Cyclohexyl Isothiocyanate.—Diethyl N-cyclohexylphosphoramidate, 23.6 g. (0.1 mole), dissolved in 50 ml. of 1,2-dimethoxyethane was added slowly at room temperature to a slurry of 50% sodium hydride, 4.8 g. (0.1 mole), in 100 ml. of 1,2-dimethoxyethane. The mixture was stirred until gas evolution ceased and the solution had become homogeneous. Carbon disulfide, 7.6 g. (0.1 mole), was added dropwise at room temperature after which the solution was heated at 70° for 0.5 hr. The solution was cooled, decanted from a gummy residue, stripped, and distilled. The infrared spectrum of the distillate, 9.5 g. (71%), b.p. 117–118° (10 mm.), was identical with that of an authentic sample of cyclohexyl isothiocyanate.

O-Methylbenzaldoxime.[17]—Diethyl N-methoxyphosphoramide, 9.85 g. (0.05 mole), was added dropwise to a slurry of 50% sodium hydride, 2.4 g. (0.05 mole), in 100 ml. of 1,2-dimethoxyethane. The solution was stirred at room temperature until gas evolution ceased. Benzaldehyde, 5.3 g. (0.05 mole), was added slowly at approximately 25°. After the addition, the mixture was warmed at 60° for 0.5 hr. and cooled. The solution was decanted away from a gummy precipitate and stripped; the residue was distilled giving 5.5 g. (82%) of clear liquid distillate, b.p. 90° (15 mm.).

(17) K. V. Auwer and B. Ottens, *Ber.*, **57**, 456 (1924).

New Methods of Introducing the Carbo-*t*-butoxy Amino-Protecting Group. Preparation and Use of *t*-Butyl Cyanoformate and *t*-Butyl Iminodicarboxylate[1]

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A new route to the potentially useful carbo-*t*-butoxylating agent, *t*-butyl cyanoformate (I), is described which involves treatment of a *t*-butyl α-alkoxyacetate with N-bromosuccinimide followed by hydrolysis of the intermediate α-bromo ester (IV) and reaction of the resulting glyoxylate solution with hydroxylamine to yield *t*-butyl oximinoacetate (II). Dehydration of the oxime by means of acetic anhydride and triethylamine gave the cyanoformate (I). As an approach to the synthesis of various biscarbo-*t*-butoxylated amino compounds the preparation of several precursors was examined. Treatment of ethyl *t*-butyl oxalate with hydrazine gave *t*-butyl oxalyl hydrazide (VII) which on diazotization gave the unstable *t*-butyl oxalyl azide (VIII). The pure axide (VIII) could not be isolated but was converted directly to *t*-butyl iminodicarboxylate (IX) by warming with *t*-butyl alcohol. It was shown that the sodium salt of the imino compound (IX) reacted with alkyl halides to give the biscarbo-*t*-butoxylated amino derivatives which by hydrogen chloride cleavage were converted to the corresponding primary amines. Amination of the sodium salt of IX by means of mesitoxyamine gave *t*-butyl hydrazine-1,1-dicarboxylate (XI).

In view of the increasing importance of the carbo-*t*-butoxy group as an amino-protecting function, studies are continuing aimed at the development of new carbo-*t*-butoxylating agents having special advantages over those currently available.[2] To date, the acylating agent of choice from the point of view of availability, acylating power, and shelf stability is *t*-butyl azidoformate.[3] A related acylating agent, *t*-butyl cyanoformate (I), which has been described recently,[4] was first

$$\underset{\text{I}}{NC\text{–}COOCMe_3} \qquad \underset{\text{II}}{HON{=}CHCOOCMe_3}$$

obtained by the dehydration of *t*-butyl oxamate by means of trifluoroacetic anhydride. In the present paper we report a more convenient route to this potentially useful cyanoformate, namely dehydration of the corresponding oxime, *t*-butyl oximinoacetate (II). The oxime (II) was obtained through the corresponding glyoxylate. Previously the most convenient routes to alkyl glyoxylates involved the oxidative cleavage of dialkyl tartrates[5] and the reaction of alkyl bromoacetates with dimethyl sulfoxide.[6] Since *t*-butyl bromoacetate is readily obtainable, numerous attempts were made to oxidize this compound by the method of Hunsberger and Tien.[6] Although this method has been shown to give ethyl glyoxylate in 70–75% yields, the results were unsatisfactory with the *t*-butyl analog. Some aldehydic material was indeed obtained as shown by isolation of small amounts of the phenylhydrazone of *t*-butyl glyoxylate from the reaction mixture. A number of potential routes to *t*-butyl glyoxylate through the corresponding dichloroacetate were also found to lack promise. It was eventually found that *t*-butyl α-alkoxyacetates undergo ready bromination in the α-position on treatment with N-bromosuccinimide in carbon tetrachloride in the presence of benzoyl peroxide. The α-bromo-α-alkoxyacetates (IV) proved to be satisfactory intermediates in the synthesis of glyoxylate derivatives. Both *t*-butyl α-methoxy- (III, R = CH_3; R′ = *t*-Bu) and α-*t*-butoxyacetate (III, R = R′ = *t*-Bu) were converted easily to the desired oximinoacetate (II). The best yields were obtained using the α-methoxyacetate. It was not necessary to isolate the intermediate bromo ester (IV) or the glyoxylate derived therefrom. Bromoacetates such as IV undergo hydrolysis extremely readily on contact with water.[7,8] In order to avoid cleavage or hydrolysis of

$$\underset{\text{III}}{ROCH_2COOR'} \qquad \underset{\text{IV}}{ROCH(Br)COOR'}$$

(1) Supported by a grant (GM-09706-02) from the National Institutes of Health.

(2) For references to earlier work, see L. A. Carpino, *J. Org. Chem.*, **28**, 1909 (1963).

(3) L. A. Carpino, C. A. Giza, and B. A. Carpino, *J. Am. Chem. Soc.*, **81**, 955 (1959).

(4) L. A. Carpino, *ibid.*, **82**, 2725 (1960). NOTE ADDED IN PROOF (AUG. 11, 1964).—M. Leplawy and W. Stec [*Bull. acad. polon. sci., ser. sci. chim.*, (6) **12**, 21 (1964); *Chem. Abstr.*, **61**, 1933 (1964)] have shown that *t*-butyl cyanoformate can be obtained by reaction of *t*-butyl alcohol with carbonyl cyanide. These investigators also showed the cyanoformate to be generally useful in the carbo-*t*-butoxylation of amino acid derivatives.

(5) F. J. Wolf and J. Weijlard, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p. 124.

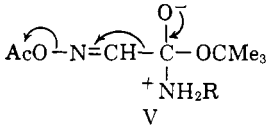
(6) J. Tien and I. M. Hunsberger, *Chem. Ind.* (London), 88 (1959).

(7) A. Bendich and G. C. Clements, *J. Am. Chem. Soc.*, **75**, 4075 (1953).

(8) R. Quelet and J. Gavarret, *Bull. soc. chim. France*, 1075 (1950).

the resulting *t*-butyl ester by the hydrogen bromide produced in the reaction, hydrolysis was carried out in the presence of sodium bicarbonate. Such aqueous solutions were then used in the preparation of glyoxylate derivatives. The exact nature of the species present in the aqueous glyoxylate solution was not determined. Continuous ether extraction of the aqueous solution prepared from either *t*-butyl α-methoxy- or α-*t*-butoxyacetate followed by removal of solvent and distillation gave a mobile liquid, b.p. 43° (15 mm.), which on standing at room temperature for several days became extremely viscous. Redistillation of the sirupy material gave again a mobile liquid. This liquid may be a mixture of the various possible hydrates.

Addition of hydroxylamine hydrochloride to the aqueous glyoxylate solution derived from *t*-butyl α-methoxyacetate gave the oximinoacetate (*II*) in 58% yield. Dehydration to *t*-butyl cyanoformate (I) was achieved in 75% yield by means of acetic anhydride–triethylamine. Substitution of pyridine for the triethylamine allowed isolation of the intermediate acetyl derivative, *t*-butyl acetoximinoacetate. The acetyl derivative was of interest in connection with possible fragmentative acylation (*cf.* V). However, the acet-



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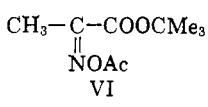
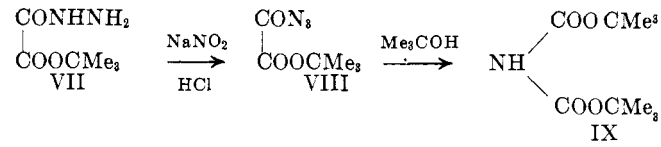


VI

oximino ester proved not to react in this manner as shown by the fact that acylation of amino compounds in its presence did not occur except under conditions known to cause prior conversion to the cyanoformate (I) which appeared to be the active acylating species.[9] In accord with this observation, *t*-butyl 2-acetoximinopropionate (VI) showed no carbo-*t*-butoxylating ability toward ammonia, benzylamine, hydrazine, or other amino compounds. The *t*-butyl α-alkoxyacetates used in these reactions were obtained in each case by sulfuric acid catalyzed addition of the free acid to isobutylene in a pressure bottle.[10] In the case of glycolic acid this gave primarily *t*-butyl α-*t*-butoxyacetate (55%). A small amount (*ca.* 7%) of *t*-butyl glycolate could be isolated from the reaction mixture when equimolar amounts of isobutylene and glycolic acid were used.

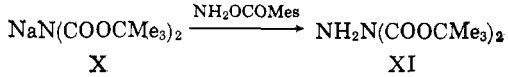
Up to the present time only the monocarbo-*t*-butoxylated derivatives of primary amino compounds have been reported. Although normally during protection of a primary amino function the remaining hydrogen atom does not interfere with further reactivity, in some cases it would be desirable to have both hydrogen atoms replaced by the carbo-*t*-butoxy group. One approach to such compounds involves acylation of the sodium salt of the monocarbo-*t*-butoxy derivative.

As a useful intermediate in a second approach to such systems, the synthesis of *t*-butyl iminodicarboxylate (IX) was examined. The preparation of IX was ac-

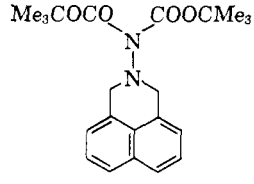


VII VIII IX

complished by treatment of ethyl *t*-butyl oxalate[4] with hydrazine to give the ester hydrazide (VII), diazotization of which gave *t*-butyl oxalyl azide (VIII). Because of its instability, the azide (VIII) was not isolated but converted directly to the iminodicarboxylate through the Curtius rearrangement by warming with *t*-butyl alcohol. *t*-Butyl iminodicarboxylate (IX) was obtained in two polymorphic modifications: A, m.p. 88.5–90.5°, and B, m.p. 119–121°. These exhibited identical infrared and n.m.r. spectra and reactivity. Availability of IX now makes possible a convenient Gabriel-like synthesis of primary amines. The sodium salt of IX reacts readily with alkyl halides and subsequent hydrogen chloride cleavage of the intermediate biscarbo-*t*-butoxy derivatives yields the corresponding amine hydrochlorides under mild conditions. As examples, α,α′-dibromo-*o*-xylene and ethyl bromoacetate were converted to the amine hydrochlorides without isolation of intermediates in yields of 50–60%. Substitution of an aminating agent for an alkylating agent allowed conversion of IX to a long-sought derivative of hydrazine, *t*-butyl hydrazine-1,1-dicarboxylate (XI),



X XI



XII

a compound which promises to be as valuable in the synthesis of special hydrazine derivatives as is *t*-butyl carbazate[11] and the isomeric *t*-butyl hydrazodiformate.[12]

The hydrazino compound (XI) was obtained by amination of the sodium salt (X) of the iminodicarboxylate by means of mesitoxyamine.[13] As evidence for the structure of XI, its benzal derivative proved to be identical with the compound obtained by treatment of the sodium salt of the benzal derivative of *t*-butyl carbazate with *t*-butyl azidoformate. Spectral evidence also supports structure XI. The infrared spectrum shows the expected imide carbonyl absorptions at 5.74 and 5.91 μ (Nujol) and the n.m.r. spectrum exhibits a sharp singlet at δ 1.52 for the *t*-butyl protons (18H) and a broad band at about δ 4.15 due to the amino protons (2H). As an illustration of the reactivity of XI, reaction with 1,8-bis(bromomethyl)naphthalene gave the bis-protected derivative (XII) of 2-amino-2,3-dihydro-1H-benz[*de*]isoquinoline. Cleavage of XII

(9) Compare A. F. Ferris, G. S. Johnson, and F. E. Gould, *J. Org. Chem.*, **25**, 496, 1813 (1960).

(10) A. L. McCloskey, G. S. Fonken, R. W. Kluiber, and W. S. Johnson, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p. 261.

(11) L. A. Carpino, *J. Am. Chem. Soc.*, **79**, 98 (1957).

(12) L. A. Carpino, *ibid.*, **79**, 4427 (1957).

(13) L. A. Carpino, *ibid.*, **82**, 3133 (1960). For the sake of convenience the important aminating agent, O-mesitoylhydroxylamine, will be referred to as mesitoxyamine.

with hydrogen chloride under mild conditions gave the expected hydrochloride.[14]

Experimental[15]

t-Butyl α-*t*-Butoxyacetate.—In a 500-ml. pressure bottle there was condensed approximately 180 g. of isobutylene; 100 g. of glycolic acid[16a] was added followed by cautious addition of 3 ml. of concentrated sulfuric acid. A stopper was wired in and the mixture was placed on a continuous shaker for 3–4 hr. until the solid dissolved. The bottle was then removed from the shaker and allowed to stand at room temperature for 12–15 hr. After addition of 250 ml. of ether, the organic layer was washed with three 100-ml. portions of water and two 75-ml. portions of 1 *M* sodium bicarbonate solution. After removal of solvent, distillation from a water bath gave 137 g. (55.3%) of the ester, b.p. 42–45° (0.9 mm.). A center cut distilled through a 30-cm., helices-packed column had b.p. 37° (0.4 mm.).

Anal. Calcd. for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71. Found: C, 63.64; H, 10.84.

When equimolar amounts of isobutylene and glycolic acid were used, it was possible to isolate in 7% yield *t*-butyl glycolate, b.p. 76–78° (20 mm.), lit.[16b] b.p. 56° (12 mm.), identified by infrared comparison with an authentic sample prepared by the method of Müller and Huber-Emden.[16b]

t-Butyl α-Methoxyacetate.—The reaction was carried out as indicated for the corresponding *t*-butoxy derivative utilizing 100 g. of methoxyacetic acid (Eastman Kodak Co., practical grade) and approximately 180 g. of isobutylene. There was obtained 124 g. (75.5 %) of the ester, b.p. 53–55° (15 mm.), lit.[17] b.p. 62–64° (22–23 mm.).

The n.m.r. spectrum showed three singlets at δ 1.47 [9H, $(CH_3)_3C$], 3.39 (3H, CH_3O), and 3.87 (2H, CH_2).

t-Butyl α-Bromo-α-methoxyacetate.—To a solution of 50 g. of *t*-butyl α-methoxyacetate in 1 l. of dry carbon tetrachloride were added 61 g. of N-bromosuccinimide and a few crystals of benzoyl peroxide. The mixture was refluxed with stirring for 1 hr. After the first 20 min. of refluxing the reflux rate increased spontaneously but not sufficiently so that the heating mantle had to be removed. An orange color developed after 25–30 min. and then gradually disappeared after an additional 10–15 min. of refluxing. The mixture was cooled in an ice bath and filtered to remove succinimide. The carbon tetrachloride was removed from the filtrate by distillation from a water bath (70–75°) at 25 mm. Distillation of the residue from a water bath gave 58 g. (75.2%) of the bromo ester, b.p. 63–65° (0.5 mm.).

All attempts to obtain analytical samples of the bromo ester gave low results for bromine content. This may have been due to rapid hydrolysis by atmospheric moisture. The n.m.r. spectrum taken immediately after distillation showed the three expected singlets at δ 1.51 [9H,$(CH_3)_3C$], 3.57 (3H, CH_3O), and 5.92 (1H, CHBr). Additional peaks appeared in the n.m.r. spectrum when it was rerun after the bromo ester had been allowed to stand at room temperature for several days.

t-Butyl Oximinoacetate.—Although the oximinoacetate could be obtained by reaction of hydrated *t*-butyl glyoxylate (see below) with hydroxylamine, it was more convenient to prepare the oxime directly from *t*-butyl α-methoxy- or α-*t*-butoxyacetate without isolation of any intermediates. As described previously 162.5 g. of *t*-butyl α-methoxyacetate was converted to the α-bromo ester by treatment with 198 g. of N-bromosuccinimide in 3 l. of carbon tetrachloride. The oil remaining after removal of the carbon tetrachloride by flash distillation at 15 mm. from a water bath (70–75°) was added at room temperature to a vigorously stirred mixture of 110 g. of sodium bicarbonate in 1.3 l. of water. Most of the oil had dissolved in about 20 min. A second 110-g. portion of sodium bicarbonate was added followed by 90.5 g. of hydroxylamine hydrochloride added portionwise to avoid excessive frothing. The mixture was stirred at room temperature for 5 hr. and then extracted with ether in a continuous extractor for 48 hr. The ether extract was dried (magnesium sulfate) and distilled to give 93.5 g. (58%) of the oximinoacetate, b.p. 81–83° (0.6 mm.).

It was absolutely necessary to avoid overheating the distillation flask during the purification of the oximinoacetate. On two separate occasions when the bath temperature was allowed to rise above 100° violent explosions of the remaining ester occurred which shattered the distillation apparatus. It is best not to attempt the distillation unless pressures below 1 mm. can be maintained throughout the distillation. Decomposition appeared to be autocatalytic and if a rise in pressure is noted it is best to discontinue the distillation. The following method which was used in the distillation above was found to be perfectly safe. The crude liquid was contained in a flask to which was attached directly a simple distillation head of the short-path type (such as Corning No. 8980) which had been wound with heating wire. Before starting the distillation, the system was evacuated to minimum pressure and the temperature in the head coil was adjusted so that the thermometer registered 66°. The liquid was then heated in an oil or water bath maintained at 89° and the distillate was collected as rapidly as possible (60 g./hr.). The n.m.r. spectrum (CCl_4) showed two singlets at δ 1.50 [9H, $C(CH_3)_3$] and 7.39 (1H, CH=) and a very broad hydroxyl absorption at δ 9.30.

Anal. Calcd. for $C_6H_{11}NO_3$: C, 49.65; H, 7.64; N, 9.65. Found: C, 49.26; H, 7.75; N, 9.44.

t-Butyl Acetoximinoacetate.—A solution of 25 g. of *t*-butyl oximinoacetate and 34.5 g. of pyridine in 100 ml. of ether was cooled in an ice bath and with stirring over a period of 5 min. 19.1 ml. of acetic anhydride was added dropwise. The cooling bath was removed and the solution was allowed to stir at room temperature for 4 hr. and then washed twice with 50-ml. portions of water, five times with 50-ml. portions of 10% hydrochloric acid, and three times with 50-ml. portions of 1 *M* sodium bicarbonate. Removal of the solvent followed by distillation gave 22.4 g. (69.5%) of the ester, b.p. 75–76.5° (0.8 mm.). The n.m.r. spectrum showed three singlets at δ 1.54 [9H, $(CH_3)_3C$], 2.20 (3H,CH_3CO), and 7.70 (1H, CH=).

Anal. Calcd. for $C_8H_{13}NO_4$: C, 51.33; H, 7.00; N, 7.48. Found: C, 51.36; H, 6.90; N, 7.41.

t-Butyl Cyanoformate.—To a mechanically stirred solution of 15.2 g. of *t*-butyl oximinoacetate and 30.4 ml. of triethylamine (4% excess) in 60 ml. of methylene dichloride, 10.3 ml. (4% excess) of acetic anhydride was dropped in at a rate to maintain gentle spontaneous refluxing (10 min.). The solution was allowed to stir 30 min. longer at room temperature and washed with 60-ml. portions of the following solvents in order: twice with water, three times with 5% hydrochloric acid, and three times with 1 *M* sodium bicarbonate. After removal of solvent from a 45° water bath at 130 mm., 10 g. (75%) of the cyanoformate was collected at 62–63°(50 mm.), lit.[4] b.p. 64–65° (55 mm.), identified by comparison of its infrared spectrum with that of an authentic sample.

t-Butyl Glyoxylate (Hydrated).—As described above 81 g. of *t*-butyl α-methoxyacetate was converted to the α-bromo derivative by treatment with 98.6 g. of N-bromosuccinimide in 1.46 l. of carbon tetrachloride in the presence of benzoyl peroxide. After removal of the carbon tetrachloride from the filtered reaction mixture, the undistilled residual bromo compound was added to a stirred solution of 55 g. of sodium bicarbonate in 650 ml. of water. After stirring for 12 hr. at room temperature, the solution was extracted with ether in a continuous extractor for 48 hr. The ether was removed from the dried (magnesium sulfate) extract by distillation from a water bath at 60° (130 mm.). The residue was distilled to give 68 g. of faintly yellow, mobile liquid, b.p. 55–60° (16 mm.). In order to remove excess water (about 2 ml.) the distillate was dissolved in 300 ml. of benzene and the solution refluxed under a Dean–Stark trap for 8 hr. Distillation gave 54 g. of the hydrated glyoxylate, b.p. 59–61° (20 mm.). After each distillation the yellowish mobile liquid became colorless and sirupy on standing at room temperature for several days. When tested just after distillation, the liquid dissolved readily in 2–3 volumes of water but after becoming viscous it was no longer soluble. The infrared spectrum (5% in carbon tetrachloride) showed a sharp band due to the hydroxyl group at 2.83 μ, and a strong, broad carbonyl absorption at 5.71 μ. Identical hydrated gloxylate material was obtained in lower yield starting from *t*-butyl α-*t*-butoxyacetate as shown by infrared spectral comparison.

(14) L. A. Carpino, A. A. Santilli, and R. W. Murray, *J. Am. Chem Soc.*, **82**, 2728 (1960).

(15) Melting points and boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 21 instrument (sodium chloride optics) and n.m.r. data were obtained with a Varian A-60 spectrometer in deuteriochloroform solution using tetramethylsilane as internal standard. Elemental analyses are by Dr. A. Bernhardt, Mülheim (Ruhr), Germany.

(16) (a) The Matheson Co., m.p. 77–79°. (b) E. Müller and H. Huber-Emden, *Ann.*, **660**, 59 (1962).

(17) M. H. Palomaa, E. J. Salmi, J. I. Jansson, and T. Salo, *Ber.*, **68**, 303 (1935).

Treatment with phenylhydrazine gave the **phenylhydrazone**,[18] m.p. 186–187.5°, obtained in the form of yellow needles from nitromethane.

Anal. Calcd. for $C_{12}H_{16}N_2O_2$: C, 65.43; H, 7.32; N, 12.72. Found: C, 65.31; H, 7.46; N, 12.90.

Treatment with methylhydrazine gave the methylhydrazone, m.p. 74–76°, lit.[16] m.p. 74.5°.

***t*-Butyl Glycolate.**[19]—To a suspension of 268 g. of sodium bicarbonate in 600 ml. of formamide (b.p. 118.5–120° at 25 mm.) and 46 g. of water there was added 403 g. of *t*-butyl bromoacetate and the mixture was stirred vigorously and heated in an oil bath at 125° (external temperature) for 70 min. The reaction mixture was then distilled to remove all material which collected between 45° (25 mm.) and 90° (70 mm.). The distillation was stopped when frothing became excessive. The distillate was diluted with 100 ml. of methylene dichloride and dried over anhydrous potassium carbonate. Distillation from a water bath gave 71 g. (26%) of the ester, b.p. 74–76° (25 mm.), which was identified by infrared comparison with a sample obtained by the method of Müller and Huber-Emden.[16b]

***t*-Butyl α-Oximinopropionate.**—A mixture of 88.1 g. of pyruvic acid, 140 g. of isobutylene, and 5 ml. of concentrated sulfuric acid was placed on a shaking machine for 12 hr. and worked up in the usual manner. Distillation of the ester through a Claisen flask and then through a 30-cm., helices-packed column gave 34.1 g. of crude *t*-butyl pyruvate, b.p. 54.5–56° (15 mm.), which was added to a solution of 18.3 g. of hydroxylamine hydrochloride and 21.6 g. of sodium acetate in 150 ml. of water. The mixture was stirred in a water bath at 70–75° for 20 min. and cooled in an ice bath, and the snow-white solid was filtered and washed with water. There was obtained 29 g. (18.2%) of the oxime, m.p. 72.5–73.5°. There was no depression of the melting point on admixture with a sample prepared in trace amounts by reaction of *t*-butyl α-bromopropionate and sodium nitrite in water–*t*-butyl alcohol solution.[20] The compound showed infrared absorption (2% in carbon tetrachloride) at 3.05 (m) and 5.79 μ (s).

Anal. Calcd. for $C_7H_{13}NO_3$: C, 52.82; H, 8.23; N, 8.80. Found: C, 53.24; H, 8.29; N, 9.01.

The **acetyl derivative** obtained by reaction with acetic anhydride and pyridine in methylene dichloride solution (55% yield) had b.p. 87.5–88° (1.0 mm.). The product showed infrared absorption (2% in carbon tetrachloride) at 5.57 (s), 5.79 (s), and 6.12 μ (m) and three sharp n.m.r. peaks at δ 1.50 (9H), 2.20 (3H), and 2.30 (3H).

Anal. Calcd. for $C_9H_{15}NO_4$: C, 53.72; H, 7.51; N, 6.96. Found: C, 53.94; H, 7.28; N, 7.16.

***t*-Butyl Oxalyl Hydrazide.**—A solution of 169.5 g. of ethyl *t*-butyl oxalate[4] in 490 ml. of methylene dichloride was cooled in an ice bath and stirred vigorously while 53.5 g. of 64% hydrazine solution was dropped in over a period of 1.5 hr. A white solid separated from the beginning and gradually increased in amount during the addition. The mixture was stirred in the ice bath for an additional 3 hr., the solid (24 g.) was filtered, and the filtrate was dried over magnesium sulfate. Removal of solvent from a water bath with the aid of a water aspirator gave a thick oil which was dissolved in about 250 ml. of benzene. The benzene solution was filtered by suction and the clear filtrate was diluted to a total volume of 1 l. by the addition of ligroin (b.p. 60–70°). Filtration gave 90 g. (58%) of shiny white crystals, m.p. 60–66°. This was pure enough for conversion to *t*-butyl iminodicarboxylate. Recrystallization from benzene–ligroin (b.p. 60–70°) gave white crystals, m.p. 69.5–71.5°.

Anal. Calcd. for $C_6H_{12}N_2O_3$: C, 44.99; H, 7.55; N, 17.49. Found: C, 45.50; H, 7.49; N, 17.20.

***t*-Butyl Iminodicarboxylate.**—A mixture of 225 ml. of water, 45 ml. of concentrated hydrochloric acid, and 300 ml. of ether contained in a 2-l. round-bottomed flask was cooled in a sulfuric acid–ice bath. When the internal temperature fell to −3°, 74 g. of *t*-butyl oxalyl hydrazide was added. While stirring vigorously and keeping the temperature between −1 and 1°, there was added dropwise over a period of 45 min. a solution of 31.5 g. of sodium nitrite in 225 ml. of water. Just as soon as the addition was completed, the two layers were filtered in order to remove a trace of suspended solid, and the ether layer was separated and rapidly washed once with 75 ml. of ice-cold water. The ether solution was then dried over calcium chloride for 4 min. in an ice bath and filtered into 150 ml. of *t*-butyl alcohol contained in a 500-ml. flask set up for distillation. The *t*-butyl alcohol–ether solution was warmed in a water bath to 40–50° in order to distil the ether. The bath temperature was raised to 70–80° for 30 min. and then the *t*-butyl alcohol was distilled with the aid of a water aspirator. The residual oil was triturated with water which gave 31 g. (31%) of white crystals, m.p. 80–86° (softening at 70°). The 31 g. of crude iminodicarboxylate was added to a boiling solution of 7.4 g. of potassium carbonate in 74 ml. of water. The mixture was removed immediately from the source of heat, stirred for 3–4 min., and then cooled rapidly in an ice bath. Filtration gave 28 g. (28%) of the diester, m.p. 86–88.5°. Recrystallization from ligroin (b.p. 60–70°) gave 24 g. (24%) of the iminodicarboxylate as snow-white crystals, m.p. 88.5–90.5°. The compound showed infrared absorption (Nujol) at 3.06 (m), 5.55 (shoulder), and 5.65 μ (s). The n.m.r. spectrum showed a sharp singlet due to the carbo-*t*-butoxy groups at δ 1.47 and a broad NH peak at 6.80.

Anal. Calcd. for $C_{10}H_{19}NO_4$: C, 55.28; H, 8.81; N, 6.45. Found: C, 55.63; H, 8.74; N, 6.82.

At times the diester isolated by following exactly the same work-up as described above exhibited a melting point of 119–121°.

Anal. Calcd. for $C_{10}H_{19}NO_4$: C, 55.28; H, 8.81; N, 6.45. Found: C, 55.35; H, 8.99; N, 6.47.

The lower melting form was converted to the higher melting modification by shaking with dilute aqueous sodium hydroxide solution, filtering, acidifying the filtrate, and recrystallizing from ligroin. The two modifications showed identical infrared and n.m.r. spectra.

Conversion of α,α′-Dibromo-*o*-xylene to *o*-Xylylenediamine.—A suspension of 0.55 g. of dry sodium hydride in a solution of 4.94 g. of *t*-butyl iminodicarboxylate (m.p. 88.5–90.5°) in 25 ml. of dry dimethylformamide was stirred magnetically while heating in a water bath at 60° for 6 hr. There was added in one portion 2.64 g. of α,α′-dibromo-*o*-xylene and the resulting mixture was heated with stirring at 60° for 4 hr. and diluted to 100–150 ml. with water. The mixture was extracted with four 25-ml. portions of methylene dichloride. The crude oil left on removal of solvent was cleaved by warming with 25 ml. of concentrated hydrochloric acid to give 1.25 g. (57%) of the hydrochloride hemihydrate. In a melting point capillary the compound darkened at 275° and became darker and darker but didn't melt up to 335°. A sample dropped into a bath preheated to 225° melted at once to a clear liquid which then darkened gradually (lit.[21] m.p. 310° dec.). The dibenzoyl derivative had m.p. 189.5–190.5° (lit.[21] m.p. 189–190°).

Conversion of Ethyl Bromoacetate to Ethyl Glycinate Hydrochloride.—The sodium salt of 4.35 g. of *t*-butyl iminodicarboxylate was prepared as indicated above from 1.07 g. of sodium hydride–oil dispersion (50%) in 25 ml. of dimethylformamide. To the frothy mixture was added 3.34 g. of ethyl bromoacetate and heating and stirring continued for 2 hr. The mixture was diluted with 300 ml. of water and extracted with four 35-ml. portions of ether; the dried ether extracts were diluted with 100 ml. of absolute ethanol and treated with a stream of hydrogen chloride gas for 10–15 min. After standing for 12 hr. at room temperature the mixture was evaporated to dryness *in vacuo* and the solid was washed out with ether. There was obtained 1.65 g. (59%) of ethyl glycinate hydrochloride, m.p. 142.5–144.5° (sealed capillary). Recrystallization from ethanol–ether did not raise the melting point. The infrared spectrum was identical with that of an authentic sample, lit.[22] m.p. 144°.

Mesitoxyamine.[13]—In previous work this compound had been obtained only as an oil. It has now been obtained as a low-melting crystalline solid. The oil obtained as described previously solidified on storage for a few hours in a freezer. The solid was dissolved in ligroin (b.p. 60–70°) by warming in a water bath at 60°. On cooling in an ice bath with scratching or seeding, the mesitoxyamine separated as a snow-white microcrystalline powder, m.p. 31–32°. The recovery was about 75%. Ordinarily

(18) This phenylhydrazone (lit. m.p. 171°) was obtained by Müller and Huber-Emden[16] by treatment of *t*-butyl diazoacetate with phenyl magnesium bromide. Comparison of the infrared spectrum of our material with a spectrum kindly provided by Müller and Huber-Emden showed the identity of the compounds prepared by the two routes. The reason for the discrepancy in the melting point is not known.

(19) The procedure is based on a general method described by H. Bredereck, R. Gompper, and G. Theilig, *Ber.*, **87**, 537 (1954).

(20) Compare N. Kornblum and J. H. Eicher, *J. Am. Chem. Soc.*, **78**, 1494 (1956).

(21) H. H. Hatt and E. M. Stephenson, *J. Chem. Soc.*, 199 (1952).

(22) T. Curtius and F. Göbel, *J. prakt. Chem.*, [2]**37**, 160 (1888).

it is not necessary to suffer the loss on recrystallization since the crude oil is sufficiently pure for use as an aminating agent.

***t*-Butyl Hydrazine-1,1-dicarboxylate.**—The sodium salt of *t*-butyl iminodicarboxylate was obtained as described above from 4.94 g. of the ester, 0.55 g. of dry sodium hydride, and 25 ml. of dimethylformamide by warming for 12 hr. in a water bath at 55–60°. The mixture was treated with 3.58 g. of mesitoxyamine in 5 ml. of dimethylformamide, heated for 6 hr. to 55–60°, diluted to 350 ml. with water, treated with decolorizing carbon, and filtered. The filtrate was extracted with about 12–15 12-ml. portions of ether. Evaporation of the combined ether extracts gave 2.7 g. of white solid, m.p. 74–92°. Two recrystallizations from ligroin (b.p. 60–70°) gave 1.2 g. (26%) of the pure N-amino compound as white needles, m.p. 104–106°. Better yields (35–40%) were obtainable by using an excess of mesitoxyamine (2 moles per mole of imide).

Anal. Calcd. for $C_{10}H_{20}N_2O_4$: C, 51.71; H, 8.68; N, 12.06. Found: C, 51.94; H, 8.69; N, 12.15.

The **benzal derivative**, obtained in the usual manner with a trace of acetic acid as catalyst, was recrystallized from ligroin (b.p. 60–70°) as white block-like crystals, m.p. 73–75°. There was no depression of the melting point on admixture with a sample prepared by acylation of the hydride-derived sodium salt of *t*-butyl 2-benzalcarbazate by means of *t*-butyl azidoformate.

Anal. Calcd. for $C_{17}H_{24}N_2O_4$: C, 63.73; H, 7.55; N, 8.74. Found: C, 63.83; H, 7.70; N, 8.73.

2-[Bis(*t*-butyloxycarbonyl)]amino-2,3-dihydro-1H-benzo[*de*]isoquinoline.—A solution of 1.02 g. of 1,8-bis(bromomethyl)naphthalene[23] and 0.75 g. of *t*-butyl hydrazine-1,1-dicarboxylate in 10 ml. of dimethylformamide was warmed to 55–60° and 0.95 ml. of triethylamine added. The mixture was stored at room temperature for 36 hr. and diluted with 100 ml. of water. Cooling and scratching caused deposition of 0.65 g. (52%) of cream-colored solid, m.p. 150–157°. Recrystallization from ethanol–nitromethane (3:1) gave 0.55 g. (44%) of the carbazate as flat white needles, m.p. 159–161°.

Anal. Calcd. for $C_{22}H_{28}N_2O_4$: C, 68.73; H, 7.34; N, 7.29. Found: C, 68.60; H, 7.25; N, 7.41.

Cleavage of 2-[Bis(*t*-butyloxycarbonyl)]amino-2,3-dihydro-1H-benzo[*de*]isoquinoline.—A stream of gaseous hydrogen chloride was passed into a solution of 0.06 g. of XII in 5 ml. of nitromethane for 2–3 min. After standing for 5–10 min., filtration gave 0.02 g. (58%) of snow-white crystalline solid, m.p. 236.5–238.5° dec. (darkening at 230°), lit.[14] m.p. 233–237° dec. The infrared spectrum was identical with that of an authentic sample[14] of the hydrochloride of 2-amino-2,3-dihydro-1H-benz[*de*]isoquinoline.

(23) L. A. Carpino, *J. Am. Chem. Soc.*, **85**, 2144 (1963).

Alkaline Degradation of 1,1-Disubstituted Sulfonhydrazides. Synthesis of a Pair of Cyclic, Benzylic Hydrazines Derived from Acenaphthene and Acenaphthylene[1]

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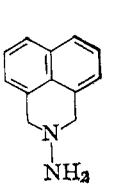
In order to test some hypotheses relating to the oxidation and sulfonhydrazide degradation of 1,1-disubstituted hydrazines two appropriate model hydrazines have been prepared for further study, namely 2-amino-2,3-dihydro-1H-indeno[1,6,7-*def*]isoquinoline (III) and 2-amino-2,3,6,7-tetrahydro-1H-indeno[1,6,7-*def*]isoquinoline (II). Treatment of acenaphthene-5,6-dicarboxylic acid anhydride with hydrazine hydrate gave the corresponding cyclic hydrazide (XI) which was reduced by means of sodium borohydride and lithium bromide to II. An alternate route to II involved lithium aluminum hydride reduction of dimethyl acenaphthene-5,6-dicarboxylate (XII) to the diol (XIII). Treatment of the diol with hydrobromic acid gave the dibromide (XIV) which upon treatment with *t*-butyl carbazate and triethylamine in dimethylformamide solution gave the carbo-*t*-butoxy derivative (XVI) which was converted to II by cleavage with hydrogen chloride. The most direct route to the corresponding unsaturated hydrazine (III) involved treatment of 5,6-bis(bromomethyl)acenaphthene with N-bromosuccinimide to give the corresponding tribromide XXII. Treatment of XXII with *t*-butyl carbazate and triethylamine in dimethylformamide was accompanied by dehydrobromination to give the protected unsaturated hydrazine derivative XXIII which on removal of the carbo-*t*-butoxy group gave the unsaturated hydrazine III. An alternate route to III involved bromination of the saturated diester XII with N-bromosuccinimide followed by dehydrobromination with lithium bromide in dimethylformamide to the unsaturated diester XVIII, reduction of which by means of lithium aluminum hydride gave the unsaturated diol XX. The diol (XX) was converted to the dichloride XXI by reaction with thionyl chloride in benzene and the dichloride was cyclized to the protected unsaturated hydrazine (XXIII) by reaction with *t*-butyl carbazate and triethylamine in dimethylformamide. The ultraviolet and n.m.r. spectra of the substituted acenaphthene and acenaphthylene derivatives obtained during the course of this work were examined and correlated with the spectra of the parent hydrocarbons.

Based on studies of the oxidation and sulfonhydrazide degradation of benzylic hydrazines such as 1,1-dibenzylhydrazine,[2,3] N-aminodihydroisoindole,[4] and the corresponding dibenzazepine[3a] it was expected that similar treatment of 2-amino-2,3-dihydro-1H-benz[*de*]-isoquinoline (I) would yield acenaphthene. However this proved not to be the case.[5] Instead, mercuric oxide oxidation of I yielded a small amount of the tetrazene, considered to be the "normal" oxidation product of nonbenzylic 1,1-disubstituted hydrazines. Treatment



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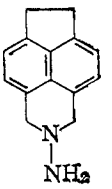

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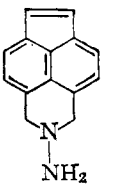

III

of the *p*-toluenesulfonyl derivative of I with aqueous alkali gave a high-melting isomer of the tetrazene, the structure of which is currently under study. In order to explain this unusual result it was postulated that the differences between the dihydroisoindoles and dibenzazepines on the one hand and compound I on the other might be ascribed to the opportunity for a low-energy

(1) Supported by a grant (NSF G-19506) from the National Science Foundation.

(2) M. Busch and B. Weiss, *Ber.*, **33**, 2701 (1900).

(3) (a) L. A. Carpino, *J. Am. Chem. Soc.*, **79**, 4427 (1957); (b) C. G. Overberger, *Record Chem. Progr.*, **21**, 21 (1960).

(4) L. A. Carpino, *ibid.*, **84**, 2196 (1962).

(5) L. A. Carpino, *ibid.*, **85**, 2144 (1963).