with benzene-chloroform (3:1), taken up in acetic acid, and hydrogenated using platinum catalyst to yield the dihydrodiols (m.p. 220-227°, no color with tetranitromethane). A solution of the dihydrodiols (0.85 g.) in acetone (300 cc.) was cooled to 10° and treated with a solution (1 cc.) of chromium trioxide in dilute sulfuric acid (prepared by dissolving 2.672 g. of chromium trioxide in 2.3 cc. of concd. sulfuric acid and making up to 10 cc. with water). After 5 min., the mixture was poured into water (500 cc.), the precipitate collected, dried, and crystallized from methanol to give dihydrofaradione, m.p. 184–187°, $[\alpha]_D$ −18° (*c*, 2.9), undepressed by a specimen, m.p. 187—189°, $[\alpha]_D$ −22°, isolated similarly from arnica flowers; reported[9] for dihydrofaradione (dihydroarnidione), m.p. 183° $[\alpha]_D$ −61°.

(b) The mixed diols (1.0 g.) were oxidized with 1.2 cc. of the standard chromium trioxide agent, the crude water-insoluble precipitate dissolved in a mixture (40 cc.) of ethanol-benzene-sulfuric acid (volume ratio, 10:5:1) and heated under reflux for 4 hr. The product, isolated in the usual way by aqueous dilution and ether extraction, was dissolved in benzene and chromatographed. The fraction eluted by benzene was crystallized once from ether-petroleum ether and once from methanol to give faradione as long laths, m.p. 247–250°, $[\alpha]_D$ +15° (*c*, 2.0); reported[14] m.p. 249-250°, $[\alpha]_D$ +22°.

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Pyridine 1-Oxides. X. pK_a Values for Some 4-Substituted Nicotinic Acid 1-Oxides

John S. Driscoll, Wolfgang Pfleiderer, and Edward C. Taylor

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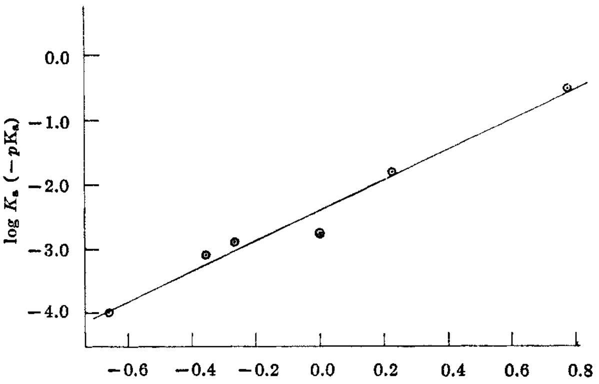
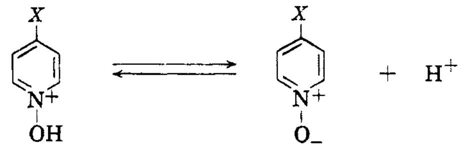


Figure 1

TABLE I

Compound	pK_a
4-Aminonicotinic acid 1-oxide	3.98 ± 0.03
4-Hydroxynicotinic acid 1-oxide	3.08 ± 0.02
4-Methoxynicotinic acid 1-oxide	2.88 ± 0.04
Nicotinic acid 1-oxide	2.74 ± 0.03
4-Chloronicotinic acid 1-oxide	1.80 ± 0.1
4-Nitronicotinic acid 1-oxide	0.50 ± 0.1

During the course of recent investigations in pyridine 1-oxide chemistry,[1] a number of 4-substituted nicotinic acid 1-oxide derivatives were prepared and were thus available for study.[2] The pK_a values of these compounds have now been determined (see Table I, where pK_a refers to the dissociation of the neutral molecule relative to the monoanion). All the values were determined potentiometrically except for 4-nitronicotinic acid 1-oxide, which was done spectrophotometrically because of its high acidity. The pK_a values have been correlated with the appropriate sigma constants by means of the Hammett equation, and a satisfactory statistical fit in all respects ($\rho = 2.347$; $r = 0.988$; $S = 0.207$) has been found. This may be compared with a rho value of 1.89 for the equilibrium (a) below involving the dissociation of the conjugate acid of 4-substituted pyridine 1-oxides to the neutral molecule.[3,4] The statistical calculations were carried out according to the procedure suggested by Jaffé;[5] the sigma values were chosen from the same source. Since the substituent group in the 4-position is *ortho* to the carboxyl group in these compounds, it would seem that these compounds should exhibit an *ortho* or proximity effect[6] and therefore not be amenable to treatment by the Hammett equation. However, since excellent correlation has been found (see Fig. 1) it would appear that the determined pK_a value is not a measure of the equilibrium (b) but rather a measure of the ionization of the zwitterionic form of the nicotinic acid 1-oxide, as shown below in (c). Thus, the substituents affecting the group bearing the acidic proton are *para* (—*X*) and *meta* (—COO⁻), and it is well known that substituents in these positions are



(a)

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[1] For the previous paper in this series, see E. C. Taylor and J. S. Driscoll, *J. Org. Chem.*, 26, 3796 (1961).

[2] E. C. Taylor and J. S. Driscoll, *J. Am. Chem. Soc.*, 82, 3141 (1960).

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[4] H. H. Jaffé, *J. Org. Chem.*, 23, 1790 (1958).

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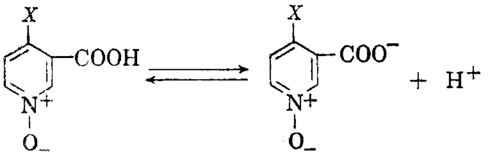
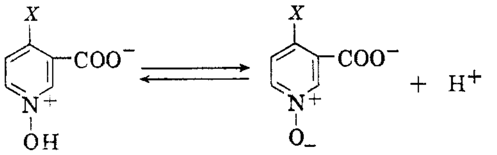


(b)



(c)

successfully correlated by the Hammett equation.

It should be pointed out that, when a compound has substituents both *meta* and *para* to the reacting group, the substituent constants are additive.[5] In the present instance, the *meta* substituent (the —COO⁻ group) is the same in every case.

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By-products Formed during the Hunsdiecker Decarboxylation and Debromination of Linolenic Acid Hexabromide[1]

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Gas chromatographic analysis of 1-bromo-*cis*,*cis*,*cis*-8,11,14-heptadecatriene, a precursor of α-linolenic-1-C^{14} acid, showed it to be contaminated by two compounds in addition to the hydrocarbon described by the original investigators.[3] The combined quantity of these impurities varied according to the conditions used in the synthesis, and ranged from 10 to 25% of the desired bromide. The concern that these two components might become labeled during the C^{14} carbonation to linolenic acid and thus interfere with metabolism studies compelled us to identify them.

The infrared spectrum of a pure sample of each of the unidentified impurities (obtained as gas chromatographic fractions) permitted the identification of one as an ether (strong absorption at 8.95 μ) and the other as a chloro compound (13.7 μ). Positive identification of these as 1-ethoxy- and 1-chloroheptadecatriene was obtained by comparative gas chromatographic behavior.

The synthetic sequence involves a Hunsdiecker reaction on silver hexabromooctadecanoate with subsequent debromination to the unsaturated bromide. Using conditions for the decarboxylation specified by the original investigators (addition of bromine to a refluxing carbon tetrachloride suspension of the silver salt), the chloro compound was obtained in a yield of 20% of the bromide. By modifying these conditions so that the bromine was added to a carbon tetrachloride suspension of the silver salt in an ice bath followed by slow heating to reflux, the yield of chloride was reduced to 8%. During this modified procedure, decarboxylation occurred below reflux temperature.

The formation of alkyl chloride could result either from an intrusion of solvent into a radical-chain mechanism or by attack on solvent by radicals escaping from the solvent cage of a radical-recombination-type mechanism for the Hunsdiecker reaction.[4] The effect of forming the hypobromite in the cold was two-fold. The decarboxylation occurred below reflux temperature, and secondly, the concentration of hypobromite was higher during decarboxylation. Assuming that the reaction proceeds by a radical-chain mechanism, a chain transfer to carbon tetrachloride, being inversely proportional to concentration of the hypobromite,[4c] would account for the decrease in chloroheptadecatriene formation with increased concentration of hypobromite. In deference to the radical-recombination mechanisms, however, it should be stated that an escape-to-recombination ratio which was proportional to temperature would also explain the observed decrease in chloro compound formation.

The 1-ethoxyheptadecatriene presumably arises *via* solvolysis of the 1-bromide during the seven hours of refluxing with zinc in ethanol to affect removal of vicinal bromine substituents from the heptabromoheptadecane. The yield of ether was 2–5% of that of the 1-bromoheptadecatriene.

Neither one of these impurities interferes in the carbonation of the Grignard of the 1-bromoheptadecatriene (to form α-linolenic-1-C^{14} acid) or effect the radio-purity of the product, but knowledge of their presence and concentrations is important in making efficient use of $C^{14}O_2$.

EXPERIMENTAL

1-Bromo-cis,cis,cis,-8,11,14-heptadecatriene was prepared according to the method of Nevenzel and Howton.[3] In some runs the conditions for the Hunsdiecker reaction were modified as given in the text.

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[1] Supported by grant H-4120 from the United States Public Health Service.

[2] Present address, Dept. of Fisheries, Tohoku University, Sendai, Japan.

[3] J. C. Nevenzel and D. R. Howton, *J. Org. Chem.*, **23**, 933 (1958).

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