Reactions of Lead Tetra-acetate. Part III.[1] Formation of Pyrimidine-iones and Related Compounds from Dicarboxylic Acid Amides

By A. L. J. Beckwith* † and R. J. Hickman, Organic Chemistry Department, University of Adelaide, South Australia

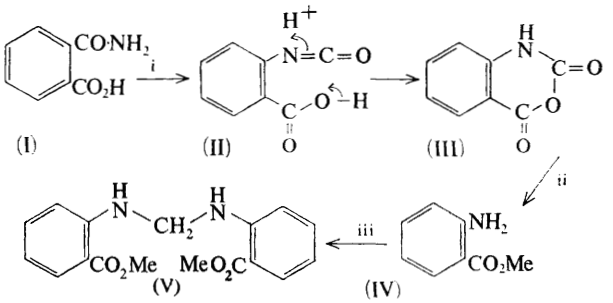
Treatment of phthalamide (X) with lead tetra-acetate in dimethylformamide affords 1,2,3,4-tetrahydro-2,4-dioxoquinazoline (XI). Pyridine-2,3- and -3,4-dicarboxamide, succinamide, 2-phenylsuccinamide, and suitable *N*-monoalkyl diamides undergo similar cyclization reactions. Phthalamic acid (I) and 2-carbamylnicotinic acid (VI) yield appropriate oxazine derivatives (III) and (VII), when heated with lead tetra-acetate, but the method fails with 2-phenylsuccinamic acid (VIII). The mechanism of these transformations appears to involve initial formation of isocyanates.

PRIMARY amides react readily with lead tetra-acetate in suitable media and, in the presence of appropriate co-reactants, yield acylamines,[2] urethanes [1,3], and other compounds [3] derived from the isocyanates initially produced. The reaction is highly selective; it has been successfully applied to substrates containing such reactive functions as aromatic, benzylic, olefinic, and ester groups,[1,2] and it can be conducted in the presence of alcohols and amines.[1,3] Thus, it represents a useful simple alternative to the Hofmann reaction both for synthesis and for degradation.

The present study is concerned with application of the amide–lead tetra-acetate reaction to substrates containing a carboxy or second carbamyl function in close juxtaposition to the reactive centre, and so disposed as to allow intramolecular reaction with the initially formed isocyanate group to give six-membered heterocyclic systems. Examples of such cyclizations have been encountered in studies of the Hofmann [4,5], Curtius [4,6], and Lossen [4,7] transformations and include reactions of value for the synthesis of biologically significant heterocyclic compounds.[8]

Exploratory work was conducted with phthalamic acid (I) since the expected product, isatoic anhydride (III), is unusually stable for a derivative of 2,5-dioxo-1,3-oxazine, and is readily characterised. When the amido-acid (I) was treated with lead tetra-acetate in boiling benzene a slow reaction ensued and the expected anhydride (III) was obtained in 44% yield. In the light of the previous evidence supporting the intermediacy of isocyanates in the amide–lead tetra-acetate reaction,[1-3] and the analogy with the Curtius transformation applied to a phthalic acid derivative,[9] there can be little doubt that isatoic anhydride is formed *via* an isocyanate (II) as shown. The reaction was conducted in a variety of solvents without substantial improvement in yield; however, it was observed that it proceeded very much more rapidly in dimethylformamide and this proved to be the best solvent for most subsequent reactions.

The use of methanol as solvent for reaction of lead tetra-acetate with phthalamic acid was investigated. At room temperature isatoic anhydride was obtained, but when the experiment was conducted in boiling methanol the only product isolated was dimethyl *NN'*-methylenedianthranilate (V).[10] The formation of this compound may involve condensation of methyl anthranilate (IV),



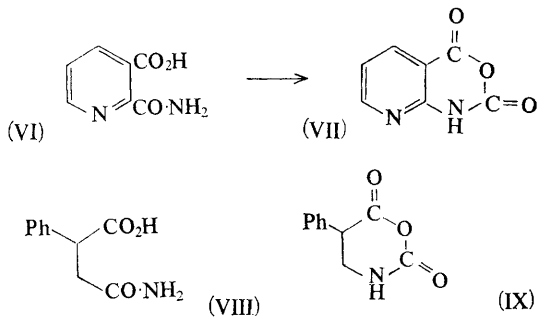
Reagents: i, $Pb(OAc)_4$; ii, MeOH; iii, H·CHO.

formed by attack of methanol on the anhydride (III), with formaldehyde arising from lead tetra-acetate oxidation of the solvent. However, less obvious routes cannot be discounted since isatoic anhydride and methanolic formaldehyde, when heated, failed to yield the condensation product (V). Further work is needed to discover whether lead salts are involved in the condensation or hydrolysis mechanisms.

Treatment of 2-carbamylnicotinic acid (VI) with lead tetra-acetate afforded, in good yield, the expected cyclic anhydride (VII) which was characterized by hydrolysis to 2-aminonicotinic acid. Reaction of 2-phenylsuccinamic acid (VIII) with lead tetra-acetate in dimethylformamide gave an amorphous yellow solid which underwent slow decomposition. The expected product (IX) is a 2,6-dioxotetrahydro-1,3-oxazine which, like the lower homologous Leuchs anhydrides,[11] readily form polyamides by intermolecular elimination of carbon dioxide.[12]

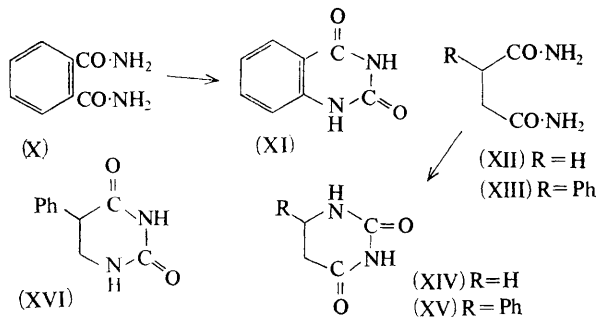
† *Present address:* Department of Chemistry, University of York.

[1] Part II, B. Acott, A. L. J. Beckwith, and A. Hassanali, *Austral. J. Chem.*, 1968, **21**, 197.
[2] B. Acott, A. L. J. Beckwith, and A. Hassanali, *Austral. J. Chem.*, 1968, **21**, 185.
[3] B. Acott, A. L. J. Beckwith, A. Hassanali, and J. W. Redmond, *Tetrahedron Letters*, 1965, 4039; H. E. Baumgarten and A. Staklis, *J. Amer. Chem. Soc.*, 1965, **87**, 1141.
[4] P. A. S. Smith in 'Molecuar Rearrangements,' ed. P. de Mayo, Interscience, New York, 1963, Part I, p. 457.
[5] E. S. Wallis and J. F. Lane, *Org. Reactions*, 1946, **3**, 267.
[6] P. A. S. Smith, *Org. Reactions*, 1946, **3**, 337.
[7] H. L. Yale, *Chem. Rev.*, 1943, **33**, 209; F. Mathis, *Bull. Soc. chim. France*, 1953, D9.
[8] G. A. Howard, A. C. McLean, G. T. Newbold, F. S. Spring, and A. R. Todd, *J. Chem. Soc.*, 1949, 232.
[9] T. Curtius and A. Semper, *Ber.*, 1913, **46**, 1162.
[10] P. Grammaticakis, *Bull. Soc. chim. France*, 1950, 158.
[11] H. D. Springall, 'The Structural Chemistry of Proteins,' Academic Press, New York, 1954, p. 51.
[12] L. Birkofer and R. Modic, *Annalen*, 1957, **604**, 56; S. P. A. Lepetit, Belg.P. 622,901/1963 (*Chem. Abs.*, 1963, **59**, 7534); H. E. Winberg, U.S.P. 2,600,596/1952 (*Chem. Abs.*, 1953, **47**, 7536).

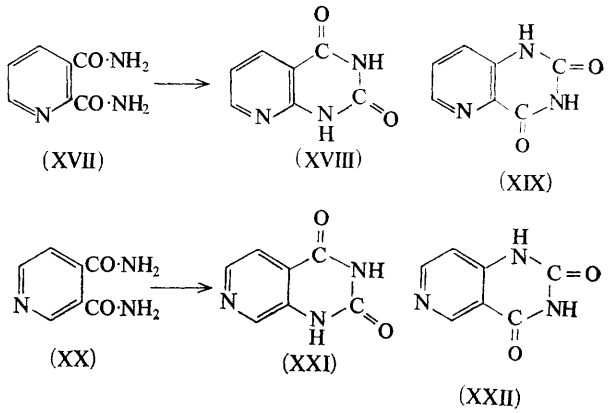


The reaction of lead tetra-acetate with suitably constituted diamides generally proceeded rapidly and afforded good yields (80—100%) of cyclized products. Phthalamide (X) gave 1,2,3,4-tetrahydro-2,4-dioxoquinazoline (XI). The same compound has been obtained by the Hofmann [13] reaction where it undoubtedly arises by intramolecular addition of one amide group to the isocyanate formed by rearrangement of the other, a reaction which proceeds much more readily than its intermolecular analogue.[14] Numerous examples of the formation of derivatives of 1,3-dioxopyrimidine by the Hofmann reaction of 1,2-amides have been recorded.[15-23]

As expected, treatment of succinamide (XII) and of 2-phenylsuccinamide (XIII) with lead tetra-acetate afforded, respectively, dihydrouracil (XIV) and its 6-phenyl derivative (XV), the structure of which was confirmed by its hydrolysis to cinnamic acid. The other possible isomeric product (XVI) was not detected in the mixture from the reaction of phenylsuccinamide with lead tetra-acetate. Similar specificity has been noted in the Hofmann reaction with phenylsuccinamide.[22]



Reaction of pyridine-2,3-dicarboxamide (XVII) and of pyridine-3,4-dicarboxamide (XX) gave the pyridopyrimidine derivatives (XVIII) and (XXI) respectively; the possible isomeric products (XIX) and (XXII) were not detected. A similar specificity has been recorded for Hofmann reaction of pyridine dicarboxamides,[15,16,19,20,23] but in some cases assignment of product structure rests on analogy.[15,20] In our experiments the nature of the products was unambiguously defined by degradation to simple pyridine derivatives.

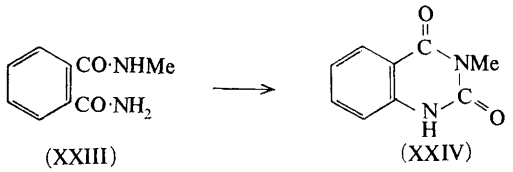


The observed specificity of the reactions of phenylsuccinamide (XIII), pyridine-2,3-dicarboxamide (XVII), and pyridine-3,4-dicarboxamide (XX) with lead tetra-acetate and with hypobromite cannot be readily rationalised on simple electronic grounds, since the initial reaction appears to proceed at the least-basic amide function * in phenylsuccinamide (XIII) and pyridine-2,3-dicarboxamide (XVII) and at the more basic in pyridine-3,4-dicarboxamide (XX). However, other factors, such as initial complex formation between the attacking reagent and the aromatic ring or heterocyclic nitrogen may affect the course of the reaction; it may, for example, be relevant that pyridine forms a stable complex with lead tetra-acetate.[24]

Lead tetra-acetate has been shown to be unreactive towards secondary amides [2,25] and hence it was expected that substrates containing both primary and secondary amide functions would undergo smooth and selective reaction as the former. This proved to be the case; *N*-methylphthalamide (XXIII), *N*-methylsuccinamide (XXV), *N*-benzylsuccinamide (XXVI), and *N*-cyclohexylsuccinamide (XXVII) were each readily converted into the expected pyrimidine derivative; *viz.* 1,2,3,4-tetrahydro-3-methyl-2,4-oxoquinazoline (XXIV), 3-methyl-5,6-dihydrouracil (XXVIII), 3-benzyl-5,6-dihydrouracil (XXIX), and 3-cyclohexyl-5,6-dihydrouracil (XXX). Similar transformations have been effected by the Hofmann reaction but in smaller yield.[26]

* We have assumed that the relative basicities of the different amide functions are predictable on the basis of the normal electronic affects of the substituents. That this approach is not necessarily valid is shown by the observation that picolinic acid has the *least* acidic carboxy-function of the three pyridinecarboxylic acids (R. W. Green and H. K. Tong, *J. Amer. Chem. Soc.*, 1956, **78**, 4896).

[13] M. M. Hoogewerff and W. A. van Dorp, *Rec. Trav. chim.*, 1891, **10**, 4; 1896, **15**, 107.
[14] P. F. Wiley, *J. Amer. Chem. Soc.*, 1949, **71**, 1310.
[15] R. G. Jones, *J. Org. Chem.*, 1960, **25**, 956.
[16] S. Blumenfeld, *Monatsch.*, 1895, **16**, 702; S. Gabriel and J. Colman, *Ber.*, 1902, **25**, 2831.
[17] I. J. Rinkes, *Rec. Trav. chim.*, 1927, **46**, 268.
[18] A. Braun and J. Tcherniac, *Ber.*, 1907, **40**, 2709.
[19] S. Gabriel and A. Sorn, *Ber.*, 1907, **40**, 4850.
[20] M. J. Reider and R. C. Elderfield, *J. Org. Chem.*, 1942, **7**, 286.
[21] H. Weidel and E. Roithner, *Monatsch.*, 1896, **17**, 174; M. W. van Dam, *Rec. Trav. chim.*, 1896, **15**, 101; J. A. McRae and W. A. McGinnis, *Canad. J. Res.*, 1940, **18***B*, 90.
[22] J. A. McRae, A. W. Weston, and C. F. Hubbs, *Canad. J. Res.*, 1937, **15***B*, 434.
[23] A. C. McLean and F. S. Spring, *J. Chem. Soc.*, 1949, 2582; and earlier papers in this series.
[24] R. Partch and J. Monthony, *Tetrahedron Letters*, 1967, 4427.
[25] R. M. Moriarty, H. G. Walsh, and H. Gopal, *Tetrahedron Letters*, 1966, 4363.
[26] F. S. Spring and J. C. Woods, *J. Chem. Soc.*, 1945, 625.



(XXIII) (XXIV)

(XXV) R = Me
(XXVI) R = $PhCH_2$
(XXVII) R = cyclohexyl

(XXVIII) R = Me
(XXIX) R = $PhCH_2$
(XXX) R = cyclohexyl

In summary, it appears that the lead tetra-acetate–amide reaction applied to the formation of dioxopyrimidine derivatives proceeds in higher yield than the Hofmann reaction, is more selective, of wider application, and is technically simpler. Since many heterocyclic 1,2-dicarboxamides are relatively easily obtained the method may be useful for the synthesis of complex heterocyclic systems.

Preliminary experiments have indicated that the lead tetra-acetate–amide reaction is not suitable for the synthesis of dioxoimidazoline derivatives. No pure product could be isolated by treatment of malondiamide or its *N*-phenyl derivative with lead tetra-acetate.

EXPERIMENTAL

General methods.—I.r. spectra were determined with a Perkin-Elmer **337** or a Perkin-Elmer **237** instrument. ^1H N.m.r. spectra were measured in deuteriochloroform with tetramethylsilane as internal standard on a Varian DP 60 spectrometer operating at 60 Mc./sec. Mass spectra were determined with an Hitachi Perkin-Elmer RMU-6D single focus instrument.

Materials.—Lead tetra-acetate was a commercial specimen which was stored *in vacuo* over phosphorous pentoxide and potassium hydroxide pellets. Benzene was dried over sodium wire. Dimethylformamide was dried over calcium hydride and fractionally distilled. Methanol and ethanol were each treated with magnesium, and then heated under reflux, and distilled. Acetic acid was boiled under reflux with potassium permanganate, distilled, heated with acetic anhydride, and fractionated. Triethylamine was dried over potassium hydroxide, and distilled.

The following amides were each prepared by published procedures: phthalamic acid,[27] m.p. 147—148°; 2-phenylsuccinamic acid,[28] m.p. 145—146°; 2-carbamylnicotinic acid,[29] m.p. 174—176°; *N*-methylsuccinamide,[26] m.p. 160°; *N*-benzylsuccinamide,[26] m.p. 194—195° (lit.,[30] m.p. 189°) (Found: C, 63·8; H, 6·6; N, 13·35. Calc. for $C_{11}H_{14}N_2O_2$: C, 64·1; H, 6·8; N, 13·6%); *N*-cyclohexylsuccinamide,[26] m.p. 205° (lit.,[31] m.p. 190°) (Found: C, 61·0; H, 9·0; N, 13·7. Calc. for $C_{10}H_{18}N_2O_2$: C, 60·6; H, 9·15; N, 14·1%); *N*-methylphthalamide,[26] m.p. 181°; and *N*-phenylmalonamide,[32] m.p. 159—160°.

[27] E. Chapman and H. Stephen, *J. Chem. Soc.*, 1925, **127**, 1791.
[28] M. Naps and I. B. Johns, *J. Amer. Chem. Soc.*, 1940, **62**, 2450.
[29] F. G. Mann and J. A. Reid, *J. Chem. Soc.*, 1952, 2057.
[30] E. A. Werner, *J. Chem. Soc.*, 1889, **55**, 627.
[31] T. V. Sheremeteva, V. A. Gusinskaya, and V. V. Kudryavtsev, *Izvest. Akad. Nauk. S.S.S.R. Ser. Khim.*, 1963, 1821.

The following diamides were each obtained from the appropriate diacids *via* the imides (formed by pyrolysis of ammonium salts), which were stirred with concentrated aqueous ammonia for 24 hr.: pyridine-2,3-dicarboxamide, m.p. 205—206° (lit.,[23] m.p. 209°); pyridine-3,4-dicarboxamide, m.p. 177—179° (lit.,[16] m.p. 175—176°); 2-phenylsuccinamide, m.p. 209—211° (lit.,[22] m.p. 211°).

1,4-*Dihydro*-2,4-*dioxo*-2H-3,1-*benzoxazine* (III).—(*a*) Lead tetra-acetate (5·4 g.) was added in one portion to a boiling suspension of phthalamic acid (2·0 g.) in dry benzene (100 ml.), and the mixture was heated under reflux with stirring for 48 hr., then cooled and filtered. The residue was washed with water and crystallised from dioxan to yield the benzoxazine (III) (0·87 g., 44%), m.p. 243—245° (lit.,[33] m.p. 243°), $\nu_{max.}$ (Nujol) 3240, 1840, 1770, and 1730 cm.$^{-1}$; *m/e* 163 ($C_8H_5NO_3$). On treatment with an alkaline solution of β-naphthol, the benzoxazine (III) was converted into β-naphthyl anthranilate,[34] m.p. 118°.

(*b*) When the preceding experiment was conducted in dimethylformamide (20 ml.) at room temperature for 40 min., the yield of benzoxazine, isolated by pouring the reaction mixture into water (30 ml.), was 1·07 g. (54%) (from dioxan).

Reaction of Lead Tetra-acetate with Phthalamic Acid in Methanol.—Lead tetra-acetate (16 g.) was added in one portion to phthalamic acid (3·6 g.) in methanol (60 ml.) and the mixture was stirred at 25° for 1 hr.; it was then heated under reflux for 20 min. The solvent was evaporated under reduced pressure and the residual oil was treated with cold water and set aside when it slowly solidified. Repeated recrystallization of the crude product from hexane gave dimethyl *NN'*-methylenedianthranilate (1·7 g. 50%), m.p. 116—117° (lit.,[10] m.p. 118°) (Found: C, 65·05; H, 5·7; N, 8·8; O, 20·6. Calc. for $C_{17}H_{18}N_2O_4$: C, 64·95; H, 5·8; N, 8·9; O, 20·4%), $\nu_{max.}$ (CCl_4) 3350 and 1690 cm.$^{-1}$; τ (CCl_4) 6·27 (6H, s, 2 × CH_3), 5·27 (2H, t, *J* 6 c./sec., CH_2) 2·1—3·6 (8H, broad signals, aromatic H), 1·8 (2H, t, *J* 6 c./sec., 2 × N–H); *m/e* 314 ($C_{17}H_{18}N_2O_4$). After exchange with D_2O the compound showed no absorption at τ 1·8 and the triplet at 5·27 collapsed to a singlet. When treated with dilute acid the compound was rapidly hydrolysed to methyl anthranilate and formaldehyde, identified by formation of the 2,4-dinitrophenylhydrazone.

3,4-*Dihydro*-1,3-*dioxo*-1H-*pyrido*[2,3-d][1,3]*oxazine* (VII).—Lead tetra-acetate (5·5 g.) was added in one portion to a suspension of 2-carbamylnicotinic acid (2·0 g.) in dimethylformamide (20 ml.), and the mixture was stirred at 50—60° for 1 hr., then poured into water (20 ml.) and filtered. Crystallization of the residue gave the expected *pyridooxazine* (1·48 g., 75%), m.p. 217—219° (Found: C, 51·3; H, 2·7; N, 17·05. $C_7H_4N_2O_3$ requires C, 51·2; H, 2·5; N, 17·1%), $\nu_{max.}$ (Nujol) 3150, 3080, 1850, and 1770 cm.$^{-1}$; *m/e* 164 ($C_7H_4N_2O_3$).

A sample (0·50 g.) of the product was heated under reflux for 20 min. with 5% aqueous sodium hydroxide (5 ml.). The reaction mixture was then cooled, saturated with carbon dioxide, and the pH was adjusted to 5 by addition of dilute hydrochloric acid. 2-Aminonicotinic acid (0·2 mg., 63%), m.p. 307° (lit.,[35] m.p. 306—307°) was deposited.

[32] J. V. Backes, R. W. West, and M. A. Whitely, *J. Chem. Soc.*, 1921, **119**, 359.
[33] E. C. Wagner and F. Fegley, *Org. Synth.*, Coll. Vol. III, 1955, 488.
[34] R. P. Steiger and E. M. Miller, *J. Org. Chem.*, 1959, **24**, 1214.
[35] E. C. Taylor and A. J. Crovetti, *J. Org. Chem.*, 1954, **19**, 1633.

Reaction of Lead Tetra-acetate with 2-Phenylsuccinamic Acid (VIII).—Lead tetra-acetate (2·5 g.) and the acid (1·0 g.) in dimethylformamide (10 ml.) were stirred at 50—60° for 1 hr., then cooled, poured into water, and continuously extracted with ether to give the product as an amorphous yellow solid, which decomposed on standing. Similarly, no pure product was isolated when the reaction was repeated in methanol and in benzene solution at various temperatures.

1,2,3,4-*Tetrahydro*-2,4-*dioxoquinazoline* (XI).— Lead tetra-acetate (2·7 g.) was added in one portion to a suspension of phthalamide (1·0 g.) in dimethylformamide (10 ml.) and the mixture was stirred at 50—60° for 1 hr., then cooled, diluted with water (15 ml.), and filtered. Sublimation of the residue at 200°/0·01 mm. gave the dioxoquinazoline (0·80 g., 81%), m.p. 351—352° (lit.,[36] m.p. 353—354°) (Found: C, 59·3; H, 3·9; N, 17·0. Calc. for $C_8H_6N_2O_2$: C, 59·3; H, 3·7; N, 17·3%), $\nu_{max.}$ (Nujol) 3250, 3160, 3060, 1690, and 1670 cm.$^{-1}$, *m/e* 162 ($C_8H_6N_2O_2$).

1,2,3,4,5,6-*Hexahydro*-2,4-*dioxopyrimidine* (XIV).— Succinamide (1·0 g.) and lead tetra-acetate (3·9 g.) in dimethylformamide (11 ml.) were stirred at 50—60° for 20 min., and the mixture was then cooled and filtered. Crystallization of the residue from acetic acid afforded the dioxopyrimidine (XIV) (0·92 g., 94%), m.p. 275°, identical with an authentic specimen prepared by catalytic hydrogenation of uracil.

1,2,3,4,5,6-*Hexahydro*-2,4-*dioxo*-6-*phenylpyrimidine* (XV). —2-Phenylsuccinamide (0·8 g.), lead tetra-acetate (1·8 g.), and dimethylformamide (8 ml.) were stirred at 50—60° for 15 min. and then poured into water, to give a precipitate of the phenylpyrimidine (XV) (0·63 g., 80%), m.p. 220—222° (lit.,[37] m.p. 220—222°), $\nu_{max.}$ (Nujol) 3200, 3080, 1740, and 1695 cm.$^{-1}$, τ (DMSO) 3·6 (s, aromatic H), 3·0 (broad absorption, –CONH–) 0·8 (br, S, –CONHCO–); *m/e* 190 ($C_{10}H_{10}N_2O_2$).

When a sample (68 mg.) of the product was heated with concentrated hydrochloric acid (1 ml.) in a sealed tube at 100° for 8 hr., it was hydrolysed to cinnamic acid (32 mg., 60%), identical with an authentic specimen.

1,2,3,4-*Tetrahydro*-2,4-*dioxo-pyrido*[2,3,-d]*pyrimidine* (XVIII).—Pyridine-2,3-carboxamide (0·9 g.) was treated with lead tetra-acetate (2·4 g.) in dimethylformamide (10 ml.) at 50—60° for 20 min. after which the mixture was filtered. Sublimation of the crude product at 200°/0·01 mm. gave the pyridopyrimidine (XVIII) (0·8 g., 90%), m.p. 360° (lit.,[38] m.p. 365°), $\nu_{max.}$ (Nujol) 3180, 3060, 1730, and 1680 cm.$^{-1}$; *m/e* 163 ($C_7H_5N_3O_2$).

A sample (0·26 g.) of the product was heated in a sealed tube at 170° for 4 hr. with 14% aqueous sodium hydroxide (3 ml.). The reaction mixture was then saturated with carbon dioxide, filtered, and acidified to pH 4·5 with dilute hydrochloric acid. Filtration of the mixture afforded 2-aminonicotinic acid (84 mg., 38%), m.p. 303—305°, identical with that obtained by hydrolysis of 3,4-dihydro-1,3-dioxo-1*H*-pyrido[2,3-*d*][1,3]oxazine.

1,2,3,4-*Tetrahydro*-2,4-*dioxopyrido*[3,4-d]*pyrimidine* (XXI).—Pyridine-3,4-dicarboxamide (1·0 g.), lead tetra-acetate (2·4 g.), and dimethylformamide (10 ml.) were stirred at 50—60° for 1 hr. Filtration of the cooled mixture gave the pyridopyrimidine (XXI) (1·0 g., quantitative) which, after sublimation at 210°/0·01 mm., had m.p. 365° (lit.,[39] m.p. >320°) (Found: C, 51·6; H, 3·4; N, 25·6. Calc. for $C_7H_5N_3O_2$: C, 51·6; H, 3·1; N, 25·8%), $\nu_{max.}$ (Nujol) 3220, 3060, 1730, and 1710 cm.$^{-1}$; *m/e* 163 ($C_7H_5N_3O_2$).

A sample (0·27 g.) of the crude product, when hydrolysed with aqueous sodium hydroxide as in the preceding experiment afforded 3-aminopyridine-4-carboxylic acid (80 mg., 35%) m.p. 306—309° (lit.,[16] m.p. 306—310°), $\nu_{max.}$ (Nujol) 3370, 3250, 2400, 1670, and 1580 cm.$^{-1}$, *m/e* 138 ($C_6H_6N_2O_2$). Fusion of the amino-acid with potassium hydroxide and distillation of the product *in vacuo* gave 3-aminopyridine identical with an authentic sample.

1,2,3,4-*Tetrahydro*-3-*methyl*-2,4-*dioxoquinazoline* (XXIV). —*N*-Methylphthalamide (1·0 g.), lead tetra-acetate (2·6 g.), and dimethylformamide (11 ml.) were stirred at 40—50° for 2 hr., and the mixture was then diluted with water (15 ml.) and cooled. The crystalline precipitate of the methylquinazoline (XXIV) (0·89 g., 88%) had m.p. 230—232° (lit.,[40] m.p. 230—233°), $\nu_{max.}$ (Nujol) 3170, 3050, 1720, and 1670 cm.$^{-1}$; *m/e* 176 ($C_9H_8N_2O_2$).

1,2,3,4,5,6-*Hexahydro*-3-*methyl*-2,4-*dioxopyrimidine* (XXVIII).—*N*-Methylsuccinamide (1·0 g.) was stirred at 60—70° for 2 hr. with lead tetra-acetate (3·5 g.) in dimethylformamide (10 ml.), and the mixture was then evaporated under reduced pressure. Extraction of the residue with hot ether, and crystallization of the extracted material from ethanol gave the dioxopyrimidine (XXVIII) (0·57 g., 56%), m.p. 125—127° (lit.,[41] m.p. 129—131°), $\nu_{max.}$ (Nujol) 3360, 3280, 3230, 1730, and 1670 cm.$^{-1}$; τ ($CDCl_3$) 7·29 (t, 2H, *J* 7 c./sec., 2H — 5), 6·59 (sextet, 2H, *J* 7 c./sec., *J′* 3 c./sec. (2H — 6), 6·86 (s, 3H, CH_3), and 3·3 (broad peak, 1H, N–H); *m/e* 128 ($C_5H_8N_2O_2$).

3-*Benzyl*-1,2,3,4,5,6-*hexahydro*-2,4-*dioxopyrimidine* (XXIX).—Treatment of *N*-benzylsuccinamide (1·0 g.) with lead tetra-acetate (2·3 g.) as in the preceding experiment gave dioxopyrimidine (XXIX) (0·76 g., 75%), m.p. 130—131° (lit.,[42] m.p. 132—134°), $\nu_{max.}$ (Nujol) 3360, 1720, and 1680 cm.$^{-1}$; τ ($CDCl_3$) 7·33 (t, 2H, *J* 7 c./sec. 2H-5), 6·68 (sextet, 2H, *J* 7 c./sec., *J′* 3 c./sec., 2H — 6), 5·1 (s, 2H, Ph–CH_2–), 3·6 (broad peak, 1H, N–H), and an unresolved 2·8 (unresolved doublet, 5H, Ar–H); *m/e* 204 ($C_{11}H_{12}N_2O_2$).

3-*Cyclohexyl*-1,2,3,4,5,6-*hexahydro*-2,4-*dioxopyrimidine* (XXX).—*N*-Cyclohexylsuccinamide (1·0 g.), lead tetra-acetate (2·3 g.) and dimethylformamide (10 ml.) were stirred together at 60—70° for 2 hr. The mixture was then filtered to remove an unidentified compound (0·24 g.), m.p. 270°, and then evaporated under reduced pressure. Addition of water (3 ml.) to the residue gave the dioxopyrimidine (XXX) (0·34 g., 33%) which, after sublimation at 150°/0·01 mm., had m.p. 210° (Found: C, 61·4; H, 8·4; N, 14·0. $C_{10}H_{16}N_2O_2$ requires C, 61·2; H, 8·2; N, 14·3%), τ ($CDCl_3$) 8·0—9·0 (10H, broad absorption, cyclohexyl), 7·36 (2H, t, *J* 7 c./sec., 2H — 5), 6·67 (2H, sextet, *J* 7 c./sec., *J′* 3 c./sec. 2H — 6), 5·6 (1H, broad absorption, N–C–H), and 3·7 (1H, broad absorption, N–H); *m/e* 196 ($C_{10}H_{16}N_2O_2$).

One of us (R. J. H.) thanks the Government of South Australia for a Grant-in-Aid.

[8/643 *Received, May 8th,* 1968]

[36] M. T. Bogart and G. Scatchard, *J. Amer. Chem. Soc.*, 1916, **38**, 1606.
[37] A. Rahman and M. O. Farooq, *Current Sci.*, 1952, **21**, 338.
[38] R. K. Robins and G. H. Hitchings, *J. Amer. Chem. Soc.*, 1955, **77**, 2256.
[39] H. H. Fox, *J. Org. Chem.*, 1952, **17**, 547.
[40] M. T. Bogart and G. Scatchard, *J. Amer. Chem. Soc.*, 1919, **41**, 2052.
[41] R. D. Hotchkiss and T. B. Johnson, *J. Amer. Chem. Soc.*, 1936, **58**, 525.
[42] K. Schlögl, *Monatsh.*, 1958, **89**, 61.