Anal. Calcd. for $C_9H_{11}NO_2S$: N, 7.39; S, 16.54. Found: N, 7.10; S, 16.26.

2-(3,4-Dichlorophenyl)-4-thiazolidone-1-dioxide.—To a solution of 8 g. (0.0322 mole) of 2-(3,4-dichlorophenyl)-4-thiazolidone in 200 ml. of acetic acid was added with stirring 7.5 g. (0.0475 mole) of potassium permanganate in 75 ml. of water. The temperature was kept below 30° by external cooling. After the addition was complete, sodium bisulfite solution was added to the reaction mixture to dissolve the manganese dioxide. The mixture was diluted with an equal volume of water and the colorless product was filtered off, washed thoroughly with water and dried. The yield of product melting at 192.4–193.4° (cor.) was 7.5 g. (83%).

Anal. Calcd. for $C_9H_7Cl_2NO_3S$: Cl, 25.31; S, 11.45. Found: Cl, 25.30; S, 11.49.

The following 1-dioxides were prepared in a similar manner: **2-(4-Bromophenyl)-4-thiazolidone-1-dioxide** (crude yield 70%) was recrystallized by dissolving it in a large volume of hot nitromethane and cooling quickly, m.p. 196.2–196.6° (cor.). *Anal.* Calcd. for $C_9H_8BrNO_3S$: Br, 27.55; S, 11.05. Found: Br, 27.10; S, 11.08. **2-(4-Chlorophenyl)-4-thiazolidone-1-dioxide** (90% yield), m.p. 172–173.5° dec. *Anal.* Calcd. for $C_9H_8ClNO_3S$: N, 5.70; S, 13.05. Found: N, 5.86; S, 13.08. **2-(4-Chlorophenyl)-2-methyl-4-thiazolidone-1-dioxide** (crude yield 75%) was recrystallized from methanol, m.p. 145.7–146.8° (cor.). *Anal.* Calcd. for $C_{10}H_{10}ClNO_3S$: Cl, 13.65; S, 12.35. Found: Cl, 13.62; S, 12.42.

RENSSELAER, NEW YORK

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF KANSAS]

Formation of N,N'-Dibenzoylurea from Nitromethane and Benzoyl Chloride in Pyridine Solution

BY ROBERT H. TERSS[1] AND WILLIAM E. MCEWEN

RECEIVED JULY 20, 1953

The reaction of nitromethane and benzoyl chloride in pyridine solution afforded N,N'-dibenzoylurea (III) together with small amounts of 3,5-diphenyl-1,2,4-oxadiazole (IV), benzamide, benzonitrile and a compound of formula $C_{15}H_{10}N_2O_2$, which has tentatively been assigned the structure 2,6-diphenyl-4-keto-1,3,5-oxadiazine (V). Carbon dioxide was evolved during the course of the reaction. Evidence is presented which indicates that fulminic acid (VII) and benzoyl isocyanate (VIII) are intermediates in the formation of N,N'-dibenzoylurea (III). The reaction of phenylnitromethane with benzoyl chloride in pyridine solution gave dibenzhydroxamic acid (XI) as the main isolable organic product.

The chemistry of acylpyridinium salts, particularly acylpyridinium chlorides I, has been investigated fairly extensively during the past half century. Attention has been directed to: (1) the preparation of crystalline acylpyridinium salts,[2] (2) the acylating properties of these salts (or, what amounts to the same thing, solutions of the acid chlorides in pyridine) toward water, hydrogen sulfide, alcohols, phenols, enols, primary and secondary amines and amides and other compounds containing active hydrogen[2a,3] (3) their use in the cleavage of ethers[2b]; (4) the condensation of these salts with a variety of nucleophilic reagents to form either 4-substituted pyridines or 4-substituted-1-acyl-1,4-dihydropyridines[4]; and (5) the self condensation reactions of the various acylpyridinium cations in the presence of reducing agents to give, at least initially, N,N'-diacyltetrahydro-4,4'-bipyridyls.[5] Many analogous reactions of acyl-quinolinium salts are also known, the condensation reactions with nucleophilic reagents to form 2-substituted-1-acyl-1,2-dihydroquinolines[4b,6] being of particular interest with respect to our work. The addition of bases to the 2- and 4-positions of alkylpyridinium and alkylquinolinium cations are also well known reactions.[7]

In all of the condensation reactions involving external bases and acylpyridinium or acylquinolinium salts in which the structures of the products have been firmly established the results have indicated

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[1] Pan-American Oil Refining Corporation Fellow, 1952–1953.

[2] (a) H. Adkins and Q. E. Thompson, THIS JOURNAL, **71**, 2242 (1949); (b) V. Prey, *Ber.*, **75**, 537 (1942); (c) W. M. Dehn, THIS JOURNAL, **34**, 1399 (1912); (d) W. M. Dehn and A. A. Ball, *ibid.*, **36**, 2091 (1914); (e) G. L. Schwartz and W. M. Dehn, *ibid.*, **39**, 2444 (1917); (f) S. I. Lur'e, *J. Gen. Chem.* (*U. S. S. R.*), **18**, 1517 (1948); (g) K. Freudenberg and D. Peters, *Ber.*, **52**, 1463 (1919); (h) M. Dennstedt and J. Zimmermann, *ibid.*, **19**, 75 (1886); (i) G. Minunni, *Gazz. chim. ital.*, [II], **22**, 213 (1892); (j) H. Staudinger and H. Stockmann, *Ber.*, **42**, 3485 (1909); (k) H. O. Jones and H. Tasker, *Proc. Chem. Soc.*, **24**, 271 (1908); (l) E. Gebauer-Fulnegg and F. Riesenfeld, *Monatsh.*, **47**, 185 (1926); (m) H. E. Baumgarten, THIS JOURNAL, **75**, 1239 (1953).

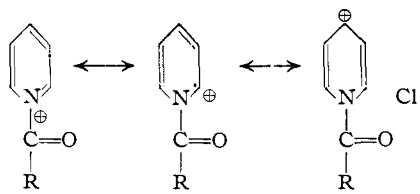
[3] (a) L. Claisen, *Ann.*, **291**, 25 (1896); (b) D. M. Smith and W. M. D. Bryant, THIS JOURNAL, **57**, 61 (1935); (c) W. R. Gilkerson, Ph.D. Thesis, Kansas University (1953); (d) L. Claisen and E. Haase, *Ber.*, **33**, 1242 (1900); (e) Q. E. Thompson, THIS JOURNAL, **73**, 5841 (1951); (f) J. Mitchell, Jr, and C. E. Ashby, *ibid.*, **67**, 161 (1945); (g) S. M. McElvain and D. Kundiger, *ibid.*, **64**, 254 (1942); (h) W. Dieckmann and R. Stein, *Ber.*, **37**, 3370 (1904); (i) S. L. Bafna and V. Gold, *J. Chem. Soc.*, 1406 (1953).

[4] (a) W. von E. Doering and W. E. McEwen, THIS JOURNAL, **73**, 2104 (1951); (b) W. E. McEwen, R. H. Terss and I. W. Elliott, *ibid.*, **74**, 3605 (1952); (c) E. Ghigi, *Ber.*, **73**, 677 (1940); **75**, 764 (1942); *Gazz. chim. ital.*, **76**, 352 (1946); (d) E. Koenigs and E. Ruppelt, *Ann.*, **509**, 142 (1934); (e) V. C. Lowman, Ph.D. Thesis, Columbia University, 1948.

[5] (a) O. Dimroth and R. Heene, *Ber.*, **54**, 2934 (1921); (b) O. Dimroth and F. Frister, *ibid.*, **55**, 1223 (1922); (c) J. P. Wibaut and J. F. Arens, *Rec. trav. chim.*, **60**, 119 (1941); (d) J. F. Arens and J. P. Wibaut, *ibid.*, **61**, 59 (1942); (e) D. A. VanDorp and J. F. Arens, *ibid.*, **66**, 189 (1947); (f) E. Weitz, A. Roth and A. Nelken, *Ann.*, **425**, 161 (1921).

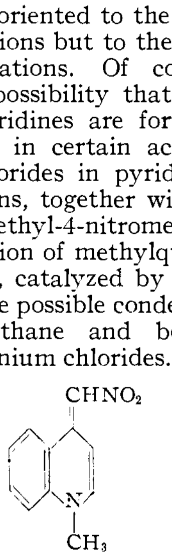
[6] (a) A. Reissert, *Ber.*, **38**, 1603, 3415 (1905); (b) A. Gasmann and H. Rupe, *Helv. Chim. Acta*, **22**, 1241 (1939); (c) S. Sugasawa and T. Tsuda, *J. Pharm. Soc. Japan*, **56**, 557 (1936); (d) W. E. McEwen and R. N. Hazlett, THIS JOURNAL, **71**, 1949 (1949); (e) R. H. Glazier, Ph.D. Thesis, Kansas University, 1952; (f) R. B. Woodward, THIS JOURNAL, **62**, 1626 (1940); (g) J. M. Grosheintz and H. O. L. Fischer, *ibid.*, **63**, 2021 (1941); (h) G. L. Buchanan, J. W. Cook and J. D. Loudon, *J. Chem. Soc.*, 325 (1944); (i) V. C. Lowman and R. Seider as quoted in R. C. Elderfield, "Heterocyclic Compounds," Vol. 4, John Wiley and Sons, Inc, New York, N. Y., 1952, p. 244.

[7] (a) N. J. Leonard, H. A. DeWalt, Jr., and G. W. Leubner, THIS JOURNAL, **73**, 3325 (1951); (b) N. J. Leonard and R. L. Foster, *ibid.*, **74**, 2110, 3671 (1952); (c) N. J. Leonard and G. W. Leubner, *ibid.*, **71**, 3405 (1949); (d) O. Wahl, U. S. Patent 1,878,557; *C. A.*, **27**, 1195 (1933); (e) E. Q. Adams and H. L. Haller, THIS JOURNAL, **42**, 2389 (1920); (f) M. Freund and L. Richard, *Ber.*, **42**, 1101 (1909); (g) J. von Braun and E. Aust, *ibid.*, **47**, 3023 (1914); (h) M. Freund and G. Bode, *ibid.*, **42**, 1746 (1909); (i) H. Schmid and P. Karrer, *Helv. Chim. Acta*, **32**, 960 (1949); (j) A. Kaufmann, *Ber.*, **51**, 116 (1918); (k) J. G. Aston and P. A. Lasselle, THIS JOURNAL, **56**, 426 (1934).



I

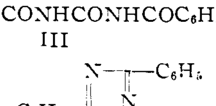
that the bases are oriented to the 4-position of the acylpyridinium cations but to the 2-position of the acylquinolinium cations. Of course, this does not preclude the possibility that 2-substituted 1-acyl-1,2-dihydropyridines are formed as non-isolable intermediates in certain acylation reactions involving acid chlorides in pyridine solution.[4a,2m] These considerations, together with the reported[7a] isolation of 1-methyl-4-nitromethylenequinolane (II) from the reaction of methylquinolinium iodide with nitromethane, catalyzed by sodium ethoxide, led us to investigate possible condensation reactions involving nitromethane and benzoylpyridinium and benzoylquinolinium chlorides.



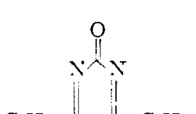
II

The reaction involving pyridine, benzoyl chloride and nitromethane proved to be complex and surprising. During a six-day reaction period at room temperature carbon dioxide was evolved, and N,N'-dibenzoylurea (III) was formed, together with small amounts of 3,5-diphenyl-1,2,4-oxadiazole (IV), benzamide, benzonitrile and a compound of formula $C_{15}H_{10}N_2O_2$ and m.p. 159.1–159.9°, which has tentatively been assigned the structure 2,6-diphenyl-4-keto-1,3,5-oxadiazine (V). Some nitromethane was recovered, 68% of the benzoyl chloride was recovered in the form of benzoic acid, and not less than 89% of the pyridine was recovered. The use of a catalytic amount of pyridine, however, failed to bring about any appreciable reaction between benzoyl chloride and nitromethane even after a reaction period of a month at room temperature. Allowing the usual reaction mixtures to stand at room temperature for longer periods of time (up to three weeks) did not increase the yield of III. A reaction mixture that had stood for five hours at room temperature afforded only a trace of III together with some benzamide. The effect of temperature on the reaction was not investigated, but an increase in room temperature seemed to accelerate the evolution of gas.

$C_6H_5CONHCONHCOC_6H_5$
III



IV



V

On the basis of some speculation and considerable experimentation we suggest the following sequence of reactions to account for the formation of N,N'-dibenzoylurea (III) and some of the by-products

$$C_6H_5COCl + CH_3NO_2 + C_5H_5N \longrightarrow$$
$$\underset{\text{VI}}{CH_2{=}\overset{+}{N}(\overset{-}{O})OCOC_6H_5} + C_5H_5NH^+Cl^- \quad (1)$$

$$VI + C_5H_5N \longrightarrow (C{=}NOH \rightleftharpoons$$
$$\underset{\text{VII}}{H{-}C{\equiv}\overset{+}{N}{-}\overset{-}{O})} + C_5H_5NH^+C_6H_5CO_2^- \quad (2)$$

$$C_6H_5COCl + C_5H_5N + VII \longrightarrow$$
$$\underset{\text{VIII}}{C_6H_5CO{-}N{=}C{=}O} + C_5H_5NH^+Cl^- \quad (3)$$

$$VIII + H_2O \longrightarrow C_6H_5CONH_2 + CO_2 \quad (4)$$

$$VIII + C_6H_5CONH_2 \longrightarrow III \quad (5)$$

The arguments in support of step 1 are the following: (a) Although the O-benzoyl derivative VI of the aci-form of nitromethane has never been isolated,[8] its formation as an unstable intermediate as a result of the action of benzoyl chloride on nitromethane in pyridine solution is reasonable on the basis of analogy with the known reaction of acid chlorides with β-ketoesters in pyridine to form exclusively the O-acyl derivatives.[3a,c,d,4a] (b) Other conceivable intermediates, ω-nitroacetophenone (IX)[9] and formhydroxamic acid (X),[10,11] were prepared and caused to react with benzoyl chloride and pyridine. Neither N,N'-dibenzoylurea (III) nor any of the by-products obtained in the nitromethane reaction were isolated. In both cases, furthermore, dibenzhydroxamic (XI) was isolated, a product not formed in the nitromethane reaction.

$C_6H_5COCH_2NO_2$	$HCONHOH$	$C_6H_5CONHOCOC_6H_5$
IX	X	XI

There is a somewhat remote analogy in the literature for step 2, which involves an elimination reaction to give fulminic acid (VII)[12]: Nef[12a] prepared mercury fulminate by the action of the sodium salt of nitromethane on mercuric chloride in a cold aqueous solution.

Step 3, which involves the formation of benzoyl isocyanate (VIII) from benzoyl chloride and fulminic acid (VII), seems entirely reasonable because of the following observations taken from the literature. (a) Scholl[13] discovered that acetyl chloride

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(8) *Cf.* (a) L. W. Jones, *Am. Chem. J.*, **20**, 1 (1898); (b) A. F. Holleman, *Rec. trav. chim.*, **15**, 356 (1896); (c) H. Wieland and Z. Kitasato, *Ber.*, **62**, 1250 (1929); (d) E. P. Stefl and M. F. Dull, THIS JOURNAL, **69**, 3037 (1947); (e) T. Urbanski, *J. Chem. Soc.*, 3374 (1949).

(9) *Cf.* S. Gabriel, *Ber.*, **36**, 570 (1903).

(10) (a) E. Bamberger and A. Landau, *ibid.*, **52**, 1093 (1919); (b) O. Baudisch, *ibid.*, **49**, 1159 (1916); (c) E. Hirschlaff and R. G. W. Norrish, *J. Chem. Soc.*, 1580 (1936); (d) E. Bamberger and E. Rust, *Ber.*, **35**, 45 (1902); (e) E. Bamberger, *J. prakt. Chem.*, **101**, 328 (1921); (f) C. D. Nenitzescu and D. A. Isacescu, *Bull. soc. chim. Romania*, **14**, 53 (1932); *C. A.*, **27**, 964 (1933); (g) S. B. Lippincott, U. S. Patent 2,168,305; *C. A.*, **33**, 9326 (1939); (h) S. B. Lippincott and H. Hass, *Ind. Eng. Chem.*, **31**, 118 (1939).

(11) Other, more complex products have also been obtained by the action of amines and other bases on primary aliphatic nitro compounds. *Cf.* (a) W. R. Dunstan and T. S. Dymond, *J. Chem. Soc.*, **59**, 410 (1891); (b) W. R. Dunstan and E. Goulding, *ibid.*, **77**, 1262 (1900); (c) W. Steinkopf, *Ber.*, **42**, 3925 (1909); (d) S. B. Lippincott, THIS JOURNAL, **62**, 2604 (1940).

(12) (a) J. U. Nef, *Ann.*, **280**, 291 (1894); (b) A. Steiner, *Ber.*, **16**, 1484 (1883); (c) E. Carstanjen and A. Ehrenberg, *J. prakt. Chem.*, [II], **25**, 232 (1882); (d) L. Wohler, *Ber.*, **38**, 1351 (1905); (e) F. C. Palazzo, *Gazz. chim. ital.*, **431**, 563 (1913); **78**, 647 (1948); (f) H. Wieland and B. Rosenfeld, *Ann.*, **484**, 236 (1930); (g) R. Scholl, *Ber.*, **27**, 2816 (1894).

(13) R. Scholl, *ibid.*, **23**, 3505 (1890).

reacts with mercury fulminate to give acetyl isocyanate, a reaction which he classified as essentially a Beckmann rearrangement. (b) Holleman[14] reported that reaction of benzoyl chloride with mercuric fulminate, followed by addition of water to the reaction mixture, afforded carbon dioxide, N,N'-dibenzoylurea (III), a trace of benzonitrile and a trace of a compound, m.p. 107°, which was not further characterized. Inasmuch as 3,5-diphenyl-1,2,4-oxadiazole (IV) melts at 109°, it is probable, in view of our results, that Holleman had also obtained IV. (c) Wieland and Hochtlen[15] also obtained III on reaction of benzoyl bromide with silver fulminate.

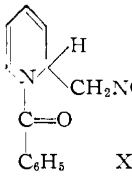
Step 4 represents an obvious isocyanate reaction and has actually been demonstrated for both acetyl isocyanate[13] and benzoyl isocyanate (VIII).[16] In the latter case benzamide was obtained in 75% yield and N,N'-dibenzoylurea (III) in 25% yield.[16] There was no report, however, of the formation of the product of m.p. 159.1–159.9°, which has tentatively been assigned the structure 2,6-diphenyl-4-keto-1,3,5-oxadiazine (V). It is therefore of interest that we obtained both III (56%) and V (22%) in the reaction of authentic benzoyl isocyanate (VIII) with water in a pyridine–benzoyl chloride medium. Since V could not be obtained from III in a separate experiment as a result of the dehydrating action of benzoyl chloride and dry pyridine (nor by use of a much more vigorous set of dehydration conditions, *viz.*, phosphorus pentoxide in refluxing benzene), it is clear that V results from VIII by a mechanism not involving III. This fact affords good support for the postulation of benzoyl isocyanate (VIII) as an intermediate in the nitromethane reaction.

Step 5 also represents a known reaction of acyl isocyanates, having been demonstrated by Scholl,[13] who converted acetyl isocyanate to N,N'-diacetylurea by the addition of acetamide.

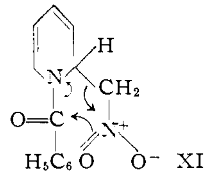
The source of the water needed for step 4 has not been determined precisely. Part of it might have been present in the pyridine added to the reaction mixture, for it has been found[3c] that even carefully purified pyridine contains about 0.01 mole of water per liter of pyridine. Water from this source, however, would account for only 4–10% of the N,N'-dibenzoylurea (III) actually obtained. Until further evidence becomes available, it can be assumed that most of the water needed in step 4 arose from side reactions.

Examination of the gross mechanism of the reaction, as represented by equations 1–5, suggested that the addition of benzamide to the original reaction mixture might increase the yield of N,N'-dibenzoylurea (III). Actually the addition of benzamide to the reaction mixture decreased the yield of III, and dibenzamide turned out to be the major product of the reaction. It is known[3e,17] that benzoyl chloride reacts with benzamide in excess pyridine to give dibenzamide in nearly theoretical yield. Although no dibenzamide was isolated in the nitromethane reaction, this fact does not invalidate the proposed mechanism. According to the mechanism, no benzamide is formed until after benzoyl isocyanate (VIII) has first been formed. Provided that VIII reacts with benzamide to give III much faster than benzoyl chloride reacts with benzamide to give dibenzamide, no appreciable amount of dibenzamide would be obtained in the nitromethane reaction.

Although the results of the reaction of nitromethane with benzoyl chloride, catalyzed by pyridine, do not require the postulation of the formation of an intermediate addition product, XII, it is our opinion that such a product is a transient species in the reaction. In conformity with the previously suggested mechanism[4a] of O-acylation of β-ketoesters in pyridine solution, it can be proposed that XII affords VI *via* the quasi six-membered ring transition XIII. Our basis for this opinion is that pyridine seems to be a unique tertiary amine for the catalysis of the reaction of benzoyl chloride with nitromethane to give III, just as pyridine seems to be a unique tertiary amine for the catalysis of the reactions of acid chlorides with β-ketoesters to give the O-acyl derivatives.[3c,4a] We have found, for example, that the use of quinoline with benzoyl chloride and nitromethane gives no N,N'-dibenzoylurea (III), nor any of the other reported by-products, but instead affords a complex red crystalline substance of formula $C_{27}H_{19}N_3O$. It is highly probable, on the basis of the formula given, that this represents an addition product containing two quinoline nuclei. We will reserve further discussion of this reaction for a future paper.[18] Also, the use of dimethylaniline as the solvent gives, even after five weeks at room temperature, only a trace of III. Of course, this result indicates that III can be formed from benzoyl chloride and nitromethane in the presence of a tertiary amine by a mechanism other than one involving XII as an intermediate. This does not, however, eliminate the possibility that the use of pyridine provides a much more favorable reaction path which does involve XII as an intermediate and XIII as a transition species.



XII



XIII

On the basis of the mechanism proposed for the formation of III from benzoyl chloride and nitromethane, it is clear that no other nitroalkane would be expected to give the same type of reaction. Specifically, a nitroalkane such as phenylnitromethane might very well undergo reactions analogous to those shown in equations 1 and 2, but the product of step 2, benzonitrile oxide (XIV),[19] would prob-

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[14] (a) A. F. Holleman, *Ber.*, **23**, 2998 (1890); (b) A. F. Holleman, *Rec. trav. chim.*, **10**, 65 (1891).

[15] H. Wieland and A. Hochtlen, *Ann.*, **505**, 237 (1933).

[16] O. C. Billeter, *Ber.*, **36**, 3218 (1903).

[17] A. W. Titherley, *J. Chem. Soc.*, **85**, 1673 (1904).

[18] On superficial examination one might assume that quinoline, benzoyl chloride and nitromethane would afford VI and all the subsequent products by way of an intermediate analogous to XII and a transition state analgous to XIII, in much the same way as the pyridine reaction mixture. Yet our experiences, only part of them published,[4b] have led to the conclusion that the differences between the systems benzoyl chloride–pyridine and benzoyl chloride–quinoline are far more numerous than the similarities.

[19] Triphenylacetonitrile oxide, $(C_6H_5)_3C—C\equiv N^+—O^-$, has been prepared and characterized by Wieland and Rosenfeld.[12f]

ably not react with benzoyl chloride to give an isocyanate. In the actual reaction of phenylnitromethane with benzoyl chloride and pyridine there was obtained dibenzhydroxamic acid (XI) as the main isolable organic product. Possibly this arose from XIV by the addition of water and subsequent benzoylation.

$$C_6H_5-C\equiv\overset{+}{N}-\overset{-}{O}$$

XIV

Experimental[20]

Reaction of Pyridine, Benzoyl Chloride and Nitromethane.—In a 500 ml., 3-necked, round-bottomed flask equipped with a mercury sealed stirrer and a Drierite tube connected to a gas-collecting bottle over water, was placed 39.3 g. (0.497 mole) of dry pyridine freshly distilled from anhydrous barium oxide and 46.4 g. (0.330 mole) of freshly distilled benzoyl chloride. The red solution was cooled in an ice-bath with stirring and 13.2 g. (0.216 mole) of nitromethane[21] was added in one portion. The reaction mixture, deep red after 10 minutes, was allowed to stand at room temperature with occasional stirring. After 14 hours a slow, irregular evolution of carbon dioxide began, evidenced by the precipitation of barium carbonate from a dilute barium hydroxide solution. The gas evolution continued for 5.5 days, during which time approximately 900 cc. of gas was collected. Slightly before (after about an hour) and during this period precipitation of a nearly colorless material was noted.

The dark, semi-solid reaction mixture was hydrolyzed with an excess of 10% sodium bicarbonate solution after six days, and the alkaline mixture was filtered. A dark, oily material was collected which, after successive washings with cold ether, water and then cold ether again, afforded 7.7 g. of a tan crystalline material. Additional solid was isolated upon concentration of the ether wash solution. A dark oil, 3.3 g., which separated from the alkaline filtrate on standing, was cooled in an ice-bath and treated with an acetone–ether solution, whereupon more of the tan solid was isolated. Altogether 8.6 g. of tan crystalline material was obtained, m.p. 151–157° dec. This solid material was dissolved in acetone, and the acetone solution was allowed to concentrate in an open flask at room temperature. Nearly colorless, diamond-shaped plates, 1.00 g., m.p. 165.0–166.6°, gradually formed as the solution became more concentrated. Three crystallizations from anhydrous acetone afforded colorless needles, m.p. 159.1–159.9° dec. This material has tentatively been assigned the structure 2,6-diphenyl-4-keto-1,3,5-oxadiazine (V).

Anal. Calcd. for $C_{15}H_{10}N_2O_2$: C, 71.99; H, 4.03; N, 11.20. Found: C, 71.87; H, 4.10; N, 10.89.

The compound was found to be identical with the diamond-shaped crystalline material of the same m.p. obtained from the reaction of pyridine, benzoyl chloride, water and benzoyl isocyanate (see below), as evidenced by a mixed m.p. test and the identity of the infrared spectra (in chloroform solution). A mixed m.p. with authentic dibenzhydroxamic acid (XI) of m.p. 160.5–161.4° showed a large depression.

Further concentration of the original acetone mother liquor afforded 5.8 g. of N,N′-dibenzoylurea (III), nearly colorless needles, m.p. 207–209° dec. Three crystallizations from acetone gave colorless, shining needles, m.p. 216.4–216.8° dec. A mixed m.p. test with authentic N,N′-dibenzoylurea (see below) showed no depression. The infrared spectrum of the product (in chloroform solution) was identical with that of authentic N,N′-dibenzoylurea.

The sodium bicarbonate solution previously decanted from the dark oil was steam distilled. A trace of dark, resinous material was filtered from the distillation residue. The filtrate was cooled to 0° and extracted with successive portions of ether, chloroform and again ether. No organic material was recovered from these extracts (see below for the results of the second and third runs, however). The sodium bicarbonate solution was acidified with hydrochloric acid, whereupon 27.2 g. (67.5%) of benzoic acid was obtained.

From the steam distillate, possessing the characteristic pyridine odor, was isolated, after cooling and standing overnight, a small quantity of 3,5-diphenyl-1,2,4-oxadiazole (IV). The cold portion of the condenser contained more of this material. Altogether 0.04 g. of IV was isolated, m.p. 108.5–109.0°. Crystallization from aqueous ethanol did not change the m.p. A mixed m.p. with an authentic sample of 3,5-diphenyl-1,2,4-oxadiazole (see below) showed no depression. The infrared spectrum of the product (in chloroform solution) was identical with that of the authentic material.

The filtrate of the steam distillate (pyridine odor) was acidified with hydrochloric acid, saturated with sodium chloride and extracted several times with ether and then chloroform. The extracts were combined, dried over anhydrous magnesium sulfate and distilled on the steam-bath through a short Vigreux column. In the distillation flask remained a small amount of liquid possessing a characteristic aromatic odor. The infrared spectrum of this material was very nearly identical with that of a mixture containing 67% of benzonitrile and 33% of nitromethane.

The aqueous-acid layer, saturated with sodium chloride, was made alkaline with sodium hydroxide solution and extracted with ether in a continuous extraction apparatus. From the ether extract there was recovered 36.9 g. of pyridine. An aliquot of this material, reacting with an excess of ethanolic picric acid, afforded pyridine picrate, m.p. 165.0–166.0°, in 94.4% yield. Thus not less than 88.7% of the original pyridine was recovered.

From a second run, in which 34.2 g. (0.432 mole) of pyridine, 30.3 g. (0.216 mole) of benzoyl chloride and 13.2 g. (0.216 mole) of nitromethane were allowed to react at room temperature for six days, but without stirring, there was isolated 5.0 g. of N,N′-dibenzoylurea (III), 0.01 g. of 2,6-diphenyl-4-keto-1,3,5-oxadiazine (V), 0.05 g. of 3,5-diphenyl-1,2,4-oxadiazole (IV), a trace amount of benzonitrile and 16.4 g. (62.2%) of benzoic acid. In addition, from the ether and chloroform extracts of the alkaline steam distillation residue, there was isolated 0.70 g. of benzamide, m.p. 129.0–130.0°, also in admixture with an authentic sample of benzamide.

From a third run, in which 39.4 g. (0.498 mole) of pyridine, 30.3 g. (0.216 mole) of benzoyl chloride and 12.5 g. (0.205 mole) of nitromethane were allowed to react for only five hours at room temperature, with stirring, there was isolated 0.40 g. of N,N′-dibenzoylurea (III), 0.30 g. of benzamide and 25.5 g. (97%) of benzoic acid.

In a fourth run, a mixture containing 0.20 mole of benzoyl chloride, 0.20 mole of nitromethane and 0.03 mole of pyridine was set aside. Even after a month at room temperature no precipitate had formed and no carbon dioxide had been evolved.

Reaction of Dimethylaniline, Benzoyl Chloride and Nitromethane.—To a solution of 46.4 g. (0.383 mole) of freshly distilled dimethylaniline and 28.1 g. (0.202 mole) of freshly distilled benzoyl chloride was added, with stirring, 12.3 g. (0.200 mole) of nitromethane.[21] After five weeks at room temperature about 100 cc. of carbon dioxide had been evolved. The blue reaction mixture which contained no precipitate was hydrolyzed with an excess of 10% sodium bicarbonate solution. To the separated amine layer was added 150 cc. of ether, and the ether solution was extracted with several portions of 6 *M* hydrochloric acid. A small amount of colorless solid precipitated from the ether solution, and more of this solid was obtained upon concentration of the ether solution. Altogether, 0.14 g. of crude N,N′-dibenzoylurea (III) was isolated, m.p. 191–193° dec. Crystallization from acetone gave colorless needles, m.p. 215.5–216.5°, also in admixture with an authentic sample of N,N′-dibenzoylurea.

On acidification of the sodium bicarbonate solution there was obtained 23.0 g. (94%) of benzoic acid.

N,N′-Dibenzoylurea (III).—A 61% yield of III was obtained from the reaction of benzoyl chloride and guanidine carbonate according to the procedure of Walther and Wlodkowski.[22] The substance melted at 216.0–217.0° (reported 210°,[22] 218°[23]).

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[20] All m.p.'s are corrected.

[21] Nitromethane (Eastman Kodak Co.) was dried over phosphorus pentoxide and fractionated through a 30-cm. packed column. The fraction, b.p. 100.5–101.0° (750 mm.), and $n^{29}\mathrm{D}$ 1.3789, was collected.

[22] R. Walther and S. Wlodkowski, *J. prakt. Chem.*, [2] **59**, 266 (1899).

[23] H. Biltz, *Ann.*, **391**, 169 (1912).

3,5-Diphenyl-1,2,4-oxadiazole (IV).—Very small yields of IV were obtained by reaction of benzamidoxime[24] with benzoyl chloride according to the procedure of Tiemann and Kruger,[25] and by reaction of benzamidoxime with chlorine by the method of Krummel.[26] The material possessed a m.p. of 108.5–109.1° (reported 108°,[25] 110°[27]).

Attempted Cyclization of N,N′-Dibenzoylurea (III) to Form 2,6-Diphenyl-4-keto-1,3,5-oxadiazine (V). (a) With Pyridine and Benzoyl Chloride.—Attempted reaction of 1.00 g. of III with 23 cc. of freshly distilled benzoyl chloride and 32 cc. of anhydrous pyridine for a period of nine days at room temperature led only to the nearly quantitative recovery of III.

(b) With Phosphorus Pentoxide.—A solution of 2.00 g. of III in 110 cc. of anhydrous benzene was mixed with 3.5 g. of phosphorus pentoxide and refluxed for five hours. On working up the reaction mixture, III was recovered in 97% yield.

Ultraviolet and Infrared Spectral Data of the Compound of Formula $C_{15}H_{10}N_2O_2$ Obtained from the Nitromethane Reaction.—The compound of m.p. 159.1–159.9°, tentatively assigned the structure V, exhibited two maxima in the C=O and C=N region of the infrared spectrum, at 1718 and 1642 cm.$^{-1}$, in chloroform solution. There was no absorption corresponding to an OH or NH group. In the ultraviolet region the compound exhibited a sloping shoulder in the 2600–2800 Å. region ($\log \epsilon$ 3.3 to 3.5) in ethanol solution. The compound absorbed at longer wave lengths than III over the entire ultraviolet region, but the general shapes of the two curves were similar.

Formhydroxamic Acid (X).—This was prepared from hydroxylamine and ethyl formate by the method of Jones,[8a] m.p. 81.5–82.0° (reported[8a] 81–82°).

Reaction of Pyridine, Benzoyl Chloride and Formhydroxamic Acid (X). (a) In the Presence of Benzamide and Water.—To an ice-cold solution of 31.6 g. (0.40 mole) of pyridine and 28.1 g. (0.20 mole) of benzoyl chloride was slowly added with stirring a mixture containing 6.10 g. (0.10 mole) of formhydroxamic acid (X), 6.10 g. (0.05 mole) of benzamide, 1.00 g. of water and 20 cc. (0.248 mole) of pyridine. A vigorous reaction ensued, and carbon dioxide was evolved.

After eight days at room temperature with intermittent stirring, the semisolid, light brown reaction mixture was hydrolyzed with a slight excess of 10% sodium bicarbonate solution. The alkaline mixture was cooled to 0° and filtered. A tan solid was collected, washed several times with water and finally washed with cold ether. There remained 13.3 g. (55%) of crude dibenzhydroxamic acid (XI), m.p. 146.8–148.9° dec. Two crystallizations from aqueous ethanol gave XI as colorless needles, m.p. 159.1–160.0°, alone and on admixture with an authentic sample of dibenzhydroxamic acid (XI).

The alkaline filtrate, combined with the aqueous and ether wash solutions, was cooled to 5°, saturated with sodium chloride and extracted with ether and chloroform. The extracts were combined, washed with cold 6 *M* hydrochloric acid, then water. Distillation of the ether–chloroform solution, dried over anhydrous magnesium sulfate, left a semisolid, pale yellow mixture. This was washed with small portions of 10% sodium bicarbonate solution and hot water, whereupon 1.2 g. of colorless solid, m.p. 102–114°, was obtained. Crystallization from 95% ethanol gave 0.60 g. (2.5%) of dibenzhydroxamic acid (XI).

The hot water washes, after cooling and standing for 24 hours, afforded 0.20 g. of colorless needles, m.p. 136.2–138.2°. Two recrystallizations from water provided 0.05 g. of unidentified material, colorless needles, m.p. 145.5–146.5°.

Anal. Found: C, 74.96, 74.65; H, 5.12, 5.12; N, 6.82, 7.00.

(b) Addition of Benzamide and Water After Twenty-Two Hours.—In this run dibenzhydroxamic acid (XI) was isolated in only 22% yield.

Dibenzhydroxamic Acid (XI).—This was prepared from hydroxylamine and benzoyl chloride by the method of Lossen,[28] m.p. 160.5-161.4° (reported 165°,[29] 161°,[30] and 159°[31]).

Reaction of Pyridine, Benzoyl Chloride and Phenylnitromethane.—An ice-cold solution of 31.6 g. (0.40 mole) of anhydrous pyridine and 28.1 g. (0.20 mole) of freshly distilled benzoyl chloride was stirred and then treated with 27.4 g. (0.20 mole) of phenylnitromethane, which was prepared[32] and distilled just prior to its use. From the red-violet solution an orange material precipitated immediately, and just as quickly redissolved. About one minute later a yellow solid separated from the solution. The reaction mixture was allowed to stand at room temperature for a period of 12 days, with occasional stirring. About 100 cc. of gas was evolved during this period, the evolution beginning about 60 hours after the addition of the phenylnitromethane. The red-black reaction mixture was hydrolyzed with an excess of 10% sodium bicarbonate solution, and a brown solid was removed by filtration. This was washed with water, then cold ether, leaving 8.9 g. (19%) of crude dibenzhydroxamic acid (XI), m.p. 146.5–148.0°. Two crystallizations from 95% ethanol gave 6.1 g. (13%) of XI, colorless needles, m.p. 159.2–159.7°, also in admixture with an authentic sample of dibenzhydroxamic acid. Additional XI, 1.4 g. (3%), was isolated from the ether wash solution on concentration.

The alkaline filtrate and wash solutions were combined and steam distilled. The distillate was acidified with hydrochloric acid and extracted with ether. Distillation of the ether solution, dried over anhydrous magnesium sulfate, left 1.1 g. of crude benzaldehyde. Treatment with an excess of 2,4-dinitrophenylhydrazine provided 2.7 g. of benzaldehyde 2,4-dinitrophenylhydrazone, m.p. 236.5–238.5° dec., also in admixture with an authentic sample of the compound.

The steam distillate was made alkaline and extracted with ether in a continuous extraction apparatus. Pyridine (93%) was recovered from the ether solution.

The alkaline steam distillation residue was extracted with ether and chloroform (thereby removing 4.0 g. of red-black liquid), then made acid with hydrochloric acid. Filtration and ether extraction provided 14.0 g. (57%) of benzoic acid.

Reaction of Pyridine, Benzoyl Chloride and ω-Nitroacetophenone (IX).—A solution of 31.6 g. (0.40 mole) of anhydrous pyridine and 28.1 g. (0.20 mole) of freshly distilled benzoyl chloride was cooled to 0°. To the cold, red solution was added slowly with stirring 10.0 g. (0.0605 mole) of ω-nitroacetophenone (IX), prepared by the method of Long and Troutman.[33] Heat was evolved on addition of the nitro compound, and after 45 minutes the reaction mixture became light brown.

The reaction mixture was allowed to stand at room temperature for nine days, and then the semi-solid mass was hydrolyzed with an excess of 10% sodium bicarbonate solution. The dark solution was extracted with ether, and the ether extract was washed with 6 *M* hydrochloric acid, then water. There was obtained 2.5 g. of crude dibenzhydroxamic acid (XI) upon concentration of the ether solution. Treatment with Norit in acetone followed by three crystallizations from 95% ethanol provided 0.05 g. of pure XI.

Acidification of the alkaline solution afforded 18.5 g. (76%) of benzoic acid.

The Benzoyl Isocyanate (VIII).—Benzoyl chloride reacted with silver cyanate[34] by the procedure of Hill and Degnan.[35] VIII was obtained in 49% yield, b.p. 72.5–73.0° (6 mm.); reported b.p. 88° (20 mm.),[35] 88° (10 mm.),[16] 202.5–204° (724 mm.).[16]

Reaction of Pyridine, Benzoyl Chloride and Benzoyl Isocyanate (VIII). (a) In the Presence of Water.—To an ice-cold, stirred solution of 31.6 g. (0.40 mole) of anhydrous pyridine and 28.2 g. (0.20 mole) of freshly distilled benzoyl chloride was added 14.7 g. (0.10 mole) of benzoyl isocyanate (VIII), which was prepared and distilled just before its use.

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[24] F. Tiemann, *Ber.*, **17**, 126 (1884).

[25] F. Tiemann and P. Kruger, *ibid.*, **17**, 1685 (1884).

[26] H. Krummel, *ibid.*, **28**, 2227 (1895).

[27] H. Wieland, *ibid.*, **42**, 803 (1909).

[28] W. Lossen, *Ann.*, **161**, 347 (1872).

[29] R. Marquis, *Compt. rend.*, **140**, 1398 (1905).

[30] A. Werner, *Ber.*, **25**, 27 (1892).

[31] W. Lossen, *Ann.*, **281**, 221 (1894).

[32] A. P. Black and F. H. Babers, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 512.

[33] L. M. Long and H. D. Troutman, THIS JOURNAL, **71**, 2469 (1949).

[34] L. Birkenbach and M. Linhard, *Ber.*, **62**, 2261 (1929).

[35] A. J. Hill and W. M. Degnan, THIS JOURNAL, **62**, 1595 (1940).

After ten minutes 1.00 cc. (0.05 mole) of cold water was added dropwise to the stirred solution, whereupon a vigorous, exothermic reaction occurred with evolution of carbon dioxide. The reaction mixture was allowed to stand at room temperature for 36 hours with occasional stirring. Then the mixture was hydrolyzed with 200 cc. of 10% sodium bicarbonate solution, and an insoluble oily material was filtered off, then washed with cold ether, water and again cold ether. There remained 11.4 g. of pink, crystalline material, m.p. 156.5–158.5° dec. Fractional crystallization from acetone gave, as the first crops, a total of 2.7 g. (22%) of the compound which has tentatively been assigned the structure 2,6-diphenyl-4-keto-1,3,5-oxadiazine (V), diamond-shaped plates, m.p. 158.2–158.8°.

The acetone mother liquor upon concentration to progressively smaller volumes afforded a total of 7.3 g. (54%) of N,N′-dibenzoylurea (III), m.p. 214.0–215.0° dec., also in admixture with authentic III.

The dark, alkaline filtrate was combined with the wash solutions and steam distilled. The steam distillate was acidified with hydrochloric acid and extracted with ether. Upon distillation of the ether solution, dried over anhydrous magnesium sulfate, there remained 2 cc. of liquid having the odor of benzonitrile.

An additional 0.30 g. (2%) of III was obtained by filtration of the alkaline residue from the steam distillation. The alkaline filtrate was extracted with ether and chloroform, then made acid with hydrochloric acid. There was obtained 21.3 g. (87%) of benzoic acid on filtration and by ether extraction.

(b) **Addition of Water After 36 Hours.**—Another reaction mixture identical to the one above, but without the immediate addition of water, turned dark and gave off 150 cc. of carbon dioxide during the course of 36 hours at room temperature. One cc. of water was then added dropwise to the stirred reaction mixture, whereupon a vigorous reaction occurred with evolution of carbon dioxide. From the dark mixture, treated with sodium bicarbonate solution as above, was filtered 9.0 g. of violet-black solid. The substance could not be purified by attempted crystallization from acetone.

After steam distillation of the alkaline filtrate there was obtained 1.1 g. of brown gummy material from the distillation residue. Several recrystallizations from acetone finally gave a trace of N,N′-dibenzoylurea (III).

From the alkaline filtrate, after acidification, there was obtained 25.3 g. (103%, based on the original benzoyl chloride) of benzoic acid.

LAWRENCE, KANSAS

[CONTRIBUTION FROM THE CENTRAL RESEARCH LABORATORIES, MONSANTO CHEMICAL COMPANY]

Aralkyl and Carbanilinoalkyl Thiocyanates[1]

BY ARTHUR H. SCHLESINGER AND DAVID T. MOWRY

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The synthesis of various aralkyl and carbanilinoalkyl thiocyanates, R–CH_2SCN, is described. Structures wherein R = phenyl, monosubstituted phenyl, benzyl, phenylethyl, phenacyl, phenoxymethyl and 2,4-dichlorophenoxymethyl are of equal phytotoxicity in seed germination tests. When R = carbanilinomethyl and substituted carbanilinomethyl the phytotoxicity is comparable to that of the corresponding halide.

Reports in the literature concerning the insecticidal activity of various thiocyanates are numerous.[2] However, investigation of the phytotoxicity of various members of this class appears to have been neglected except for the work of Jones[3] concerning α-naphthylmethyl thiocyanate. Therefore, it was of interest to prepare and study various thiocyanates, in order to determine the relation of structure to phytotoxicity.

The thiocyanates I of Table I were prepared by the reaction of the appropriate bromide or chloride with an equivalent or slight excess of potassium thiocyanate in hot ethanol or acetone. Yields varied from 29–96% but were mostly of the order of 80%. The reaction was allowed to progress

$$\underset{\text{I}}{R_1\text{—}CH_2\text{—}X + KSCN \longrightarrow R_1\text{—}CH_2\text{—}SCN + KX}$$

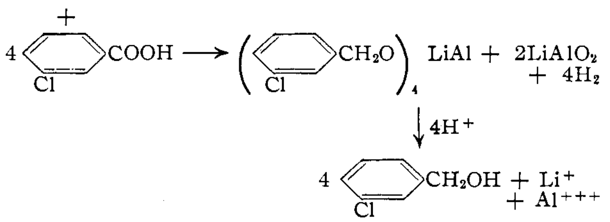
until the near-theoretical amount of potassium halide had been deposited. Intermediate carbanilates were prepared in 38–87.5% yields either by method A, which consisted of the reaction of a halohydrin with the appropriate aromatic isocyanate, or method B, the reaction of 2-chloroethyl chloroformate with the appropriate aromatic amine and pyridine in benzene.

$$\text{(A)}\quad X\text{—}R\text{—}OH + ArNCO \longrightarrow ArNHCO_2\text{—}R\text{—}X$$

$$\text{(B)}\quad ClCO_2CH_2CH_2Cl + ArNH_2 + C_5H_5N \longrightarrow ArNHCO_2CH_2CH_2Cl + C_5H_5N\cdot HCl$$

Table II lists the yields and physical properties of the haloalkyl carbanilates that were prepared as intermediates.

Incidental to the preparation of 3-chlorobenzyl thiocyanate, 3-chlorobenzyl alcohol was prepared in 91% yield by reduction of 3-chlorobenzoic acid with lithium aluminum hydride. The alcohol was converted in 60% yield by thionyl chloride to 3-chlorobenzyl chloride along with a small amount (17%) of 3-chlorobenzyl ether.



Examination of the thiocyanates and other related materials for phytotoxicity was done by a slight modification of the method of Thompson, Swanson and Norman.[4] Cucumber and wheat seeds (representing dicotyledenous and monocotyledenous species) were germinated in petri dishes

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[1] Presented before the 124th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 7, 1953.

[2] R. Metcalf, Chem. Biol. Coördination Center, National Research Council, Washington, D. C., Review No. 1 (1948), reviews the insecticidal action of thiocyanates and presents the leading references. See also ref. 3.

[3] F. Jones, U. S. Patent 2,394,915 (1946).

[4] H. Thompson, C. Swanson and A. Norman, *Bot. Gaz.*, **107**, 476 (1946).