As in Table II the uncertainty in these values is several tenths of a unit.

TABLE IV

CYCLOHEXENE, THERMODYNAMIC FUNCTIONS

(Units: cal./degree mole)

T, °K.	$\frac{(H^0 - H^0_0)}{T}$	C^0_p	$-\frac{(F^0 - H^0_0)}{T}$	S^0
200	10.75	16.32	55.43	66.18
298.16	13.98	25.10	60.29	74.27
300	14.05	25.28	60.38	74.43
400	18.04	34.64	64.96	83.00
500	22.20	42.78	69.43	91.63
600	26.20	49.45	73.84	100.04
700	29.93	54.92	78.16	108.09
800	33.35	59.49	82.38	115.73
900	36.47	63.34	86.49	122.96
1000	39.33	66.62	90.48	129.81
1100	41.94	69.43	94.36	136.30
1200	44.34	71.85	98.12	142.46
1300	46.53	73.92	101.75	148.28
1400	48.55	75.72	105.27	153.82
1500	50.42	77.27	108.68	159.10

Appendix I

In order to calculate thermodynamic functions for the mode of oscillation with potential energy given by equation (2) above, the partition function is needed

$$Q = \frac{(2\pi mkT)^{1/2}}{h} \int_{-\infty}^{+\infty} e^{-V(Z)/kT} dZ \qquad (3)$$

On integration the result is

$$Q = \frac{(2\pi mkT)^{1/2}}{h} [2a + (\pi kT/b)^{1/2}) \qquad (4)$$

Let us define $y = 2a(b/\pi kT)^{1/2}$, in terms of which the thermodynamic functions may be written as

$$\frac{-(F - H_0)}{T} = R\left[\ln \frac{2a(2\pi mk)^{1/2}}{h} + \frac{1}{2}\ln T + \ln\left(1 + \frac{1}{y}\right)\right]$$

$$\frac{H - H_0}{T} = \frac{R}{2}\left[\frac{2 + y}{1 + y}\right]$$

$$C = R\left[\frac{1}{2} + \frac{3}{4(1 + y)} - \frac{1}{4(1 + y)^2}\right]$$

Summary

By the use of bond bending and bond twisting (internal rotation) potential constants from related molecules the potential or strain energy of cyclopentene and cyclohexene was calculated for various configurations. It was found that cyclopentene can pucker by moving the carbon opposite to the double bond out of the plane of the other four carbon atoms by about 0.3 Å. without significant change in energy from the planar configuration. Cyclohexene, by contrast, shows two tautomeric forms related to chair and boat cyclohexane which differ by about 2.7 kcal./mole.

The available Raman and infrared spectroscopic data are interpreted for cyclopentene and cyclohexene. With reasonable adjustments of otherwise somewhat uncertain parameters, agreement is obtained with the thermodynamic data for the two substances. The thermodynamic functions ($-(F^0 - H^0_0)/T$, $(H^0 - H^0_0)/T$, S^0 and C^0_p) are then calculated for the ideal gas state from 200 to 1500°K.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Amine Exchange Reactions of Mannich Bases

BY H. R. SNYDER AND JAMES H. BREWSTER[1]

Amine exchange reactions occur when quaternary ammonium salts are heated with ammonia or primary or secondary amines[2] (eqn. A1). Similar reactions have been observed with Mannich bases of nitromethane[3] and of indole[4] (eqn. B1); the phenylhydrazones of ketonic Mannich bases form pyrazolines by internal amine exchange[5] (eqn. C).

Since these reactions appear to be similar in their mechanisms to the corresponding amine replacement reactions which occur in alkylations with quaternary salts of benzylamine[6,7,8] (eqn. A2), and with Mannich bases[4,8,9] (eqn. B2) and their quaternary salts[8,10] (eqn. A2), it seemed desirable to determine whether amine exchange reactions occur readily with ketonic and phenolic Mannich bases.

A. 1 $R'\!-\!\overset{+}{N}R_3 + :B \longrightarrow R'\overset{+}{B} + :NR_3$

$R' =$  $—CH_2—, CH_3—$, etc.; $B = HNR_2''$

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[2] Scholtz, *Ber.*, **24**, 2402 (1891); **31**, 414, 1700 (1898); von Braun and Zobel, *Ann.*, **445**, 247 (1925); *Ber.*, **59**, 1786 (1926); von Braun, Kuhn and Goll, *ibid.*, **59**, 2330 (1926); Hultquist, *et al.*, THIS JOURNAL, **70**, 23 (1948).

[3] Duden, Bock and Reid, *Ber.*, **38**, 2036 (1905).

[4] Howe, Zambito, Snyder and Tishler, THIS JOURNAL, **67**, 38 (1945).

[5] Mannich and Bauroth, *Ber.*, **57**, 1108 (1924); Nisbet and Gray, *J. Chem. Soc.*, 839 (1933); Levvy and Nisbet, *ibid.*, 1053, 1572 (1938); Nisbet, *ibid.*, 1237, 1568 (1938); 126 (1945); Harradence and Lions, *J. Proc. Roy. Soc. N. S. Wales*, **73**, 14 (1939) [*C. A.*, **33**, 8196 (1939)].

[6] von Meyer, *Abhandl. math.-phys. Klasse sächs. Akad. Wiss.*, **31**, 179 (1908) [*Chem. Zentr.*, **80**, II, 1800 (1909)].

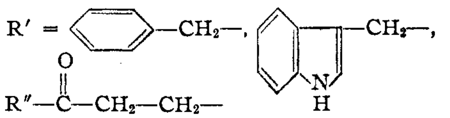
[7] Snyder and Speck, THIS JOURNAL, **61**, 668, 2895 (1939).

[8] Snyder, Smith and Stewart, *ibid.*, **66**, 200 (1944).

[9] Mannich, Koch and Borkowsky, *Ber.*, **70**, 355 (1937); Reichert and Posemann, *Arch. Pharm.*, **275**, 67 (1937).

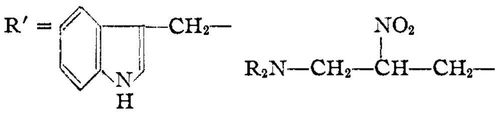
[10] duFeu, McQuillin and Robinson, *J. Chem. Soc.*, 53 (1937).

$2\quad R'-\overset{+}{N}R_3 + :B^- \longrightarrow R'B + :NR_3$

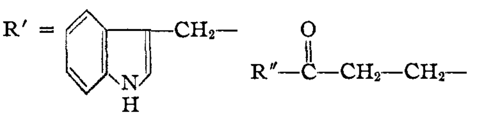


$B = -CH(CO_2Et)_2,\ -CN$, etc.

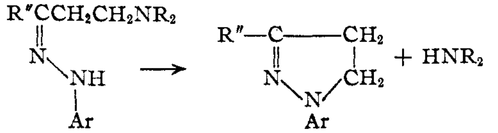
B. $R'NR_2 + HB \longrightarrow R'B + HNR_2$

1. 

$HB = HNR_2''$

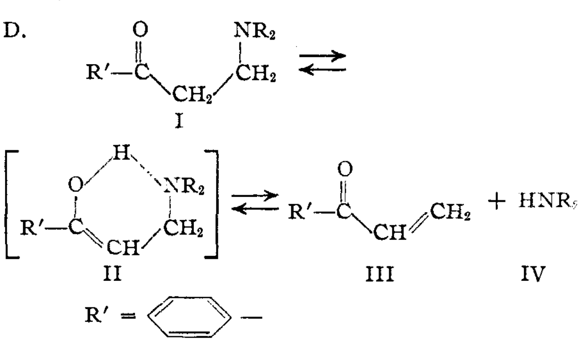
2. 

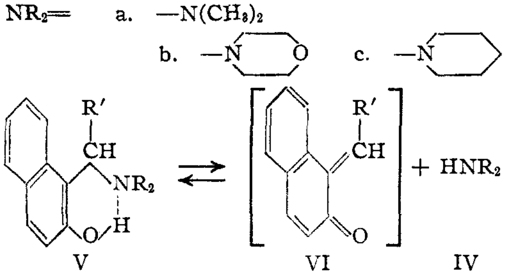
$HB = H_2C(CO_2Et)_2\quad HCN$, etc.

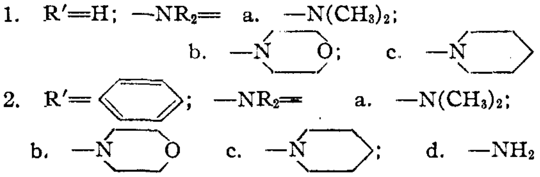
C. 

In common with other β-aminoketones, the Mannich bases of ketones (I) undergo amine elimination reactions to form α,β-unsaturated carbonyl compounds (III).[11] Ammonia and primary and secondary amines add in a 1,4 manner to α,β-unsaturated ketones,[12] perhaps by way of a six-membered chelate ring intermediate (II) such as that suggested by Cromwell and Cram.[13] This intermediate could also participate in amine elimination reactions; if so, bimolecular amine exchange reactions would be expected to occur readily with ketonic Mannich bases (eqn. D).

o-Aminomethylphenols (V) are essentially enolic forms of ketonic Mannich bases. The phenolic hydrogen atom appears to be bound largely to the nitrogen atom.[14] Amine exchange reactions would be expected to occur with particular ease with such compounds, perhaps by way of a methylene quinone (VI) (eqn. E).

D. 





It was found that β-dimethylaminopropiophenone (Ia) reacts with boiling morpholine (IVb) to form β-morpholinopropiophenone (Ib) and dimethylamine (IVa). The hydrochloride and methiodide of Ia reacted only a little more rapidly with morpholine than did the tertiary amine (Ia).

Similarly, α-dimethylaminomethyl-β-naphthol (V 1a) reacted by amine exchange with morpholine and with piperidine (IVc). The morpholine and piperidine Mannich bases of β-naphthol (V 1b and V 1c) could be converted one to the other by reaction with an excess of the appropriate secondary amine.

The Betti bases (V 2) formed by condensation of β-naphthol with benzaldehyde and ammonia or dimethylamine likewise reacted by amine exchange with morpholine and with piperidine.

Good yields of pure products were obtained in all cases when one of the secondary amines was present in large excess or when dimethylamine or ammonia was removed from the mixture by volatilization. Side reactions and resin formation were not observed, even when no inert gas was passed through the system.

Experimental

Ketonic Mannich Bases (Ia, Ib).—The hydrochlorides of β-dimethylaminopropiophenone (Ia)[15] and β-morpholinopropiophenone (Ib)[16] were prepared from acetophenone, paraformaldehyde and the appropriate secondary amine hydrochloride. The thrice-distilled,[17] free tertiary amines had the following properties. Ia: n^{20}_D 1.5299; d^{20}_4 1.017;[18] *RMD* calcd. 53.34; *RMD* found, 53.82; b. p. 94–97° (7 mm.), 83–87° (1–2 mm.) [lit.[15] 110–112° (14 mm.)]; hydrochloride, m. p. 156°.[15,19] Ib: n^{20}_D 1.5433; d^{20}_4 1.103[18]; *RMD* calcd. 62.73; *RMD* found 62.02; b. p. 83° (1.5 mm.); hydrochloride, m. p. 177°.[16]

Reactions of β-Dimethylaminopropiophenone and its Salts with Morpholine.—β-Dimethylaminopropiophenone (Ia) (0.18 g., 0.001 mole) was heated with morpholine (4.35 g., 0.050 mole) under reflux in an atmosphere of nitrogen for two hours. Water (10 ml.) and 10% sodium

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[11] Blicke, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 303.

[12] Cromwell, *Chem. Revs.*, **38**, 83 (1946).

[13] Cromwell, and Cram. THIS JOURNAL, **65**, 301 (1943).

[14] Decombe, *Compt. rend.*, **197**, 258 (1933); German Patent 89,979; *Frdl.*, **4**, 98 (1899).

[15] Mannich and Heilner, *Ber.*, **55**, 356 (1922).

[16] Harradence and Lions, *J. Proc. Roy. Soc. N. S. Wales*, **72**, 233, 273, 284 (1939) [*C. A.*, **33**, 5855, 6841, 6825 (1939)].

[17] A distillation flask with a wide side-arm (10 mm.) set near the bulb was used.

[18] Fischer-Davidson Gravitometer.

[19] All melting points are corrected.

hydroxide (1 ml.) were added to the cooled solution, and the mixture was extracted with three 5-ml. portions of ether. The ether solution was dried over magnesium sulfate, filtered and treated with dry hydrogen chloride. The white precipitate was collected by filtration and crystallized from alcohol–ether to yield the hydrochloride of β-morpholinopropiophenone (Ib); weight 0.20 g. (78%), m. p. 175–176°. No melting point depression occurred when this material was mixed with authentic Ib hydrochloride; marked melting point depressions (20–30°) occurred when it was mixed with the hydrochloride of Ia or with morpholine hydrochloride.

β-Dimethylaminopropiophenone (Ia) hydrochloride (0.22 g., 0.001 mole) was heated with morpholine (4.35 g., 0.050 mole) for one and one-half hours. The reaction mixture was worked up as described above to yield the hydrochloride of Ib, weight 0.20 g. (78%), m. p. 175–177°.

The methiodide of Ia (0.32 g., 0.001 mole) was heated with morpholine (4.35 g., 0.050 mole) under nitrogen. The reaction appeared to be complete after an hour. The hydrochloride of Ib, 0.21 g. (81%), m. p. 175–176°, was isolated from the reaction mixture as described above.

Phenolic Mannich Bases (V 1).—The Mannich bases of β-naphthol (V 1) form rapidly in good yield when one equivalent of 38% formalin is added to a solution of equivalent amounts of β-naphthol and a secondary amine in water or alcohol. The following were prepared: α-dimethylaminomethyl-β-naphthol (V 1a), yield 80%, m. p. 76.0–76.5°;[14] α-piperidinomethyl-β-naphthol (V 2c), yield 73%, m. p. 93–94°;[14,20] and α-morpholinomethyl-β-naphthol (V 1b), yield 90%, m. p. 116.5–117.0°.[21]

Amine Exchange Reactions of Naphthol Mannich Bases (V 1).—α-Dimethylaminomethyl-β-naphthol (V 1a) (1 g. 0.005 mole) was heated under reflux with an excess of a secondary amine (0.025 mole) until the evolution of dimethylamine had ceased (about one hour). A slow stream of nitrogen was passed through the system to sweep out the dimethylamine formed by the reaction. Water (5 ml.) was added to the cooled residue, and the solid which precipitated was crystallized from alcohol. The products were identified by melting point and mixed melting point.

With piperidine as the secondary amine, 1.12 g. (92%) of α-piperidinomethyl-β-naphthol (V 1c), m. p. 93–94°, was obtained.

With morpholine as the secondary amine, 1.0 g. (83.5%) of α-morpholinomethyl-β-naphthol (V 1b), m. p. 116.5–117.0°, was obtained.

α-Morpholinylmethyl-β-naphthol (V 1b) (0.24 g., 0.001 mole) was heated under reflux for two hours with piperidine (0.42 g., 0.005 mole). Water was added to the cooled solution, and the solid which precipitated was crystallized once from alcohol. Pure α-piperidinomethyl-β-naphthol (V 1c), 0.12 g. (50%), m. p. 94–95°, was so obtained.

Similarly, α-piperidinomethyl-β-naphthol (V 1c) (0.24 g., 0.001 mole) was heated with morpholine (0.44 g., 0.005 mole). The product obtained by addition of water to the solution melted at 102–107°. A small amount of α-morpholinomethyl-β-naphthol (V 1b), m. p. 116–117°, the more soluble of the two Mannich bases, was obtained in pure state by fractional crystallization of the crude product from 50% ethanol.

Betti Bases (V 2).—The method of "Organic Syntheses"[22] was used in the preparation of 1-α-aminobenzyl-2-naphthol (V 2d). This material melted sharply at 113–114° (lit.[22] 125°); its melting point was not raised by seven recrystallizations from ether, nor by repeated crystallization from benzene–petroleum ether. The amine formed a hydrochloride, m. p. 190° (dec.), and a benzaldehyde condensation product, m. p. 144–145°, both of which were identical with intermediates in the preparation.[22] The acetamido derivative prepared from the amine by use of acetic anhydride and the product formed by condensation of benzaldehyde, β-naphthol and acetamide were identical and melted at 223–225° (lit. 236°).[23] The method of Littman and Brode[24] was used in the preparation of 1-α-dimethylaminobenzyl-2-naphthol (V 2a), m. p. 163–164° (lit.[24] 164–165°), 1-α-piperidinobenzyl-2-naphthol (V 2c), m. p. 198–199° (lit.[24] 198–198.5°), and 1-α-morpholinobenzyl-2-naphthol (V 2b). The last-named compound has not previously been prepared. A solution of morpholine (8.7 g., 0.1 mole), β-naphthol (14.4 g., 0.1 mole) and benzaldehyde (10.6 g., 0.1 mole) in ethanol (12 ml.) was let stand for two days. The solid which separated was thrice crystallized from benzene–petroleum ether to yield 28.0 g. (88%) of coarse white crystals of V 2b, m. p. 176.5–177.0°.

Anal.[25] Calcd. for $C_{21}H_{21}NO_2$: C, 78.97; H, 6.63; N, 4.39. Found: C, 78.89; H, 6.85; N, 4.30.

Amine Exchange Reactions of Betti Bases (V 2).—A solution of 1-α-aminobenzyl-2-naphthol (V 2d) (0.29 g., 0.001 mole) and morpholine (0.44 g., 0.005 mole) in xylene (2 ml.) was heated under reflux for four hours. When the evolution of ammonia had ceased, the solution was cooled and high-boiling petroleum ether (10 ml.) was added to it. 1-α-Morpholinobenzyl-2-naphthol (V 2b) crystallized slowly from the solution. There was obtained 0.31 g. (87.5%) of the tertiary amine, m. p. 175–176°.

Similar results were obtained when 1-α-dimethylaminobenzyl-2-naphthol (V 2a) was heated with morpholine in xylene. 1-α-Piperidinobenzyl-2-naphthol (V 2c) was formed when either V 2d or V 2a was heated with piperidine in xylene.

Summary

Ketonic and phenolic Mannich bases react with secondary amines by amine exchange. The process is reversible and occurs without appreciable side reactions. The mechanism of this reaction appears to be analogous to that of other amine replacement reactions of Mannich bases.

URBANA, ILLINOIS RECEIVED JULY 26, 1948

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[20] Auwers and Dombrowski, *Ann.*, **344**, 280 (1906).

[21] Shriner, Grillot and Teeters, THIS JOURNAL, **68**, 946 (1946).

[22] Betti, "Organic Syntheses," Coll. Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 303.

[23] Betti, *Gazz. chim. ital.*, **331**, 5 (1903).

[24] Littman and Brode, THIS JOURNAL, **52**, 1655 (1930).

[25] Microanalyses by Miss Emily Davis and Mr. Howard Clark.