them by glpc on a Porapak Q column. Nitrogen was determined in the same way by thermal conductivity chromatography on a 4A molecular sieve column.

Aldehydes were identified and determined in the electrolysis solution itself by ultraviolet spectroscopy and by chromatography on 9N9, THFP, and Porapak columns.

Registry No.—Butylamine, 109-73-9; hexylamine, 111-26-2; isobutylamine, 78-81-9; benzylamine 100-46-9; ammonia, 7664-41-7; propylamine, 107-10-8; cyclohexylamine, 108-91-8; allylamine, 107-11-9; methylamine, 74-89-5; *t*-butylamine, 75-64-9.

Acknowledgment.—The authors wish to acknowledge financial support from the National Institutes of Health through Grant GM-10064 and from the National Science Foundation for a fellowship for K. K. B.

ortho Metalations of Ring-Substituted Benzyldimethylamines by *n*-Butyllithium and Condensations with Benzophenone. Nucleophilic Mechanism. Cyclizations to Phthalans[1]

KARL P. KLEIN AND CHARLES R. HAUSER

Department of Chemistry, Duke University, Durham, North Carolina

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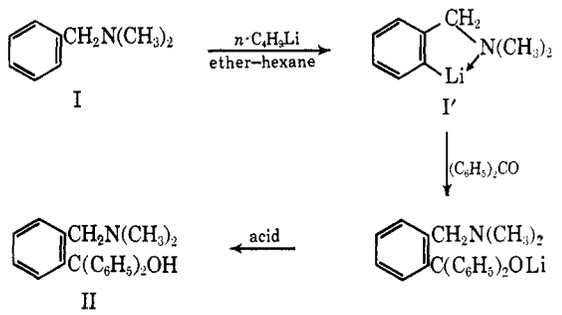
Several 2-, 3-, and 4-substituted and one 3,5-disubstituted benzyldimethylamines were lithiated with *n*-butyllithium in ether–hexane for 1 and 24 hr, and the resulting lithioamines were condensed with benzophenone to form the corresponding carbinolamines. The two 3-substituted benzyldimethylamines afforded only one of the two possible isomers: that which arose through lithiation at the position *ortho* to both the dimethylaminomethyl group, and the ring substituent. The yields were generally good to excellent after the longer lithiation period. Also, deuterations of certain of the lithioamines were effected after the 1-hr period. The results indicated that a nucleophilic mechanism operated. Six of the carbinolamines were cyclized through their methiodides to form substituted phthalans, generally in good yields. Both the lithiation–condensation and the cyclization methods should be useful in synthesis.

Recently,[2] benzyldimethylamine (I) was lithiated with *n*-butyllithium in ether–hexane at 25–30° to form *o*-lithioamine I′ which was condensed with benzophenone to give the *o*-carbinolamine (II, Scheme I).

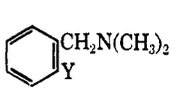
SCHEME I



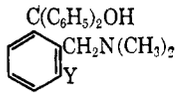
I I′ II

In the present investigation, nine ring-substituted benzyldimethylamines were similarly *ortho* lithiated and condensed with benzophenone to produce the corresponding carbinolamines, all of which were new. The lithiations were effected for both 1- and 24-hr periods before adding the ketone; the condensation period after adding the ketone was 4 hr. The results are summarized in Tables I and II; also in Table I are included, for comparison, the yields of the known carbinolamine (II) after the two lithiation periods.

The three 2-substituted benzyldimethylamines (IIIa–c) afforded the 2,6-disubstituted benzyldimethylamines (IVa–c), respectively. The structures of these products were supported by their infrared spectra which showed peaks in the region 790–800 cm^{-1}, ascribable to the three adjacent aromatic hydrogens.[3]

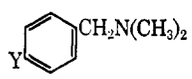


IIIa, Y = Cl
b, Y = F
c, Y = CH=C(C6H5)2

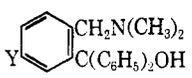


IVa, Y = Cl
b, Y = F
c, Y = CH=C(C6H5)2

The three 4-substituted benzyldimethylamines (Va–c) produced the 2,5-disubstituted benzyldimethylamines (VIa–c), respectively. The structures of these products were supported by infrared spectra which showed peaks in the region 800–820 and 870–893 cm^{-1}, indicating the two adjacent and one free aromatic hydrogen, respectively.[3]

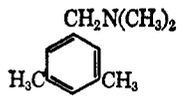


Va, Y = CH_3
b, Y = OCH_3
c, Y = Cl

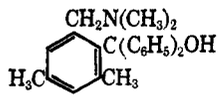


VIa, Y = CH_3
b, Y = OCH_3
c, Y = Cl

The 3,5-dimethylbenzyldimethylamine (VII) afforded the 2,3,5-trisubstituted benzyldimethylamine (VIII). The structure of VIII was indicated by its infrared spectrum which exhibited a peak at 863 cm^{-1}, consistent with a structure having one free aromatic hydrogen.[3]



VII



VIII

The two 3-substituted benzyldimethylamines (IXa, b), each of which might conceivably form isomers, nevertheless afforded only a single product. Evidently, lithiation occurred preferentially at the

(1) Supported by Army Research Office (Durham) and the National Science Foundation.

(2) F. N. Jones, R. L. Vaulx, and C. R. Hauser, *J. Org. Chem.*, **28**, 3461 (1963).

(3) See L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958, pp 76–79.

TABLE I

CONDENSATIONS OF RING-SUBSTITUTED BENZYLDIMETHYLAMINES WITH BENZOPHENONE TO FORM CARBINOLAMINES BY MEANS OF *n*-BUTYLLITHIUM

Starting amine	Carbinolamine	Yield, % at metalation period of 1 hr	24 hr	Mp, °C
I	2-(Dimethylaminomethyl)triphenylcarbinol (II)	32	75	152–154[a]
IIIa	3-Chloro-2-(dimethylaminomethyl)triphenylcarbinol (IVa)	73 (71)[b]	81	151–152[a]
IIIb	2-(Dimethylaminomethyl)-3-fluorotriphenylcarbinol (IVb)	33	0	164–165[a]
IIIc	2-(Dimethylaminomethyl)-3-(diphenylvinyl)triphenylcarbinol (IVc)	23	32	188–189.5[c]
Va	2-(Dimethylaminomethyl)-5-methyltriphenylcarbinol (VIa)	29 (26)[b]	82 (88)[d]	165.5–166[a]
Vb	2-(Dimethylaminomethyl)-5-methoxytriphenylcarbinol (VIb)	29	70	129–129.5[a]
Vc	5-Chloro-2-(dimethylaminomethyl)triphenylcarbinol (VIc)	72	82	157.5–158.5[a]
VII	2,4-Dimethyl-6-(dimethylaminomethyl)triphenylcarbinol (VIII)	14	52	121–121.5[a]
IXa	2-(Dimethylaminomethyl)-6-methoxytriphenylcarbinol (Xa)	26 (23)[b]	75	104–104.5[c]
IXb	2-(Dimethylaminomethyl)-6-trifluoromethyltriphenylcarbinol (Xb)	72	70	131–132[e]

[a] Recrystallized from hexane. [b] Duplicate experiments. [c] Recrystallized from ethanol. [d] Lithiation period was 48 hr. [e] Recrystallized from hexane–ethanol.

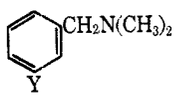
TABLE II

NMR SPECTRA AND ANALYSES OF CARBINOLAMINES

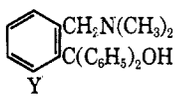
	Nmr (τ), ppm[a]						Anal., %					
	Protons						Calcd			Found		
Compd	N-Methyl[b]	N-Benzyl	Aromatic[c]	Hydroxyl[b]	Other[b]	Formula	C	H	N	C	H	N
IVa	7.80	6.65	2.40–3.40	0.40	...	$C_{22}H_{22}ClNO$	75.09	6.30	3.98	75.26	6.35	4.07
IVb	7.85	6.90[d]	2.50–3.55	0.75[e]	...	$C_{22}H_{22}FNO$	78.78	6.61	4.18	78.84	6.62	4.40
IVc	...	...	...	...	...	$C_{36}H_{33}NO$	87.23	6.71	2.83	87.03	6.82	3.01
VIa	8.00	7.20	2.75–3.20	3.75	7.90[f]	$C_{23}H_{25}NO$	83.34	7.60	4.23	83.02	7.59	4.11
VIb	7.90	7.10	2.50–3.20	0.00[e]	6.45[g]	$C_{23}H_{25}NO_2$	79.50	7.25	4.03	79.31	7.29	4.09
VIc	7.90	7.05	2.55–3.20	0.85	...	$C_{22}H_{22}ClNO$	79.09	6.30	3.98	75.26	6.36	4.15
VIII	7.90	6.95	2.70–3.30	...	8.55[f] 7.75[f]	$C_{24}H_{27}NO$	83.44	7.88	4.05	83.30	8.02	4.12
Xa	7.90	6.95	2.50–3.25	1.15	6.45[g]	$C_{23}H_{25}NO_2$	79.50	7.25	4.03	79.44	7.22	4.15
Xb	8.00	7.00	2.50–3.55	2.10	...	$C_{23}H_{22}F_3NO$	71.67	5.75	3.63	71.57	6.03	3.66

[a] Determined in carbon tetrachloride except VIa–b which were determined in deuteriochloroform. [b] Singlet. [c] Multiplet. [d] Doublet. [e] Center of broad peak. [f] Methyl protons. [g] Methoxy protons.

position *ortho* to both the dimethylaminomethyl group and the ring substituent. Thus, the product from IXa was shown to be Xa, and that from IXb was indicated to be Xb. The structures of these products were supported by their infrared spectra which showed peaks in the region 786–790 cm^{-1}, ascribable to the three adjacent aromatic hydrogens.[3]



IXa, Y = OCH_3
b, Y = CF_3



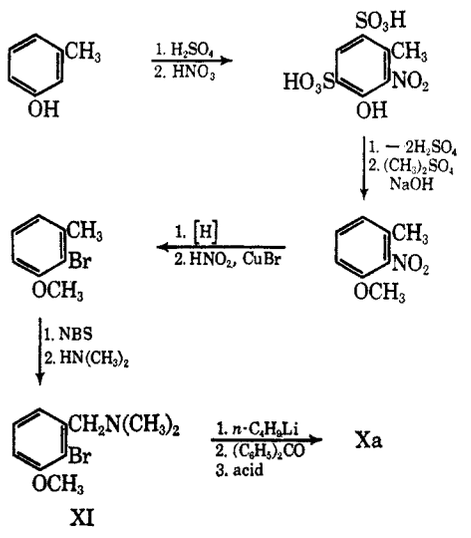
Xa, Y = OCH_3
b, Y = CF_3

The structure of the methoxy compound (Xa) was confirmed by independent synthesis from *m*-cresol (Scheme II). The conversion of *m*-cresol to the bromo compound (XI) involved a modification of the method of Gibson,[4] and that of this bromide to the carbinolamine (Xa) a halogen–metal interchange with *n*-butyllithium.[5]

Also, the 2,5-disubstituted benzyldimethylamine (XII), which would be the other possible isomer from the lithiation and condensation reactions of 3-methoxybenzyldimethylamine (IXa), was prepared from 2-methyl-4-methoxyaniline (Scheme III) and shown not to be the isomer from IXa.

Since anisole is known to readily undergo *ortho* metalation with *n*-butyllithium under similar conditions,[5a] it was possible that the position of lithiation of

SCHEME II



XI

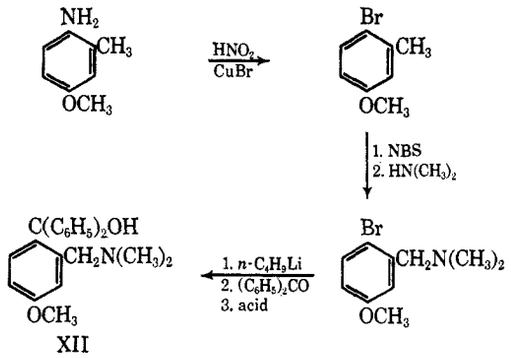
amine IXa was determined by the methoxy group. However, the dimethylaminomethyl group of IXa evidently controlled the lithiation, since treatment of a mixture of equimolar amounts of anisole and benzyldimethylamine with 1 molecular equiv of *n*-butyllithium, followed by 1 equiv of benzophenone, afforded exclusively the carbinolamine (II).

In addition to the infrared peaks mentioned above, the infrared spectrum for each of the carbinolamines showed a strong peak in the region 837–855 cm^{-1}, which can be attributed to the unaltered dimethylam-

(4) G. P. Gibson, *J. Chem. Soc.*, **123**, 1269 (1923).

(5) (a) See F. N. Jones and C. R. Hauser, *J. Org. Chem.*, **27**, 4389 (1962); (b) R. G. Jones and H. Gilman, *Org. Reactions*, **6**, 339 (1954).

SCHEME III



XII

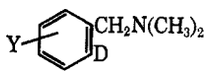
inomethyl group.[6] Hydroxyl peaks were observed in the spectra of all the adducts. Moreover, all the spectra exhibited peaks in the regions 739–763 and 694–704 cm^{-1}, ascribable to the five adjacent aromatic hydrogens[3] in the monosubstituted aromatic portions of the molecules.

The nmr spectra for certain of the carbinolamines were determined (see Table II). These spectra indicated the presence of the N-methyl, N-benzyl, hydroxyl, and aromatic protons.

The lithiations of most of the substituted benzyldimethylamines appeared to be essentially free of side reactions; however, lithiation of amine IIIb may have been accompanied by the benzyne reaction,[7] and that of amine IIIc by attack of the reagent at the double bond (see the Experimental Section). It should be mentioned that the method failed with 3-fluoro-, 3-chloro-, and the 3,5-dichlorobenzyldimethylamines which afforded dark reaction mixtures (heat generated); presumably the benzyne type of reaction predominated.

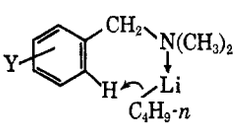
Table I shows that, with the exceptions of amines IIIb, c (see above), the amines afforded the corresponding carbinolamines in good to excellent yields (52–82%) after the 24-hr lithiation period and, in certain cases, after even the 1-hr period. This method could presumably be extended, not only to other ring-substituted benzyldimethylamines, but also to various electrophilic compounds. Actually, the unsubstituted benzyldimethylamine I has previously been condensed with a number of electrophilic compounds.[2]

Table I further shows that, compared to the unsubstituted benzyldimethylamine (I), the electron-withdrawing atoms or groups, 2-chloro, 4-chloro, and 3-trifluoromethyl, greatly facilitated the lithiation, whereas the electron-donating groups, especially the 3,5-dimethyl group, retarded the lithiation. Presumably the relative ease of lithiation would parallel the anticipated relative acidities of the *ortho* hydrogens. The relative order of lithiation of three of the amines, the 2-chloro (IIIa), the 4-methyl (Va), and the 3-methoxy (IXa) compounds, was supported by deuterations to form presumably the *ortho* deuterioamines (IIIaD, VaD, and IXaD, respectively[8]); the percentage deuterations after a 1-hr lithiation period were 70, 35, and 30%, respectively (see Table III). Since the reactants appeared to remain in solution during the 1-hr lithiation period, the relative order of the yields of the carbinolamines (see Table I) and percentage deuterations may be considered to represent relative rates of lithiation.

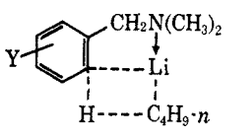


IIIaD, Y = 2-Cl
VaD, Y = 4-CH_3
IXaD, Y = 3-OCH_3

These observations are in line with a nucleophilic mechanism, which may involve removal of an *ortho* proton by the potential *n*-butyl carbanion within coordination complex XIII. Also the mechanism may be represented as four-centered system XIV in which the abstraction of the *ortho* proton furnishes the main driving force.



XIII



XIV

TABLE III

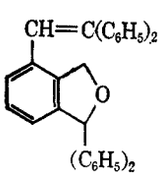
NMR DATA[a] OF DEUTERATED AMINES

Substituent	Type of proton	Chemical shift, cps (±1)	Calcd area ratio	Obsd area ratio
2-Chloro[b] (IIIaD)	Methyl	131[c]	6.0	5.95
	Benzyl	208	2.0	2.05
	Aromatic	418–441	4.0	3.30
4-Methyl[d] (VaD)	Methyl	127,[c] 134[e]	9.0	9.0
	Benzyl	196	2.0	2.0
	Aromatic	413–436	4.0	3.65
3-Methoxy[f] (IXaD)	Methyl	129,[c] 220[g]	9.0	9.05
	Benzyl	198	2.0	1.95
	Aromatic	396–437	4.0	3.70

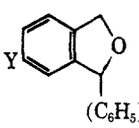
[a] Determined in carbon tetrachloride. [b] Recovered 92% of IIIa, bp 91–92° (12 mm). [c] N-Methyl protons. [d] Recovered 80% of Va, bp 80–81° (12 mm). [e] Ring methyl protons. [f] Recovered 87% of IXa, bp 101–102° (9.5 mm). [g] Methoxy protons.

Similar nucleophilic mechanisms have been assumed for the metalation of other types of aromatic compounds.[9,10] However, an electrophilic mechanism has also been suggested for certain metalations.[11]

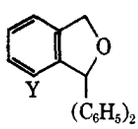
Cyclizations to Form Carbinolamines through Methiodides to Form Ring-Substituted Phthalans.—The carbinolamines IVc, VIa–c, and Xa, b were converted through their methiodides to their corresponding phthalans (XV, XVIa–c, and XVIIa, b, respectively); the yields were generally good (Table IV).



XV



XVIa, Y = CH_3
b, Y = OCH_3
c, Y = Cl



XVIIa, Y = OCH_3
b, Y = CF_3

(6) See W. Q. Beard, Jr. and C. R. Hauser, *J. Org. Chem.*, **25**, 334 (1960).
(7) See G. Wittig and W. Merkle, *Ber.*, **76**, 109 (1943).
(8) A similar *ortho* deuteration of lithiobenzyldimethylamine I′ has been effective previously: F. N. Jones, M. F. Zinn, and C. R. Hauser, *J. Org. Chem.*, **28**, 663 (1963).
(9) See J. D. Roberts and D. Y. Curtin, *J. Am. Chem. Soc.*, **68**, 1685 (1946); D. Bryce-Smith, *J. Chem. Soc.*, 1079 (1954); H. Gilman and J. W. Morton, Jr., *Org. Reactions*, **8**, 258 (1954).
(10) D. Bryce-Smith, V. Gold, and D. P. N. Satchell, *J. Chem. Soc.*, 2743 (1954); D. A. Shirley and K. R. Barton, *Tetrahedron*, **22**, 515 (1966).
(11) A. A. Morton, *J. Am. Chem. Soc.*, **69**, 969 (1947).

TABLE IV

CYCLIZATIONS OF CARBINOLAMINES THROUGH METHIODIDES TO FORM PHTHALANS

Carbinolamine	Phthalan	Recrystn solvent	Mp, °C	Yield,[a] %
IVc	3-(2,2-Diphenylvinyl)-1,1-diphenylphthalan (XV)	Hexane–ethanol	171–172	59
VIa	5-Methyl-1,1-diphenylphthalan (XVIa)	Hexane	136–136.5	82
VIb	5-Methoxy-1,1-diphenylphthalan (XVIb)	Hexane–ethanol	91.5–92.5	80
VIc	5-Chloro-1,1-diphenylphthalan (XVIc)	Ethanol	119.5–120.5	67
Xa	6-Methoxy-1,1-diphenylphthalan (XVIIa)	Pentane	103.5–104	20
Xb	6-Trifluoromethyl-1,1-diphenylphthalan (XVIIb)	Hexane	136.5–137	84

[a] Based on carbinolamine.

TABLE V

ABSORPTION SPECTRA AND ANALYSES OF PHTHALANS

		Nmr[a] (τ), ppm				Anal., %			
		Protons				Calcd		Found	
Phthalan	Infrared data, cm^{-1}	Benzyl[b]	Aromatic[c]	Other[b]	Formula	C	H	C	H
XV	1022, 797, 757, 699	4.30	2.45–3.35	...	$C_{34}H_{26}O$	90.63	5.82	90.65	5.83
XVIa	1030, 877, 803, 750, 697	5.05	2.60–3.25	7.70[d]	$C_{21}H_{18}O$	88.08	6.34	87.92	6.30
XVIb	1042, 877, 826, 766, 699	5.00	2.55–3.40	6.40[e]	$C_{21}H_{18}O_2$	83.42	6.00	83.21	6.05
XVIc	1030, 870, 812, 757, 690	4.95	2.60–2.90	...	$C_{20}H_{15}ClO$	78.30	4.93	78.32	4.95
XVIIa	1010, 733, 752, 690	4.95	2.50–3.35	6.45[e]	$C_{21}H_{18}O_2$	83.42	6.00	83.65	6.11
XVIIb	1016, 797, 757, 699	5.20	2.25–2.90	...	$C_{21}H_{15}F_3O$	74.11	4.44	74.38	4.47

[a] Determined in carbon tetrachloride. [b] Singlet. [c] Multiplet. [d] Methyl protons. [e] Methoxy protons.

The structures of the phthalans were supported by analyses and absorption spectra (see Table V). Their infrared spectra showed peaks for a cyclic ether[12] in the region 1010–1042 cm^{-1} and peaks in the regions 746–766 and 690–699 cm^{-1} ascribable to five adjacent aromatic hydrogens[3] which were present in the 1,1-diphenyl group. The spectra of compounds XV and XVIIa, b exhibited peaks in the region 773–797 cm^{-1}, attributable to three adjacent aromatic hydrogens.[3] Peaks in the regions 870–877 and 803–826 cm^{-1} appeared in the spectra of cyclic ethers XVIa–c and are consistent with the structures having one free and two adjacent aromatic hydrogens.[3] The phthalans gave quite simple nmr spectra which consisted of singlets at τ 4.30–5.20, assigned to the methylene protons, and an aromatic multiplet in the region 2.25–3.35.

All of the present phthalans appeared to be new. The method should be useful for the syntheses of various other substituted phthalans, in which the substituents could be varied, not only in the ring, but also in the 1,1 positions.

Experimental Section[13]

Preparation of Ring-Substituted Benzyldimethylamines.—Amines IIIb,[14] IIIc,[15] Va–c,[16] and IXb[17] were prepared as described previously. Amines IIIa, VI, and IXa were prepared by alkylation of dimethylamine with the corresponding benzyl halide; they were identified by comparisons of their methiodides or methobromides with authentic samples.[17,18]

Metalations of Ring-Substituted Benzyldimethylamines and Condensations with Benzophenone to Form Adducts.—In Tables I and II are summarized the yields and physical constants of the carbinolamines IVa–c, VIa–c, VII, and Xa, b. The details are given below.

To 0.025 mole of the ring-substituted benzyldimethylamine in a 125-ml erlenmeyer flask was added 0.03 mole of *n*-butyllithium (approximately 1.6 *M*). The flask was filled completely with anhydrous ether, tightly stoppered, and allowed to stand at room temperature (25–30°) for 1 or 24 hr. The solution of the resulting *o*-lithioamine was added slowly to a boiling solution of 0.03 mole of benzophenone in anhydrous ether. The resulting mixture was allowed to stand at room temperature for 4 hr and then hydrolyzed by cautious addition of water. The layers were separated and the ether layer was extracted twice with 4 *N* hydrochloric acid. The acid extracts were combined and made basic with potassium hydroxide (cooled and stirred). The resulting mixture was extracted three times with ether and the combined etheral solution was dried over anhydrous magnesium sulfate. The solvent was removed, and the residue was recrystallized from an appropriate solvent (see footnotes to Table I). Most of the amine fractions remaining after removal of the solid adducts were shown by vpc to consist essentially of the corresponding starting amines, and the neutral fractions obtained by evaporation of the original ether layer were shown to consist mainly of benzophenone and *n*-butyldiphenylcarbinol (from condensation of the ketone with the reagent). However, lithiations of amines IIIb, c produced dark mixtures and generated appreciable heat; vpc determinations on the amine fractions after removal of solid adduct indicated the presence of several products.

Similar results were obtained in several cases when the reaction was effected on twice the scale.

Carbinolamine I was identified by melting points and mixture melting point with an authentic sample.[2]

Independent Synthesis of Carbinolamine Xa.—2-Nitro-*m*-cresol, bp 102–105° (10 mm), was prepared in 40% yield from 70 ml of *m*-cresol, 305 ml of 20% fuming sulfuric acid, and 28 ml of fuming nitric acid according to the modification of Hodgson and Beard[19] of the method of Gibson.[4]

2-Nitro-3-methylanisole, mp 47–48° (lit.[20] mp 49°), was obtained in 90% yield by treatment of 38.40 g of 2-nitro-*m*-cresol with an excess of dimethyl sulfate and sodium hydroxide.

2-Amino-3-methylanisole, bp 114–116° (15 mm) [lit.[4] bp 124–126° (15 mm)], was obtained in 62% yield by reduction of 36.70 g of 2-nitro-3-methylanisole with iron powder in glacial acetic acid.

(12) R. L. Vaulx, F. N. Jones, and C. R. Hauser, *J. Org. Chem.*, **29**, 505 (1964).

(13) Melting and boiling points are uncorrected. Elemental analyses preformed by Ilse Beetz, Kronach, West Germany, and Janssen Pharmaceutica, Beerse, Belgium. Vapor phase chromatography was carried out on F and M Models 500 and 700 gas chromatographs using 5-ft Apiezon L and 2- and 6-ft silicone gum rubber columns. Infrared spectra were taken on a Perkin-Elmer Infracord Model 137, using the potassium bromide pellet method for solids and the neat liquid between sodium chloride plates for liquids. Nmr spectra were obtained with a Varian A-60 spectrometer using tetramethylsilane as an internal reference.

(14) H. Hellmann and W. Unseld, *Ann.*, 195 (1960).

(15) R. L. Vaulx, F. N. Jones, and C. R. Hauser, *J. Org. Chem.*, **29**, 1387 (1964).

(16) E. L. Eliel, T. N. Ferdinand, and M. C. Herrmann, *ibid.*, **19**, 1693 (1954).

(17) W. Q. Beard, Jr., D. N. Van Enam, and C. R. Hauser, *ibid.*, **26**, 2310 (1961).

(18) W. Q. Beard, Jr., and C. R. Hauser, *ibid.*, **25**, 334 (1960).

(19) H. H. Hodgson and H. G. Beard, *J. Chem. Soc.*, **127**, 498 (1925).

(20) P. Chuit and F. Bolsing, *Bull. Soc. Chim. France*, [3] **35**, 143 (1906).

2-Bromo-3-methylanisole, mp 33–36° (lit.[19] mp 35.5–36.5°), was obtained in 85% yield by the Sandmeyer reaction on 18.6 g of 2-amino-3-methylanisole using the sulfuric acid procedure.[21]

2-Bromo-3-methoxybenzyldimethylamine (XI), bp 112–114° (2.1 mm), was prepared in 55% yield by alkylation of dimethylamine with α,2-dibromo-3-methoxytoluene which, in turn, was prepared in 62% yield by the Wohl–Ziegler reaction of 31.5 g of 2-bromo-3-methylanisole.

Anal. Calcd for $C_{10}H_{14}BrNO$: C, 44.19; H, 5.77; N, 5.74. Found: C, 44.03; H, 5.81; N, 6.00.

2-Dimethylaminomethyl-6-methoxytriphenylcarbinol (Xa) was prepared by treatment of 4.50 g (0.18 mole) of 2-bromo-3-methoxybenzyldimethylamine (XI) with 15 ml (0.025 mole) of *n*-butyllithium in 125 ml of ether for 4 hr as described for the metalations of the ring-substituted benzyldimethylamines. The resulting lithioamine was added to a boiling solution of 0.025 mole of benzophenone in ether and allowed to stand for 4 hr.[5a] After a work-up as described above for the carbinolamines, there was isolated 5.05 g (80%) of Xa, mp 106–107°. A mixture melting point of this adduct and that obtained from the metalation of IXa was undepressed, mp 105–107°. Also, the infrared spectra of the two samples were superimposable.

Preparation of 2-Dimethylamino-5-methoxytriphenylcarbinol (XII).—4-Methoxy-2-methylbromobenzene, bp 106–109° (11 mm) [lit.[22] bp 108.5° (12 mm)], was obtained in 64% yield from the Sandmeyer reaction of 0.025 mole of 4-methoxy-2-methylaniline. This halide was converted by the Wohl–Ziegler reaction in 65% yield to 2-bromo-5-methoxybenzyl bromide which, in turn was treated with excess anhydrous dimethylamine to afford 2-bromo-5-methoxybenzyldimethylamine, bp 116–119° (1.8 mm), in 90% yield.

Anal. Calcd for $C_{10}H_{14}BrNO$: C, 44.19; H, 5.77; N, 5.74. Found: C, 44.48; H, 6.00; N, 5.69.

This bromoamine (2.50 g, 0.01 mole) was treated with 7 ml (0.011 mole) of *n*-butyllithium and 0.011 mole of benzophenone essentially as described for the metalations of the ring-substituted benzyldimethylamines to afford 1.35 g (47%) of XII, mp 118–119° after recrystallization from hexane. A mixture melting point of XII with Xa melted at 91–119°.

Anal. Calcd for $C_{23}H_{25}NO_2$: C, 79.50; H, 7.25; N, 4.03. Found: C, 79.65; H, 7.42; N, 3.91.

Deuteration of Amines IIIa, Va, and IXa.—The results of these reactions are summarized in Table III. The details are given below. The *o*-lithioamine, obtained by treating 0.025 mole of the appropriate amine with 0.03 mole of *n*-butyllithium for 1 hr as described above for the lithiations of the ring-substituted amines, was added to a stirred mixture of 0.05 mole of deuterium oxide (99.8% deuterium) in 100 ml of anhydrous ether. After stirring for 1 hr, the reaction mixture was worked-up as described for isolation of the carbinolamines to afford an oil which was distilled (see footnotes *b*, and *d* of Table III).

Cyclizations of Carbinolamines through Methiodides to Form Phthalans.—The results of these reactions are summarized in Tables IV and V. The details are given below.

Carbinolamines IIIc, VIa–c, and Xa, b were treated with excess methyl iodide in acetonitrile, and the resulting methiodides were recrystallized from this solvent. These methiodides were thermally cyclized at 200–210° for 15 min as described previously[12] to afford the cyclic ethers which were recrystallized from the appropriate solvents (see Table IV).

Registry No.—Butyllithium, 109-72-8; benzophenone, 119-61-9; II, 6969-98-8; IIIaD, 10126-18-8; IVa, 10169-24-1; IVb, 10126-19-9; IVc, 10126-20-2; VaD, 10126-21-3; VIa, 10126-22-4; VIb, 10126-23-5; VIc, 10126-24-6; VIII, 10126-25-7; IXaD, 10126-26-8; Xa, 10126-27-9; Xb, 10126-28-0; XI, 10126-29-1; XII, 10126-30-4; XV, 10126-31-5; XVI, 10126-32-6; XVIb, 10126-33-7; XVIc, 10126-34-8; XVIIa, 10126-35-9; XVIIb, 10126-36-0; 2-bromo-5-methoxybenzyldimethylamine, 10126-37-1.

(21) A. I. Vogel, "Textbook of Practical Organic Chemistry," 3rd ed, Longmans, Green and Co., New York, N. Y., 1956, p 602.

(22) R. Pschorr, *Ann.*, **391**, 50 (1912).

Acetylation and Cyclization of 1,3,5-Triketones with Acetic Anhydride by Boron Fluoride to Form Acyl-4-pyrones. Conversion into Acyl-4-pyridones. Mass Spectroscopy[1]

EDWIN M. KAISER, STEWART D. WORK, JAMES F. WOLFE, AND CHARLES R. HAUSER

Department of Chemistry, Duke University, Durham, North Carolina 27706

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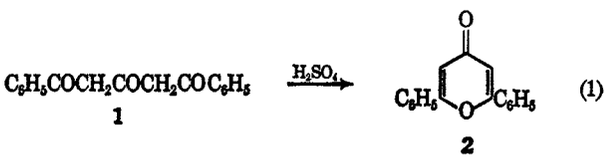
Acetylations and cyclizations of 1,5-diphenyl-1,3,5-pentanetrione, 1-phenyl-1,3,5-hexanetrione, and *o*-hydroxybenzoylacetone were effected with acetic anhydride by means of boron fluoride to form the corresponding acylpyrones, the last compound being a chromone. The first two products were subsequently converted to corresponding acylpyridones. Mass spectroscopy was employed to elucidate structures.

1,3,5-Triketones are known to be cyclized readily by acids such as cold, concentrated sulfuric acid[2] or liquid hydrofluoric acid[3] to form 4-pyrones. For example, triketone **1** affords pyrone **2** (eq 1).



1 **2** (1)

We have now found that certain 1,3,5-triketones can be acetylated and cyclized with acetic anhydride by boron fluoride to form acyl(acetyl or benzoyl)-4-pyrones. Thus, triketone **1** was converted in 90% yield to the acylpyrone **4a** which was subsequently converted to the acylpyridone **5a** (Scheme I). Isomeric structures **4b** and **5b** for these products, respectively, were eliminated by spectral methods (see below).

That the triketone did not first undergo cyclization to form pyrone **2** which was then acetylated was shown by failure of **2** to undergo acetylation under similar conditions. That the product was indeed an acylpyrone, not acetylated triketone **3** which was presumably formed initially (see Scheme I), was supported by analysis, by a negative enol test, and by similarity of the absorption spectra and other properties to those of known 4-pyrones.

Interestingly, this acetylation–cyclization of triketone **1** with acetic anhydride and boron fluoride differs from the reaction of a β-diketone such as acetylacetone

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(2) R. J. Light and C. R. Hauser, *J. Org. Chem.*, **25**, 538 (1960); M. L. Miles, T. M. Harris, and C. R. Hauser, *ibid.*, **30**, 1007 (1965).

(3) K. G. Hampton, T. M. Harris, C. M. Harris, and C. R. Hauser, *ibid.*, **30**, 4263 (1965).