An analytical sample was obtained by recrystallization of the combined crops from a large volume of methanol as small yellow-orange plates.

*Anal.* Calcd. for $C_3H_7KN_2O_6$: C, 26.1; H, 3.1; K, 17.0; N, 12.2. Found: C, 26.2, 25.9; H, 3.1, 3.4; K, 16.9, 16.7; N, 12.5, 12.2.

Principal infrared absorption bands were carbonyl, 1690; hydroxyl, 3375; $-C(NO_2)_2^-$, 1160 and 1243 cm.$^{-1}$. The ultraviolet absorption maximum was $\lambda_{max}^{dil\ KOH}$ 378 m$\mu$ (log $\epsilon$ 4.22).

**3,3-Dinitropropionaldehyde (potassium salt)** was prepared by treating 0.1 mole (22.7 g.) of potassium trinitromethide, 0.1 mole (9.8 g.) of potassium acetate, and 0.1 mole (5.3 g.) of acrylonitrile in 200 ml. of 50% dioxane at about 60°. Samples of the reaction mixture were analyzed spectrophotometrically throughout the 150-min. reaction period. During this time there was a gradual shift of $\lambda_{max}$ from 350 to about 357 m$\mu$.

At the end of 150 min., the mixture was cooled to ambient temperature and extracted with three 100-ml. portions of ether. The aqueous phase was cooled to about −5°, whereupon a yellow crystalline solid separated. This product after washing with methanol and ether weighed 5.28 g. and proved to be unchanged potassium trinitromethide, $\lambda_{max}$ 350 m$\mu$.

Diluting the mother liquors with an equal volume of methanol and cooling to about −30 to −40° in Dry Ice–acetone gave only small amounts of a gummy solid. This material had $\lambda_{max}$ 368 m$\mu$ while the mother liquors after removal of the unchanged potassium trinitromethide had $\lambda_{max}$ 360 m$\mu$.

**Reaction of Potassium Methyl 4,4-Dinitro-2-hydroxybutyrate (DNS) with Methyl Acrylate.**—Fifteen thousandths of a mole (3.69 g.) of DNS, 0.03 mole (2.58 g.) of methyl acrylate, 25 ml. of 1 *M* acetic acid in dioxane, and 50 ml. of water were heated on the steam bath for 3 hr. The resulting mixture was diluted with 200 ml. of water and extracted with five 100-ml. portions of ether, after first adjusting the pH of the solution to between 7 and 8 with sodium carbonate. The combined ether extracts were dried over calcium sulfate and the ether was removed on the steam bath to leave a viscous oil. This oil solidified on cooling to yield 3.42 g. of a white solid melting at 72–75°.

After recrystallization from ether, this product melted at 74–75° and did not depress the melting point of an authentic sample of dimethyl 4,4-dinitro-2-hydroxypimelate ($C_9$). Spectrophotometric analysis of the residual aqueous phase showed that less than $10^{-4}$ moles of DNS remained in solution.

**Acknowledgment.**—This work was supported by the Foundational Research Fund of the U. S. Naval Ordnance Laboratory, Task F.R.-44. The assistance of Messrs. F. Taylor, Jr., and B. Wilkerson in preparing some of the intermediates used in this work and discussions with Drs. D. V. Sickman and M. J. Kamlet are appreciated.

# Cyclization of Isothiocyanates as a Route to Phthalic and Homophthalic Acid Derivatives[1,2]

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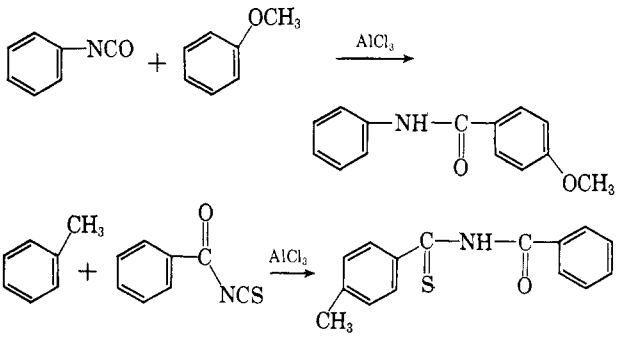
Under Friedel–Crafts conditions, benzoyl isothiocyanates undergo cyclization to monothiophthalimides, and phenylacetyl isothiocyanates give monothiohomophthalimides. The thioimides may be converted to their oxygen analogs, reduced to isoquinoline derivatives, or hydrolyzed to the dicarboxylic acids. The cyclization shows great selectivity when two different *ortho* positions are open for ring closure.

Although there exist numerous methods for the introduction of a carboxyl group into an aromatic ring, they are almost exclusively limited to bimolecular electrophilic substitution reactions, with concomitant uncertainty about the site of introduction, the *para* position usually being favored over the *ortho* position. Prominent examples of such methods include the Gattermann and the Gattermann–Koch reactions,[3,4] the Hoesch reaction,[5] the Vilsmeier–Haack reaction,[6] the Reimer–Tiemann reaction,[7] the Kolbe reaction,[8] bromination followed by the Grignard reaction with carbon dioxide, and the Friedel–Crafts acylation reaction. The use of isocyanates as acylating agents has been studied intermittently since 1885, when Leuckart first produced *p*-methoxybenzanilide by treatment of anisole with phenyl isocyanate and aluminum chloride,[9] but the yields in these and other studies were often low owing in part to the rapid decomposition of the reagents. The use of acyl isothiocyanates was first reported by Wheeler[10] in the reaction of toluene with benzoyl isothiocyanate.




It occurred to us that aromatic acyl and alkyl isothiocyanates would possess sufficient reactivity to serve as intramolecular acylating agents in order to provide a synthetic route to phthalic acids from benzoic acids and to homophthalic acids from phenylacetic acids. This paper reports the results of these studies.[11]

(1) Taken in part from the doctoral thesis of R. O. Kan, University of Michigan, 1961.

(2) For a preliminary communication describing some of the results reported here, see P. A. S. Smith and R. O. Kan, *J. Am. Chem. Soc.*, **82**, 4753 (1960).

(3) (a) L. Gattermann, *Ber.*, **31**, 1149 (1898); (b) N. O. Calloway, *Chem. Rev.*, **17**, 327 (1935).

(4) (a) L. Gattermann and J. A. Koch, *Ber.*, **30**, 1622 (1897); (b) N. N. Crounse, *Org. Reactions*, **5**, 290 (1949).

(5) (a) J. Houben and W. Fischer, *Ber.*, **66**, 339 (1933); (b) P. E. Spoerri and A. S. DuBois, *Org. Reactions*, **5**, 387, 1949.

(6) L. F. Fieser, J. L. Hartwell, J. E. Jones, J. H. Wood, and R. W. Frost, *Org. Syn.*, **20**, 11 (1940).

(7) K. Reimer and F. Tiemann, *Ber.*, **9**, 824 (1876).

(8) (a) H. Kolbe, *J. prakt. Chem.*, [2]**10**, 89 (1874); (b) R. Schmitt, *ibid.*, [2]**31**, 397 (1885).

(9) R. Leuckart and M. Schmidt, *Ber.*, **18**, 2338 (1885).

(10) H. L. Wheeler, *Am. Chem. J.*, **26**, 345 (1901).

(11) One such example had been previously reported in the conversion of α-naphthyl isothiocyanate to thionaphthacarbostyril [N. S. Dokunikhin and L. A. Gaeva, *Zh. Obshch. Khim.*, **24**, 1871 (1954)], but, in view of our results, the structure of the product should be reinvestigated.

TABLE I

ISOTHIOCYANATES, R—NCS, AND CORRESPONDING N-PHENYLTHIOUREAS, RNHCSNHC$_6$H$_5$

| Isothiocyanate | B.p. (mm.) or m.p., °C. | Yield, % | N-Phenylthiourea, m.p., °C. | Analyses, % Calcd. C | Calcd. H | Calcd. N | Found C | Found H | Found N |
|---|---|---|---|---|---|---|---|---|---|
| Benzoyl[a] | 143 (20) | 77.5 | | | | | | | |
| *m*-Toluyl | 95 (0.7) | 82.5 | 113 | 66.64 | 5.23 | 10.37 | 66.64 | 5.24 | 10.27 |
| *p*-Toluyl | 92 (0.4) | 72 | 132–133 | 66.64 | 5.23 | 10.37 | 66.61 | 5.23 | 10.32 |
| 3,5-Dimethylbenzoyl | 99 (1.5)[b] | 62.5 | | | | | | | |
| *m*-Methoxybenzoyl | 104 (0.3) | 77 | 104–105 | 62.91 | 4.93 | 9.78 | 62.78 | 5.03 | 10.00 |
| 3,5-Dimethoxybenzoyl | 158 (1.3) | 22 | 125.5 | 60.64 | 5.10 | 8.86 | 60.64 | 5.03 | 8.68 |
| 3,4,5-Trimethoxybenzoyl[c] | 98 | 76.3 | | | | | | | |
| Benzyl[d] | 141 (21) | 60–82 | | | | | | | |
| β-Phenylethyl[e] | 95 (0.8) | 75[f] | | | | | | | |
| Phenylacetyl | 103 (1.7) | 50–79 | 107–108 | 66.64 | 5.22 | 10.36 | 66.77 | 5.33 | 10.44 |
| *m*-Tolylacetyl | 98 (0.2) | 65.3 | 132 | 67.57 | 5.68 | 9.85 | 67.69 | 5.76 | 9.77 |
| *p*-Tolylacetyl | [g] | | 150–151 | 67.57 | 5.68 | 9.85 | 67.60 | 5.64 | 9.66 |
| *m*-Methoxyphenylacetyl | 128 (0.3) | 24.7 | 104 | 63.97 | 5.38 | 9.33 | 63.96 | 5.41 | 9.30 |
| *p*-Methoxyphenylacetyl | 123 (0.4) | 66.5 | 123 | 63.97 | 5.38 | 9.33 | 64.12 | 5.42 | 9.48 |
| *p*-Chlorophenylacetyl | 116 (0.5) | 63 | 136–137 | 59.11 | 4.30 | 9.20 | 59.22 | 4.35 | 9.36 |
| Diphenylacetyl | [g] | | 173 | 72.80 | 5.24 | 8.09 | 72.59 | 5.29 | 8.11 |
| Cinnamoyl | 119 (0.2) | 75 | 163–164 | 68.05 | 5.00 | 9.92 | 68.20 | 5.00 | 10.04 |
| 3-Thenoyl | 76 (0.3) | 72 | 152 | 54.94 | 3.84 | 10.68 | 55.01 | 4.00 | 10.74 |
| 3-Phenanthreneacetyl | [g] | | 198–198.5 | 74.48 | 4.90 | 7.56 | 74.35 | 4.80 | 7.24 |
| 3-Phenanthroyl | [g] | | 183–184 | 74.13 | 4.53 | 7.86 | 74.39 | 4.64 | 7.80 |
| α-Naphthoyl | 152 (0.7), 35 | 52.7 | 154 | 70.56 | 4.60 | 9.14 | 70.58 | 4.72 | 9.22 |
| β-Naphthoyl | 74 | 43.8 | 148.5 | 70.56 | 4.60 | 9.14 | 70.49 | 4.59 | 9.23 |
| α-Naphthylacetyl | [g] | 72 | 125 | 71.22 | 5.03 | 8.75 | 71.04 | 6.26 | 8.82 |
| Cyclohexene-1-acetyl | 77 (0.5) | 31–44 | 110 | 65.70 | 6.57 | 10.22 | 65.68 | 6.47 | 10.29 |
| Cyclohexene-1-carbonyl | 90 (0.5) | 54–82 | 121–122 | 64.60 | 6.15 | 10.77 | 64.68 | 6.14 | 10.82 |
| Benzhydryl[h] | 58 | 41.7[f] | | | | | | | |

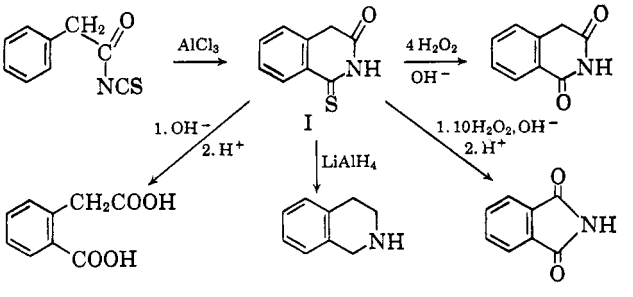
[a] J. C. Amberlang and T. S. Johnson, *J. Am. Chem. Soc.*, **61**, 632 (1939). [b] *Anal.* Calcd. for $C_9H_9NO_2S$: C, 62.80; H, 4.75; N, 7.32. Found: C, 62.74; H, 4.91; N, 7.26. [c] W. H. Perkins and C. Weizmann, *J. Chem. Soc.*, **89**, 1649 (1906). [d] W. Schneider, D. Glibbens, G. Hüllweck, and W. Steibelt, *Ber.*, **47**, 1248 (1914). [e] J. v. Braun and H. Deutsch, *ibid.*, **45**, 2188 (1912). [f] Prepared following the procedure of M. L. Moore and F. S. Crossley, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 599. [g] Not distilled, but used as such. [h] O. H. Wheeler and I. Lerner, *Am. Chem. J.*, **26**, 345 (1901).

## Results

Acyl isothiocyanates used in these studies are conveniently prepared from lead thiocyanate and the corresponding acyl halide[12]; alkyl isothiocyanates were prepared from the amine, carbon disulfide, and ethyl chloroformate by the modified Kaluza reaction.[13] The isothiocyanates were converted to the N-substituted N′-phenylthioureas by treating with aniline for characterization purposes. A list of those prepared is given in Table I.

When phenylacetyl isothiocyanate was refluxed with 2.2 molar equiv. of aluminum chloride in carbon disulfide for a few hours, or stirred in *sym*-tetrachloroethane on a steam bath for 30 min., and the reaction mixture decomposed with ice and water, a bright orange solid (I) remained, which melted at 221–222° after recrystallization from glacial acetic acid. Prolonged hydrolysis with concentrated potassium hydroxide converted I to homophthalic acid; lithium aluminum hydride reduction resulted in the formation of 1,2,3,4-tetrahydroisoquinoline, while treatment with hydrogen peroxide produced the sulfur-free homophthalimide, or, when used in excess, the phthalimide. These conversions (Chart I) unequivocally identified the compound as 2a-thiohomophthalimide [or 1-thio-1,2,3,4-tetrahydro-1,3(2H,4H)-isoquinolinedione by *Chemical Abstracts* nomenclature].

CHART I




Similarly, a variety of ring- and also methylene-substituted phenylacetyl isothiocyanates underwent such intramolecular ring closure in yields varying from 40 to 74% (Table II). The products were degraded in a manner similar to that depicted in Chart I, in order to establish their identities. Where the corresponding homophthalimides or homophthalic acids were not previously reported, the imides were also oxidized to the corresponding phthalimides[14] for identification.

Not unexpectedly, benzoyl isothiocyanates underwent such ring closure with much greater reluctance; the attachment of the carbonyl group directly to the aromatic ring greatly deactivates the ring towards electrophilic substitution, necessitating the presence of other electron-donating groups in order to overcome

(12) A. E. Dixon and J. Taylor, *J. Chem. Soc.*, **93**, 684 (1908).

(13) W. R. Vaughan, M. V. Anderson, H. S. Blanchard, and D. I. McCane *J. Org. Chem.*, **20**, 819 (1955).

(14) The mechanism of this oxidation, which involves ring contraction by benzilic acid rearrangement, is to be discussed in another paper; a preliminary report has been given [P. A. S. Smith and R. O. Kan, *J. Am. Chem. Soc.*, **83**, 2580 (1961)].

TABLE II

CYCLIZATION OF ISOTHIOCYANATES

A. Arylacetyl Isothiocyanates, $R_2CHCONCS$

| R | Thioimide [substituted 1-thio-1,3(2H,4H)-isoquinolinedione] | M.p., °C. | Reaction time, hr. | Yield, % |
|---|---|---|---|---|
| Phenyl, H | Unsubstituted[a] | 221–222 | 3 | 74 |
| *m*-Tolyl, H | 6-Methyl[b] | 198–199 | 4 | 42 |
| *p*-Tolyl, H | 7-Methyl[c] | 230 | 4 | 48 |
| *m*-Methoxyphenyl, H | 6-Methoxy[d] | 224–225 | 4 | 42 |
| *p*-Chlorophenyl, H | 7-Chloro[e] | 238–239 | 4 | 40 |
| Diphenyl | 4-Phenyl[f] | 166–167 | 0.5 | 40 |
| α-Naphthyl, H | 5,6-Benzo[g] | 254–255 | 16 | 41 |
| 3-Phenanthryl, H | (?)[h] | 240–280 | | |
| 1-Cyclohexenyl, H | 5,6,7,8-Tetrahydro, hydrate (?)[i] | 197 | 0.5–4 | 48 |

B. Aroyl Isothiocyanates, ArCONCS

| Ar | Thioimide (substituted 1-thio-1,3-isoindolinedione) | M.p., °C. | Reaction time, hr. | Yield, % |
|---|---|---|---|---|
| Phenyl | None | | | |
| *m*-Tolyl | 7-Methyl[j] | 192 | 96 | 45 |
| *p*-Tolyl | None | | | |
| 3,5-Xylyl | 5,7-Dimethyl[k] | 209–210 | 24 | 65 |
| *m*-Methoxyphenyl | None | | | |
| 3,5-Dimethoxyphenyl | None | | | |
| 3,4,5-Trimethoxyphenyl | None | | | |
| α-Naphthyl | None | | | |
| β-Naphthyl | 6,7-Benzo[l] | 248–249 | 48 | 25 |
| 3-Thienyl | 4-Thio-4,6(5H)-thieno[2,3-*c*]-pyrroledione[m] | 183 | 24 | 12 |

C. Other Isothiocyanates, RNCS

| R | Product | M.p., °C. | Reaction time, hr. | Yield, % |
|---|---|---|---|---|
| Benzyl | None | | | |
| β-Phenylethyl | 1-Thiodihydroisocarbostyryl[n] | 98–99 | 30 | 40 |

[a] *Anal.* Calcd. for $C_9H_7NOS$: C, 61.00; H, 3.98; N, 7.91. Found: C, 61.03; H, 4.16; N, 7.88. [b] *Anal.* Calcd. for $C_{10}H_9NOS$: C, 62.82; H, 4.75; N, 7.32. Found: C, 62.80; H, 4.88; N, 7.42. [c] *Anal.* Calcd. for $C_{10}H_9NOS$: C, 62.82; H, 4.75; N, 7.32 Found: C, 63.13; H, 4.40; N, 7.39. [d] *Anal.* Calcd. for $C_{10}H_9NO_2S$: C, 57.96; H, 4.36; N, 6.76. Found: C, 57.74; H, 4.58; N, 6.54. [e] *Anal.* Calcd. for $C_9H_6ClNOS$: C, 51.07; H, 2.86; N, 6.62. Found: C, 51.19; H, 2.99; N, 6.57. [f] *Anal.* Calcd. for $C_{15}H_{11}NOS$: C, 71.12; H, 4.38; N, 5.55. Found: C, 70.96; H, 4.41; N, 5.39. [g] *Anal.* Calcd. for $C_{13}H_9NOS$: C, 68.89; H, 3.99; N, 6.16. Found: C, 68.73; H, 4.17; N, 6.32. [h] Orange powder. *Anal.* Found: C, 62.74; H, 3.69; N, 4.32; ash, 2.99. All attempts at purification by recrystallization from a variety of solvents were unsuccessful. [i] White powder after crystallization from benzene–petroleum ether mixture. *Anal.* Calcd. for $C_9H_{11}NOS$: C, 59.67; H, 6.08; N, 8.85. Calcd. for $C_9H_{13}NO_2S$: C, 54.25; H, 6.54; N, 7.03. Found: C, 54.89; H, 6.56; N, 7.02. [j] *Anal.* Calcd. for $C_9H_7NOS$: C, 61.00; H, 3.98; N, 7.91. Found: C, 61.20; H, 4.25; N, 7.89. [k] *Anal.* Calcd. for $C_{10}H_9NOS$: C, 62.82; H, 4.75; N, 7.32. Found: C, 63.04; H, 4.76; N, 7.41. [l] *Anal.* Calcd. for $C_{12}H_7NOS$: C, 67.61; H, 3.30; N, 6.58. Found: C, 67.40; H, 3.45; N, 6.68. [m] *Anal.* Calcd. for $C_6H_3NOS_2$: C, 42.58; H, 1.79; N, 8.28. Found: C, 42.70; H, 2.02; N, 8.06. [n] *Anal.* Calcd. for $C_9H_9NOS$: C, 66.25; H, 5.52; N, 8.59. Found: C, 66.64; H, 5.50; N, 8.57.

this effect. Thus, benzoyl isothiocyanate failed to cyclize at all under a wide variety of conditions, while the substituted benzoyl isothiocyanates, which are listed in Table II, did so only after considerably longer reaction times.

1-Cyclohexeneacetyl isothiocyanate gave an unexpectedly colorless product, whose analysis indicated the presence of the elements of one molecule of water more than required by the thioimide structure. Although the infrared spectrum (amide doublet at 1700 and 1780 plus strong bands at 1040–1060 and 1200–1200, $cm.^{-1}$, part of which may be due to thionamide) and tests for unsaturation with bromine and with permanganate were consistent with the thioimide structure, the indentification should be regarded as uncertain.

It is of interest to note that *m*-toluyl isothiocyanate formed exclusively the product resulting from carboxylation in the position *ortho* to the methyl group, II, thus providing a facile route to 3-methylphthalic acid and its derivatives. *m*-Tolylacetyl isothiocyanate, on the other hand, cyclized to the opposite side, *para* to the methyl group, to give III, the structure of which was established by oxidation to trimellitic acid (Chart II) and degradation to 4-methylphthalimide.

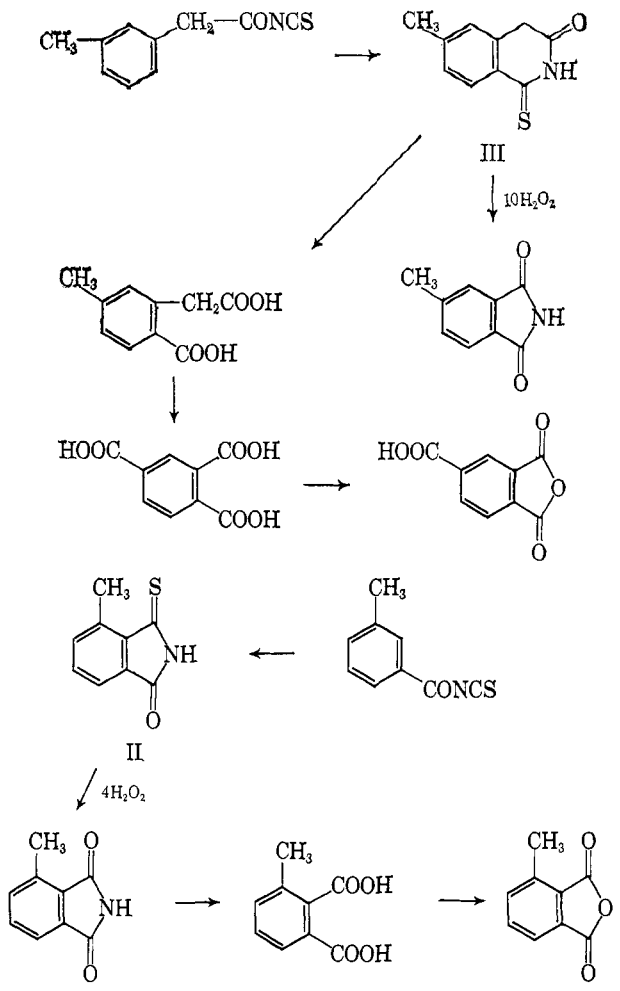
An attempt to extend this synthetic method to other systems met with only partial success. Thus α-naphthylacetyl isothiocyanate produced the thioimide resulting from attack on the β-position, whereas α-naphthoyl isothiocyanate could not be made to react. β-Naphthoyl isothiocyanate reacted by closure to the α-position, however. In addition, 3-thenoyl isothiocyanate cyclized to the 2-position, but in poor yield.

Finally, aralkyl isothiocyanates were briefly examined; only phenethyl isothiocyanate was cyclized successfully, to form 1-thiodihydroisocarbostyril in 40% yield.

The thioimides as a class, of which previously only one example has been reported,[15] were rose red when five-membered (except for brown thionaphthalimide), and brown-orange to yellow-orange when six-membered.

(15) M. E. Baguley and J. A. Elvidge, *J. Chem. Soc.*, 709 (1957).

CHART II




The electronic absorption spectra in ethanol solution showed four or more bands, of which that of lowest frequency, presumably resulting from an n–$\pi^*$ transition in the thiocarbonyl group,[16] fell in the region of 3250 to 4500 Å. (log $\epsilon$ 3–3.9). The infrared spectra showed amide doublets, at 1700–1740 cm.$^{-1}$ for the five-membered rings, and at 1680–1690 cm.$^{-1}$ for the six-membered rings.

Hydrolysis of the products to the dicarboxylic acids was difficult; reflux periods up to several days with 25% potassium hydroxide solution were sometimes required, although the result was always eventually successful.

The processes of cyclization of aroyl isothiocyanates, or of arylacetyl isothiocyanates followed by ring contraction, open a general route to aromatic *ortho* dicarboxylic acids hitherto available only with difficulty or not at all.

## Experimental[17]

**Preparation of Isothiocyanates.**—A mixture of 1 mole of the acid chloride, 140 g. (1 mole) of lead thiocyanate, and 250 ml. of benzene was refluxed for 5 hr., after which a small amount of Norit was added, and refluxing continued for an additional 5 min. Subsequently the mixture was filtered twice through the same Büchner funnel, where the solid collected in the first pass removed the last traces of finely divided solid from initial filtrate. The solvent was removed under aspirator vacuum, and the residual isothiocyanate was distilled *in vacuo* just prior to use since, after a few hours standing in air, the light yellow liquids rapidly decomposed and turned dark. For this reason, most of the products were not analyzed but, for characterization, were converted to the corresponding phenylthioureas by warming for 5 min. with aniline in methanol solution.

The acyl isothiocyanates showed the characteristic infrared absorption in the form of a broad band or a doublet in the range 1930–2000 cm.$^{-1}$, and carbonyl stretching at or near 1700 cm.$^{-1}$. The acyl isothiocyanate absorption thus falls at distinctly lower frequencies than that of alkyl isothiocyanates (*e.g.*, benzyl, 2025 and 2040 cm.$^{-1}$; $\beta$-phenylethyl, 2020 and 2040 cm.$^{-1}$).

**Cyclization of Isothiocyanates.**—One equivalent of the isothiocyanate was added slowly with stirring over 5–15 min., during which time the vessel was cooled in ice–water, to 250 ml. of carbon disulfide and 2.2 molar equiv. (86 g.) of anhydrous powdered aluminum chloride. After the addition, the cooling bath was removed, and the mixture was refluxed (infrared lamp) for periods varying from 4 hr. to 4 days. It was cooled again in an ice bath, and a mixture of 100 ml. of water and 20 ml. of concentrated hydrochloric acid was added dropwise over 0.5 hr. Stirring was continued until most of the solid that had deposited had been decomposed, after which it was collected by suction filtration. Evaporation of the filtrate yielded only 3 to 4% additional product. The solid thus obtained was dried in an oven at 40° or in a vacuum desiccator to remove all traces of carbon disulfide and was recrystallized from glacial acetic acid after treatment with a little Norit. The thioimides obtained in this manner are listed in Table III.

*sym*-Tetrachloroethane was used as solvent also in some cases. It was removed at the end of the reaction by steam distillation. The reaction times needed were generally lower. Phenylacetyl isothiocyanate required 12 min. of warming on a steam bath in *sym*-tetrachloroethane, against 3 hr. of refluxing in carbon disul-

TABLE III

CARBOXYLIC ACIDS OBTAINED FROM CYCLIZED ISOTHIOCYANATES

| Acid | Yield, % | M.p., °C. |
|---|---|---|
| Homophthalic | 61 | 181[a] |
| 5-Methylhomophthalic[b] | 87 | 202 |
| 4-Methylhomophthalic[c] | 91 | 201 |
| 5-Methoxyhomophthalic | Good | 225[d] |
| 4-Chlorohomophthalic | >50 | 197[e] |
| $\alpha$-Phenylhomophthalic | 94 | 173[f] |
| 1-Homo-1,2-naphthalic[g] | 10, >50[h] | 214–215 |
| 2-Carboxycyclohexene-1-acetic | Good | 166[i] |
| 3-Methylphthalic | 80 | 157–158[j] |
| 3,5-Dimethylphthalic | Good | 176[k] |
| 1,2-Naphthalic | 40 | 175[l] |
| Thiophene-2,3-dicarboxylic | 75 | 270[m] |
| *o*-(2-Aminoethyl)benzoic, hydrochloride | Good[n] | 194–198[o] |

[a] Lit. m.p. 181° [W. Davies and H. G. Poole, *J. Chem. Soc.*, 1616 (1928)]. [b] *Anal.* Calcd. for $C_{10}H_{10}O_4$: C, 61.85; H, 5.20; equiv. wt., 97. Found: C, 61.90; H, 5.28; equiv. wt., 94, 97. [c] *Anal.* Calcd. for $C_{10}H_{10}O_4$: C, 61.85; H, 5.20; equiv. wt., 97. Found: C, 61.66; H, 5.31; equiv. wt., 95.5, 99.5. [d] Lit. m.p. 222° [S. N. Chakravarti and N. Swaminathan, *J. Indian. Chem. Soc.*, 11, 101 (1934)]. [e] Lit. m.p. 191–192° [D. E. Adams and T. F. Grey, *J. Chem. Soc.*, 3518 (1955)]. [f] G. F. Koelsch, *J. Am. Chem. Soc.*, **58**, 1321 (1936). [g] *Anal.* Calcd. for $C_{13}H_{10}O_4$: C, 67.83; H, 4.38; equiv. wt., 115. Found: C, 67.68; H, 4.47; equiv. wt., 116. [h] From hydrolysis in 90% orthophosphoric acid for 5 hr. at 140°. [i] Lit. m.p. 166° [G. A. R. Kon and H. R. Nanji, *J. Chem. Soc.*, 2426 (1932)]. [j] Lit.[26] m.p. 154°. [k] Lit. m.p. 183° [L. Ruzicka, *Helv. Chim. Acta*, **19**, 419 (1936)]. [l] Lit.[24] m.p. 175°. [m] Lit. m.p. 268–270° [B. R. Baker, R. E. Schaub, J. P. Joseph, F. J. McEvoy, and J. H. Williams, *J. Org. Chem.*, **18**, 138 (1953)]. [n] From hydrolysis in refluxing concentrated hydrochloric acid. [o] Lit.[18] m.p. 199–200°. Neutralizing a small sample with sodium bicarbonate solution, evaporation of the water, and heating of the residue for 2 hr. at 170° gave 3,4-dihydroisocarbostyryl, m.p. 68° (lit.[18] m.p. 70–71°).

(16) M. J. Janssen, *Rec. trav. chim.*, **79**, 454, 464, 1066 (1960).

(17) Melting points are corrected and boiling points are uncorrected. Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich., and by Micro-Tech Laboratories, Skokie, Ill. Infrared spectra were recorded on a Perkin-Elmer Model 21 spectrophotometer, from films or Nujol mulls. Ultraviolet-visible spectra were recorded with a Cary recording spectrophotometer, Model 11.

fide to obtain a similar yield. The product required more extensive purification, however, and the yields never exceeded those obtained by the use of carbon disulfide. Other catalysts, such as stannic chloride and ferric chloride, proved to be ineffective.

**Conversion of Thioimides to Dicarboxylic Acids.**—In a 100-ml., round-bottom, one-necked copper flask were placed 3 g. of a thioimide and 40 ml. of 25% aqueous potassium hydroxide. The mixture was refluxed until no evolution of ammonia was observed (24–72 hr.), followed by acidification, extraction with ether, and evaporation of the extracts under a stream of air. In this manner the acids listed in Table III were obtained. The melting points recorded were those observed with rapid heating or in a preheated bath; slow heating gave lower, less sharp, melting points. Melting was in all cases accompanied by gas evolution, presumably resulting from anhydride formation.

**Reduction of 2-Thiohomophthalimides.**—To 100 ml. of anhydrous ether containing 1.071 g. of lithium aluminum hydride (5 molar equiv.) was added 1 g. of 2a-thiohomophthalimide [1-thio-1,3(2H,4H)-isoquinolinedione] in two portions, over 2 min. The mixture was stirred under reflux for 15 hr., after which it was cooled. A mixture of 2 ml. of water and 2 ml. of 10% sodium hydroxide solution was added carefully and stirring was continued for another hour. After filtration and washing of the precipitate with anhydrous ether, the solvent was removed under the aspirator, and a saturated solution of picric acid in ethanol was added to the residue. The picrate of 1,2,3,4-tetrahydroisoquinoline formed in 47% yield on standing, m.p. 195°, lit.[18] m.p. 195–196°. Similarly, a 50% yield of 1,2,3,4-tetrahydroisoquinoline, isolated as its picrate, was obtained from the reduction of thio-3,4-dihydroisocarbostyril. A yield of 40% of 6-methyl-1,2,3,4-tetrahydroisoquinoline (as its picrate, m.p. 214°, lit.[19] m.p. 205°) was obtained by the reduction of 5-methyl-2a-thiohomophthalimide [1-thio-6-methyl-1,3(2H,4H)-isoquinolinedione].

**Oxidation of Homophthalic Acids.**—An aqueous solution of 0.5 g. of 5-methylhomophthalic acid and an excess of potassium permanganate was refluxed for 8 hr., filtered, and acidified. Evaporation to dryness in an air stream, extraction of the residue with boiling, glacial acetic acid, and cooling of the extract gave 0.3 g. (55%) of trimellitic acid, m.p. 225° dec. (lit. m.p. 226–227°,[20] 238°[21]). Refluxing this product with acetic anhydride for 2 hr., removal of reagent and acetic acid *in vacuo*, and sublimation of the residue at 200–220° (12 mm.) gave trimellitic anhydride, m.p. 160°, lit.[22] m.p. 162.5–163.5°.

Similar treatment of 5-methoxyhomophthalic acid gave 4-methoxyphthalic acid, m.p. 170°, lit.[23] m.p. 171–172°. Sublimation at 220° gave 4-methoxyphthalic anhydride, m.p. 95°, lit.[23] m.p. 94–95°.

**Oxidation of Thiohomophthalimides to Phthalimides.**—To a solution of 0.5 g. of 1-thio-1,3(2H,4H)-benzo[*d*]isoquinolinedione (the thiohomophthalimide from α-naphthylacetyl isothiocyanate) in 5 ml. of water containing 0.5 g. of potassium hydroxide was slowly added 2.8 ml. (10 molar equiv.) of 30% hydrogen peroxide. After 4 hr. at room temperature, the solution was acidified with concentrated hydrochloric acid and heated on the steam bath for 20 min. Upon chilling, there was obtained 0.35 g. (81%) of 1,2-naphthalimide as yellow needles, m.p. 223° after recrystallization from acetic acid, lit.[24] m.p. 224°.

*Anal.* Calcd. for $C_{12}H_7NO_2$: C, 72.42; H, 3.55; N, 7.04. Found: C, 72.25; H, 3.65; N, 7.00.

In a similar manner, 6-methyl-1-thio-1,3(2H,4H)-isoquinolinedione (the thiohomophthalimide from *m*-tolylacetyl isothiocyanate) was converted in 61% yield to 4-methylphthalimide, m.p. 196° (lit.[25] m.p. 196°, depressed by admixture with the known 3-methyl isomer).

*Anal.* Calcd. for $C_9H_7NO_2$: C, 67.08; H, 4.38; N, 8.70. Found: C, 67.39; H, 4.49; N, 8.91.

**3-Methylphthalimide.**—Sublimation at 110° (20 mm.) of the 3-methylphthalic acid obtained from *m*-tolulyl isothiocyanate by cyclization and hydrolysis gave 3-methylphthalic anhydride, m.p. 117–118°, lit.[26] m.p. 117–118°. Equal weights of 28% ammonium hydroxide and the 3-methylphthalic anhydride were heated for 2 hr. at 150–180°. Recrystallization of the crude product from hot water gave 3-methylphthalimide, m.p. 188–189° (lit.[27] m.p. 189–190°) in good yield.

(18) E. Bamberger and W. Dieckmann, *Ber.*, **26**, 1205 (1893).
(19) J. von Braun, G. Blessing, and R. S. Cahn, *ibid.*, **57**, 908 (1924).
(20) W. H. Perkin and J. F. S. Stone, *J. Chem. Soc.*, **127**, 2275 (1925).
(21) G. T. Morgan and E. A. Coulson, *ibid.*, 2551 (1929).
(22) W. Schultze, *Ann.*, **359**, 129 (1908).
(23) W. W. Prichard, *J. Am. Chem. Soc.*, **78**, 6137 (1956).
(24) E. F. Bradbrook and R. P. Linstead, *J. Chem. Soc.*, 1739 (1936).
(25) S. von Niementowski, *Monatsh.*, **12**, 620 (1891).
(26) F. Mayer and O. Stark, *Ber.*, **64**, 2003 (1931).
(27) S. Gabriel and A. Thieme, *ibid.*, **52**, 1079 (1919).

# Optically Active Amines. II. The Optical Rotatory Dispersion Curves of the N-Benzylidene and Substituted N-Benzylidene Derivatives of Some Open-Chain Primary Amines[1,2]

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Most of the optically active N-benzylidene, N-*o*-methoxybenzylidene, N-salicylidene, N-5-nitrosalicylidene, N-5-chlorosalicylidene, and N-5-bromosalicylidene derivatives of α-phenyl- and α-benzylethylamine and of *sec*-butylamine were prepared and their electronic absorption spectra and optical rotatory dispersion curves were measured. Cotton effects could be observed only in the rotatory dispersion curves of the N-salicylidenes and the N-5-chloro- and N-5-bromosalicylidenes of α-phenyl- and α-benzylethylamine. A comparison of these curves with that displayed by N-salicylidene-*sec*-butylamine suggests that, for the aralkylamine derivatives, there may be present rotationally significant interactions of the π-electron systems of the phenyl and benzyl groups with the N-salicylidene moiety which, for the derivatives with the (*S*)-configuration, result in strong positive Cotton effects near 410 and 315 mμ.

Many Schiff bases derived from aldehydes and ketones and optically active open-chain amines exhibit notably high rotatory powers at the sodium D-line. Betti[5] has recorded values for numerous derivatives of benzaldehyde and substituted benzaldehydes and (+)-1-(α-aminobenzyl)-2-naphthol ($[\phi]_D$ +147°) and observed marked differences, apparently related to the strengths of the acids corresponding to the aldehydes. For example, the derivative prepared from *p*-N,N-dimethylaminobenzaldehyde has an extremely high posi-

(1) Paper I: H. E. Smith, M. E. Warren, Jr., and A. W. Ingersoll, *J. Am. Chem. Soc.*, **84**, 1513 (1962).
(2) A preliminary report of some of this work was presented before the Combined Southeast and Southwest Regional Meeting of the American Chemical Society, New Orleans, La., 1961, Abstract 162.
(3) Part of this work is from the M.A. Thesis of S. L. Cook, Vanderbilt University, June, 1962, and part from the Ph.D. Thesis of M. E. Warren, Jr., Vanderbilt University, June, 1963.
(4) National Defense Education Act Fellow, 1959–1962.
(5) M. Betti, *Trans. Faraday Soc.*, **26**, 337 (1930).