M+ 409.428630 (1.4) (calcd, 409.428344), 366 (1), 240 (100), 198 (81); m* (409 → 240) 140.83; m* (240 → 198) 163.65.

Registry No.—Sodium, 7440-23-5; calcium, 7440-70-2; ammonia, 7664-41-7; cycloheptylnitrile, 32730-85-1; cycloheptylmethylamine, 4448-77-5, 32730-87-3 (*N*-phenylthiourea derivative); adiponitrile, 111-69-3; dodecyl cyanide, 629-60-7; tridecylamine, 2869-34-3; acetamide of 1-amino-1-dodecyltridecane, 32730-89-5.

Acknowledgment.—The author gratefully acknowledges the analytical assistance of Mr. B. E. Wilkes, Mr. J. T. Hildebrand, and Mr. W. H. Joyce.

A New Synthesis of Unsymmetrical Azo Compounds[1]

JOANNA S. FOWLER

Brookhaven National Laboratory, Upton, New York 11973

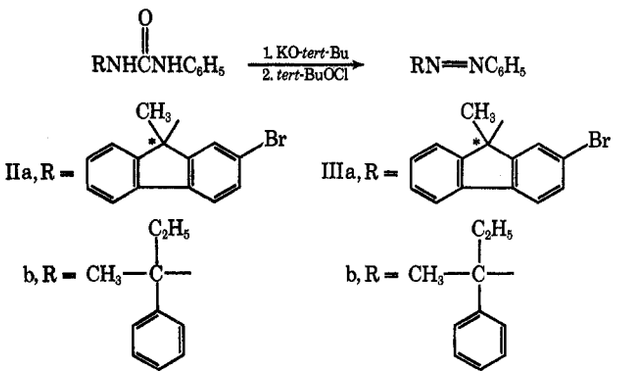
Received July 26, 1971

The relative rates of bond breaking of the two carbon–nitrogen bonds in the thermal decomposition of unsymmetrical azo compounds has been investigated recently.[2] This and other studies have resulted in the modification of old and development of new synthetic procedures for the preparation of the requisite unsymmetrical azo compounds.[3]

In connection with our studies, we required an azo compound of the general formula I in which the tertiary carbon is optically active. Since none of the existing methods for the preparation of unsymmetrical azo compounds could be modified to give a compound of type I, we explored new routes to this structure.[4]

RN=NAr
I, R = *tert*-alkyl

The treatment of unsymmetrical ureas (IIa,b) with potassium *tert*-butoxide in *tert*-butyl alcohol followed by the addition of *tert*-butyl hypochlorite at room temperature for 15 min produced azo compounds IIIa,b in approximately 20% yield. The ureas are readily obtained by the reaction of phenyl isocyanate with a *tert*-alkylamine. In addition, IIIa was produced optically active by beginning with resolved 2-bromo-9-methyl-9-aminofluorene, which was prepared from 2-bromofluorenone.



This method resembles the sequence which Greene[5] reported in the synthesis of diaziridones. However, it is not known if a diaziridone is an intermediate in this reaction.

Experimental Section[6]

2-Bromofluorenone.—2-Bromofluorene was oxidized according to the procedure of Ross and coworkers[7] to give 2-bromofluorenone in 73% yield, mp 144–146° (lit.[7] mp 146–148°), after recrystallization from ethanol.

2-Bromo-9-methylfluoren-9-ol.—To 22 g of 2-bromofluorenone in 700 ml of dry benzene was added 100 ml of CH_3MgBr (Aldrich, 2.2 *M*) over 20 min. The solution was stirred at room temperature for 1 hr and poured into 1 *N* H_2SO_4. The benzene layer was separated and the acid extracted with benzene. The benzene was dried ($MgSO_4$) and evaporated and the residue crystallized from chloroform–petroleum ether (bp 30–60°) to give 15.7 g (67%) of product, mp 143.5–144.5° (lit.[8] mp 148–149°).

2-Bromo-9-methyl-9-azidofluorene.—2-Bromo-9-methylfluoren-9-ol was converted to the azide according to the procedure of Coombs[9] in 85% yield and used as the oil without further purification: nmr spectrum (CCl_4) δ 1.67 (s, CH_3) and 7.1–7.8 (m, aromatics).

2-Bromo-9-methyl-9-aminofluorene.—To 9 g of $LiAlH_4$ (Ventron) in 225 ml of dry ether cooled in an ice bath was added with stirring 51.4 g of 2-bromo-9-methyl-9-azidofluorene at a rate which maintained vigorous refluxing. After addition was complete the reaction mixture was stirred at room temperature for 30 min. The excess $LiAlH_4$ was decomposed by the *slow* addition of 39 ml of 20% NaOH to the cooled reaction mixture. The white granular precipitate was filtered and the ether evaporated (frothing!) to give 42 g (89%) of a very viscous nearly colorless oil: nmr spectrum (CCl_4) δ 1.55 (s, CH_3), 7.1–7.8 (m, 7 aromatic H's), 1.41 (s, broad, NH_2).

Resolution of 2-Bromo-9-methyl-9-aminofluorene.—The amine (27.4 g) in 350 ml of ethyl ether was added to 12.5 g of *d*-10-camphorsulfonic acid in 50 ml of ethyl alcohol. The solution was allowed to stand at room temperature for 2 hr and at 16° for 1 hr and filtered to give 12.1 g of the camphorsulfonate salt. The amine from this salt was used to prepare the (+) azo compound. The filtrate was evaporated and the amine liberated. To 19.4 g of this amine was added 10.6 g of *d*-tartaric acid in 350 ml of ethanol. This was allowed to stand at 25° overnight and yielded 11.9 g of the tartrate salt. The amine liberated from this salt was used to prepare the (−) azo compound. In order to ascertain the rotation of the respective amines, they were each converted to the urea with phenyl isocyanate as described below and the rotations measured. The urea from the camphor-

(1) Research performed under the auspices of the U. S. Atomic Energy Commission.

(2) S. Seltzer and F. T. Dunne, *J. Amer. Chem. Soc.*, **87**, 2628 (1965); S. Seltzer, *ibid.*, **83**, 2625 (1961), **85**, 14 (1963); S. Seltzer and S. G. Mylonakis, *ibid.*, **89**, 6584 (1967); S. E. Scheppele and S. Seltzer, *ibid.*, **90**, 358 (1968); S. G. Mylonakis and S. Seltzer, *ibid.*, **90**, 5487 (1968); S. Seltzer, personal communication; W. A. Pryor and K. Smith, *J. Amer. Chem. Soc.*, **92**, 5403 (1970), **89**, 1741 (1967); N. A. Porter, M. E. Landis, and L. J. Marnett, *ibid.*, **93**, 795 (1971).

(3) For a summary of the synthetic methods which have been used in the preparation of azo compounds, see C. G. Overberger, J. P. Anselme, and J. G. Lombardino, "Organic Compounds with Nitrogen–Nitrogen Bonds," Ronald Press, New York, N. Y., 1966, Chapter 4; H. Zollinger, "Azo and Diazo Chemistry, Aliphatic and Aromatic Compounds," Interscience, New York, N. Y., 1961, Chapter 9. For specific examples of unsymmetrical azo compounds, see S. G. Cohen, F. Cohen, and C. H. Wang, *J. Org. Chem.*, **28**, 1479 (1963); S. Seltzer and F. T. Dunne, ref 2; N. A. Porter, M. E. Landis, and L. J. Marnett, ref 2.

(4) Since this method was developed Porter, *et al.*,[2] have reported a synthetic sequence which also leads to this type of compound and involves the unsymmetrical sulfamide.

(5) F. D. Greene, J. C. Stowell, and W. R. Bergmark, *J. Org. Chem.*, **34**, 2254 (1969).

(6) Melting points were taken on a Reichert melting point apparatus and are uncorrected. Nmr spectra were recorded on a Varian A-60 instrument and ultraviolet spectra were recorded on a Cary Model 14 spectrophotometer. Microanalyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. 11377.

(7) S. D. Ross, M. Finkelstein, and R. C. Petersen, *J. Amer. Chem. Soc.*, **80**, 4327 (1958).

(8) A. Weizmann, *J. Org. Chem.*, **16**, 1851 (1951).

(9) M. M. Coombs, *J. Chem. Soc.*, 3454 (1958).

sulfonate salt gave $\alpha_{DMF}^{5461\,Å}$ = +26° and the urea from the tartrate salt gave $\alpha_{DMF}^{5461\,Å}$ = −28°. A second crystallization of the salts gave ureas with $\alpha_{DMF}^{5641\,Å}$ = +40° and $\alpha_{DMF}^{5641\,Å}$ = −40°. For preparation of optically active azo compounds various batches of +(−) ureas having specific rotation from +(−)23 to +(−)40° were used.

N-Phenyl-*N'*-2-bromo-9-methyl-9-fluorenylurea (IIa).—To 1.98 g of 2-bromo-9-methyl-9-aminofluorene in 40 ml of benzene was added 0.79 ml of phenyl isocyanate. The solution was heated to boiling on a steam bath and allowed to cool, and 2.4 g of colorless crystals was collected, mp 269.5–270°, after two crystallizations from acetone.

Anal. Calcd for $C_{21}H_{17}BrN_2O$: C, 64.13; H, 4.36; N, 7.12. Found: C, 64.67; H, 4.41; N, 7.09.

2-Bromo-9-methyl-9-fluorenylazobenzene (IIIa).—Potassium *tert*-butoxide (2.70 g) was dissolved in 430 ml of *tert*-butyl alcohol, 9.65 g of *N*-phenyl-*N'*-2-bromo-9-methyl-9-fluorenylurea was added, and the resulting slurry was stirred for 15 min at room temperature. *tert*-Butyl hypochlorite (4.58 ml) was added dropwise from a syringe over 2 min. The reaction mixture became bright yellow and the temperature rose to 30°. Stirring was continued for 15 min and the mixture poured onto ice and water and extracted with ether until the water was colorless. Some unreacted urea remained suspended at the interface. The ether was thoroughly washed with water (2 l.) to remove the *tert*-butyl alcohol. (Since emulsions result from shaking while extracting, it is better to pour the water through the ether and not to shake it.) The ether is filtered from 2.7 g of unreacted urea and dried with K_2CO_3 and evaporated leaving a red oil. This was chromatographed using a cold dry column of alumina eluting with 20% benzene in petroleum ether (bp 30–60°).[10] The fractions of the chromatograph were monitored by tlc. The first few fractions contained two faster running compounds in addition to the yellow azo compound and these fractions were discarded. The yield of azo compound was 1.5 g (23% based on recovered urea). This material could be crystallized with difficulty from petroleum ether, mp 67–73° dec. However, the oil and crystals had identical infrared and nmr, and the elemental analyses of the oil and the solid were identical. The nmr spectrum ($CDCl_3$) showed δ 1.85 (s, CH_3) and 7.26–8.05 (m, aromatic H's), and the uv spectrum of the oil showed λ^{EtOH} 404 nm (ε 202).

Anal. Calcd for $C_{20}H_{15}BrN_2$ (oil): C, 66.12; H, 4.16; N, 7.71. Found: C, 66.34; H, 4.24; N, 7.63.

The azo compound prepared from the partially resolved ureas gave $\alpha_{EtOH}^{5461\,Å}$ = +(−)150°. The optical purity of the azo compound was not determined. However, when attempts were made to recrystallize the partially resolved material it was found that the racemate crystallized leaving a more highly resolved oil in the mother liquors. Hence the oil was used without crystallization.

[(α-Phenyl-α-methyl)propyl]azobenzene (IIIb).—To 2.36 g of IIb[11] in 100 ml of *tert*-butyl alcohol was added 1.06 g of potassium *tert*-butoxide. This was stirred for 15 min at room temperature and 2.04 ml of *tert*-butyl hypochlorite was added dropwise over 2 min. After the addition was complete the reaction mixture was poured into 120 ml of cold water and extracted with petroleum ether. The petroleum ether extracts were washed well with water, then dried, and evaporated. The petroleum ether soluble portion of the residue was chromatographed over neutral alumina and 0.6 g of a yellow oil was eluted with petroleum ether. Nmr showed this material to be a 1:3 mixture of an unidentified compound and azo compound IIIb. The analytical sample was prepared by fractional molecular distillation: nmr (CCl_4) δ 0.77 (t, 3 H, J = 7 Hz, CH_2CH_3), 1.57 (s, 3 H, CH_3), 2.12 (q, 2 H, J = 7 Hz, CH_2CH_3); uv λ_{vis}^{EtOH} 410 nm (ε 120).

Anal. Calcd for $C_{16}H_{20}N_2$: C, 79.95; H, 8.38; N, 11.65. Found: C, 80.22; H, 7.82; N, 11.59.

Registry No.—IIa, 32659-22-6; (±)-IIa, 32659-23-7; (+)-IIIa, 32659-24-8; (−)-IIIa, 32659-25-9; IIIb, 32722-87-5; 2-bromo-9-methyl-9-azidofluorene, 32670-62-5; 2-bromo-9-methyl-9-aminofluorene, 32659-26-0.

(10) The alumina used for the dry column (240 g) was deactivated by the addition of 7 ml of water to 380 g of neutral alumina and heating the resulting mixture at ~50° for 1 hr on the rotary evaporator. The jacketed chromatograph column (1.2 × 14 in.) was cooled with an ice–water mixture.

(11) M. Thiel, W. Schafer, and F. Asinger, *Justus Liebigs Ann. Chem.*, **613**, 128 (1958).

The Synthesis of 3-Alkyl-2-pyrazinyl Methyl Ketones and Related Compounds

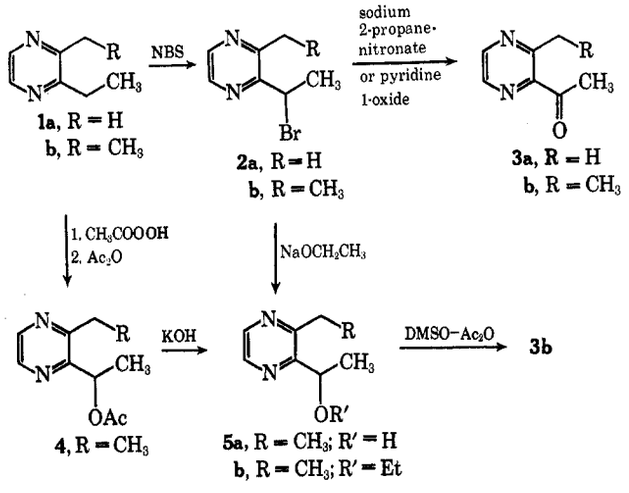
B. D. MOOKHERJEE* AND E. M. KLAIBER

International Flavors & Fragrances Inc., Union Beach, New Jersey 07735

Received September 2, 1971

Acetylpyrazines, which are important flavoring materials,[1a–d] are not readily available. The literature contains no convenient synthetic route involving less than four steps.

We now report a simple two-step synthesis of acetylpyrazines from the corresponding alkylpyrazines. Monobromoalkylpyrazines, obtained by treatment of alkylpyrazines with *N*-bromosuccinimide (NBS),[2,3] are readily oxidized to the corresponding ketones by either sodium-2-propanenitronate[4] or pyridine 1-oxide.[5] Thus, 2-ethyl-3-methylpyrazine (**1a**) on treatment with NBS in the presence of benzoyl peroxide gave 2-(1-bromoethyl)-3-methylpyrazine (**2a**) (≈100%) which in turn was converted to ketone **3a**[1c] by both sodium 2-propanenitronate and pyridine 1-oxide in 66 and 25% overall yield, respectively. Similarly, 2-(1-bromoethyl)-3-ethylpyrazine (**2b**), obtained from 2,3-diethylpyrazine (**1b**), was converted to ketone **3b** in 54% overall yield with sodium 2-propanenitronate. When bromide **2b** was treated with excess sodium ethoxide in ethanol, ethyl ether **5a** was obtained in 43% yield.



In another experiment ketone **3b** was prepared from **1b** using the *N*-oxide rearrangement.[6] Treatment of **1b**

(1) (a) D. L. Roberts, to R. J. Reynolds Tobacco Co., U. S. Patent 3,402,051 (Sept 17, 1968); *Chem. Abstr.*, **72**, 11496*d* (1970); (b) M. Winter, F. Gautschi, I. Flament, and M. Stoll, to Firmenich et Cie., French Patent 1,530,436 (June 28, 1968); *Chem. Abstr.*, **71**, 90131*m* (1969); (c) Polak's Frutal Works, U. S. Patent Application 666,980; (d) V. K. Smith, Jr., P. River, and S. Kushner, to American Cyanamid Co., U. S. Patent 2,677,686 (May 4, 1954).

(2) *N*-Chlorosuccinimide has previously been used for the chlorination of 2,3-dimethylpyrazine: R. A. Pages and P. E. Spoerri, *J. Org. Chem.*, **28**, 1702 (1963).

(3) For bromination of methylpyrimidine derivatives with *N*-bromosuccinimide, see M. Hasegawa, *Pharm. Bull.*, **1**, 387 (1953); *Chem. Abstr.*, **49**, 10970*g* (1955).

(4) H. B. Hass and M. L. Bender, *J. Amer. Chem. Soc.*, **71**, 1767 (1949); *Org. Syn.*, **30**, 99 (1950).

(5) W. Feely, W. L. Lehn, and V. Boekelheide, *J. Org. Chem.*, **22**, 1135 (1957).

(6) G. Kobayashi and S. Furukawa, *Pharm. Bull.*, **1**, 347 (1953); *Chem. Abstr.*, **49**, 10948*e* (1955); V. Boekelheide and W. J. Linn, *J. Amer. Chem. Soc.*, **76**, 1286 (1954); B. Klein, J. Berkowitz, and N. E. Hetman, *J. Org. Chem.*, **26**, 126 (1961).