rarely, but, since lactam formation has been shown to be faster than glycylglycyl cleavage, a significant degree of selectivity should be obtainable in all cases.

Experimental[8]

Dicarbobenzoxy-L-ornithine Methyl Ester.—This compound was prepared from dicarbobenzoxy-L-ornithine[9] and ethereal diazomethane, m.p. 71–72° from chloroform–ligroin.

Anal. Calcd. for $C_{22}H_{26}N_2O_6$: C, 63.75; H, 6.32; N, 6.76. Found: C, 63.83; H, 6.37; N, 6.04.

Dicarbobenzoxy-L-ornithinamide.—Dicarbobenzoxy-L-ornithine methyl ester, 1 g., was stored overnight at 0° in 10 ml. of methanolic ammonia. Filtration yielded 600 mg. of amide, 62%, m.p. 168.

Anal. Calcd. for $C_{21}H_{25}N_3O_5$: C, 63.14; H, 6.31; N, 10.52. Found: C, 62.93; H, 6.34; N, 9.84.

L-Ornithylglycylglycine was prepared by a modification of the method used by Goldschmidt and Rosculet.[10] Dicarbobenzoxy-L-ornithylglycylglycine was synthesized by direct coupling of dicarbobenzoxy-L-ornithine[9] and sodium glycylglycinate with ethyl chloroformate[11]; m.p. 169–171° from ethyl acetate–ligroin; Goldschmidt and Rosculet[10] reported m.p. 125–126°. Because of discrepancy in melting point, our preparation was analyzed.

Anal. Calcd. for $C_{25}H_{30}N_4O_8$: C, 58.35; H, 5.88; N, 10.89; neut. equiv., 514. Found: C, 58.18; H, 5.89; N, 11.31; neut. equiv., 513.

Hydrogenolysis at room temperature and 1 atm. in the presence of palladium black, 75 mg./mmole, in 80% aqueous acetic acid containing a slight excess of hydrochloric acid yielded noncrystalline L-ornithylglycylglycine hydrochloride, R_f 0.08, purple color with ninhydrin; $[\alpha]^{25}D$ +22.0° (*c* 1%, 0.5 *N* HCl); Goldschmidt and Rosculet[10] reported $[\alpha]^{25}D$ +25.9° (*c* 2%, 0.5 *N* HCl).

Anal. Calcd. for $C_9H_{18}N_4O_4 \cdot HCl$: C, 38.23; H, 6.77; Cl, 12.54; N, 19.82. Found: C, 38.39; H, 6.80; Cl, 12.90; N, 19.70.

The naphthylamide derivatives were prepared by the coupling procedure of Vaughan and Osato.[11] Physical constants and analytical data for these compounds are listed in Table II. In addition to the chromatographic data recorded in Table II, the R_f values and ninhydrin colors of the compounds listed below were obtained: ornithinamide prepared by hydrogenolysis of the dicarbobenzoxy derivative, 0.04, purple; L-ornithine hydrochloride, 0.08, purple; ornithine methyl ester dihydrochloride,[12] 0.10, purple; 2,4-diaminobutyric acid hydrochloride, 0.12, purple; glycylglycine, 0.12, yellow; glycine, 0.18, brown; 3-amino-2-pyrrolidone hydrochloride,[13] 0.24, yellow; 3-amino-2-piperidone hydrochloride,[12] 0.28, yellow; and α-naphthylamine, 0.91, tan.

Cleavage Procedures.—Peptides at concentrations of 2 mg./ml. were allowed to react at controlled temperatures between 25 and 85° in 2-ml. sealed glass ampoules, and the reaction was terminated by cooling or mild acidification. Aliquots (10 μl.) were spotted in triplicates on Whatman No. 1 filter paper and chromatographed at room temperature using *n*-butyl alcohol–acetic acid–water, 4:1:5 (v./v.) as the mobile phase, and the products were detected qualitatively either by ninhydrin sprays or with a Mineralite, Model SL 2537 hand lamp. The sections containing the ultraviolet-absorbing compounds were cut out, the substances were eluted with water, and the eluates were made up to 4 ml. Under the elution conditions used, variable amounts of ultraviolet-absorbing impurities were detected which we could not remove satisfactorily. However, the interference of these compounds could be minimized by using aqueous extracts from the sections of the chromatograms adjacent to the naphthylamide spots as spectrophotometric blanks and taking readings at 292 mμ. The choice of this wave length rather than the absorption maximum, 281 mμ, represents a compromise between minimum interference by the impurities and loss of sensitivity of the detection procedure. Corrections for losses during chromatography and elution of the compounds were made through the use of calibration curves. The average molar extinction coefficient, ε, of the six naphthylamide salts in aqueous solutions at 292 mμ was 5190 ± 4%, and at 281 mμ it was 6100 ± 4%. The average molar extinction coefficient for the carbobenzoxynaphthylamides in 95% ethanol at 290 mμ, their absorption maximum, was 7050 ± 1%.

(8) All melting points were determined with a Mel-Temp heating block in capillary tubes and are uncorrected. Analyses are by George Robertson, Florham Park, N. J. R_f values were obtained on Whatman No. 1 filter paper with *n*-butyl alcohol–acetic-acid–water, 4:1:5 (v./v.), descending.

(9) R. L. M. Synge, *Biochem. J.*, **42**, 99 (1948).

(10) S. Goldschmidt and G. Rosculet, *Chem. Ber.*, **93**, 2387 (1960).

(11) J. R. Vaughan and R. L. Osato, *J. Am. Chem. Soc.*, **74**, 676 (1952).

(12) E. Fischer and G. Zemplén, *Chem. Ber.*, **42**, 4878 (1909).

(13) S. Wilkinson, *J. Chem. Soc.*, 104 (1951).

A Carbon-by-Carbon Degradation of Carbon-14-Labeled Nicotinic Acid[1]

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A carbon-by-carbon chemical degradation of carbon-14-labeled nicotinic acid is presented which is capable of giving the specific activity of each carbon atom in the molecule directly. With reasonably good counting equipment, the method can be applied to nicotinic acid containing 5 μc. of activity in 2–3 mmoles. Randomly labeled acid containing this level of activity would produce carbon dioxide in the final stages with a specific activity of about 0.1 mμc./mg. of carbon.

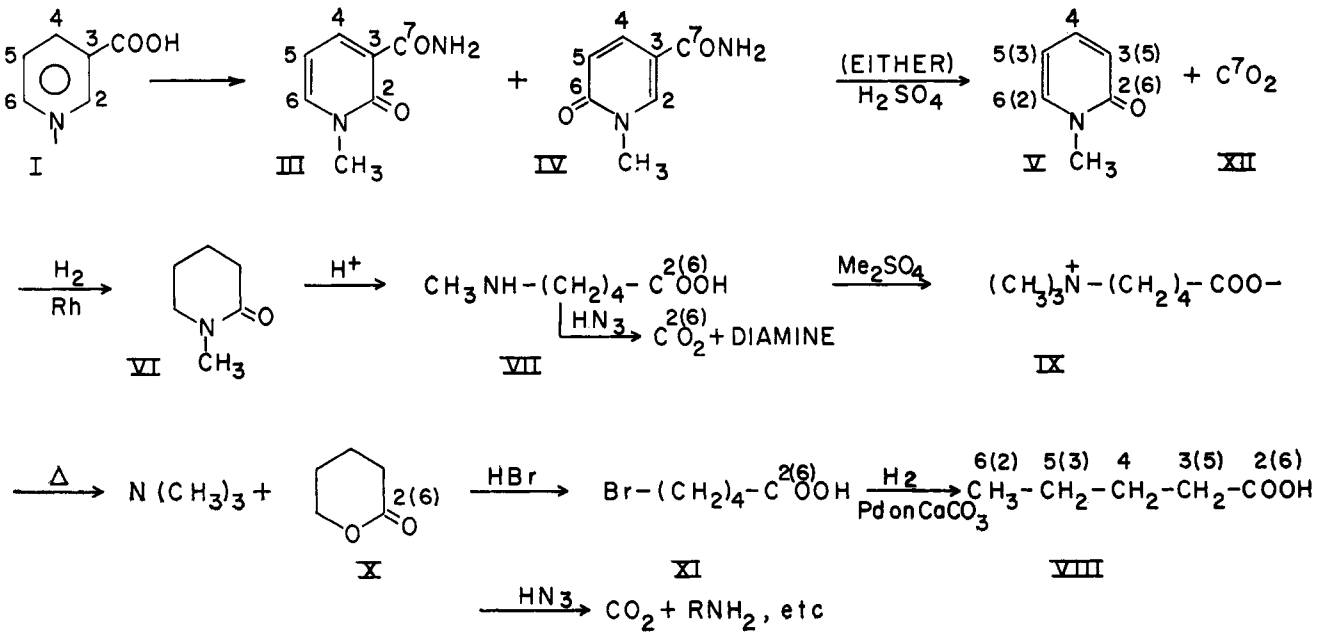
The carbon-by-carbon degradation of the pyridine ring of nicotinic acid (I) has become an increasingly necessary step in the elucidation of some biochemical pathways by C^{14} tracer methods. No complete degradation scheme applicable directly to I has been available so far, although several partial degradations of the pyridine ring of I and of ricinine have been published which have made the specific activity of each of the ring carbon atoms potentially available.[2] Starting from I, these would require total amounts of activity of the order of 0.2–0.5 mc., however.[2f] A scheme is presented here which is capable of yielding the specific activity of each of the pyridine ring carbon atoms of labeled I unambiguously, in essentially a single sequence of reactions. This method can easily be applied to an amount of I containing 5 μc. of total C^{14} activity if reasonably good counting equipment is available[3] (low level liquid scintillation, or, preferably, low level gas

(1) Research performed under the auspices of the U. S. Atomic Energy Commission at Brookhaven National Laboratory and under Grants G12855 and GB1129 from the National Science Foundation at Columbia University.

(2) (a) T. Griffith, K. P. Hellman, and R. U. Byerrum, *J. Biol. Chem.*, **235**, 800 (1960); (b) T. Griffith and R. U. Byerrum, *Biochem. Biophys. Res. Commun.* **10**, 293 (1963); (c) A. R. Friedman and E. Leete, *J. Am. Chem. Soc.*, **85**, 2141 (1963); (d) P. F. Juby and L. Marion, *Can. J. Chem.*, **41**, 117 (1963); (e) J. M. Essery, P. F. Juby, L. Marion, and E. Trumbull, *ibid.*, **41**, 1142 (1963); (f) R. K. Gholson, Oklahoma State University, private communication.

(3) D. R. Christman, *Nucleonics*, **19**, No. 5, 51 (1961).

SCHEME I



counting methods). Even using solid counting of barium carbonate, the scheme should give reasonable results starting with 50–100 μc. of total C^{14} activity in I. Each reaction is run on a desirable mass scale, dilutions with inactive material being made at various appropriate stages.

The sequence of reactions used is shown in Scheme I. I, in the form of its amide methioidide (II), is oxidized to a mixture of the corresponding 2- (III) and 6-pyridones (IV),[4,5] which are separated by means of an alumina column. Each of these pyridones is then decarboxylated in 60% sulfuric acid over a period of several days, during which time carbon dioxide (XII) is trapped and counted to give the specific activity of the original carboxyl group of the nicotinic acid. This reaction is analogous to the known decarboxylation of ricinine under similar conditions.[6]

The mother liquor from it contains N-methyl-2-pyridone (V) regardless of the pyridone carboxamide used. In one case, the carbonyl group is at the original ring position 2, and in the other at the original position 6. These pyridones are reduced to the corresponding piperidone (VI) by hydrogen, using 5% rhodium on alumina as the catalyst, and VI is hydrolyzed with dilute hydrochloric acid to δ-methylaminovaleric acid (VII). In one case the carboxyl carbon is the original C-2 of the pyridine ring, and in the other case the C-6.

Although δ-dimethylaminovaleric acid has been degraded to allylacetic acid *via* its N-oxide,[2d] in our hands a better yield of the ultimately desired valeric acid (VIII) has been more readily obtained by conversion of VII to its betaine (IX) by means of dimethyl sulfate,[7] thermal decomposition of IX (in an inert atmosphere) to δ-valerolactone (X),[8] hydrolysis of X in concentrated hydrobromic acid to give δ-bromovaleric acid (XI),[9] and the nearly quantitative hydrogenolysis of this compound, using palladium on calcium carbonate as catalyst.[10] Allylacetic acid, once obtained, can be reduced equally easily to VIII by hydrogen, using various catalysts. Attempts to deaminate IX to allylacetic acid *via* the Emde reduction were unsuccessful however.

To this point, the over-all yield of the series of reactions from *each* pyridone is about 1%, and each portion of VIII contains about 10 mμc. of activity, total, starting with 5 μc. of acid.

Each portion of VIII can be completely degraded carbon by carbon by the Schmidt reaction,[11,12] starting in one case with the original C-2 and in the other with the original C-6. However, a total of five consecutive Schmidt reactions, two starting from one of the valeric acids and three from the other, gives the activity of each of the original ring carbons directly, and any additional Schmidt reactions duplicate results already obtained. It is necessary to purify (preferably by gas chromatography) each subsequent acid, since some chain cleavage occurs during the oxidation of the amine product of the Schmidt reaction.[11b] It is possible easily to run a series of three Schmidt reactions starting from 0.5 g. of thallium valerate (XIII, the most convenient form in which to handle and purify these acids in the running of this reaction).[12]

This degradation scheme is currently being applied in this laboratory to the degradation of the pyridine ring of nicotine. The nicotine is obtained by feeding various precursors related to the Krebs cycle to excised tobacco roots growing in sterile culture medium.[13] The results of these biochemical studies will be published later, although some representative results of several

(4) M. E. Pullman and S. P. Colowick, *J. Biol. Chem.*, **206**, 121 (1954).
(5) R. F. Dawson, D. R. Christman, A. D'Adamo, M. L. Solt, and A. P. Wolf, *J. Am. Chem. Soc.*, **82**, 2628 (1960).
(6) E. Winterstein, J. Keller, and A. B. Weinhagen, *Arch. Pharm.*, **255**, 513 (1917).
(7) E. M. Gal, R. E. Spenger, and D. M. Greenberg, *J. Org. Chem.*, **15**, 1261 (1950).
(8) R. Willstätter and W. Kuhn, *Ber.*, **37**, 1853 (1904).
(9) N. Isenberg, J. B. Liebsohn, and V. E. Merola, *Can. J. Chem.*, **40**, 831 (1962).
(10) M. Busch and H. Stöve, *Ber.*, **49**, 1073 (1916),
(11) (a) E. F. Phares, *Arch. Biochem. Biophys.*, **33**, 173 (1951); (b) E. F. Phares, and S. F. Carbon, *ibid.*, **33**, 179 (1951).
(12) R. C. Anderson and A. P. Wolf, Brookhaven National Laboratory Report BNL-3222, 1957.
(13) D. R. Christman and R. F. Dawson, *Biochem.*, **2**, 182 (1963).

TABLE I

COMPARISON OF NICOTINIC ACID AND PYRIDONE DECARBOXYLATIONS[a,b]

Compound[c]	Sp. act.[d]	C^7O_2 sp. act.[d]	% C^7O_2/total act.[e]
Nicotinic acid	75.1	65.5	87.0
2-Pyridone	0.182	0.174	95.6
6-Pyridone	0.248	0.211	85.0
Nicotinic acid	27.0	5.39	20.0
2-Pyridone	35.3	7.31	20.7
6-Pyridone	32.4	6.19	19.1
Nicotinic acid	6.12	0.678	11.1
2-Pyridone	14.9	1.63	10.9
6-Pyridone	39.6	4.58	11.7

[a] Nicotinic acid decarboxylated by pyrolysis of its calcium salt.[5] [b] Each compound was diluted separately after its preparation, before decarboxylation. [c] The first group was obtained from feeding of alanine-2-C^{14}; the second from alanine-3-C^{14}; the third from glycerol-1-C^{14}.[13] [d] Specific activities are expressed in mμc./mmole. Standard deviation is 3%. [e] Standard deviation is ±5%.

TABLE II

SCHMIDT DECARBOXYLATION OF δ-METHYLAMINOVALERIC ACIDS[a]

Source of acid[b]	Sp. act.[c]	CO_2 sp. act.[c]	% of total pyridine ring[d]
2-Pyridone	0.0158	0.00390	24.6 (C^2)
6-Pyridone	0.0186	0.00152	8.2 (C^6)

[a] From feeding of alanine-2-C^{14}. [b] Each compound was diluted separately after its preparation, before decarboxylation. [c] Specific activities are expressed in mμc./mmole. Standard deviation is 3%. [d] Standard deviation is ±5%.

stages of this degradation scheme are shown in Tables I and II.

In cases where very little activity is incorporated into the pyridine ring or where a rapid result is desired for C-2 or C-6 of the ring, the Schmidt reaction can be applied directly to VII, obtained by hydrolysis of VI. About 25–50 mg. of the acid is required for this procedure when gas counting is employed. This precludes the further degradation of this portion of the available material, however, since unsatisfactory results are obtained in the oxidation of diamines to dicarboxylic acids and in their subsequent degradation by the Schmidt method.

Experimental[14]

Nicotinamide.—I (200–400 mg.) is refluxed for 3 hr. with redistilled thionyl chloride (4 ml./100 mg. of acid) in a small round-bottomed flask with a neck about 4 in. long. A drying tube is used at the top of the reflux condenser. The condenser is then connected to the flask by a 120° elbow, and a receiver with a vacuum takeoff is provided. While the receiver is cooled in dry ice, a vacuum of about 1 cm. is applied and the reaction vessel is shaken gently while being heated to 30–40° by a heating mantle. After the excess thionyl chloride has distilled off, the flask containing nicotinoyl chloride is cooled with Dry Ice while a stream of gaseous ammonia is passed into the vessel until about 15 ml. of liquid ammonia are present. The flask is then lifted above the Dry Ice level and held there while the excess ammonia slowly boils off. The residue is then dissolved in a little water and passed onto a column of AG 3-X4 resin about 6 cm. long and 2 cm. in diameter. The resin (a specially prepared equivalent of IRA-400) is base washed, then thoroughly water washed, before use. The first 20 ml. of eluate (containing much ammonium chloride) is discarded, then the nicotinamide is eluted with about 500 ml. of water (unreacted I is retained by the resin). The water is then evaporated under vacuum, and the dry residue extracted with about 5 ml. of hot methanol (some ammonium chloride is carried along, but most remains undissolved at this point).

For 200 mg. of I, the volume of methanol is reduced to about 0.5 ml.; then about 0.15 ml. of methyl iodide is added and II is prepared as previously described, in an over-all yield of about 70%.[5]

From this II, the corresponding pyridones (III and IV) are prepared by oxidation with basic potassium ferricyanide, as previously described.[5] The yield of each pyridone is 20–25% from the methiodide.

Decarboxylation of Pyridones.[6]—Either III or IV (1–2 mmoles) is placed in a 50-ml. flask fitted with both a gas inlet tube and a long neck with a cold finger reflux condenser. The outlet of the condenser leads to a spiral gas trap, fitted with stopcocks at each end, *via* a joint for later attachment to a vacuum line. About 15 ml. of 60% sulfuric acid is added to the reaction flask and helium is bubbled through the solution at a rate of about 1 bubble per second. After the air in the system has been displaced by helium, the flask temperature is raised to just under reflux temperature and held there for 2–5 days until approximately the calculated amount of XII has been evolved. A much slower evolution may be noted after this point, owing to slow decomposition of the reaction products. During the first half of the reaction, the specific activity of the evolved XII agrees closely with that obtained by the pyrolysis of the corresponding calcium nicotinate (Table I). However, after that point the specific activity changes slowly, probably owing to the above mentioned decomposition. This is especially true during the decarboxylation of IV, which proceeds more slowly than does that of III. The water content should be maintained at roughly its starting level throughout the decarboxylation process.

When it is desired to trap XII (from the original carb oxyl group) for counting purposes, liquid nitrogen is applied to the trap until sufficient XII has accumulated; the stopcocks are closed and the trap is removed to a vacuum system, where XII is measured and transferred to a counter. After the helium has been pumped away, the liquid nitrogen is replaced by a Dry Ice bath in order that XII can be removed without liberating water from the trap. This XII shows no discernible impurities when subjected to gas chromatographic analysis. From III, XII evolves at a rate of about 1 mg. of carbon in 2 hr., and from IV it evolves at less than half this rate.

After evolution of XII about equals the calculated amount, the solution is cooled and diluted to about 50 ml. with water. It is taken to pH 8 with solid sodium carbonate and then is continuously extracted for 1 day with chloroform. The chloroform is evaporated under mild vacuum at room temperature. The residual oil (V) is taken up in about 20 ml. of glacial acetic acid and about an equal weight of 5% rhodium on alumina is added. This mixture takes up the maximum amount of hydrogen at atmospheric pressure within 30 min., and the yield of pyridone can be indirectly ascertained from the amount of hydrogen taken up. The solution is then filtered, most of the acetic acid is removed under vacuum at room temperature, and the residual oil is refluxed for 2 days with 10 ml. of 6 *N* hydrochloric acid. The excess acid is removed under vacuum and the solid residue is dissolved in water; then small portions of thoroughly washed, base-form AG3-X4 resin are added until the pH is raised to 6.5. After filtration, the water is removed and the residue is thoroughly dried, and VII, m.p. 134–135°, is obtained by recrystallization from about 1:3 ethanol–ether (yield ~30% from pyridone).

Betaine of VII[7] (IX).—About 3 mmoles of VII is dissolved in 3 ml. of water containing 1 equiv. of potassium hydroxide. While the reaction mixture is shaken vigorously, 1 ml. of dimethyl sulfate and 5 ml. of water containing 10 mequiv. of potassium hydroxide are added alternately, dropwise over about 0.5 hr. The solution is refluxed for 15 min., cooled, and taken to pH 7 with sulfuric acid, then evaporated to dryness. The dry solid is triturated with hot ethanol to extract the IX from inorganic material, and it can be crystallized as the dihydrate from a little ethanol plus about five times the volume of ether (m.p. 225° dec.). If sulfate is still present in the ethanol extract, it can be removed by adding dilute barium hydroxide solution until the pH has again been raised to about 6 and no more barium sulfate precipitates, then filtering, and repeating the evaporation and trituration.

(14) All C^{14} counting was performed by proportional gas counting of carbon dioxide. *Cf.* D. R. Christman, N. E. Day, P. R. Hansell, and R. C. Anderson, *Anal. Chem.*, **27**, 1935 (1955).

Formation of δ-Valerolactone (X).[8]—About 0.5 g. of IX is placed in an L-shaped side arm on an ordinary, straight vacuum trap. The outlet of this trap goes to a second trap and thence to a vacuum line. The first trap is provided with a joint so that it can be dismantled in the subsequent operations. The first trap is cooled with Dry Ice and the second with liquid nitrogen, after a pressure of about 0.8 atm. of helium has been introduced. The side arm, containing the betaine, is heated to 225°, and after about 1 min. the helium is slowly bled out of the system *via* the vacuum line. The system is then pumped for about 15 min., during which time trimethylamine collects in the second trap and X distils into the first trap.

δ-Bromovaleric Acid (XI).—X is washed out of the first trap with about 10 ml. of 48% hydrobromic acid and the solution is refluxed overnight.[9] Ether extraction gives XI, m.p. 137–139° (recrystallized from petroleum ether, b.p. 30–60°), in about 10% yield from IX.

Thallium Valerate (VIII).—A solution of 135 mg. of XI in 10 ml. of ethanol is dehalogenated with hydrogen at 1 atm., using 0.5 g. of 5% palladium on calcium carbonate as the catalyst.[10] The calculated amount of hydrogen is taken up in about 10 min., after which the solution is filtered and the ethanol removed under vacuum. The residue is taken up in water, acidified with sulfuric acid, and continuously extracted overnight with ether. A little less than 1 equiv. of an aqueous solution of thallous hydroxide is added to the ether extract and the mixture is stirred vigorously while the base is added to a phenolphthalein end point. This is taken to dryness and the crude XIII is triturated with several milliliters of absolute ethanol (inorganic thallium salts are insoluble). Then about twice the amount of ether is added to the supernatant ethanol and the product is obtained by refrigeration. The yield is about 90%, m.p. 160–164°. This salt can be used directly in running the Schmidt reaction.[12] The subsequent acids, made by the oxidation of the next lower amine (obtained in running the Schmidt reaction), are treated similarly after having been purified by gas chromatography. Each Schmidt reaction, from material based on either pyridone, gives XII representing one specific carbon atom in the original pyridine ring of nicotinic acid. The average activity level from 5 μc. of randomly labeled I is about 0.1 mμc./mg. of carbon.

Peroxytrifluoroacetic Acid–Boron Fluoride as a Source of Positive Hydroxyl[1,2]

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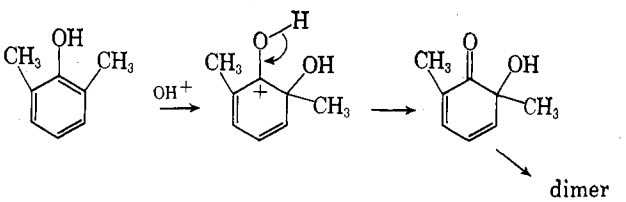
Peroxytrifluoroacetic acid–boron fluoride is shown to be an excellent reagent for effecting electrophilic aromatic hydroxylations with efficient use of the peracid. Mesitylene gave mesitol (88%), isodurene gave isodurenol (65%), but benzene gave only trace amounts of phenol. Prehnitene gave isodurenol, 2,3,5- and 2,3,6-trimethylphenol, 4,5,6,6-tetramethylcyclohexadienone, and 2,2′,3,3′,4,4′,5,5′-octamethyldiphenylmethane in addition to the expected prehnitol. These products can be rationalized by electrophilic attack of positive hydroxyl at substituted, as well as unsubstituted, aromatic carbon atoms, with 1,2-alkyl shifts in the former instance, and by hydride abstraction from methyl groups *para* to a phenolic hydroxyl.

It has long been recognized that organic peracids are sources of electrophilic (positive) hydroxyl in their reactions with the carbon–carbon double bond[4] and with certain aromatic hydrocarbons.[5] The hydroxyl cation was the assumed intermediate in the conversion of mesitylene to mesitol by hydrogen peroxide in acetic–sulfuric acid.[6] A Lewis acid (boron fluoride etherate) has been used in place of mineral acid with hydrogen peroxide to oxidize *m*-xylene, in low yield, to phenols and quinones.[7]

Peroxytrifluoroacetic acid was considered[8] to be an excellent source of positive hydroxyl, because the trifluoroacetate ion is a good leaving group. Using excess peracid, Musgrave, *et al.*, obtained 30–40% conversions of alkylbenzenes to phenols and quinones.[9] The orientation of the xylenols (2,4- and 2,6-) from *m*-xylene supported the contention that the reaction involved positive hydroxyl, rather than hydroxyl radicals.[10] The reaction has been extended to the preparation of *o*- and *p*-methoxyphenols from anisole and analogous phenoxyphenols from diphenyl ether.[11] The products from 2,6-dimethylphenol and peroxytrifluoroacetic acid depend upon reaction conditions; either 2,6-dimethylbenzoquinone or 6-hydroxy-2,6-dimethyl-2,4-cyclohexadienone dimer may predominate, slow addition of peroxide to the phenol favoring the latter (2,6-dimethyl-3-hydroxybenzoquinone is a minor reaction product).[12] Dienone dimer is presumably formed by attack of OH^+[13] at an already substituted position.[14]



It was considered likely that, if a Lewis acid facilitates the cleavage of hydrogen peroxide[7] and of certain diacyl

(1) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for financial support (G-488C).

(2) For a preliminary account, see C. A. Buehler and H. Hart, *J. Am. Chem. Soc.*, **85**, 2177 (1963).

(3) National Science Foundation Cooperative Fellow, 1962–1963.

(4) For a review, see D. Swern, *Org. Reactions*, **7**, 378 (1953).

(5) I. M. Roitt and W. A. Waters, *J. Chem. Soc.*, 3060 (1949).

(6) D. H. Derbyshire and W. A. Waters, *Nature*, **165**, 401 (1950); no experimental details are given.

(7) J. D. McClure and P. H. Williams, *J. Org. Chem.*, **27**, 24 (1962); this reagent converts aliphatic ketones to esters at room temperature in good yield.

(8) R. D. Chambers, P. Goggin, and W. K. R. Musgrave, *J. Chem. Soc.*, 1804 (1959).

(9) Conversions were calculated on the basis of hydrocarbon consumed: in fact, if calculated on amount of peracid used, they are much lower. The experimental technique described in the present paper (*vide infra*) affords much better conversions than previously reported,[8] even without boron fluoride.

(10) The hydroxyl radical, however, is also electrophilic; see R. O. C. Norman and G. K. Radda, *Proc. Chem. Soc.*, 138 (1962). The question of whether the hydroxyl radical or the cation is involved in certain metal-catalyzed aromatic hydroxylations of biochemical interest is still unsettled; see R. Stewart, "Oxidation Mechanisms," W. A. Benjamin, Inc., New York, N. Y., 1964, p. 159; also, G. A. Hamilton and J. P. Friedman, *J. Am. Chem. Soc.*, **85**, 1008 (1963).

(11) J. D. McClure and P. H. Williams, *J. Org. Chem.*, **27**, 627 (1962).

(12) J. D. McClure, *ibid.*, **28**, 69 (1963).

(13) The symbol OH^+ is used for convenience throughout this paper. It is recognized that the precise nature of the positive hydroxyl species is unknown; it may have trifluoroacetate or other ligands attached.

(14) The author[12] prefers a cyclic transition state involving initial hydrogen bonding of peracid to the phenolic hydroxyl, but this does not appear to be required.[15]

(15) A. J. Waring and H. Hart, *J. Am. Chem. Soc.*, **86**, 1454 (1964).