that the mechanism (ii) is more likely in the oxidation of arylacetic acids and either the rate of oxidation of carboxylate ion have been underestimated or the rate of oxidation of the aromatic compounds have been overestimated. The relative ease with which aromatic rings and carboxylate ions are oxidized could obviously be strongly affected by the reversibility of equation (5), while the oxidation of the carboxylate anion is certainly irreversible. The mechanism discussed here assumes that the observed oxidations are caused exclusively by the sulphate radical anion and the copper(II) salt has no role in the initial electron-transfer. This could be an oversimplification of a more complex mechanism.

EXPERIMENTAL

Potassium and copper(II) acetates and potassium peroxydisulphate were obtained from Carlo Erba and Fluka, respectively. All the benzylacetates (prepared by acetyl-

ation of the corresponding benzyl alcohols), 3-phenylpropene (2), 3-phenylprop-2-enyl acetate (3), 5-phenyl-4,5-dihydrofuran-2(3H)-one (1), and methyl acetate were isolated and identified by comparison with authentic samples. Methyl esters of acetoxy(phenyl)acetic acid and *p*-(acetoxyethyl)-phenylacetic acid, and 1,4-bis(acetoxyethyl)benzene were isolated by g.l.c. and identified by their n.m.r. (Varian A 90) and mass spectra (g.l.c.-m.s. System, Varian MAT 112 S).

General Procedure.—A mixture of potassium peroxydisulphate (20 mmol), copper(II) acetate hydrate (10 mmol), potassium acetate (45 mmol), and the arylacetic acid (or 4-phenylbutanoic acid) (20 mmol) in acetic acid (50 ml) was heated at reflux under nitrogen with vigorous stirring. Carbon dioxide evolution was complete in 2–4.5 h. The mixture was cooled, the solid filtered off, and the solution diluted with water and extracted with diethyl ether. The combined extracts were washed with 0.2M-hydrochloric acid. Acidic and basic components were separated by extraction with saturated aqueous sodium carbonate and 10% hydrochloric acid. The neutral fraction, after addition of methyl benzoate as internal standard, was analysed by g.l.c. on a glass column (2 m) of 10% UCC W 982 on Chromosorb (80–100 mesh) with a Hewlett-Packard model 575 chromatograph with flame-ionisation detector. The acidic fraction was treated with diazomethane and analysed by g.l.c.

Yields, from the g.l.c. analysis and calculated on the basis of the amount of arylacetic acid (or 4-phenylbutanoic acid), which had been converted, are reported in the Table. In the oxidation of phenylacetic acid, methyl acetate was isolated by fractional distillation of the reaction mixture (8% yield based on $K_2S_2O_8$).

Competitive Oxidation of 4-Phenylbutanoic acid and Phenylacetic Acid.—The reaction was carried out as in the previous section, in the presence of phenylacetic acid (10 mmol), 4-phenylbutanoic acid (10 mmol), and potassium peroxydisulphate (3 mmol). G.l.c. analysis showed that the acidic fraction contained phenylacetic acid (8.20 mmol) and 4-phenylbutanoic acid (9.75 mmol) (ratio of conversion 8 : 1); the neutral fraction contained benzyl acetate (1.6 mmol), the propene (1) (0.13 mmol), and the acetate (2) (0.03 mmol).

Oxidation of Pivalic Acid by Peroxydisulphate in the Presence of Naphthalene and Quinoline.—A mixture of potassium acetate (45 mmol), copper(II) acetate hydrate (20 mmol), quinoline (10 mmol), naphthalene (10 mmol), pivalic acid (40 mmol), and potassium peroxydisulphate (20 mmol) in acetic acid (50 ml) was refluxed for 5 h. The cooled solution was filtered and diluted with water, and the acidic and basic components were separated. The neutral fraction contained 1-acetoxynaphthalene (0.6 mmol) which was identified by comparison with an authentic sample;

from the basic fraction 2-t-butylquinoline (0.15 mmol) was isolated by column chromatography and identified by comparison with an authentic sample.

Oxidation of the Methyl Esters of Phenylacetic Acid or 4-Phenylbutanoic Acid.—The general procedure was used for 4 h at reflux with the methyl esters of phenylacetic acid or 4-phenylbutanoic acid (20 mmol; purity 98% by g.l.c.) instead of the arylacetic acid. Carbon dioxide was evolved, and the separation was carried out as described. For methyl phenylacetate, the neutral fraction contained methyl phenylacetate (18.6 mmol by g.l.c.) and a small amount of benzyl acetate (0.7 mmol); the acidic fraction contained only a trace of phenylacetic acid. With methyl 4-phenylbutanoate, the neutral fraction contained the starting ester (12 mmol, 40% conversion), compound (1) (3.2 mmol, 40% of the converted 4-phenylbutanoate), methyl 4-acetoxy-4-phenylbutanoate (1.6 mmol 20%), and two unidentified products.

Competitive Experiment with Methyl *p*-Tolyl Acetate and Phenylacetic Acid.—A mixture of potassium peroxydisulphate (4 mmol), copper(II) acetate hydrate (10 mmol), potassium acetate (45 mmol), phenylacetic acid (10 mmol), and methyl *p*-tolyl acetate (10 mmol) in acetic acid (50 ml) was heated at reflux under nitrogen with stirring for 4 h. Separation as in the previous experiments gave an acidic fraction containing phenylacetic acid (8.6 mmol) and carboxy(phenyl)methyl acetate (0.6 mmol) and a neutral fraction containing methyl *p*-tolylacetate (9.8 mmol) and benzyl acetate (2.1 mmol, 52% of the converted acid).

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