The solution was found to contain 0.71 millimole of total nitrogen and 0.73 millimole of primary amino nitrogen. Thus, of the original nitrogen, 11% was evolved as ammonia, and all that remained in the hydrolysate (85%) was as primary amino nitrogen (87%).

A second sample of 200 mg. (0.80 millimole) of the cyanocinnamic acid (I) was treated in the same way. After 0.33 millimole, 41%, of the original nitrogen had been evolved as ammonia, the hydrolysate contained 0.47 millimole, 59%, total nitrogen and 0.47 millimole, 59%, primary amino nitrogen. The acid lactam (III) gave no primary amino nitrogen with the analytical procedure used.

BERKELEY, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF ORGANIC CHEMISTRY, SHARP AND DOHME, INC.]

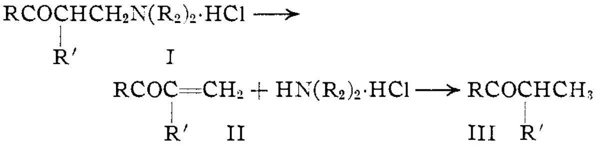
A Convenient Deamination of β-Dialkylamino Ketones

BY EVERETT M. SCHULTZ AND JOHN B. BICKING

RECEIVED OCTOBER 24, 1952

It has been found that β-*t*-amino ketone hydrochlorides of the type prepared by the Mannich reaction are deaminated by hydrogen over Raney nickel. The products are an amine and a ketone having the same carbon skeleton as the Mannich base.

As is well known, the hydrochloride of a Mannich base (I) may be decomposed into an unsaturated ketone (II) and an amine by steam distillation or dry distillation.[1,3] The reduction of the unsaturated ketone so obtained leads to the next higher homolog (III) of the ketone used in the Mannich reaction.[2,3] This procedure may be used in synthesis to lengthen the carbon chain of a ketone.[2] It is also useful to prove the structures of Mannich bases since from the structure of the homologous ketone, which usually is readily determined, the structure of the Mannich base can be deduced easily.



$$\underset{\underset{R'}{|}}{\mathrm{RCOCHCH_2N(R_2)_2{\cdot}HCl}}\ \longrightarrow\ \text{I}$$

$$\underset{\underset{R'}{|}}{\mathrm{RCOC{=}CH_2}}\ \text{II} + \mathrm{HN(R_2)_2{\cdot}HCl} \longrightarrow \underset{\underset{R'}{|}}{\mathrm{RCOCHCH_3}}\ \text{III}$$

The process of decomposing the β-amino ketone by steam distillation is frequently tedious especially with compounds producing ketones of high molecular weight which have a low volatility with steam. Furthermore, much of the vinyl ketone (II) that is produced may be lost through polymerization during the distillation.[3] In addition, a second step, hydrogenation, is still required in order to obtain the homologous ketone (III). Hence, the procedure is time consuming and the yields may be low.

A simple, one-step method of degradation that provides a good yield of the homologous ketone (III) from a Mannich base has been found in this Laboratory. In this process, a solution or suspension of the hydrochloride of the amino ketone in absolute alcohol is submitted to hydrogenolysis over Raney nickel at a pressure of 60–100 atmospheres and a temperature of 80°. One mole of hydrogen per mole of amino ketone is absorbed at a moderate rate and then the consumption of hydrogen ceases. Of course, if the Mannich base contains an olefinic double bond (*e.g.*, M, Table I), additional hydrogen is required. The other product of the reaction, in addition to the homologous ketone (III), is the hydrochloride of the secondary amine used in the preparation of the Mannich base. The reaction mixture when freed of catalyst occasionally was colorless but usually was green due to dissolved nickel compounds. In any event, the color was removed readily in the subsequent purification. The ketones obtained were colorless, possessed very sharp boiling points and yielded derivatives that reached a maximum melting point after one recrystallization. Hence, the products were apparently very pure.

TABLE I

MANNICH BASES (I)

No.	Formula
A[13]	$\underset{\mathrm{CH_2N(CH_3)_2{\cdot}HCl}}{\mathrm{C_6H_5\underset{|}{C}HCOCH_3}}$

$\mathrm{C_6H_5C(R)(R_1)COCH(R_2)CH_2Am{\cdot}HCl}$

	R	R_1	R_2	Am
B	H	Methyl	H	Dimethylamino
C	H	Ethyl	H	Dimethylamino
D	H	*n*-Propyl	H	Dimethylamino
E	H	*n*-Propyl	H	1-Piperidyl
F	H	Isopropyl	H	Dimethylamino
G	H	Benzyl	H	Dimethylamino
H	H	Phenyl	H	Dimethylamino
I	H	Phenyl	Methyl	Dimethylamino
J	Benzyl	Phenyl	H	Dimethylamino

$\mathrm{RCOCH_2CH_2Am{\cdot}HCl}$

	R	Am
K	Phenyl	Dimethylamino[1]
L	*m*-Hydroxyphenyl	Dimethylamino
M	Styryl	Diethylamino[12]
N	*p*-Methoxyphenyl	Dimethylamino[3]

Fourteen Mannich bases having a variety of structures (Table I) were submitted to the degradation and in all cases deamination occurred and a good yield of the homologous ketone (III) was obtained. The age of the Raney nickel catalyst employed or the use of catalyst from different preparations did not influence the result of the reaction. Therefore, the procedure appears to have general application.

The amino ketones used in this work are listed in Table I. The homologous ketones derived

---

[1] C. Mannich and G. Heilner, *Ber.*, **55**, 356 (1922).

[2] F. F. Blicke, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., p. 322.

[3] C. Mannich and D. Lammering, *Ber.*, **55**, 3510 (1922).

TABLE II

HYDROGENOLYSIS OF MANNICH BASES (I)

Mannich base no.[12,13]	Product	Yield, %	B.p. or m.p. °C.	Mm.	$n^{25}\text{D}$	Derivative, m.p., °C.			Reference
							Found	Reported	
IA	$C_6H_5CH(CH_3)COCH_3$	56	107	22	1.5091	Smc.[a]	169–170	172–173[b]	4a,b,c
			104	18					
B	$C_6H_5CH(CH_3)COC_2H_5$	73	106–107	14	1.5030	Smc.	135–136	136	5
C	$C_6H_5CH(C_2H_5)COC_2H_5$	70	113–114	13	1.5000	Smc.	139–140	139–140	4a
D	$C_6H_5CH(n\text{-}C_3H_7)COC_2H_5$	72	125	14	1.4961	Smc.	122–123[c]	108–109	6
E		86							
F	$C_6H_5CH(i\text{-}C_3H_7)COC_2H_5$	96	118–119	14[d]	1.4943	Smc.[e]	172–173	.....	
						Smc.	204–206[f]	215–216	
G	$C_6H_5CH_2CH(C_6H_5)COC_2H_5$	80	123–124	1.5	1.5548	Ox.	102–103	106–107	6
						Dnp.	124–125	.....	
H	$(C_6H_5)_2CHCOC_2H_5$	72	125–127	1.5	....	Smc.	189–190	189–190	7
			M. 35–36						
I	$(C_6H_5)_2CHCO(i\text{-}C_3H_7)$	51	M. 72–73	..	....		.....		8
J	$C_6H_5CH_2C(C_6H_5)_2COC_2H_5$	57	167–170	1[g]	....		.....		
			M. 72–30						
K	$C_6H_5COC_2H_5$	86	108–110	21	1.5243	Dnp.	189–190	187–189	9
L	$m\text{-}OH\text{–}C_6H_4\text{–}COC_2H_5$	74	M. 75–77[h]		....		.....		10
M	$C_6H_5CH_2CH_2COC_2H_5$	79	130–131	18	1.5068		.....		11
N	$p\text{-}CH_3OC_6H_4COC_2H_5$	73	151–152	16		Smc.	170–171	176	3

[a] Smc. = semicarbazone; Dnp. = 2,4-dinitrophenylhydrazone; Ox. = oxime. [b] Structure verified by mixed m.p. with semicarbazone (m.p. 169–170°) of an authentic sample of the ketone.[4c] [c] The semicarbazone of the ketone from IE first melted at 106–109°. Inoculation with the semicarbazone m.p. 122–123° raised m.p. to 122–123°. [d] *Anal.* Calcd. for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.97; H, 9.60. [e] *Anal.* Calcd. for $C_{14}H_{21}N_3O$: N, 16.99. Found: N, 16.88. [f] Structure verified by mixed melting points of semicarbazone, oxime and 2,4-dinitrophenylhydrazone with authentic samples of these derivatives of 4,5-diphenyl-3-pentanone prepared from α,β-diphenylpropionitrile and ethylmagnesium bromide.[6] [g] *Anal.* Calcd. for $C_{23}H_{22}O$: C, 87.86; H, 7.06. Found: C, 87.79; H, 7.02. [h] We are indebted to Dr. E. L. Engelhart for an authentic sample of *m*-hydroxypropiophenone prepared by the procedure of Hartung, *et al.*,[10] and for the sample of β-dimethylamino-*m*-hydroxypropiophenone used in this work.

from them were identified by their physical properties and by the melting points of their derivatives. In some cases, where the melting points of the derivatives of the ketones did not agree with the published values, the ketone was prepared by an unequivocal method and the derivatives of both preparations were demonstrated to be identical by melting points and mixed melting points. Details of this work are summarized in Table II.

Experimental[14]

All of the deaminations were carried out in the same manner and may be illustrated by this example.

Deamination of 4-Dimethylamino-1,1-diphenyl-2-butanone Hydrochloride (IH).—The hydrochloride (IH) (30.3 g., 0.1 mole) was suspended in absolute ethanol (150 ml.) and Raney nickel in absolute alcohol (1/4 teaspoonful) was added. The mixture was sealed into a stainless-steel lined hydrogenation autoclave. Hydrogen was admitted to a pressure of 1180 p.s.i. and the autoclave was rocked for about three minutes to saturate the solvent with hydrogen. The temperature then was raised to 80° and rocking was resumed. Hydrogen absorption commenced at once and ceased after 2.5 hours when 0.1 mole of hydrogen had been used. After removal of the catalyst by filtration, the alcohol was evaporated on a steam-bath. The residue on cooling consisted of a mixture of a dark oil and white crystals of dimethylamine hydrochloride, water was added to dissolve the amine salt and the oil was extracted with ether. The greenish-brown ether layer was washed with 5% hydrochloric acid and with 5% sodium hydroxide solution whereupon the color was extracted to the aqueous phase and the ether layer became pale yellow. After drying the latter over sodium sulfate, the ether was evaporated and the residue was distilled.

WEST POINT, PENNSYLVANIA

---

(4) (a) M. Tiffeneau and J. Levy, *Bull. soc. chim.*, [4] **33**, 767 (1923); *C. A.*, **17**, 3029 (1923); (b) M. Tiffeneau and A. Orechoff, *ibid.*, [4] **29**, 817 (1921); *C. A.*, **16**, 1232 (1927); (c) C. M. Suter and A. W. Weston, THIS JOURNAL, **64**, 535 (1942).

(5) M. Tiffeneau, *Ann. chim.*, [8] **10**, 364 (1907); [8] **11**, 144 (1907).

(6) J. Levy and P. Jullien, *Bull. soc. chim.*, [4] **45**, 942 (1929); *C. A.*, **24**, 1104 (1930).

(7) (a) A. McKenzie and R. Roger, *J. Chem. Soc.*, 2154 (1924); (b) N. Maxim, *Ann. chim.*, **9**, 55 (1928); *C. A.*, **22**, 2153 (1928); *Compt. rend.*, **18**, 2393 (1926); *C. A.*, **20**, 2997 (1926).

(8) M. Tiffeneau and A. Orechoff, *Bull. soc. chim.*, **33**, 195 (1923); *C. A.*, **18**, 71 (1924).

(9) (a) O. Wallach, *Ann.*, **332**, 317 (1904); (b) T. Thomas and T. S. Stevens, *J. Chem. Soc.*, 2611 (1932).

(10) W. H. Hartung, J. C. Munch, E. Miller and F. Crossley, THIS JOURNAL, **53**, 4154 (1931).

(11) C. Harries and G. H. Müller, *Ber.*, **35**, 969 (1902).

(12) C. Mannich and M. Schütz, *Arch. Pharm.*, **265**, 684 (1927); *C. A.*, **22**, 963 (1928).

(13) For preparation of compounds A through J, see E. M. Schultz, J. B. Bicking and J. M. Sprague, to be published.

(14) All boiling points and melting points are uncorrected.