$n^{25}D$ 1.4704; 25.6 g. (26%) of a mixture of 3-methyl-2-methylene-1-acetoxymethylcyclohexane (VIIa) and 3-methyl-1-methylene-2-acetoxymethylcyclohexane (VIIb), b.p. 72° (2.2 mm.), $n^{25}D$ 1.4641; and 6.0 g. (4.5% recovery) of unchanged diacetate VI. The yield of the diene I, based on unrecovered VI and VII, was 84%. Strong absorption bands in the infrared at 895 and 2900 cm.$^{-1}$ and medium strong bands at 839, 860, 1450 and 1555 cm.$^{-1}$ confirm the structure of I.[9]

Anal. Calcd. for C_9H_{14}: C, 88.45; H, 11.55. Found: C, 88.73; H, 11.50. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.79; H, 9.74.

8-Methyl-$\Delta^{9(10)}$-octahydronaphthalene-2,3-dicarboxylic Anhydride (VIII).—A mixture of 3.0 g. (0.025 mole) of 3-methyl-1,2-dimethylenecyclohexane (I), 2.0 g. (0.020 mole) of maleic anhydride and 50 ml. of ether was heated under reflux for 1 hour. The reaction mixture was cooled and the resulting precipitate was recrystallized from ether to yield 2.25 g. (41%) of 8-methyl-$\Delta^{9(10)}$-octahydronaphthalene-2,3-dicarboxylic anhydride (VIII), m.p. 124.5–125°.

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 71.07; H, 7.27.

1-Methyl-1,2,3,4,5,5a,6,11,11a,12-decahydronaphthacene-6,11-dione (IX).—A mixture of 2.0 g. (0.0125 mole) of 1,4-naphthoquinone, 4.0 g. (0.0328 mole) of 3-methyl-1,2-dimethylenecyclohexane (I), and 100 ml. of ether was heated under reflux for 12 hours. The warm solution was filtered and the filtrate was cooled to precipitate white crystals. Recrystallization from petroleum ether (30–60°) yielded 1.0 g. (29%) of 1-methyl-1,2,3,4,5,5a,6,11,11a,12-decahydronaphthacene-6,11-dione (IX), m.p. 138–139°. Two additional recrystallizations from the same solvent produced an analytical sample, m.p. 141.5–142°.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.17; H, 6.97.

COLLEGE PARK, MARYLAND

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BUCKNELL UNIVERSITY]

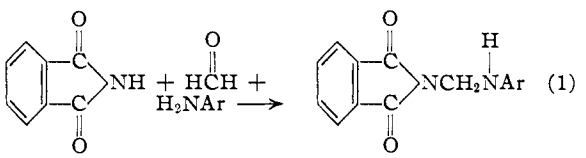
Identification of Amines. II. Phthalimidomethyl Derivatives of Primary and Secondary Amines[1]

BY HAROLD W. HEINE, MELDRUM B. WINSTEAD AND ROBERT P. BLAIR

RECEIVED SEPTEMBER 23, 1955

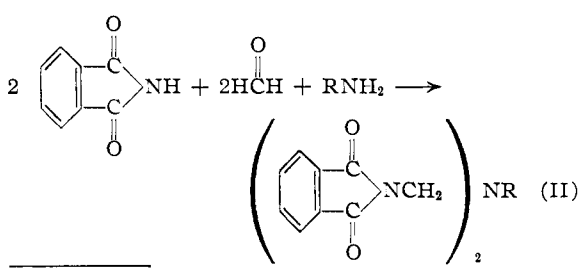
The condensation of phthalimide and formaldehyde with primary aliphatic amines has been shown to yield bis-(phthalimidomethyl)-alkylamines. In addition the syntheses of some N-(arylaminomethyl)-, N-(alkylarylaminomethyl)- and N-(dialkylaminomethyl)-phthalimides are reported.

Recently it has been shown that the condensation of primary aromatic amines with formaldehyde and phthalimide can be used successfully for the syntheses of N-(arylaminomethyl)-phthalimides,[2] *i.e.*



(1)

These compounds are useful for the characterization of amines since they are easily prepared and purified and have sharp melting points. The scope of the reaction which in some aspects is similar to the Mannich condensation has now been extended to aliphatic primary and secondary amines as well as aromatic secondary amines. No difficulty was encountered with the formation of the phthalimidomethyl derivatives of the aliphatic and aromatic secondary amines listed in Table I except that the yields were lower than were observed for the primary aromatic amines.[2] The primary aliphatic amines differed markedly, however, from the primary aromatic amines in that they readily formed the bis-(phthalimidomethyl)-alkylamines, (II). The results are in harmony with the recent observations of Haworth and co-workers[3] who reported that the condensation of the N-hydroxymethyl derivatives of benzamide, phenylacetamide and β-phenylpropionamide (formed by reaction of formaldehyde and the amides under alkaline conditions) with methylamine formed tertiary amino derivatives of the type shown in equation II. A similar product was reported for the reaction of N-hydroxymethylbenzamide with *n*-butylamine.[3]



(II)

Table I lists twenty-four additional N-(arylaminomethyl)-phthalimides of primary aromatic amines as well as seven N-(alkylarylaminomethyl)-phthalimido derivatives of secondary aromatic amines. Also included in Table I are six N-(dialkylaminomethyl)-phthalimide derivatives of secondary aliphatic amines. The bis-(phthalimidomethyl)alkylamines are presented in Table II.

Experimental

N-(Arylaminomethyl)-phthalimide and N-(Alkylarylaminomethyl)-phthalimide Derivatives.—It was found convenient to modify the original procedure for the preparation of these compounds as follows.[2] Three grams (0.0204 mole) of phthalimide was suspended in 35 ml. of 95% ethanol. Two milliliters of 37% formaldehyde was added and reflux was begun. Next 0.023 mole of the primary or secondary aromatic amine was added to the hot alcoholic solution. The solution turned yellow immediately. At this point the alcoholic solution was usually homogeneous and was refluxed for one-half hour. In a few cases the derivative began to separate from the boiling solution shortly after reflux was begun. Whenever this occurred reflux was discontinued

(1) This paper represents a portion of a thesis submitted by Robert P. Blair, in partial fulfillment of the requirements for the degree of Master of Science, Bucknell University, July, 1955.

(2) M. B. Winstead and H. W. Heine, THIS JOURNAL, **77**, 1913 (1955).

(3) R. D. Haworth, D. H. Peacock, W. R. Smith and R. MacGillivray, *J. Chem. Soc.*, 2972 (1952).

TABLE I

PHTHALIMIDOMETHYL DERIVATIVES OF PRIMARY AND SECONDARY AROMATIC AND SECONDARY ALIPHATIC AMINES

Amine used	M.p., °C.	Yield, %	Formula	Nitrogen, % Calcd.	Found
m-Aminoacetophenone[a]	147–148.5	82	$C_{17}H_{14}N_2O_3$	9.52	9.60
2-Amino-3,5-diiodobenzoic acid[a,b]	195–197	40	$C_{16}H_{10}I_2N_2O_4$	5.11	5.05
p-Aminohippuric acid	211 d.	68	$C_{18}H_{15}N_3O_5$	11.89	11.80
p-Amino-N-methylacetanilide	203–203.5	32	$C_{18}H_{17}N_3O_2$	13.00	12.58
p-Aminophenol	159–160	55	$C_{15}H_{12}N_2O_3$	10.44	10.52
p-Aminophenylacetic acid	151–152	27	$C_{17}H_{14}N_2O_4$	9.03	9.02
o-Aminophenylethyl alcohol	162–163	39	$C_{17}H_{16}N_2O_3$	9.46	9.36
p-Aminopropiophenone	145.5–146.5	57	$C_{18}H_{16}N_2O_3$	9.09	8.91
3-Aminoquinoline[a]	190.5–191.5	57	$C_{18}H_{13}N_3O_2$	13.86	13.72
p-*sec*-Amylaniline[c]	102–103.5	17	$C_{20}H_{22}N_2O_2$	8.61	8.69
2-Anilinoethanol[a]	95.5–96	23	$C_{17}H_{16}N_2O_3$	9.46	9.40
4-Bromo-2-methylaniline[d]	167–169	45	$C_{16}H_{13}BrN_2O_2$	8.12	8.12
5-Chloro-2-methoxyaniline	152.5–153.5	37	$C_{16}H_{13}ClN_2O_3$	8.84	8.78
3-Chloro-2-methylaniline[d]	194–194.5	48	$C_{16}H_{13}ClN_2O_2$	9.32	9.24
3-Chloro-4-methylaniline[e]	179–180	61	$C_{16}H_{13}ClN_2O_2$	9.32	9.38
5-Chloro-2-methylaniline[d]	192–193	23	$C_{16}H_{13}ClN_2O_2$	9.32	9.40
p,*p*'-Diaminodiphenylmethane[f,g,h]	208–210	63	$C_{31}H_{24}N_4O_4$	10.85	10.70
Diisoamylamine	52–53	33	$C_{19}H_{28}N_2O_2$	8.85	8.79
Dibenzylamine	145–146.5	53	$C_{23}N_{20}N_2O_2$	7.83	7.95
2,6-Dibromo-4-aminophenol[d]	166–168 d.	53	$C_{15}H_{11}Br_2N_2O_3$	6.58	6.33
Diisobutylamine	63–64	73	$C_{17}H_{24}N_2O_2$	9.72	9.85
2,5-Diethoxyaniline	89–91	17	$C_{19}H_{20}N_2O_4$	8.28	8.24
N,N-Diethyl-*p*-phenylenediamine	101–102	62	$C_{19}H_{21}N_3O_2$	12.99	12.96
Di-*n*-propylamine	37–38	12	$C_{15}H_{20}N_2O_2$	10.76	10.81
N-Ethylaniline	80–81.5	58	$C_{17}H_{16}N_2O_2$	10.00	10.18
Ethyl anthranilate	151.5–152.5	45	$C_{18}H_{16}N_2O_4$	8.64	8.64
N-Ethyl-*m*-toluidine	82–83.5	40	$C_{18}H_{18}N_2O_2$	9.52	9.51
N-Methylaniline	93	64	$C_{16}H_{14}N_2O_2$	10.54	10.52
N-Methyl-*m*-toluidine	92–93.5	40	$C_{17}H_{16}N_2O_2$	10.00	9.52
M-Methyl-*p*-toluidine	105–108	58	$C_{17}H_{16}N_2O_2$	10.00	10.20
2-Naphthylamine[d]	170–171 (162–163)	63	$C_{19}H_{14}N_2O_2$	9.27	9.21
m-Phenetidine[d,f]	170–171	65	$C_{17}H_{16}N_2O_3$	9.46	9.27
p-Phenylazoaniline[d,f]	196.5–197.5	50	$C_{21}H_{16}N_4O_2$	15.72	15.38
N-Phenylbenzylamine[i]	164–165	76	$C_{22}H_{18}N_2O_2$	8.18	8.07
p-Phenylenediamine[f,g,h]	245–247 d. (258)	51	$C_{24}H_{18}N_4O_4$	13.14	13.11
Piperidine[c,j]	119.5–120.5	23	$C_{14}H_{16}N_2O_2$	11.47	11.50
Pyrrolidine	123–124	59	$C_{13}H_{14}N_2O_2$	12.16	12.14

[a] Reaction medium refluxed one hour. [b] One hundred and fifty milliliters of ethanol used as reaction solvent. [c] Recrystallized from acetone–petroleum ether (65–110°). [d] Recrystallized from dioxane–petroleum ether (65–110°). [e] Recrystallized from ethanol–acetone. [f] Derivative precipitates in boiling solvent. [g] 0.011 mole of amine used in this reaction. [h] Recrystallized from nitrobenzene–petroleum ether (65–110°). [i] Recrystallized from ethanol–dioxane. [j] Sachs reported m.p. 117–118° (F. Sachs, *Ber.*, **31**, 3233 (1898)); other investigators reported m.p. 119–119.5° (J. R. Feldman and E. C. Wagner, *J. Org. Chem.*, **7**, 31 (1942); hydrate of this derivative m.p. 94–95° (M. B. Moore and R. T. Rapala, THIS JOURNAL, **68**, 1657 (1946)).

TABLE II

BIS-PHTHALIMIDOMETHYL DERIVATIVES OF PRIMARY ALIPHATIC AMINES

Amine used	M.p., °C.	Yield, %	Formula	Nitrogen, % Calcd.	Found
Allylamine	125–126	68	$C_{21}H_{17}N_3O_4$	11.19	11.18
N-Aminoethylmorpholine	185–186	23	$C_{24}H_{24}N_4O_5$	12.49	12.39
2-Amino-4-methylpentane[a]	122–123	29	$C_{24}H_{25}N_3O_4$	10.02	10.07
N-Aminopropylmorpholine	119–121		$C_{25}H_{26}N_4O_5$	12.11	11.81
Benzylamine[b]	187–188	79	$C_{25}H_{19}N_3O_4$	9.87	9.86
n-Butylamine	143–144	63	$C_{22}H_{21}N_3O_4$	10.73	10.72
Isobutylamine	156.5–157.5	83	$C_{22}H_{21}N_3O_4$	10.73	10.71
sec-Butylamine[b]	188–190	42	$C_{22}H_{21}N_3O_4$	10.73	10.71
Dodecylamine	69.5–70	43	$C_{30}H_{37}N_3O_4$	8.35	8.34
Ethylamine[b]	172–174	90	$C_{20}H_{17}N_3O_4$	11.57	11.52
2-Ethylhexylamine	154–155	53	$C_{26}H_{29}N_3O_4$	9.39	9.39
n-Heptylamine	111–111.5	55	$C_{25}H_{27}N_3O_4$	9.70	9.73
Hexadecylamine	82–82.5	30	$C_{34}H_{45}N_3O_4$	7.51	7.57
n-Hexylamine	108.5–109.5	44	$C_{24}H_{25}N_3O_4$	10.02	9.96
3-Methoxypropylamine	114–115	60	$C_{22}H_{21}N_3O_5$	10.31	10.14

TABLE II (*Continued*)

Amine used	M.p., °C.	Yield, %	Formula	Nitrogen, % Calcd.	Found
Methylamine[b]	216–218	67	$C_{19}H_{15}N_3O_4$	12.03	11.92
Octadecylamine	77–79	49	$C_{36}H_{49}N_3O_4$	7.15	7.04
3-Isopropoxypropylamine	120.5–121	55	$C_{24}H_{25}N_3O_5$	9.65	9.48
n-Propylamine	145.5–146.5	60	$C_{21}H_{19}N_3O_4$	11.13	11.16
Isopropylamine	166–167.5	58	$C_{21}H_{19}N_3O_4$	11.13	11.04
Tetradecylamine	78.5–79	38	$C_{32}H_{41}N_3O_4$	7.90	7.83

[a] Recrystallized from 95% ethanol. [b] Recrystallized from dioxane–petroleum ether (65–110°).

and the product collected. Several amines required refluxing periods of one hour. These are indicated in Table I.

The reaction medium was thoroughly chilled, and the product was filtered and dried. Many of the derivatives precipitated in a high state of purity and were brightly colored compounds. The majority of the derivatives were recrystallized from 95% ethanol. Those derivatives which were only slightly soluble in this solvent were best recrystallized from a mixture of dioxane and petroleum ether (65–110°) or some other solvent pair, as indicated in Table I.

Bis-(phthalimidomethyl)-alkylamines.—The same procedure as described above was followed except that 0.0105 mole of the primary aliphatic amine and only 10 ml. of 95% ethanol was employed. Also the reaction mixture was refluxed only 15 minutes. If the reactants did not dissolve readily when refluxing began then more ethanol was added in 5-ml. portions until the mixture was homogeneous. The reaction mixture was then chilled overnight, filtered and dried. Recrystallization of the bis derivatives was best accomplished by dissolving the compound (usually 2–3 g.) in 10 ml. of hot acetone, filtering while hot, and adding petroleum ether (65–110°) to the hot solution until a faint cloudiness persisted. The solution was then chilled overnight and the recrystallized product filtered and dried.

Acknowledgment.—The authors wish to express their appreciation to Research Corporation for the Frederick Gardner Cottrell grant in support of this project. Grateful acknowledgment is also made to Sharples Chemical, Inc., Carbide and Carbon Chemicals Company and Armour and Company for generous samples of many of the aliphatic amines used in this work.

LEWISBURG, PENNSYLVANIA

[CONTRIBUTION NO. 955 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

The Synthesis of Nitrogen-containing Ketones. V. The Direct Acylation of 3-Picoline[1,2,3]

BY ALFRED D. MILLER, CARL OSUCH, NEWTON N. GOLDBERG AND ROBERT LEVINE

RECEIVED SEPTEMBER 12, 1955

The direct acylation of 3-picoline with aromatic and heterocyclic esters using potassium amide as the condensing agent is described. The structure of one of the ketones, 3-phenacylpyridine, was established by reducing it to 3-(2-phenylethyl)-pyridine, authentic samples of which were prepared by two independent routes.

In previous work we reported[4] that the phenyllithium-effected acylations of 2-picoline with aliphatic, aromatic and heterocyclic esters give high yields of the corresponding 2-picolyl ketones.

The present paper is concerned with the direct acylation of 3-picoline—a reaction which has not been reported previously. Apparently the only 3-picolyl ketone recorded in the literature is 3-acetonylpyridine. This ketone has been synthesized by two routes: (1) the reaction of 3-pyridylacetic acid (prepared from 3-picoline in six steps) with acetic anhydride and sodium acetate[5] and (2) the reaction of 3-pyridylmagnesium bromide with 2-methyl-3-chloropropene followed by ozonolysis of the resulting olefin.[6]

In the present study it has been found that phenyllithium cannot be used to metalate the methyl group of 3-picoline since the interaction of these reagents in the presence (or absence) of an acylating agent such as methyl benzoate gives only the azomethine addition product, 2-phenyl-5-methylpyridine, and none of the desired 3-phenacylpyridine.[7] The use of methyllithium in place of phenyllithium gave an extremely complex mixture from which we were unable to isolate any pure compounds.

Since Brown and Murphey[8] recently demonstrated that it is possible to alkylate 3-picoline with alkyl halides, using a suspension of sodium amide in liquid ammonia as the condensing agent, it was desirable to attempt acylations under similar conditions. Using methyl benzoate as the acylating agent, 3-phenacylpyridine (isolated as its picrate) was indeed obtained, but in only 10% yield. Further study showed that considerably higher yields

(1) For paper IV in this series, see N. N. Goldberg and R. Levine, THIS JOURNAL, **77**, 4926 (1955).

(2) This work was performed under Contract No. AT(30-1)-670 between the U. S. Atomic Energy Commission and the University of Pittsburgh.

(3) Presented before the Organic Division of the 128th National ACS Meeting, Minneapolis, Minn., September 11–16, 1955.

(4) N. N. Goldberg, L. B. Barkley and R. Levine, THIS JOURNAL, **73**, 4301 (1951).

(5) A. Burger and C. R. Walter, Jr., *ibid.*, **73**, 1988 (1950); the yield in the last step is 40% of theory.

(6) J. P. Wibaut and H. G. P. van der Voort, *Rec. trav. chim.*, **71**, 798 (1952); the over-all yield of ketone based on 3-bromopyridine is 15%.

(7) When the tar base was rapidly added to the phenyllithium (Standard Addition Technique), a 30.8% yield of 2-phenyl-5-methylpyridine was obtained; when the phenyllithium was added slowly to the tar base (Reverse Addition Technique), the yield of addition product dropped to 18.1%. The structure of the 2-phenyl-5-methylpyridine was established by oxidizing it to pyridine-2,5-dicarboxylic acid.

(8) H. C. Brown and W. A. Murphey, THIS JOURNAL, **73**, 3308 (1951).