TABLE V

RESOLUTION OF N-BENZENESULFONYL-N-CARBOXYMETHYL-3-SUBSTITUTED MESIDINES[a]

Sub-stituent	Alkaloid	Resolving solvent	Ml. of solv. per g. acid	Purif. solvent	Pure less-sol. salt m.p., °C.	Rotation in EtOH[b] Wt., g.	Vol., ml.	$[\alpha]_D$, l 1	t, °C.
NO₂	Cinchonine	AcOEt	22	AcOEt–MeOH (3:1)	215–216	0.0557	20	+115.0	23
F[c]	Cinchonidine	AcOEt	20	AcOEt	125–138	.0387	5	− 60.7	27
	Cinchonine	AcOEt	23	AcOEt–MeOH (10:1)	201–202	.0579	5	+ 94.1	29
Cl	Cinchonine	AcOEt–MeOH (11:1)	22	AcOEt–MeOH (6:1)	198–200	.0596	5	+106.5	26
Br	Cinchonine	AcOEt	16	AcOEt–MeOH (15:1)	200–203	.0720	20	+100.0	23
I	Cinchonine	AcOEt–MeOH (7:1)	24	AcOEt–MeOH (2:1)	204–205	.0683	5	+114.2	28
NH₂	Optically active compound prepared by reduction of optically active nitro compound.								

[a] Only the less-soluble salts are described. [b] A 1-dm. tube was used in all cases. [c] Resolution of the 3-fluoro acid was attempted with both cinchonine and cinchonidine, but the regenerated acid showed no optical rotation, and all the salt fractions exhibited similar rotation. A check for mutarotation in the cinchonidine salt was negative. Cinchonidine salt: *Anal.* Calcd. for $C_{36}H_{40}FN_3O_5S$: C, 66.95; H, 6.24. Found: C, 66.75; H, 6.15.

the acid in a manner just described afforded a comparable yield of (−)-N-benzenesulfonyl-N-carboxymethyl-3-nitro-mesidine, m.p. 199–200° (resolidified and melted again at 223–225°); rotation: 0.1225 g. made up to 10 ml. with ethanol at 25° gave α_D −0.14°, l 1; $[\alpha]^{25}_D$ −11.4°.

The resolutions of the other compounds in this investigation were carried out in a manner similar to that of the nitro compound just described; however, only the less-soluble salts were used. Details are summarized in Table V.

Racemization of (+)-N-Benzenesulfonyl-N-carboxy-methyl-3-nitromesidine.—A dimethylformamide solution of 0.9756 g. of the (+)-3-nitro acid was made up to 10 ml. and the racemization carried out at 118° (boiling point of *n*-butyl alcohol) in a manner described previously.[2] The following results were obtained: 0.0 hr., α^{30}_D +0.23°; 0.5 hr., α^{30}_D +0.17°; 1.0 hr., α^{30}_D +0.14°; 1.5 hr., α^{30}_D +0.12°; 2.5 hr., α^{30}_D +0.09°; 3.5 hr., α^{30}_D +0.04°.[18]

A plot of α *vs.* time on semi-logarithmic paper afforded a straight line typical of a first-order rate equation from whose slope was derived the rate constant, $k = 2.4 \times 10^{-1}$ hr.⁻¹ and the half-life, $t_{1/2} = 1.5$ hr.

(18) In all other cases, a minimum of five points was plotted.

TABLE VI

RACEMIZATION OF N-BENZENESULFONYL-N-CARBOXY-METHYL-3-SUBSTITUTED MESIDINES

Sub-stitu-ent	Opt. active acid m.p., °C.	Rotation in dimethylformaide Wt., g.	Vol., ml.	$[\alpha]_D$, l 1	t, °C.	$k_{av}. \times 10^{-2}$, hr.⁻¹	$t_{1/2}$, hr.
NO₂	196–198	0.9756	10	+ 2.4	30	24	1.5
Cl	202–211	.8432	20	+26.6	29	5.7	6.1
Br	219–220	.3887	20	+22.1	29	5.2	6.7[a]
I	188–195	.4606	20	+29.1	29	5.5	6.3
NH₂	110–115	.1339	10	+31.4	29	5.7	6.1

[a] Reported $k_{av} = 4.4 \times 10^{-2}$ hr.⁻¹; $t_{1/2} = 8.0$ hr. in *n*-butyl alcohol; for ref. see Table I, footnote b.

Duplicate racemization experiments were carried out in all cases in the same manner.

The average rate constants, half-lives, melting points and specific rotations of the optically active acids are summarized in Table VI.

URBANA, ILLINOIS

The Oxidation of Amines with Peracetic Acid

BY WILLIAM D. EMMONS

Under the proper experimental conditions, peracetic acid is a fairly good reagent for the oxidation of many anilines to nitrobenzenes. It also can be employed in some cases for oxidation of primary amines to nitroalkanes.

In contrast to previously described results, we have found that under suitable experimental conditions peracetic acid is a reasonably efficient reagent for oxidation of aromatic amines to nitrobenzenes. The oxidation of both aromatic and aliphatic amines with peracetic acid has been described in the literature but in most cases relatively poor yields of nitro compounds were obtained.[1-3] Thus oxidation of aniline with peracetic acid is reported to give only 11% nitrobenzene and the major product is azoxybenzene. The oxidation of aliphatic amines

(1) J. D'Ans and A. Kneip, *Ber.*, **48**, 1144 (1915).
(2) F. P. Greenspan, *Ind. Eng. Chem.*, **39**, 847 (1947).
(3) E. Bamberger and R. Seligman, *Ber.*, **35**, 4293 (1902).

also has been described but here, too, complex mixtures of products resulted.

Anhydrous solutions of peracetic acid were conveniently prepared by the acid-catalyzed reaction of acetic anhydride with 90% hydrogen peroxide. This reaction normally was carried out at ice-bath temperatures in an appropriate solvent. After the exothermic formation of peracetic acid had taken place, the aromatic amines were oxidized in the boiling solution. Peracetic acid prepared in this manner is contaminated with small amounts of hydrogen peroxide and diacetyl peroxide, but these impurities do not interfere with the subsequent oxidation reaction. The yields of some typical

oxidations of aromatic amines are summarized in Table I and refer to purified products.

TABLE I
OXIDATION OF AMINES TO NITROBENZENES

Aniline	Yield of nitrobenzene, %
Aniline	83
p-Toluidine	72
o-Toluidine	70
p-Anisidine	82
2-Amino-p-cymene	72
o-Anisidine	70
p-Chloroaniline	62
Ethyl p-aminobenzoate	66

In several cases trace amounts of highly colored impurities (possibly azoxybenzenes) were formed, but removal of these materials by passage of the crude product over a short silica gel chromatographic column proved relatively simple. In contrast to the recently described oxidation of anilines to nitrobenzenes with trifluoroperacetic acid,[4] the use of peracetic acid suffers from somewhat lower yields, its failure to oxidize cleanly weakly basic amines such as p-nitroaniline, and the impurity of some of the crude products obtained. On the other hand, peracetic acid is a considerably cheaper reagent and may be used also for the oxidation of anilines with electron donating substituents such as o- and p-anisidine. In these two cases oxidation of the amines with trifluoroperacetic acid was not successful since the reagent attacked the benzene nucleus. As indicated above, however, oxidation of aromatic amines such as p-nitroaniline with strongly electron-withdrawing groups was not a satisfactory reaction with peracetic acid and complex mixtures of products were obtained. The oxidation of β-naphthylamine with peracetic acid was also attempted but here, as was the case with trifluoroperacetic acid, an intractable tar was obtained. In summary then it appears that peracetic acid supplements trifluoroperacetic acid in its ability to oxidize anilines to nitrobenzenes and in many cases the former reagent is satisfactory.

The oxidation of aliphatic amines with peracetic acid also was examined briefly. Yields of nitroalkanes obtained from t-octylamine, cyclohexylamine, sec-butylamine and n-hexylamine were, respectively, 87, 70, 65 and 33%. Superficially it would appear that the reagent is satisfactory for oxidation of t-carbinamines and dialkylmethylamines to the corresponding nitroalkanes. This reaction un-

$$R_2CHNH_2 \longrightarrow R_2CHNOH \longrightarrow R_2CHNO \longrightarrow R_2CHNO_2$$

doubtedly proceeds through the intermediate hydroxylamine and nitrosoalkane. That this is indeed the case is indicated by the transitory blue color observed in all of these reactions. The fact that a rather poor yield of nitroalkane is obtained from n-hexylamine may be explained by a relatively rapid prototropic conversion of the nitrosoalkane intermediate to its stable tautomer, n-hexaldoxime. The ultimate fate of this oxime, if indeed it was formed, was not investigated but certainly this explanation for the poor yield obtained with this primary

(4) W. D. Emmons, THIS JOURNAL, 76, 3470 (1954).

amine is not unreasonable. It also should be pointed out that the recently described permanganate oxidation of t-carbinamines to t-nitroalkanes is a more convenient preparation of these compounds, although it does not appear applicable to the synthesis of other nitroalkanes.[5]

It is interesting to contrast the behavior of peracetic acid with that of trifluoroperacetic acid in the oxidation of aliphatic amines. Under normal conditions the attempted oxidation of an aliphatic amine simply leads to formation of the amine trifluoroacetate salt. This is not surprising, since solutions of trifluoroperacetic acid always contain considerable quantities of trifluoroacetic acid. The latter compound is a sufficiently strong acid to protonate substantially all the free amine, and hence the oxidation does not take place. If, however, the reaction is carried out in the presence of a heterogeneous sodium carbonate buffer system,[6] it is possible to obtain a reaction between an aliphatic amine and trifluoroperacetic acid. Under these conditions, however, the product obtained is the N-alkyl trifluoroacetamide.

$$RCH_2NH_2 + CF_3\overset{O}{\overset{\|}{C}}OOH \longrightarrow RCH_2\overset{H}{N}COCF_3 + H_2O_2$$
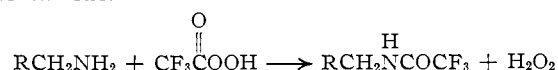
The yields of this amide were excellent even at temperatures as low as −30°. It is apparent that with strongly nucleophilic amines attack of the nucleophile takes place exclusively at the carbonyl carbon atom, while in the case of aromatic amines, no detectable acylation of the amine was observed with trifluoroperacetic acid.

Experimental[7]

Oxidation of p-Toluidine to p-Nitrotoluene.—To 60 ml. of chloroform stirred vigorously in an ice-bath was added 13.6 ml. (0.5 mole) of 90% hydrogen peroxide and two drops of sulfuric acid catalyst. Acetic anhydride (61.2 g., 0.6 mole) was then added dropwise over a 30-minute period. The mixture subsequently was stirred for 15 minutes at room temperature. The clear solution so obtained was diluted with 40 ml. of chloroform and heated fairly rapidly to boiling. The heating mantle was removed, and 10.7 g. (0.1 mole) of freshly distilled p-toluidine in 25 ml. of chloroform was added over a 20-minute period. The solution boiled vigorously during this addition. The yellow solution was then heated under reflux one hour and poured into 300 ml. of water. The organic layer was separated, washed with 2 × 100 ml. of 20% aqueous sodium hydroxide solution and 100 ml. of 10% hydrochloric acid and then finally dried over magnesium sulfate. Evaporation of the solvent gave 13.0 g. of crude product and after recrystallization from ligroin, 9.8 g. (72%) of p-nitrotoluene, m.p. 50–51°, was obtained. A mixture melting point with an authentic specimen showed no depression.

Oxidation of p-Anisidine to p-Nitroanisole.—A peracetic acid solution in chloroform was prepared as described above. The oxidation of 12.3 g. (0.1 mole) of p-anisidine also was carried out as described above and 14.0 g. of crude product isolated. After recrystallization from ethanol there was obtained 12.5 g. (82%) of p-nitroanisole, m.p. 52.5 to 53°. A mixture melting point with an authentic specimen showed no depression.

Oxidation of 2-Amino-p-cymene to 2-Nitro-p-cymene.—In the usual manner there was obtained 18.5 g. of crude oxidation product. This was dissolved in 100 ml. of methylene

(5) N. Kornblum, R. J. Clutter and W. J. Jones, ibid., 78, 4003 (1956).

(6) W. D. Emmons and A. S. Pagano, ibid., 77, 89 (1955).

(7) All preparations of peracetic acid were routinely carried out behind a safety shield. For information concerning the hazards of 90% hydrogen peroxide see E. S. Shanley and F. P. Greenspan, Ind. Eng. Chem., 39, 1536 (1947).

chloride and the resulting solution was passed over a 2 × 5 cm. column of silica gel. The column was washed with a little solvent and the combined eluates were evaporated. There was obtained 12.8 g. of 2-nitro-p-cymene, b.p. 94° (2.0 mm.), n^{20}D 1.5288. The infrared spectrum of this product was identical in all respects to that of an authentic sample.

Oxidation of Ethyl p-Aminobenzoate to Ethyl p-Nitrobenzoate.—The reaction when carried out in the usual way gave 14.7 g. of crude product which after recrystallization from ethanol weighed 12.8 g. (66%) and melted at 53–55°. It showed no depression in melting point when mixed with an authentic specimen of ethyl p-nitrobenzoate.

Oxidation of sec-Butylamine to 2-Nitrobutane.—Hydrogen peroxide (65.2 ml., 2.4 moles) was added dropwise fairly rapidly to 300 ml. of ice-cooled ethylene chloride with vigorous stirring. After addition of four drops of sulfuric acid catalyst 292 g. (2.88 moles) of acetic anhydride was added to the cooled solution over a 90-minute period. The mixture so obtained was stirred 30 minutes at 0° and 30 minutes at room temperature. It was diluted with 200 ml. of ethylene chloride and heated rapidly to reflux. At this temperature a solution of 43.8 g. (0.6 mole) of sec-butylamine in 50 ml. of ethylene chloride was added dropwise over a one-hour period. The reaction was very exothermic during this addition and rapidly developed a blue color. After the amine addition was complete the mixture was heated under reflux one hour. It was then cooled, washed with 2 × 500 ml. of cold 1:1 ammonia, and finally with 500 ml. of water. The organic extract was dried over magnesium sulfate, and the major portion of solvent removed by frac-tionation in a Todd column packed with glass helices. The residue, still containing some solvent, was fractionated in a spinning band column, and 40.2 g. (65%) of 2-nitrobutane, b.p. 64–66° (60 mm.), n^{20}D 1.4043, obtained. The infrared spectrum of this product was identical in all respects to that of an authentic sample.

Reaction of Trifluoroperacetic Acid with n-Hexylamine.—A solution of trifluoroperacetic acid was prepared by dropwise addition of 60.5 ml. (0.36 mole) of trifluoroacetic anhydride to a cooled suspension of 8.2 ml. (0.3 mole) of 90% hydrogen peroxide in 50 ml. of methylene chloride. This solution was then added over a 30-minute period to a well-stirred suspension of 85 g. (0.8 mole) of anhydrous sodium carbonate in 400 ml. of methylene chloride at −25° to −35°. At this temperature a solution of 5.0 g. (0.05 mole) of n-hexylamine in 10 ml. of solvent was added dropwise, and the resulting mixture was stirred at −30° for one hour. It was then poured into 500 ml. of water. The organic layer was dried over magnesium sulfate and the volatile solvent evaporated. There was obtained 7.9 g. (80%) of n-hexyl trifluoroacetamide, b.p. 80° (1.0 mm.). The infrared spectrum was typical of an N-substituted amide and showed carbonyl bands at 1710 and 1550 cm.$^{-1}$.

Anal. Calcd. for $C_8H_{14}NOF_3$: C, 48.72; H, 7.16; N, 7.10. Found: C, 48.76; H, 7.48; N, 7.62.

HUNTSVILLE, ALABAMA

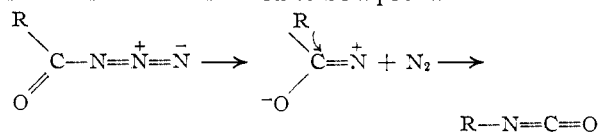# The Curtius Rearrangement. I. The Decomposition of m- and p-Substituted Benzazides in Toluene

BY YASUHIDE YUKAWA AND YUHO TSUNO

The rates of the Curtius rearrangement of various substituted benzazides in toluene were measured by collecting the nitrogen evolved; the activation energies and log PZ were calculated. The rate differences attributable to substitution were small but the activation and log PZ varied over a wide range. The rate changes were, however, found to depend on the changes in activation energy. Electron-releasing groups in the m-position of benzazide increased the reaction rate and electron-attracting groups decreased it. On the other hand, all substituents in the p-position decreased the rate. These results, which differ from those reported for the Lossen, Hofmann and Schmidt rearrangements, are discussed in terms of the polar effects of the substituents and the effect of conjugation of the carbonyl group with the benzene ring on the breaking bond.

Although the Curtius rearrangement,[1] the decomposition of acyl azide into an isocyanate and nitrogen, is an important procedure for replacing a carboxyl group by an amino group or amino derivatives, few kinetic studies[2,3] have been reported.

The Curtius rearrangement has been thought to proceed through a mechanism[4] analogous to those of similar rearrangements such as the Lossen, Hofmann and Schmidt rearrangements. Of the various mechanisms[5,6] proposed, the following expression has been considered to be a probable one.

$$R-N=C=O$$

An azide decomposes to give a molecule of nitrogen and an intermediate which contains a nitrogen atom with an incomplete octet, followed by intramolecular migration of R. In other words, the reaction in which loss of nitrogen occurs is the rate-determining step.

Newman and co-workers,[3] in their kinetic study of this rearrangement, demonstrated that the kinetics in various solvents was first order and that no salt effect was present. However, kinetic effects of structural changes in the azide, and effects of substituents on the migration of the phenyl group in benzazide have not been investigated. The study made by Hauser and others[7,8] on the Lossen and Hofmann rearrangements indicated that electron-releasing substituents in the migrating phenyl group increase and electron-attracting groups decrease the rate, the sequence being in accord with the polar effects of the respective substituents, and the experimental results were found to follow Hammett's equation. In the

(1) For a comprehensive review see, P. A. S. Smith, "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 337.

(2) C. W. Porter and L. Young, THIS JOURNAL, **60**, 1497 (1938); E. W. Barrett and C. W. Porter, *ibid.*, **63**, 3434 (1941).

(3) M. S. Newman, S. H. Lee, Jr., and A. B. Garrett, *ibid.*, **69**, 113 (1947).

(4) F. C. Whitmore, *ibid.*, **54**, 3274 (1932).

(5) C. R. Hauser and S. W. Kantor, *ibid.*, **72**, 4284 (1950).

(6) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, pp. 319–320.

(7) T. F. Bright and C. R. Hauser, THIS JOURNAL, **61**, 618 (1939); W. B. Renfrow, Jr., and C. R. Hauser, *ibid.*, **59**, 2308 (1937).

(8) C. R. Hauser and W. B. Renfrow, Jr., *ibid.*, **59**, 121 (1937).