in an evacuated but closed vacuum desiccator the compound lost bromine and benzhydrazide hydrobromide (m.p. and mixed m.p. 215–217°) remained. Since purification was not possible the substance was characterized by adding a portion to cracked ice and allowing the reaction to proceed until gaseous evolution stopped. An excess of aniline was then added, the mixture stirred and treated with dilute hydrochloric acid. The resulting solid was recrystallized from ethanol, m.p. 162–164°. The melting point was not depressed on admixture with an authentic sample of benzanilide. For analysis, samples of the hydrobromide were allowed to stand in a desiccator in contact with bromine. Values for the molar ratio of bromine to benzhydrazide hydrobromide ranged from 0.95 to 1.03.

**Formation of Benzhydrazidium Triiodide.**—A solution of 12.6 g. of iodine in 10 ml. of 47% hydriodic acid was added to a solution of 6.8 g. of benzhydrazide in 20 ml. of 47% hydriodic acid. A bronze-colored solid soon separated. The yield after drying over calcium chloride, potassium hydroxide and ceresin wax was 21 g. (the brown solid became dark green during the drying process). Recrystallization from dilute hydriodic acid gave long bronze needles (9.5 g.), m.p. in a sealed tube 149–153° dec. after the appearance of iodine vapors at 125° and previous softening at 135°. One-gram samples were analyzed roughly by solution in 25 ml. of ethanol and then addition of 100 ml. of 1 *N* sulfuric acid and titration with 0.1 *N* thiosulfate. The results (active I: 45.90, 45.95, 45.82, 46.02%) suggest that the compound is a dihydrate of benzhydrazidium triiodide although it was not obtained sufficiently pure for good elemental analysis.

***p*-Carbomethoxybenzhydrazide.**—A small amount of this compound was the only product isolated in an attempted conversion of a crude sample of dimethyl isophthalate (Brother's Chemical Co., Pract. grade) to isophthalhydrazide by refluxing with hydrazine hydrate. The monohydrazide undoubtedly is derived from dimethyl terephthalate present as an impurity. The hydrazide melted at 204–205.5° after recrystallization from nitromethane–dimethylformamide (1:1).

*Anal.* Calcd. for $C_9H_{10}O_3N_2$: C, 55.66; H, 5.19. Found: C, 55.62; H, 5.06.

**Reaction of Benzyl Carbazate with Hydrogen Chloride–Chlorine. Formation of Benzyl Chloride.**—A solution of 13.5 g. of benzyl carbazate[16] in 150 ml. of methylene dichloride was cooled in an ice-bath and saturated with hydrogen chloride. Dry chlorine was then passed into the cold mixture until the solid dissolved (two hours).[17] After removal of the solvent from a water-bath at 60° the benzyl chloride was distilled through a 30-cm. spiral-packed column, b.p. 73–75° (16 mm.), yield 7.85 g. (76.1%). The isothiuronium salt melted at 175.5–177.5°; mixed m.p. with an authentic sample 175.5–177.5°.

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[16] N. Rabjohn, THIS JOURNAL, **70**, 240 (1948).

[17] The reaction was much more rapid (10–15 min.) in nitromethane but isolation of the product was simplified in this case by use of methylene chloride.

AMHERST, MASS.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MASSACHUSETTS]

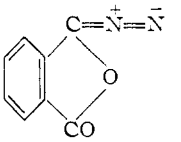
# Oxidative Reactions of Hydrazines. II. Isophthalimides. New Protective Groups on Nitrogen[1,2]

BY LOUIS A. CARPINO

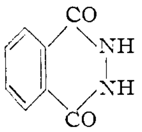
RECEIVED JULY 24, 1956

Oxidation of the hydrazones and oximes of phthalaldehydic acid by means of N-bromosuccinimide yields isophthalimides. As an aid in this and other studies new procedures for the selective and rapid removal of protective groups on nitrogen have been developed which involve cleavage of the *t*-butyloxycarbonyl (carbo-*t*-butoxy) group by means of hydrochloric, hydrofluoric or trifluoroacetic acid.

In work directed toward the synthesis of diazophthalide (I), synthetic routes to possible precursors (*e.g.*, V, R = $NH_2$, OH) were examined. Attempted syntheses of N-aminoisophthalimide (V, R = $NH_2$) gave either N-aminophthalimide (IV, R = $NH_2$) or 1,2-phthaloylhydrazine (II). The hydrazone (III, R = $NHCOOCH_2C_6H_5$) obtained from benzyl carbazate and phthalaldehydic acid, on oxidation with N-bromosuccinimide, gave a substance (V, R = $NHCOOCH_2C_6H_5$) isomeric with that (IV, R = $NHCOOCH_2C_6H_5$) obtained from benzyl carbazate and phthalic anhydride. Both isomers were cleaved by hydrogen bromide to N-aminophthalimide, a compound previously obtained from phthalimide and hydrazine.[3]



I



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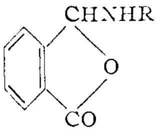

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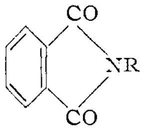
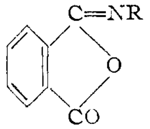


IV



V

In view of the facile isomerization of isophthalimides new methods for the removal of protective groups were sought which could be carried out under milder conditions. These methods were originally examined in connection with attempted cleavage of the carbobenzoxy group from benzyl benzoylazoformate ($C_6H_5CON{=}NCOOCH_2C_6H_5$) which underwent reduction of the azo linkage on treatment with hydrogen bromide.[4] Both the *p*-methoxybenzyloxycarbonyl (carboanisoxy) and *t*-butyloxycarbonyl (carbo-*t*-butoxy) groups were found to be cleaved instantaneously at ordinary temperatures by the strong non-reducing acid, trifluoroacetic acid. In the case of the carboanisoxy group difficulties sometimes accompanied separation of the desired product from by-products containing the *p*-methoxybenzyl group. The carbo-*t*-butoxy group did not suffer from such a dis-

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[1] This work was supported by grants from the Research Corporation, New York.

[2] Presented at the 129th National Meeting of the American Chemical Society, Dallas, Texas, April 13, 1956.

[3] H. D. K. Drew and H. H. Hatt, *J. Chem. Soc.*, 16 (1937).

[4] L. A. Carpino, THIS JOURNAL, **79**, 96 (1957).

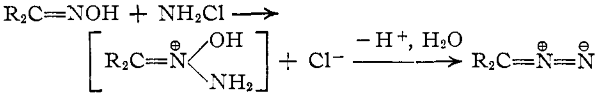
advantage and furthermore was cleaved even by the milder acid, hydrogen fluoride. Since the carbo-*t*-butoxy group undergoes cleavage by hydrogen chloride in nitromethane or water it is suggested that these reagents will be routinely useful in rapidly liberating an amino group protected by this function. Presumably all by-products (carbon dioxide and isobutylene) of the reaction are gaseous.[5]

$$\mathrm{RNHCOOCMe_3 \xrightarrow{HX} RNH_3X + CO_2 + [Me_2C{=}CH_2]}$$

In the examples reported in this paper the carbo-*t*-butoxy group has been introduced by indirect means although *t*-butyl chloroformate has been prepared and found to react normally with amines.[6]

Unfortunately the new procedures were not successful in the attempted synthesis of N-aminoisophthalimide since cleavage of V ($R = NHCOOCMe_3$ or $NHCOOCH_2C_6H_4OCH_3$-*p*) gave 1,2-phthaloylhydrazine (II).

Attention was next directed to the structure of the product obtained by reaction of phthalic anhydride and hydroxylamine for which structures IV and V (R = OH) have been proposed. This study was prompted by the observation of Forster[7] who found that diazocamphor could be obtained readily by treatment of isonitrosocamphor with chloramine, a reaction which can be considered a nucleophilic displacement on nitrogen followed by stabilization of the intermediate VI.[8]



$$\mathrm{R_2C{=}NOH + NH_2Cl \longrightarrow \left[R_2C{=}\overset{\oplus}{N}\genfrac{}{}{0pt}{}{OH}{NH_2}\right] + Cl^- \xrightarrow{-H^+,\ H_2O} R_2C{=}\overset{\oplus}{N}{=}\overset{\ominus}{N}}$$

VI

Early workers[9] suggested structure IV (R = OH), but later investigators favored V (R = OH) and the latter structure appeared to be accepted until 1955 when Ames and Grey[10] compared the infrared spectrum of the product with that of phthalimide and N-ethylphthalimide and concluded that the structure was best represented by IV (R = OH). This assignment has been verified in the present work by further spectral evidence and also additional chemical evidence in the form of an isomeric N-hydroxy compound, which was prepared by careful oxidation of phthalaldehydic acid oxime by the N-bromosuccinimide–pyridine method.

On the basis of infrared data and method of synthesis the new isomer is assigned structure V (R = OH). The conditions for the preparation of V (R = OH) must be carefully controlled during oxidation of the oxime. Phthaloxime is readily converted by acids, alkalies or mild heating to N-hydroxyphthalimide. These properties clearly preclude application of the Forster reaction to phthaloxime.

Methylation of V (R = OH) by means of diazomethane gave the rearranged ether, N-methoxyphthalimide (IV, $R = OCH_3$) although the isomeric compound could be obtained by a method analogous to that used in the synthesis of V (R = OH). The infrared spectral data for the carbonyl region of the normal and isophthalimides examined in the course of this work are shown in Tables II and III. In all cases the normal compounds showed the two expected bands at 1745–1715 and 1795–1770 $cm.^{-1}$ with the broader band characteristically at the longer wave length. All of the isoimides showed absorption at 1705–1658 $cm.^{-1}$.[11]

## Experimental[12-14]

**Preparation of *t*-Butyl Phenyl Carbonate.**—A solution of 248 g. of *t*-butyl alcohol and 430 g. of quinoline in 500 ml. of methylene dichloride was stirred and cooled by a slow stream of running tap water while 520 g. of phenyl chloroformate was added dropwise during about four hours while maintaining the temperature at 30°. The solution was allowed to stand overnight, sufficient water was added to dissolve the precipitated salt and the organic layer was washed two times with 200-ml. portions of water and 3–4 times with 200-ml. portions of 5% hydrochloric acid. The solvent was removed from the dried ($MgSO_4$) solution and the product distilled through a Claisen flask, b.p. 74–78° (0.5 mm.), amount 476 g. (73.6%).

*Anal.* Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.48; H, 7.19.

Distillation of large amounts of this compound by means of a water aspirator leads to complete decomposition to phenol and presumably carbon dioxide and isobutylene. Attempts to prepare this compound using as bases pyridine, dimethylaniline, tri-*n*-butylamine, triethylamine, sodium *t*-butoxide and potassium *t*-butoxide either did not cause reaction to occur, gave extremely low yields or gave other products.

**Preparation of *t*-Butyl Carbazate.**—A mixture of 476 g. of *t*-butyl phenyl carbonate and 252 g. of 64% hydrazine (Eastman Kodak Co. pract.) was warmed on a hot-plate. When the temperature reached 75° instantaneous solution occurred and the temperature rose spontaneously to 103°. After standing for 12 hours the solution was diluted to one liter with ether and shaken well with an aqueous solution containing 150 g. of sodium hydroxide. The mixture was extracted with ether for 24 hours in a continuous extractor, the solvent removed on a steam-bath and the carbazate distilled through a Claisen flask, b.p. 60–61° (0.5 mm.). The yield was 221 g. (68.3%).

An analytical sample was prepared by extraction of an ether solution of a small amount of the carbazate with dilute sodium hydroxide to remove any phenol, evaporation of the solvent, redistillation and finally recrystallization several times from petroleum ether, m.p. 41–42°.

*Anal.* Calcd. for $C_5H_{12}O_2N_2$: C, 45.43; H, 9.16. Found: C, 45.60; H, 9.05.

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[5] In the hydrogen halide cleavage of the carbo-*t*-butoxy group either the *t*-butyl halide or isobutylene might be formed as primary decomposition products. Referee II raised the question as to which is the more likely product. While no studies have yet been made on the exact stoichiometry of the reaction it appears that isobutylene is a primary product since passage of the gases from the hydrochloric acid cleavage of *t*-butyl carbanilate through bromine water caused decolorization and separation of a heavy oil.

[6] A. R. Choppin and J. W. Rogers, THIS JOURNAL, **70**, 2967 (1948). The method described by these workers is long and tedious. Since a convenient synthesis of *t*-butyl chloroformate is necessary for widespread utility of the present procedures a modification of the reported method is being examined.

[7] R. Forster, *J. Chem. Soc.*, **107**, 260 (1915).

[8] *Cf.* R. S. Drago and H. H. Sisler, THIS JOURNAL, **77**, 3191 (1955).

[9] For references to previous work see C. D. Hurd, C. M. Buess and L. Bauer, *J. Org. Chem.*, **19**, 1140 (1954).

[10] D. E. Ames and T. F. Grey, *J. Chem. Soc.*, 3518 (1955).

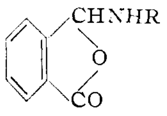
[11] L. J. Bellamy ("The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 223, 226) quotes the range 1680–1630 $cm.^{-1}$ for the stretching frequency of the C=N bond in $\alpha,\beta$-unsaturated compounds.

[12] All boiling and melting points are uncorrected.

[13] Analyses are by Geller Laboratories, Hackensack, N. J., and Drs. Weiler and Strauss, Oxford, England.

[14] Infrared spectra were taken as Nujol mulls with a Perkin–Elmer model 21 double beam spectrophotometer, sodium chloride optics. The authors are indebted to Dr. Arthur E. Martell of Clark University for making the spectrophotometer available.

TABLE I



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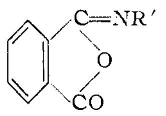

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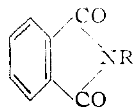
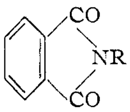


| R, R′ or R″ | Yield, % | Formula | Analyses, % Calcd. C | Calcd. H | Found C | Found H | M.p., °C. |
|---|---|---|---|---|---|---|---|
| R = -NHCOOCH$_2$C$_6$H$_5$ | 90 | $C_{16}H_{14}O_4N_2$ | 64.42 | 4.73 | 64.45 | 4.66 | 189–191 (d.) |
| R = -NHCOOC(CH$_3$)$_3$ | 56 | $C_{13}H_{16}O_4N_2$ | 59.08 | 6.10 | 59.20 | 6.19 | 179.5–180.5 |
| R = -OCH$_3$ | 87 | $C_9H_9NO_3$ | 60.33 | 5.06 | 60.60 | 5.21 | 133–134 |
| R′ = -NHCOOCH$_2$C$_6$H$_5$ | 41 | $C_{16}H_{12}O_4N_2$ | 64.86 | 4.08 | 64.83 | 4.14 | 167–168 |
| R′ = -NHCOOC(CH$_3$)$_3$ | 40 | $C_{13}H_{14}O_4N_2$ | 59.53 | 5.38 | 60.00 | 5.61 | 128–130 |
| R′ = -OCH$_3$ | 67 | $C_9H_7NO_3$ | 61.02 | 3.98 | 60.90 | 4.13 | 124–124.5 |
| R″ = -NHCOOCH$_2$C$_6$H$_5$ | 68 | $C_{16}H_{12}O_4N_2$ | 64.86 | 4.08 | 65.23 | 4.04 | 136–137 |

TABLE II[a]

CARBONYL ABSORPTION FREQUENCIES OF

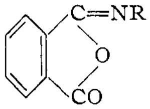


| R | Cm.$^{-1}$ |
|---|---|
| -OCH$_3$ | 1736s<br>1787s |
| -OSO$_2$C$_6$H$_5$[b] | 1743s<br>1798m |
| -NHCOOCH$_2$C$_6$H$_5$ | 1725s (very broad)<br>1795m |
| -NHCOOCH$_2$C$_6$H$_4$OCH$_3$-*p* | 1727s<br>1786m |
| -NH$_2$ | 1715s<br>1776m |
| -N=CHC$_6$H$_5$ | 1700s<br>1782m |
| -H | 1745s<br>1768s |
| -OH | $\left.\begin{matrix}1705\\1745\end{matrix}\right\}$s<br>1787s |

[a] s = strong, m = medium. [b] Prepared by the method of C. B. Buess and L. Bauer, *J. Org. Chem.*, **20**, 33 (1955).

TABLE III[a]

CARBONYL ABSORPTION FREQUENCIES OF



| R | Cm.$^{-1}$ |
|---|---|
| -OCH$_3$ | 1658m-s<br>1755 (shoulder)<br>1800s |
| -NHCOOCH$_2$C$_6$H$_5$ | 1683m<br>1745s<br>1785s |
| -NHCOOCH$_2$C$_6$H$_4$OCH$_3$-*p* | 1705w<br>1737s<br>1796s |
| -OH | $\left.\begin{matrix}1825\\1810\end{matrix}\right\}$s<br>1690m |

[a] s = strong, m = medium, w = weak.

The hydrazide was characterized as the benzal derivative which was recrystallized from ethanol–dimethylformamide (5:1) and melted at 186–188° dec.

*Anal.* Calcd. for $C_{12}H_{16}N_2O_2$: C, 65.43; H, 7.32. Found: C, 65.20; H, 7.36.

**Preparation of *t*-Butyl Hydrazodicarboxylate.**—A solution of 5 g. of crude *t*-butyl carbazate in 15 ml. of acetic acid and 30 ml. of water was cooled in an ice-bath and 2.9 g. of sodium nitrite was added during 2–3 minutes. After dilution with 30 ml. of water the top oily layer was extracted with two 30-ml. portions of ether and the extracts washed with sodium bicarbonate solution (1 molar). After drying over magnesium sulfate the ether was removed on a water-bath leaving 5 g. of brown oil. This oil was mixed with 5 g. of *t*-butyl carbazate, 3 g. of pyridine and 10 ml. of ether and allowed to stand for one week. After the addition of 50 ml. of water and 25 ml. of methylene dichloride the organic layer was washed with water, dried (magnesium sulfate) and distilled on a steam-bath with the aid of a water aspirator leaving 6 g. of red-brown oil which soon crystallized. After one recrystallization from methanol–water and another from benzene–ligroin the solid (2.5 g., 28.5%) melted at 89–91°. Two additional recrystallizations from nitromethane raised the melting point to 103–105°.

*Anal.* Calcd. for $C_{10}H_{20}O_4N_2$: C, 51.71; H, 8.70. Found: C, 51.90; H, 8.57.

**Cleavage of *p*-Methoxybenzyl N-Phenylcarbamate by Trifluoroacetic Acid.**—At room temperature[15a] 10.0 g. of the carbamate[15b] was added to 10 ml. of trifluoroacetic acid dissolved in 15 ml. of methylene dichloride. Vigorous gas evolution occurred and was allowed to subside between additions. After standing for three hours the solution was diluted with water and made alkaline with 20% sodium hydroxide solution. After two extractions of the aqueous solution with 10-ml. portions of methylene dichloride the organic layer was dried (magnesium sulfate) and distilled through a 20-cm. spiral-packed column giving 2.1 g. (58%) of aniline, b.p. 28–30° (0.1 mm.), $n^{24}D$ 1.5826. The acetyl derivative melted at 112–114°.

**Cleavage of *t*-Butyl N-Phenylcarbamate by Trifluoroacetic Acid.**—The cleavage was carried out by adding 6.5 g. of the carbamate[6] to 10 ml. of trifluoroacetic acid as indicated above for the anisyl compound except that methylene dichloride was not used to dilute the acid. Upon isolating the product as previously indicated there was obtained 1.5 g. (52%) of aniline, b.p. 76° (14 mm.).

**Cleavage of *t*-Butyl N-Phenyl Carbamate by Hydrofluoric Acid.**—To 20 ml. of 48% hydrofluoric acid there was added 5.0 g. of *t*-butyl N-phenyl carbamate[6] and the mixture warmed slightly on a hot-plate for three to five minutes. After allowing the mixture to stand at room temperature for 30 min. it was placed in the ice-chest overnight and the solid filtered and washed with ethanol. After drying in an oven at 40–50° the solid (4.05 g., 90.4%) melted at 240–243° (rapid heating). A sample of the same compound ($C_6H_5$-$NH_2 \cdot 4HF$) was prepared by adding aniline to an excess of hydrofluoric acid, m.p. 235–240° (rapid heating).[16] Acetylation of the aniline formed by adding alkali to the hydrofluoride gave acetanilide, m.p. and mixed m.p. 112–114°.

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(15) (a) Mr. Paul Terry has found that cleavage of the carbo-*t*-butoxy group occurs with moderate speed even at low temperatures. Using hydrogen chloride in nitromethane, *t*-butyl carbanilate gives a 28% yield of aniline hydrochloride at −40° over a period of five hours. At room temperature the yield is 100%. (b) H. Walbaum, Bericht von Schimmel and Co., 140 (1909) [*Chem. Zentr.*, **80**, II, 2181 (1909)].

(16) This compound has been described by J. F. T. Berliner and R. M. Honn, *J. Phys. Chem.*, **32**, 1142 (1928). These authors found that aniline hydrofluoride and most of the other hydrofluorides prepared by them sublimed on heating and did not give characteristic melting points.

**Preparation of *p*-Methoxybenzyl Carbazate.**—Phenyl *p*-methoxybenzyl carbonate was prepared as indicated above for the corresponding *t*-butyl compound except that dimethyl aniline was used in place of quinoline. The thick purplish oil which remained after removal of the methylene dichloride had to be used without purification in the next step since attempted distillation at pressures as low as 1-2 mm. always led to decomposition.

On mixing 27.6 g. of the crude carbonate and 11.7 g. of 64% hydrazine, spontaneous warming occurred and a homogeneous solution formed. After standing for two hours volatile by-products and starting materials were removed on a steam-bath, first with a water aspirator and then with an oil-pump (1-2 mm.). The residue solidified on cooling and on recrystallization from benzene-petroleum ether gave 18.0 g. (85.4%) of white crystals, m.p. 67-71°. A second recrystallization from methanol gave 12.0 g. (56.9%) of small white crystals, m.p. 72-74.5°. The analytical sample melted at 76-77°.

*Anal.* Calcd. for $C_9H_{12}O_3N_2$: C, 55.09; H, 6.16. Found: C, 55.30; H, 5.99.

**Preparation of Phthalaldehydic Acid *p*-Methoxybenzyloxycarbonylhydrazone.**—A solution of 5 g. of *p*-methoxybenzyl carbazate in 20 ml. of warm ethanol was cooled and added to a solution of 3.75 g. of phthalaldehydic acid in 50 ml. of ethanol. On standing, 7.0 g. (84%) of the condensation product separated as a mass of white crystals, m.p. 183-185°. The analytical sample was crystallized from nitromethane-dimethylformamide and melted at 184.5-185.5°.

*Anal.* Calcd. for $C_{17}H_{16}N_2O_5$: C, 62.19; H, 4.91. Found: C, 62.20; H, 4.97.

Other hydrazones and oximes were prepared similarly. The results are shown in Table I.

**N-[*p*-Methoxybenzyloxycarbonylamino]-isophthalimide** (V, R = $NHCOOCH_2C_6H_4OMe$-*p*).—A mixture of 3.3 g. of the hydrazone, 1.8 g. of N-bromosuccinimide and 50 ml. of methylene dichloride was treated with 0.8 g. of pyridine. After standing for one hour all of the solid material had dissolved and the solution was washed three times with water, dried (magnesium sulfate) and allowed to evaporate. A yellow-white solid (3.5 g. (100%) m.p. 139-141.5°) remained. On recrystallization from nitromethane 2.25 g. (68.8%) of white crystals was obtained, m.p. 139-141°. The analytical sample melted at 144-145°.

*Anal.* Calcd. for $C_{17}H_{14}N_2O_5$: C, 62.57; H, 4.33. Found: C, 62.30; H, 4.24.

Other isophthalimides were prepared similarly. The results are shown in Table I.

**N-[*p*-Methoxybenzyloxycarbonylamino]-phthalimide** (IV, R = $NHCOOCH_2C_6H_4OMe$-*p*).—A solution of phthalic anhydride was prepared by boiling 1.5 g. of the crude anhydride with 60 ml. of chloroform for 2-3 min. and filtering. The filtrate was refluxed with 2.0 g. of anisyl carbazate for 5 hours and the clear solution allowed to evaporate leaving 3.0 g. (90.5%) of the crude hydrazide. Recrystallization from ethanol-dimethylformamide (1:1) gave 1.8 g. (54.3%) of small white crystals, m.p. 158-160°. The analytical sample was crystallized from nitromethane and melted at 160-162°.

*Anal.* Calcd. for $C_{17}H_{14}N_2O_5$: C, 62.57; H, 4.33. Found: C, 62.50; H, 4.34.

Other phthalimides were prepared similarly. The results are shown in Table I.

**Isomerization of N-Methoxyisophthalimide.**—A solution of 0.2 g. of the imide dissolved in 8 ml. of nitromethane was saturated with hydrogen bromide. After standing overnight the mixture was filtered to remove a small amount of hygroscopic solid and the filtrate evaporated by a stream of air. The yellow solid (0.175 g., 87.5%) was recrystallized from 50% ethanol giving white flaky needles, m.p. 134-135°. The m.p. was not depressed on admixture with an authentic sample of N-methoxyphthalimide.[17]

**Cleavage of N-*t*-Butyloxycarbonylaminoisophthalimide.**—A solution of 0.8 g. of the imide in 5 ml. of nitromethane was saturated with dry hydrogen chloride. The yellow powder (0.5 g., m.p. 210-215°) which precipitated was shown to be phthalhydrazide by recrystallization from dimethylformamide, m.p. and mixed m.p. 340-342°.

**Cleavage of N-Benzyloxycarbonylaminoisophthalimide.**—This hydrazide, upon cleavage as described above gave N-aminophthalimide, m.p. 199-200°.[3] The same compound was obtained by cleavage of N-benzyloxycarbonylaminophthalimide as shown by identity of the corresponding infrared spectra. The benzal derivative melted at 161-163°.

**Preparation of Phthaloxime** (V, R = OH).—A slurry of 6.6 g. of powdered phthalaldehydic acid oxime in 50 ml. of methylene dichloride was cooled in an ice-bath and 3.2 ml. of pyridine then added. Immediately after addition of the pyridine, 7.2 g. of N-bromosuccinimide was added in one portion with swirling. Most of the solid dissolved at once and the remainder was brought into solution by crushing the particles against the sides of the flask. The orange solution was washed by decantation 3-4 times with water which caused the precipitation of a papery solid. After 3-5 minutes from the time the oxidizing agent was added, the mixture was filtered yielding 2.9 g. (45%) of white crystals which were washed with water. If a sample of this compound was dropped into a melting point bath heated to 175°, melting and instantaneous resolidification occurred followed by remelting at 222-232° as the temperature was gradually raised. When an ordinary melting point was taken, only the latter temperature was observed (much previous softening). The product was recrystallized from acetone giving 1.5 g. of papery needles which were shown to be free from any significant amount of N-hydroxyphthalimide by the complete absence of the strong, broad absorption band of the latter at 1705-1720 cm.$^{-1}$.

*Anal.* Calcd. for $C_8H_5NO_3$: C, 58.54; H, 3.07. Found: C, 58.70; H, 3.12.

The infrared spectrum was obtained two days after preparation. The oxime was converted to N-hydroxyphthalimide (m.p. and mixed m.p. 235-237°) by crystallization from dimethylformamide or brief treatment with hydrochloric acid.

The conditions of the preparation as described must be followed exactly in order to obtain reproducible results and even with care the yield is sometimes very low or the desired product difficult or impossible to isolate, particularly if the solution is allowed to stand for an appreciable time before washing with water. The oxime is soluble in dilute sodium bicarbonate solution. Methylation with methyl iodide and sodium ethoxide yields the O-methyl ether of N-hydroxyphthalimide (m.p. and mixed m.p. 133-135°). Diazomethane also yields the same compound (m.p. 133-135°).

AMHERST, MASS.

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[17] D. S. Pratt and H. D. Gibbs, *Philippine J. Sci.*, **8**, 165 (1913).