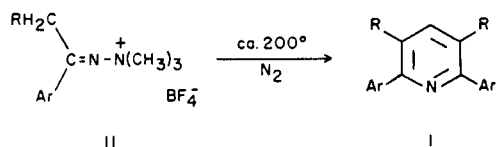


Department of Chemistry, Kent State University

Pyrolysis of Ketone *N,N,N*-Trimethylhydrazonium Fluoborates. III.
Preparation of Fused-Ring Pyridines

George R. Newkome (1a) and D. L. Fishel (1b)

Isolation of 2,6-diphenylpyridines (I) from the pyrolysis of aralkyl ketone *N,N,N*-trimethylhydrazonium fluoborates (II) (2) suggested the investigation of this route for the synthesis of fused-ring *N*-heterocycles, in which R represents a fusion to the aromatic ring, Ar. Thus, α -indanone



N,N,N-trimethylhydrazonium fluoborate, IX, or substituted α -tetralone *N,N,N*-trimethylhydrazonium fluoborates, Xa-d, should afford 10,12-dihydrodiindeno[1,2-*b*:2',1'-*e*]pyridine, XI, or substituted 5,6,8,9-tetrahydrodibenz[*c,h*]acridines, XIIa-d, respectively. The unsubstituted fused-ring pyridines (XI-XIIa) have been previously reported (3,4,5,6).

Ketone *N,N*-dimethylhydrazones (7) were readily prepared in ca. 80% yield by refluxing the ketone with an excess of anhydrous *N,N*-dimethylhydrazine (8). Data for the ketone *N,N*-dimethylhydrazones are cited in Table I. Difficulty was experienced for the preparation of 7-nitro- α -tetralone *N,N*-dimethylhydrazone, VIe, when during attempted purification by vacuum distillation, only resinous tars were obtained; no identifiable products were isolated.

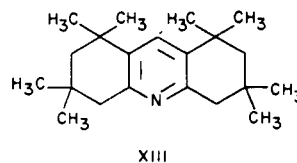
The quaternization of the *N,N*-dimethylhydrazones with methyl iodide resulted in 85-95% yields of the corresponding *N,N,N*-trimethylhydrazonium iodides (9). These iodide derivatives, upon treatment with a hot aqueous solution of sodium fluoborate, were converted to the corresponding ketone *N,N,N*-trimethylhydrazonium fluoborates in excellent yields. The properties of these intermediary iodides and fluoborates are quoted in Tables II and III, respectively. The main difficulty during conversion of the *N,N,N*-trimethylhydrazonium iodides into the fluoborates was concurrent hydrolysis of the iodide (9a,c), but this could be avoided by using neutral solutions of sodium fluoborate. The ketone *N,N,N*-trimethylhydrazonium fluoborates precipitated rapidly from the

aqueous solution with little or no hydrolysis. Their general insolubility in most organic solvents allowed their purification by simple washing techniques; analytical samples were recrystallized from absolute ethanol.

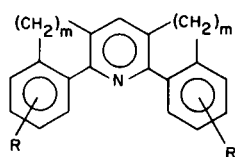
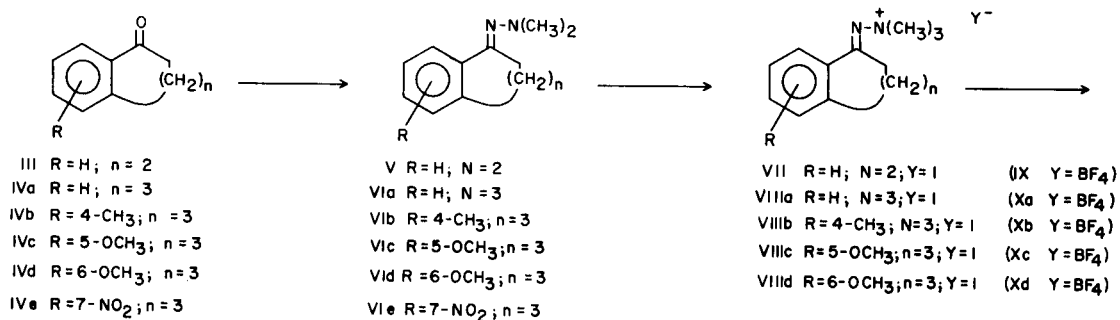
Pyrolysis of several ketone *N,N,N*-trimethylhydrazonium iodides gave in our hands only trace amounts of the desired *N*-heterocyclic products. This was perhaps to be expected in the presence of a reducing agent as powerful as the iodide counterion. Pyrolysis of the ketone *N,N,N*-trimethylhydrazonium fluoborates, however, either under a slow stream of nitrogen or *in vacuo*, resulted in conversion to the fused-ring *N*-heterocyclic compounds.

These fluoborates decomposed by a highly exothermic reaction at ca. 200° with the liberation of ammonia and the methyl amines. Better control of the decomposition was maintained by restricting *en-masse* quantities of the fluoborate to less than five grams or by preparing a "train" in a Pyrex tube. Refluxing cumene (b.p., 155°) was used in some instances as an inert solvent to suspend the fluoborate during the pyrolysis; no significant changes in overall yield were observed by this method.

The attempt was made to expand this synthesis to completely alicyclic starting materials. Cyclohexanone *N,N,N*-trimethylhydrazonium fluoborate could not be prepared since the quaternary iodide hydrolyzed under the reaction conditions. When a sterically hindered molecule, such as 3,3,5,5-tetramethylcyclohexanone, was employed, this difficulty was no longer encountered. A compound presumed to be 1,1,3,3,6,6,8,8-octamethyl-1,2,3,4,5,6,7,8-octahydroacridine, XIII, was obtained in about 40% yield from the corresponding fluoborate. Alternate routes to the alicyclic ketone *N,N,N*-trimethylhydrazonium fluoborates were not investigated.



XIII



- XI R = H; m = 1
XIIa R = H; m = 2
XIIb R = 5,8-di-CH₃; m = 2
XIIc R = 4,9-di-OCH₃; m = 2
XIId R = 3,10-di-OCH₃; m = 2

TABLE I

Ketone *N,N*-Dimethylhydrazones

Compound No.	% Yield	$n_D^{(T)}$	B.p. (mm)	Formula	C	Calcd.			Found	
						H	N	C	H	N
V	95	1.5817 (26)	73-75 (0.2)	C ₁₁ H ₁₄ N ₂	75.82	8.10	16.08	75.80	8.04	16.19
VIa	95	1.5718 (26)	76-77 (0.1)	C ₁₂ H ₁₆ N ₂	76.56	8.57	14.88	76.40	8.33	14.70
VIb	87 (a)	1.5680 (20)	83-84 (0.1)	C ₁₃ H ₁₈ N ₂						
VIc	73	1.5806 (20)	136-137 (0.7)	C ₁₃ H ₁₈ N ₂ O	71.52	8.31	12.83	71.70	8.26	12.82
VI d	86	1.5797 (26)	127-128 (0.2)	C ₁₃ H ₁₈ N ₂ O	71.52	8.31	12.83	71.57	8.30	12.63
VIe	(b)									

(a) Analysis was obtained on the methyl iodide derivative. (b) No product isolated, see text.

TABLE II

Ketone *N,N,N*-Trimethylhydrazonium Iodides

Compound No.	% Yield	M.p., °C	Formula	C	Calcd.			Found	
					H	N	C	H	N
VII	88	179-180	C ₁₂ H ₁₇ N ₂ I	45.58	5.42	8.87	45.81	5.44	8.92
VIIIa	95	167-169	C ₁₃ H ₁₉ N ₂ I	47.28	5.80	8.49	47.30	6.00	8.37
VIIIb	85	184-186	C ₁₄ H ₂₁ N ₂ I	48.85	6.15	8.14	48.85	6.14	7.97
VIIIc	90	193-194	C ₁₄ H ₂₁ N ₂ OI	46.68	5.88	7.78	46.68	5.99	7.74
VIId	92.5	188-189	C ₁₄ H ₂₁ N ₂ OI	46.68	5.88	7.78	46.71	5.86	7.80

TABLE III

Ketone *N,N,N*-Trimethylhydrazonium Fluoborates

Compound No.	% Yield	M.p., °C	Formula	Calcd.			Found		
				C	H	N	C	H	N
IX	92	166-167	C ₁₂ H ₁₇ N ₂ BF ₄	52.20	6.21	10.15	52.36	6.31	10.05
Xa	94	145-146	C ₁₃ H ₁₉ N ₂ BF ₄	53.82	6.60	9.66	53.63	6.75	9.55
Xb	82	146-147	C ₁₄ H ₂₁ N ₂ BF ₄	55.29	6.96	9.22	55.22	7.12	9.16
Xc	85	183-185	C ₁₄ H ₂₁ N ₂ OBF ₄	52.52	6.62	8.76	52.75	6.57	8.71
Xd	88	164	C ₁₄ H ₂₁ N ₂ OBF ₄	52.52	6.62	8.76	52.50	6.65	8.66

TABLE IV

Substituted 5,6,8,9-Tetrahydrodibenz[*c,h*]acridines

Compound No.	% Yield	M.p., °C	Formula	Calcd.			Found		
				C	H	N	C	H	N
XIIa	56	162-163	C ₂₁ H ₁₇ N	89.01	6.05	4.94	89.01	6.07	5.00
XIIb	53	177-178	C ₂₃ H ₂₁ N	88.71	6.80	4.50	88.65	6.91	4.56
XIIc	46	193-194	C ₂₃ H ₂₁ NO ₂	80.43	6.16	4.08	88.52	6.23	4.08
XIId	63	184-185	C ₂₃ H ₂₁ NO ₂	80.43	6.16	4.08	80.35	6.04	4.03

EXPERIMENTAL

Melting points were taken in sealed capillaries with a Hoover-Thomas melting point apparatus and are uncorrected. NMR spectra were obtained with a Varian Associates A-60 pmr spectrometer; tetramethylsilane was used as the internal standard. Refractive indices were obtained with a Bausch and Lomb Abbe-type refractometer. Molecular weights were obtained on a CEC 21-103C mass spectrometer (inlet temperature 293°, ionizing energy 70 e.v., and ionizing current 10 μ a). Microanalyses were performed by Spang Microanalytic Laboratory, Ann Arbor, Michigan.

Reagents.

Anhydrous *N,N*-dimethylhydrazine (99+%), anhydrous methyl iodide and the sodium fluoborate were purchased from Matheson Coleman and Bell. α -Indanone and the substituted α -tetralones were obtained from commercial sources.

Preparation of Ketone *N,N*-Dimethylhydrazones.

The procedure was essentially that described earlier (7). Yields and characteristic data for the *N,N*-dimethylhydrazones (V-VIa-e) are quoted in Table I.

3,3,5,5-Tetramethylcyclohexanone *N,N*-dimethylhydrazone was prepared by a similar procedure in 98% yield, b.p. 33-34° (0.25 mm), n_D^{26} 1.4622.

Anal. Calcd. for C₁₂H₂₄N₂: C, 73.42; H, 12.32; N, 14.26. Found: C, 73.41; H, 12.16. N, 14.19.

Preparation of Ketone *N,N,N*-Trimethylhydrazonium Iodides.

The following preparation of α -indanone *N,N,N*-trimethylhydrazonium iodide, VII, will exemplify the general procedure.

A mixture of α -indanone *N,N*-dimethylhydrazone (31.1 g.,

0.177 mole), absolute ethanol (35 ml.) and excess anhydrous methyl iodide was let stand several days. The crystalline precipitate was filtered and dried *in vacuo* giving α -indanone *N,N,N*-trimethylhydrazonium iodide (48.0 g., 0.152 mole) in 88% yield, m.p. 179-180° (dec.). The analytic sample was recrystallized from ethanol; the melting point was not increased.

Anal. Calcd. for C₁₂H₁₇N₂I: C, 45.58; H, 5.42; N, 8.87. Found: C, 45.81; H, 5.44; N, 8.92.

The yields and analytic data of the *N,N,N*-trimethylhydrazonium iodides (VII-VIIIa-d) are quoted in Table II.

3,3,5,5-Tetramethylcyclohexanone *N,N,N*-trimethylhydrazonium iodide was prepared in a similar manner in 75% yield, m.p. 184-186° (dec.).

Anal. Calcd. for C₁₃H₂₇N₂I: C, 46.16; H, 8.05; N, 8.28. Found: C, 46.33; H, 8.23; N, 8.18.

Preparation of Ketone *N,N,N*-Trimethylhydrazonium Fluoborates.

The following preparation of α -indanone *N,N,N*-trimethylhydrazonium fluoborate, IX, will exemplify the procedure.

A hot aqueous solution of α -indanone *N,N,N*-trimethylhydrazonium iodide (40.0 g., 0.127 mole) was refluxed with slow addition of an excess of a hot neutral aqueous sodium fluoborate solution over several minutes. The mixture was cooled in ice; the crystalline product was filtered, dried *in vacuo*, and recrystallized from absolute ethanol to give α -indanone *N,N,N*-trimethylhydrazonium fluoborate (32.2 g., 0.117 mole) in 92% yield, m.p. 166-167° (dec.).

Anal. Calcd. for C₁₂H₁₇N₂BF₄: C, 52.20; H, 6.21; N, 10.15. Found: C, 52.36; H, 6.31; N, 10.05.

The yields and analytical data of the *N,N,N*-trimethylhydrazonium fluoborates (IX-Xa-d) are quoted in Table III.

3,3,5,5-Tetramethylcyclohexanone *N,N,N*-trimethylhydrazonium fluoborate was prepared in a similar manner in 99% yield, m.p. 178–179° (dec.).

Anal. Calcd. for $C_{13}H_{27}N_2BF_4$: C, 52.36; H, 9.13; N, 9.40. Found: C, 52.34; H, 9.14; N, 9.34.

The nmr spectrum, in deuterium oxide, exhibited singlets at δ 3.52 (N-CH₃); δ 2.70, 2.26, and 1.55 (-CH₂-) and δ 1.10 and 1.02 (C-CH₃), with integration ratios of 9:2:2:2:6:6, respectively.

10,12-Dihydrodiindeno[1,2-*b*:2',1'-*e*]pyridine (XI).

α -Indanone *N,N,N*-trimethylhydrazonium fluoborate (9.0 g., 0.032 mole) was pyrolyzed, in two 4.5 gram quantities, under a slow stream of dry nitrogen. The residual tar in the pyrolysis tube was extracted with benzene (three 25 ml. portions), concentrated *in vacuo* to dryness and chromatographed on neutral Merck alumina by elution with 20% benzene in petroleum ether (b.p. 30–60°; ca. 1000 ml.). The first fraction was stripped of solvents and the pale residue was recrystallized from petroleum ether (b.p. 68–80°)-benzene (90:10) affording 10,12-dihydrodiindeno[1,2-*b*:2',1'-*e*]pyridine (1.3 g., 5.1 mmoles) in 31% yield, m.p. 204–205°; lit. (4) m.p. 206–207°.

The nmr spectrum, in deuteriochloroform, exhibited a singlet at δ 3.75 (-CH₂-) and a complex aromatic region with peaks at δ 8.17, 7.77 and 7.69, with integration ratios of 4:2:1:6, respectively.

The ultraviolet spectrum, in absolute ethanol, had λ max, 237 m μ (ϵ , 35,800), 246 (ϵ , 32,600), 270 (ϵ , 6,400), 335 (ϵ , 28,900), 343 (ϵ , 32,500), and 350 (ϵ , 27,400).

Anal. Calcd. for $C_{19}H_{13}N$: C, 89.39; H, 5.14; N, 5.49; mol. wt. 255. Found: C, 89.13; H, 5.17; N, 5.49; mol. wt. (mass spectrometry) 255.

5,6,8,9-Tetrahydrodibenz[*c,h*]acridine (XIIa).

Twenty grams of Xa were pyrolyzed in five gram quantities as above described. The crystalline XIIa weighed 4.5 g. (56.2% yield) and melted at 161°. Recrystallization from petroleum ether (b.p., 60–80°)-benzene gave an analytic sample, m.p. 162–163°; lit. (5) m.p., 162–163°.

Data for the other substituted 5,6,8,9-tetrahydrodibenz[*c,h*]acridines, XIIb-d, prepared via this procedure are summarized in Table IV.

Dibenz[*c,h*]acridine.

A mixture of 5,6,8,9-tetrahydrodibenz[*c,h*]acridine (500 mg., 2.15 mmoles) and an equal weight of palladium on carbon (10%) was heated at 250° *in vacuo* to give pale white dibenz[*c,h*]acridine in quantitative yield, m.p., 188°; lit. (6) m.p. 189–190°.

1,1,3,3,6,6,8,8-Octamethyl-1,2,3,4,5,6,7,8-octahydroacridine (XIII).

3,3,5,5-Tetramethylcyclohexanone *N,N,N*-trimethylhydrazonium fluoborate (15.0 g., 0.05 mole) was pyrolyzed in three 5 gram quantities as previously described. The pyrolysis residue was

chromatographed on neutral Merck alumina with petroleum ether (b.p. 30–60°) giving 3.5 grams of crude product. Recrystallization gave an analytic sample of XIII (3.0 g., 0.01 mole) in 40% yield, m.p. 114–115°.

The nmr spectrum, in carbon tetrachloride, exhibited two singlets at δ 1.28 and 1.02 (C-CH₃), two singlets at δ 2.58 and 1.55 (-CH₂-), and a singlet at δ 7.42 (C_{aromatic}-H), with integration ratios of 6:6:4:4:1, respectively.

The ultraviolet spectrum, in absolute ethanol, had λ max 215 m μ (ϵ , 6,350), 271 (ϵ , 6,190), 276 (ϵ , 7,500), 280 (ϵ , 7,100), and 288 (ϵ , 6,170).

Anal. Calcd. for $C_{21}H_{33}N$: C, 84.21; H, 11.11; N, 4.68. Found: C, 84.49; H, 11.11; N, 4.66.

Acknowledgment.

We are indebted to Mr. Nathan Ingber, formerly of the Sohio Research Laboratories, Cleveland, Ohio, for mass spectroscopic analyses and to the Dow Chemical Company, Midland, Michigan, for partial financial support of this investigation.

REFERENCES

- (1a) National Aeronautics and Space Administration Trainee, 1965–1966, present address: Department of Chemistry, Princeton University, Princeton, N. J.; (b) to whom inquiries should be addressed.
- (2) Previous paper: D. L. Fishel and G. R. Newkome, *J. Am. Chem. Soc.*, **88**, 3654 (1966).
- (3) G. Errera, *Gazz. Chim. Ital.*, **33I**, 424 (1903).
- (4) W. Borsche and H. Hahn, *Ann. Chem.*, **537**, 219 (1939).
- (5) J. Cologne, J. Dreux, and H. Delplace, *Bull. Soc. Chim. France*, 447 (1957). In this paper, these authors assigned the erroneous structural formula for XI as that of 5,7-dihydrodiindeno[2,1-*b*:1',2'-*e*]pyridine.
- (6) B. Mills and K. Schofield, *J. Chem. Soc.*, 4213 (1956).
- (7) G. R. Newkome and D. L. Fishel, *J. Org. Chem.*, **31**, 677 (1966).
- (8) Although no catalyst was necessary for the preparation of most *N,N*-dimethylhydrazones, acetic acid could probably have been used to increase the rate of formation of most *N,N*-dimethylhydrazones, R. H. Wiley and S. H. Chang, [*J. Med. Chem.*, **6**, 610 (1963)] found it necessary to use catalytic amounts of glacial acetic acid in the preparation of several steroid *N,N*-dimethylhydrazones.
- (9) Facile quaternization of other *N,N*-dimethylhydrazones has been reported: (a) P. A. S. Smith and E. E. Most, Jr., *J. Org. Chem.*, **22**, 358 (1957); (b) W. Theilacker and O. R. Leichte, *Ann. Chem.*, **572**, 121 (1951); (c) R. F. Smith and L. E. Walker, *J. Org. Chem.*, **27**, 4372 (1962).

Received May 15, 1967

Kent, Ohio 44240