tion, extraction with methylene chloride, and removal of the solvent a small amount of white solid. This solid was recrystallized twice from hexane to yield white needles of \( \alpha \)-t-butoxy-\( \alpha \)-mesityl-acetophenone-\( \alpha \)-carboxylic acid, m.p. 115-116°.

**Analytical.** Caled. for C\(_{24}\)H\(_{20}\)O\(_2\): C, 84.68; H, 5.92. Found: C, 84.94; H, 5.86.

**Hydrolysis of 2-Mesityl-3-mesityloxy-1-indenone.**—A solution of 885 mg. of VII in 25 ml. of dioxane and 25 ml. of 6 N hydrochloric acid was heated on a steam bath for 3 hr. The mixture was then concentrated to about 20 ml., diluted with 50 ml. of methylene chloride, and extracted five times with 1 N sodium hydroxide. The organic layer contained unchanged starting material. The red aqueous phase on acidification, extraction with methylene chloride, and removal of solvent yielded after trituration of the residue with ether 245 mg. (0.93 mmole, 40%) of pale yellow needles of 2-mesityl-1,3-indandione (VIII), m.p. 130-131° (0.05 mm.) to yield white needles, m.p. 198-199°.

The infrared spectrum showed a hydroxyl band at 3540 cm.\(^{-1}\), carbonyl bands at 1710 and 1640 cm.\(^{-1}\), the latter arising from hydrogen bonding of one of the carbonyl groups with the hydroxyl group. Other bands in the spectrum included a C=O stretching at 1100 cm.\(^{-1}\), characteristic of tertiary alcohols, along with CH\(_2\) and methylene absorption.

**Analytical.** Caled. for C\(_{24}\)H\(_{20}\)O\(_2\): C, 84.68; H, 5.92. Found: C, 84.94; H, 5.86.

**Hydrolysis of 2-Mesityl-3-mesityloxy-1-indenone.**—A solution of 885 mg. of VII in 25 ml. of dioxane and 25 ml. of 6 N hydrochloric acid was heated on a steam bath for 3 hr. During this time the solution was reduced to half the volume, with formation of light ivory colored needles. The mixture was diluted with 25 ml. of water, the solid was collected and chromatographed on silica gel. The ether eluate on removal of the solvent gave white crystals of 2-hydroxy-2-mesityl-1,3-indandione (VIII), which was purified by two sublimations at 190-200° (0.05 mm.) to yield white needles, m.p. 198-199°.

The infrared spectrum showed a hydroxyl band at 3540 cm.\(^{-1}\), carbonyl bands at 1710 and 1640 cm.\(^{-1}\), the latter arising from hydrogen bonding of one of the carbonyl groups with the hydroxyl group. Other bands in the spectrum included a C=O stretching at 1100 cm.\(^{-1}\), characteristic of tertiary alcohols, along with CH\(_2\) and methylene absorption.

**Analytical.** Caled. for C\(_{24}\)H\(_{20}\)O\(_2\): C, 84.68; H, 5.92. Found: C, 84.94; H, 5.86.

**Hydrolysis of 2-Mesityl-3-mesityloxy-1-indenone.**—A solution of 885 mg. of VII in 25 ml. of dioxane and 25 ml. of 6 N hydrochloric acid was heated on a steam bath for 3 hr. The mixture was then concentrated to about 20 ml., diluted with 50 ml. of methylene chloride, and extracted five times with 1 N sodium hydroxide. The organic layer contained unchanged starting material. The red aqueous phase on acidification, extraction with methylene chloride, and removal of solvent yielded after trituration of the residue with ether 245 mg. (0.93 mmole, 40%) of pale yellow needles of 2-mesityl-1,3-indandione (VIII), m.p. 130-131° (0.05 mm.) to yield white needles, m.p. 198-199°.

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**Hydrolysis of 2-Mesityl-3-mesityloxy-1-indenone.**—A solution of 885 mg. of VII in 25 ml. of dioxane and 25 ml. of 6 N hydrochloric acid was heated on a steam bath for 3 hr. The mixture was then concentrated to about 20 ml., diluted with 50 ml. of methylene chloride, and extracted five times with 1 N sodium hydroxide. The organic layer contained unchanged starting material. The red aqueous phase on acidification, extraction with methylene chloride, and removal of solvent yielded after trituration of the residue with ether 245 mg. (0.93 mmole, 40%) of pale yellow needles of 2-mesityl-1,3-indandione (VIII), m.p. 130-131° (0.05 mm.) to yield white needles, m.p. 198-199°.

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On modifying this procedure we found that significantly improved yields of carbamates were readily and consistently obtained: thus, the yield of 1-butyl carbamate was raised to over 90%.

The compounds prepared by this procedure are listed in Table I (pp. 3424 and 3425).

The most significant factor leading to improved yields was substitution of trifluoroacetic for trichloroacetic acid. This beneficial effect does not appear to be solely related to increased acid strength, for hydrochloric and methanesulfonic acids gave only traces of product when used in place of trifluoroacetic acid under the same conditions. Another factor markedly influencing the yield was the choice of solvent; benzene and methylene chloride gave markedly better yields than other inert solvents such as ether, carbon tetrachloride, or tetrahydrofuran.

Substitution of potassium cyanate for sodium cyanate reduced the yield to less than 5%.

The reaction is generally over in less than two hours, and the crude yields of product are high (60 to 90%). In some instances, the final yield of analytically pure product was low; this was generally due to losses occurring during purification, as the result of inherent thermal or hydrolytic instability or volatility of the products. In most cases, the "crude" product was actually quite pure.

Primary, secondary, and tertiary alcohols are all smoothly converted to the corresponding carbamates (compounds 1 to 7). Even the relatively unstable propargyl alcohol was easily converted to its carbamate (compound 8). The melting point of menthol carbamate (6) which we prepared differed from that reported by Bedos, but agrees with that reported by other investigators.

Both cyclic and acyclic 1,3-diols gave the simple carbamates (10 to 12) as the major products. However, 1,2-diols gave cyclic carbonates (25 and 26), along with mixtures of other products, probably mono- and dicarbamates.

Attempts were made to extend these reactions to the preparation of carbamates from 1,1-(gem)-diols and diothiols. Dihydroxymalonic acid (mesoxalic acid hydrate) was recovered unchanged from the reaction mixture, and biphenylylglycol hydrate gave a high melting, insoluble mixture of products.

The only simple alcohols from which carbamates could not be isolated were diphenylethylcarbinol (which gave 1,1-diphenylethylene) and trichloro- and trifluoromethylcarbinols (these gave complex mixtures of products). Phenols easily corresponded the carbamates (8 and 9).

The carbamates of surprisingly few primary and secondary mercaptans, and of no tertiary mercaptans, are known. These (15-17) and the carbamate of a 1,3-dithiol (18) were readily prepared. The odors of the freshly prepared thiolcarbamates were not particularly unpleasant; however, on prolonged standing a typical mercaptan odor developed. A gem-dithiol, 2,2-dimercapto-1,3-diphenyl propane, did not react and was recovered unchanged from the reaction mixture.

Carbamates were first prepared by Conduché in 1909 by the reaction of a carbonyl compound with isohydroxurea, but were assigned the incorrect azoxirane structures by C. Exner and M. Horak, who prepared the stereisomeric oxime carbamates corresponding to II (19-24). Syn- and anti-isobutyrophenone oximes give stereoisomeric oxime carbamates (25 and 26), along with mixtures of other products, probably mono- and dicarbamates.

In subsequent papers, only the laborious manual method of isolating the two forms has been employed (H. M. Kissman, D. S. Tarbell, and J. Williams, J. Am. Chem. Soc., 75, 2595 (1953), and B. F. Brown, N. M. van Gulik, and G. H. Rehmold, J. Org. Chem., 77, 1094 (1955)). In the Experimental, we describe a convenient synthesis of the p-carbonates.

(18) The product from chloral hydrate will be described in another communication.

(19) The thiol analog of meprobamate.


(21) A. Conduché, Ann. chim. phys., 18, 533 (1907); 12, 1 (1958): Chem. Abstr., 5, 858 (1908); 4, 999 (1908).


(23) After our work was completed, an article by G. Zinner, Arch. Pharm., 299, 1 (1959), appeared, describing the synthesis of the carbamates of some aliphatic oximes by reaction of the oximes at -10° with aqueous potassium cyanate and hydrochloric acid. Zinner points out, however, that he could only prepare the carbamates of oximes having some water solubility, and furthermore, that aromatic oximes did not react. The procedure described in the present paper worked for all oximes tried and, also, as indicated, permits synthesis of the stereoisomeric syn- and anti-ketoxyimine carbamates.

(24) The oxime prepared from isobutyrophenone was first reported having m.p. 58° (V. Meyer, et al., Ber., 90, 506 (1887); later, A. Lapworth and V. Steele, J. Chem. Soc., 1882 (1911), reported a m.p. of 96° and claimed that the earlier figure was incorrect. However, papers continued to appear reporting only 56 to 58° melting points (A. Maguer and R. M. Evans, J. Am. Chem. Soc., 60, 819 (1938); P. L. d'Bevillanville, J. Org. Chem., 6, 482 (1941); and G. P. Meshishov, J. Gen. Chem. USSR, 9, 831 (1939)). In 1950, Kissman and Williams reported that the 58° to 60° material, on slow crystallization from pentane, deposited a mixture of two different types of crystals which they separated manually and showed to be the syn (m.p. 56-58°) and anti (m.p. 59-60°) isobutyrophenone oximes (m.p. 57-60°). The oximes could not be separated satisfactorily by chromatography.

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carbamates; however, syn- and anti-p-chlorobenzaldoximes gave the same product.

The extension of this reaction to more complex alcohols, i.e., those in which still other functional groups are present, is underway. Preliminary work indicates that when a basic tertiary nitrogen is present in the molecule, the yield of carbamate is very low.

Although, as pointed out earlier, the usual products from the reaction of cyanic acid with alcohols have been reported to be allophanates, we have never observed allophanate formation in our procedure. The only by-product occasionally observed is trifluoroacetamide; however, it is not usually isolated and does not present any problem because of its very high solubility in water and in organic solvents.

When sodium thiocyanate and trifluoroacetic acid reacted with alcohols and mercaptans in attempts to extend this synthetic method to the synthesis of thionocarbamates and dithiocarbamates, only complex mixtures of odorous products resulted.

**Experimental**

**General Procedure.** Most of the study of the effect of changing the experimental variables on yield was done using t-butyl alcohol.

As already pointed out in the discussion, trifluoroacetic acid gives far better yields than trichloroacetic acid, and other acids under the same conditions give negligible yields. For each hydroxyl group 2 equiv. of trifluoroacetic acid and 2 equiv. of sodium cyanate are used. Excess trifluoroacetic acid has no effect, but smaller amounts of the acid or cyanate cause a big drop in yield.

A different important factor influencing the yield is solvent. In most instances, the use of benzene or methylene chloride gives yields superior to those obtained even using similar solvents such as carbon tetrachloride or ether. A few instances were found where benzene or methylene chloride did not give any product, but tetrahydrofuran did; but, in general, tetrahydrofuran as solvent led to negligible yields of product. With a new alcohol, therefore, the procedure was first to try benzene or methylene chloride (the choice of these depending on the solubility of the alcohol) and if this did not give any product, then to try tetrahydrofuran as solvent. In general, the yield is much higher when the alcohol is soluble in the solvent used.

Vigorous agitation markedly decreases the yield. (23) The order of addition of reagents is not important; however, the procedure we generally use involves adding the acid to a portion of this two-phase system gave the thiouronium chloride (the choice of these depending on the solubility of the alcohol) and, if this did not give any product, then to try tetrahydrofuran as solvent. In general, the yield is much higher when the alcohol is soluble in the solvent used. The order of addition of reagents is not important; however, the procedure we generally use involves adding the acid to a portion of this two-phase system gave the thiouronium chloride (the choice of these depending on the solubility of the alcohol) and, if this did not give any product, then to try tetrahydrofuran as solvent. In general, the yield is much higher when the alcohol is soluble in the solvent used.

The temperature, within the limits of 20 to 50°, has no effect on yield. A contact time of 2 hr. is usually sufficient. Increasing the reaction time to 24 hr. has no effect on the yield; for convenience the reaction mixture is usually allowed to stir overnight at room temperature.

After the reaction is completed, a small amount of water is added to the mixture to dissolve the salt: then the organic solution is separated, dried, and concentrated in vacuo (usually at 50°, since most of the carbamates proved to be thermally unstable or volatile). Ringing of the organic solution with dilute bicarbonate invariably resulted in large losses of product.

The crude product was generally isolated in good yield (60-90%), as listed in Table I, in a good state of purity; however, large losses were generally observed during further purification due to the volatility and the thermal and hydrolytic instability of many of the carbamates. The yields in parenthesis in Table I are after further purification.

In most of the experiments described subsequently, no attempt was made to determine the optimum experimental conditions.

As a typical preparation, the synthesis of t-butyl carbamate is given in detail.

**1-Butyl Carbamate.**—(25) Trifluoroacetic acid (15.5 ml., 0.21 mole was added to 200 ml. slowly to a stirred mixture of t-butyl alcohol (7.4 g., 0.1 mole) and which cyanate (16 g., 0.2 mole) in 25-100 ml. of benzene (volumes of solvent significantly larger than this decreased the yield). A mildly exothermic reaction occurred and some gas bubbled out of the system. The container was loosely stoppered, and the reaction mixture stirred for 3 hr. (or overnight, the yield was the same). Fifteen milliliters of water was added and the organic layer was separated and dried; the solvent was removed in vacuo at a pot temperature of 40-50°. The residue solidified, 92% yield, m.p. 88-90°. Recrystallization from water gave an analytical pure product, 8% (96% yield), m.p. 107-108°. (26) lit. m.p. 108°.

The preparation of the other compounds was essentially identical to that described for the preparation of t-butyl carbamate.

The specific reaction conditions are listed in Table I.

Further details of the work-up, where these are not obvious from the table, are given as follows.

**d,l-Methyl Carbamate.**—The product also was obtained, although in low yield as given in the table, when tetrahydrofuran was used as solvent. When the sodium cyanate was omitted, the reaction of methyl carbamate was quantitatively recovered showing that methyl did not undergo any rearrangement under these reaction conditions.

4-Chloro-1,2,2-methyl-1,3-nortestosterone Carbamate (7).—At the conclusion of the reaction period (Table I), the tetrahydrofuran was distilled from the reaction mixture as solvent. The semisolid residue was treated with water. The resulting solid was treated with acetone and the insoluble material discarded. The filtrate, on concentration, left an oil which was dissolved in benzene and chromatographed using neutral alumina. The crystalline fractions that were isolated were combined and recrystallized from ethanol-water.

2,2,4,4-Tetramethyl-1,3-bis(carbamylxoy)cyclobutane (12).—The starting glycol was obtained from Eastman Chemical Products; it is a mixture of cis and trans glycols and was used as such.

At the end of the reaction period the ether was removed and the residual slurry was neutralized with sodium bicarbonate. On dilution with water, the solid dicarbamate (mixture of cis and trans isomers) separated. This was recrystallized from water.

When the reaction was carried out using tetrahydrofuran as solvent and worked up as before, some other-insoluble material was isolated, which proved to be the monocarbamate (mixture of cis and trans isomers), m.p. 160-170° (10% yield).

**Teprin Carbicarbamate.** (14).—At the end of the reaction period the solvent was removed in vacuo and the residue was diluted with water, then extracted with ethyl acetate. Concentration of the extract gave an oil which was treated with 1 equiv. of thiourea, and the residue was dissolved in water. The resulting solid carbicarbamate as a solid (45% yield), and some oil that was clearly amine impure monocarinate.

2-Methyl-2-pentanolthiol. —A mixture of 1 equiv. of 2-methyl-2-pentanol (K and K Laboratories), 1.1 equiv. of thiourea, and 1.3 equiv. of concentrated hydrochloric acid was stirred at room temperature for 18 hr. After the end of this time, two layers were present. Addition of an aqueous solution of p-toluene sulfonic acid to a portion of this two-phase system gave the thiouronium p-toluene sulfonate, m.p. 124-127° dec. (from methanol-ether).

**Aspin.** Calc. for CuH2NO3S: C, 50.27; H, 7.21; N, 8.42. Found: C, 50.14; H, 7.19; N, 8.37.

The balance of the two-phase system was treated with 2 equiv. of sodium hydroxide (keeping the system under nitrogen) at 35-40°. A large oily layer separated. This was steam distilled directly from the reaction mixture. The distillate was separated and extracted with some ether and distilled. The mercuric distillate, b.p. 129-130°, m.p. 1.4470 (lit. b.p. 122-123°, m.p. 1.4359), 52% over-oil yield.

**2-Methyl-2-propyl-1,3-dithiol Carbamate.** (18). A mixture of 2-Methyl-2-propyl-1,3-dibromopropane (19).—A mixture of 2-methyl-2-propyl-1,3-dibromopropane and 1,405 g. (3.9 ml.) was stirred at room temperature for 18 hr. has no effect on the yield; for convenience the reaction mixture is usually allowed to stir overnight at room temperature.

After the reaction is completed, a small amount of water is added to the mixture to dissolve the salt: then the organic solution is separated, dried, and concentrated in vacuo (usually at 50°, since most of the carbamates proved to be thermally unstable or volatile). Ringsing of the organic solution with dilute bicarbonate invariably resulted in large losses of product.

The crude product was generally isolated in good yield (60-90%), as listed in Table I, in a good state of purity; however, large losses were generally observed during further purification due to the volatility and the thermal and hydrolytic instability of many of the carbamates. The yields in parenthesis in Table I are after further purification.

In most of the experiments described subsequently, no attempt was made to determine the optimum experimental conditions.


(23) Bayer and Co., German Patent 318,893 (1914).


(26) All melting points are corrected. The microanalyses were performed by Mrs. D. Holst and her staff of these laboratories.

Table I
SYNTHESIS OF CARBAMATES

<table>
<thead>
<tr>
<th>No.</th>
<th>Compound</th>
<th>Conditions</th>
<th>M.p., °C</th>
<th>Recrystallization solvent</th>
<th>Yield,%</th>
<th>Calcd. C</th>
<th>H</th>
<th>N</th>
<th>Found C</th>
<th>H</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>n-BuOCONH₂</td>
<td>Benzene, 2 hr., 30°</td>
<td>53-54°</td>
<td>Water</td>
<td>73</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>t-BuOCONH₂</td>
<td>Benzene, 2 hr., 30°</td>
<td>107-108°</td>
<td>Hexane</td>
<td>92</td>
<td>51.26</td>
<td>9.47</td>
<td></td>
<td>51.00</td>
<td>9.47</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Et₂C—OCONH₂</td>
<td>No solvent, 4 hr., 5°</td>
<td>55-56°</td>
<td>Hexane</td>
<td>39</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>CH₂C₂H₂N₂</td>
<td>CH₃CH₂, 18 hr., 30°</td>
<td>108-109°</td>
<td>Cyclohexane</td>
<td>78</td>
<td>58.72</td>
<td>9.15</td>
<td>9.78</td>
<td>58.84</td>
<td>9.08</td>
<td>10.02</td>
</tr>
<tr>
<td>5</td>
<td>HC≡CCH₂OCONH₂</td>
<td>Ether, 3 hr., 30°</td>
<td>47-50°</td>
<td>Benzene</td>
<td>60</td>
<td>48.48</td>
<td>5.09</td>
<td>14.14</td>
<td>48.42</td>
<td>5.15</td>
<td>14.22</td>
</tr>
<tr>
<td>6</td>
<td>MeOOCNH₂</td>
<td>AcOH, 3 hr., 30°</td>
<td>164-166°</td>
<td>Ethanol</td>
<td>87</td>
<td>66.29</td>
<td>10.62</td>
<td>7.03</td>
<td>66.24</td>
<td>10.74</td>
<td>6.77</td>
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<tr>
<td>7</td>
<td>OCONH₂</td>
<td>THF, 18 hr., 30°</td>
<td>213-216°</td>
<td>Ethanol-water</td>
<td>25</td>
<td>65.65</td>
<td>7.71</td>
<td>3.83</td>
<td>65.64</td>
<td>7.54</td>
<td>3.79</td>
</tr>
<tr>
<td>8</td>
<td>OCONH₂</td>
<td>Ether, 48 hr., 30°</td>
<td>145-148°</td>
<td>Water</td>
<td>62</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>CH₂C₂H₂N₂</td>
<td>CH₃CH₂, 18 hr., 30°</td>
<td>200-202°</td>
<td>Water</td>
<td>35</td>
<td>55.67</td>
<td>5.19</td>
<td>14.43</td>
<td>55.66</td>
<td>5.21</td>
<td>14.72</td>
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<tr>
<td>10</td>
<td>MeOOCNH₂</td>
<td>THF, 2 hr., 30°</td>
<td>102-103°</td>
<td>Water</td>
<td>75</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>11</td>
<td>CH₂C₂H₂N₂</td>
<td>THF, 18 hr., 40°</td>
<td>174-196°</td>
<td>Ethanol</td>
<td>57</td>
<td>44.03</td>
<td>6.47</td>
<td>12.84</td>
<td>44.11</td>
<td>6.38</td>
<td>12.92</td>
</tr>
<tr>
<td>12</td>
<td>Me₂OOCNMe₂</td>
<td>Ether, 18 hr., 30°</td>
<td>175-185°</td>
<td>Water</td>
<td>45</td>
<td>52.16</td>
<td>7.88</td>
<td>12.17</td>
<td>52.24</td>
<td>7.79</td>
<td>11.90</td>
</tr>
<tr>
<td>13</td>
<td>Me₂OOCNMe₂</td>
<td>THF, 18 hr., 30°</td>
<td>160-170°</td>
<td>Water</td>
<td>10</td>
<td>57.72</td>
<td>9.17</td>
<td>7.48</td>
<td>57.71</td>
<td>8.93</td>
<td>8.10</td>
</tr>
</tbody>
</table>

* In each reaction, 2 equiv. of sodium cyanate and 2 equiv. of trifluoroacetic acid were used for each hydroxyl group present. Other details are given in the Experimental section.

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mixture was poured into water and then steam distilled. The distillate was extracted with ether and dried; the solvent was removed and the dibromide distilled, b.p. 96-97° (7 mm.), nD° 1.4995, 35% yield.


B. 2-Methyl-2-propyl-1,3-propanedithiol.-A solution of sodium polysulfide was prepared by bubbling hydrogen sulfide into 40 ml. of 40% aqueous sodium hydroxide until the solution was saturated, then adding this solution to a suspension of 18 g. of sulfur in 35 ml. of ethanol. A vigorous reaction occurred with hydrogen sulfide evolution. When the reaction subsided, the solution was heated on a steam bath for 0.5 hr. The solution was diluted with 300 ml. ethanol, 17 g. of the dibromide was added, and the solution was refluxed for 24 hr. Most of the alcohol was distilled, and a large volume of water was added to the residue. The polysulfide was isolated as an oil, 12 g. This was added dropwise to a solution of 9.2 g. of sodium in 330 ml. of liquid ammonia. The ammonia was allowed to evaporate, and the residue was treated with ether and a little ethanol, then diluted with water. The system was made acidic with dilute sulfuric acid; then the ether extracts were dried and concentrated giving 9.1 g. oil, nD° 1.5095. The dimercapton was distilled, 7.5 g., nD° 1.5005, b.p. 75° (0.7 mm.).

Anal. Calcd. for C₈H₁₄S₂: C, 51.16; H, 6.22; S, 42.62. Found: C, 51.19; H, 6.21; S, 42.31.

C. Preparation of the Bis thiocarbamate.—The reaction was carried out according to our standard procedure. The reaction mixture was rinsed with water, dried, and concentrated. A
AN IMPROVED SYNTHESIS OF CARBAMATES

TABLE I
(continued)

<table>
<thead>
<tr>
<th>No.</th>
<th>Compound</th>
<th>Conditions*</th>
<th>M.p., °C.</th>
<th>Recrystallization solvent</th>
<th>Yield, %</th>
<th>C</th>
<th>H</th>
<th>N</th>
<th>C</th>
<th>H</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>Me-NHCOO- Me-OCONH₂</td>
<td>THF, 18 hr., 30°</td>
<td>203-205</td>
<td>Ethanol-water</td>
<td>(45)</td>
<td>55.80</td>
<td>8.58</td>
<td>10.85</td>
<td>56.10</td>
<td>8.82</td>
<td>10.93</td>
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<tr>
<td>15</td>
<td>n-BuSCONH₂</td>
<td>Ether, 3 hr., 30°</td>
<td>98-100°</td>
<td>Hexane</td>
<td>65</td>
<td>45.08</td>
<td>8.32</td>
<td>10.52</td>
<td>45.25</td>
<td>8.21</td>
<td>10.68</td>
</tr>
<tr>
<td>16</td>
<td>t-BuSCONH₂</td>
<td>Ether, 4 hr., 30°</td>
<td>92-95°</td>
<td>Hexane</td>
<td>50</td>
<td>45.08</td>
<td>8.32</td>
<td>10.52</td>
<td>45.23</td>
<td>8.31</td>
<td>10.67</td>
</tr>
<tr>
<td>17</td>
<td>Me-n-C-C≡S-CONHz</td>
<td>CH₂Cl₂, 18 hr., 30°</td>
<td>45-47</td>
<td>Hexane</td>
<td>(25)</td>
<td>52.13</td>
<td>9.38</td>
<td>8.69</td>
<td>52.21</td>
<td>9.70</td>
<td>8.81</td>
</tr>
<tr>
<td>18</td>
<td>Me-CH₂SCONHz</td>
<td>CH₂Cl₂, 18 hr., 30°</td>
<td>102-104</td>
<td>Isopropyl ether-hexane</td>
<td>50</td>
<td>43.17</td>
<td>7.25</td>
<td>11.19</td>
<td>43.10</td>
<td>7.36</td>
<td>11.02</td>
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<tr>
<td>19</td>
<td>n-Pr=C≡NOCONHz</td>
<td>CH₂Cl₂, 18 hr., 30°</td>
<td>94-96</td>
<td>Water</td>
<td>90</td>
<td>53.83</td>
<td>7.74</td>
<td>17.94</td>
<td>54.18</td>
<td>7.79</td>
<td>17.79</td>
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<tr>
<td>20</td>
<td>C≡NOCONHz</td>
<td>Ether, 18 hr., 30°</td>
<td>114-116</td>
<td>Water</td>
<td>77</td>
<td>57.13</td>
<td>7.19</td>
<td>16.66</td>
<td>57.15</td>
<td>7.33</td>
<td>16.74</td>
</tr>
<tr>
<td>21</td>
<td>C≡N-CH₂SCONHz</td>
<td>CH₂Cl₂, 4 hr., 30°</td>
<td>114-116</td>
<td>Cyclohexane-hexane</td>
<td>(40)</td>
<td>64.06</td>
<td>6.84</td>
<td>13.58</td>
<td>64.34</td>
<td>7.08</td>
<td>13.67</td>
</tr>
<tr>
<td>22</td>
<td>C≡N-C₄H₉SCONHz</td>
<td>CH₂Cl₂, 3 hr., 30°</td>
<td>94-96</td>
<td>Cyclohexane</td>
<td>(31)</td>
<td>64.06</td>
<td>6.84</td>
<td>13.58</td>
<td>63.87</td>
<td>6.77</td>
<td>13.65</td>
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<tr>
<td>23</td>
<td>p-ClC₆H₄.CH=NOCONHz</td>
<td>CH₂Cl₂, 157-158</td>
<td>Benzene</td>
<td>80</td>
<td>48.38</td>
<td>3.55</td>
<td>14.11</td>
<td>48.44</td>
<td>3.70</td>
<td>13.88</td>
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<tr>
<td>24</td>
<td>C₆H₅-CH=CH=C≡NOCONHz</td>
<td>CH₂Cl₂, 5 hr., 30°</td>
<td>87-89°</td>
<td>Chloroform-hexane</td>
<td>(13)</td>
<td>62.48</td>
<td>6.29</td>
<td>14.57</td>
<td>62.68</td>
<td>6.52</td>
<td>14.66</td>
</tr>
<tr>
<td>25</td>
<td>p-ClC₆H₄.CH=C≡NOCONHz</td>
<td>Ether, 3 hr., 30°</td>
<td>73-75</td>
<td>Water</td>
<td>(56)</td>
<td>59.9</td>
<td>5.42</td>
<td>14.0</td>
<td>60.0</td>
<td>5.54</td>
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<tr>
<td>26</td>
<td>p-CF₃C₆H₄.CH=C≡NOCONHz</td>
<td>CH₂Cl₂, 18 hr., 30°</td>
<td>71-74</td>
<td>Cyclohexane</td>
<td>(20)</td>
<td>56.94</td>
<td>4.78</td>
<td>14.1</td>
<td>56.81</td>
<td>4.91</td>
<td></td>
</tr>
</tbody>
</table>

106°. 1 Mixture of cis and trans isomers; see Experimental.  2 Ref. 25, m.p. 102°.  3 B.p. 110-112° (2 mm.).  4 The yields listed are based on a single run; no attempt was made to determine the optimum conditions for highest yield; the figures in parentheses are the yields after several recrystallizations during which time serious losses due to hydrolysis resulted.

white solid formed, 50% yield, m.p. 85-90°. It was recrystallized first from methanol-water, then from isopropyl ether-hexane, giving an 11% yield of analytically pure product. The combined filtrates appeared to contain some monocarbamate and some cyclic dithiocarbamate.

syn-Isobutyrophenone Oxime.—A mixture of isobutyrophenone (74 g., 0.5 mole), hydroxylamine hydrochloride (52.15 g., 0.75 mole), and anhydrous sodium acetate (82 g., 1.0 mole) in ethanol was heated at reflux for 4 hr. The suspension was filtered and the filtrate was concentrated to a solution in water which solidified to a crystalline material, m.p. 58-63°, corresponding to a mixture of syn and anti isomers; yield, 80 g. (98%).

Some of this material was dissolved in ether and treated with excess ethereal hydrogen chloride; a white solid separated immediately. The suspension was heated at reflux for 1 hr. and the solid then isolated. The melting point of this oxime hydrochloride was 113-117° dec. No attempt was made to purify it since on treatment with water, the free base separated, m.p. 85-90°. It was recrystallized several times from hexane, m.p. 89.5-92° (lit. m.p. 89-90°).

All attempts to separate the original mixture of oximes (m.p. 58-63°) by fractional crystallization or thin-layer chromatography failed.

anti-Isobutyrophenone Oxime.—The reaction was carried out as described for the preparation of the syn isomer, except that the mixture was maintained at room temperature for 8 hr. If continued for longer periods, isomerization started to occur and an inseparable mixture resulted.
The reaction mixture was filtered, and the filtrate was concentrated in vacuo keeping the pot temperature below 40°. The residual oil crystallized. On recrystallization from cyclohexane, 33 g. of pure anti-isobutyrophenone oxime was obtained, m.p. 97–100° (lit. 95–98°), m.m.p. 56–60° with the syn isomer.

Attempts to prepare the anti isomer by ultraviolet light isomerization in ethanol or benzene for varying lengths of time led only to an inseparable mixture of syn and anti forms. Brief warming with dilute alcoholic hydrochloric acid also gave an inseparable mixture of isomers, m.p. 56–60°.

Evidence obtained from thin layer chromatography experiments indicates that the mixture of carbamates prepared from the syn-anti oxime mixture could be separated on alumina using methylene chloride as eluate.

- Chlorobenzaldoxime Carbamate (22). — Syn- and anti-p-chlorobenzaldoximes were prepared as described by Erdmann. The same carbamate was obtained regardless of which isomer was used as starting material.

Benzyl Methyl Ketoxime Carbamate (23). — The ketoxime, b.p. 106° (1.5 mm.), was prepared as described by Neber. No isomer of this oxime is known.

At the end of the reaction period, the reaction mixture was treated with water, and the aqueous suspension was extracted with methylene chloride. The organic solution was dried and concentrated to give an oil which slowly solidified. The semisolid material was chromatographed in ethyl acetate solution using alumina (Fisher chromatographic alumina), and the crystalline eluates were further purified by recrystallization from a mixture of chloroform and hexane.

2-[(p-Chlorophenyl)-1-methyl-2,3-butanediol Cyclic Carbonate (25). — The starting diol was treated in the standard manner.

(29) We are indebted to Dr. Robert Lyle for providing us with a sample of anti-isobutyrophenone oxime (isolated by manual separation of crystals) it proved to be identical by mixture melting point and infrared comparisons with our material.


Sulfonyl Fluorides as Intermediates in Organic Synthesis. I. The Synthesis of Aminobenzensulfonyl Fluorides and Their Condensation with β-Ketonic Esters

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Aminobenzensulfonyl fluorides have been synthesized by decylation of acetylamino benzensulfonyl fluorides or by catalytic hydrogenation of nitrobenzensulfonyl fluorides over Raney nickel catalyst. They can be condensed in the usual way with β-ketonic esters to give N-acetylaminobenzensulfonyl fluorides which can be converted into the corresponding sulfonates by alkaline hydrolysis.

The condensation of β-ketonic esters with substituted anilines to give acetylated anilides is generally conducted in boiling xylene. Aminobenzensulfonic acids or their salts, however, possessing very low basicity and negligible solubility in this reaction medium, fail to react. Since this excluded one-step synthesis of N-acetylatedaminobenzensulfonylates III, indirect synthetic routes had to be investigated.

Esters of N-acetylatedaminobenzensulfonylic acids IIa and IIb were expected to be interesting intermediates for the preparation of N-acetylamino benzensulfonylates of type III.

However, condensation of β-ketonic esters with methyl aminobenzensulfonylates Ia gave only low yields of the expected compounds IIa, along with rather large amounts of methylaminobenzensulfonylic acids resulting from autoalkylation of methyl aminobenzensulfonylates Ia. Phenyl acetylamino benzensulfonylates

After removal of the solvent, a little water was added; then the solution was neutralized with bicarbonate, extracted with ether, dried, and concentrated to an oil that slowly set to a semisolid. The oil was dissolved in benzene and chromatographed over neutral alumina. The fractions that crystallized were combined and recrystallized from methanol, 56% yield. The infrared spectra show no NH absorption and thus agree with the elemental analysis, which corresponds to the cyclic carbonate.

Some of the other chromatographic fractions crystallized after prolonged standing. Inspection of the infrared spectra indicates that a mixture of mono- and dicarbamates was probably present.

2-[(p-Trifluoromethylphenyl)-3-methyl-2,3-butanediol Cyclic Carbonate (26). A. 2-[(p-Trifluoromethylphenyl)-3-methyl-2,3-butanediol (26). — To the Grignard reagent prepared from 113 g. (0.454 mole) of p-bromobenzotrifluoride and 12.5 g. (0.51 mole) of magnesium turnings in 1000 ml. of ether was added 21 g. (0.205 mole) of 2-methyl-2-hydroxy-3-butanol (K and K Laboratories) in 50 ml. of ether at such a rate that refluxing proceeded slowly. The mixture was stirred overnight and treated first with 100 ml. of a saturated ammonium chloride solution and then with 100 ml. of 2 N hydrochloric acid. After stirring for 30 min., the etheral layer was separated and concentrated in vacuo to give a solid. This was recrystallized from cyclohexane, a mixture of methanol-water, and a mixture of cyclohexane and benzene. White needles were obtained, m.p. 98–99°; yield, 30 g. (50%).


B. Preparation of the Cyclic Carbonate. — The starting diol was treated in the standard manner. The resulting oil was chromatographed over neutral alumina. The fractions that crystallized were combined and recrystallized from cyclohexane, 20% yield.

Acknowledgment. — We wish to thank Mr. Kenneth Snader for experimental assistance.