concentration of *aci* form present in these mixtures and the rate equation should be expressed in the form

$$\text{rate} = k_2[aci]\,[\text{methylenebisamine}]$$

or

$$\text{rate} = k_2K_e[\text{nitro}]\,[\text{methylenebisamine}]$$

where K_e is the equilibrium constant for the nitro-*aci* interconversion. That the inhibiting effect of base is not due entirely to dielectric effects is shown by the runs in excess triethylamine which fell below the curve in Fig. 1 and 2.

Synthesis and Study of Mannich Bases from 2-Naphthol and Primary Amines[1]

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Several 1-alkylaminomethyl-2-naphthols (III) were prepared from the corresponding naphthoxazines (I). These new Mannich bases (III) were found to undergo self-condensation with great ease in warm ethanol to form mainly either *N*,*N*-bis(2-hydroxy-1-naphthylmethyl)alkylamines (II) or the original naphthoxazine along with bis(2-hydroxy-1-naphthyl)methane. The course of the reaction depended largely on the structure of the primary amine used in the synthesis of I.

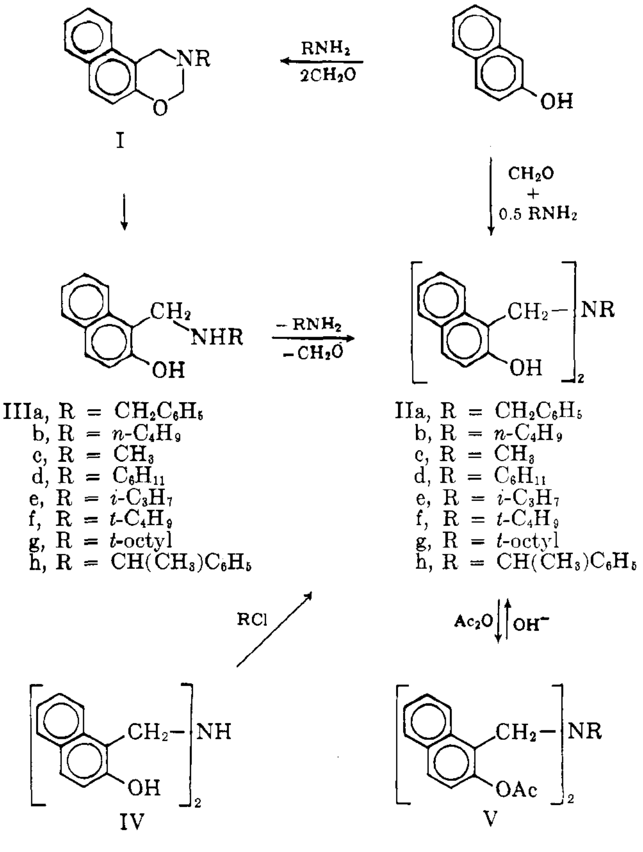
Mannich bases have been used widely as synthetic intermediates.[4,5] Work in this laboratory[6,7] on phenolic Mannich bases derived from primary amines has shown the importance of several reaction variables on the course of the condensation. These included the nature and position of substituents on the phenol, reactant ratios, temperature, and the basicity of the amine.

Marked differences in behavior also were found between phenols and naphthols. For example, phenols having a free *ortho* or *para* position reacted readily with equimolar quantities of formaldehyde and primary amines to form Mannich bases. However, use of 2-naphthol in place of the phenol led to a 2-substituted 2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazine (I) or the corresponding *N*,*N*-bis(2-hydroxy-1-naphthylmethyl)amine (II) depending on the particular amine and temperature employed.[6]

Hydrochlorides of Mannich bases (III) from 2-naphthols and primary amines were obtained indirectly, however, by the acidic hydrolysis of naphth[1,3]oxazines.[6] In the present study, neutralization of the Mannich base (IIIa) hydrochloride from benzylamine resulted in a solid product which upon recrystallization from warm ethanol did not give the corresponding free base but rather a good yield of *N*,*N*-bis(2-hydroxy-1-naphthylmethyl)benzylamine. This result was of particular interest since earlier attempts[6] to prepare the latter compound (IIa) by direct condensation of 2-naphthol with formaldehyde and benzylamine in the calculated 2:2:1 molar ratio led to an 86% yield of the corresponding naphthoxazine (Ia).

The structure of IIa was confirmed by an independent synthesis involving the condensation of benzyl chloride with *N*,*N*-bis(2-hydroxy-1-naphthylmethyl)amine (IV) and also by the synthesis of a diacetate (V). The latter was reconverted to IIa upon saponification.

The ease with which the self-condensation of IIIa occurs is rather surprising in view of the comparative stability of naphtholic Mannich bases from secondary amines although the structure of the latter would, of course, preclude an analogous reaction.



I

IIIa, R = $CH_2C_6H_5$
b, R = n-C_4H_9
c, R = CH_3
d, R = C_6H_{11}
e, R = i-C_3H_7
f, R = t-C_4H_9
g, R = t-octyl
h, R = $CH(CH_3)C_6H_5$

IIa, R = $CH_2C_6H_5$
b, R = n-C_4H_9
c, R = CH_3
d, R = C_6H_{11}
e, R = i-C_3H_7
f, R = t-C_4H_9
g, R = t-octyl
h, R = $CH(CH_3)C_6H_5$

IV

V

It was found possible to prepare the crystalline free Mannich base (IIIa) in high yield (94%), however, by neutralizing an aqueous suspension of the corresponding hydrochloride with 2-aminoethanol in the presence of ether at 0° and removing the ether under reduced pressure with cooling. The free base (IIIa) was readily converted to *N*,*N*-bis(2-hydroxy-1-naphthyl)benzylamine (IIa) in 83% yield when an ethanol solution was warmed to 60° for 5 min.

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[3] Abstracted in part from a thesis submitted by W. A. Nasutavicus to the Graduate School of the University of Utah in partial fulfillment of the requirements for the degree of Master of Arts.

[4] F. F. Blicke, *Org. Reactions*, **1**, 303 (1942).

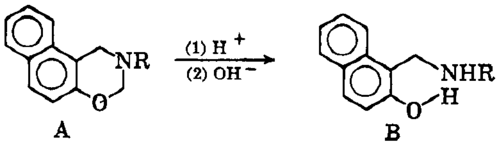
[5] J. H. Brewster and E. L. Eliel, *ibid.*, **7**, 99 (1953).

[6] W. J. Burke, M. J. Kolbezen, and C. W. Stephens, *J. Am. Chem. Soc.*, **74**, 3601 (1952).

[7] W. J. Burke, R. P. Smith, and C. Weatherbee, *ibid.*, **74**, 602 (1952); W. J. Burke, K. C. Murdock, and Grace Ek, *ibid.*, **76**, 1677 (1954); W. J. Burke, C. R. Hammer, and C. Weatherbee, *J. Org. Chem.*, **26**, 4403 (1961).

TABLE I

3-SUBSTITUTED 1*H*-2,3-DIHYDRONAPHTH[1,2-*e*][1,3]OXAZINES AND 1-SUBSTITUTED AMINOMETHYL-2-NAPHTHOLS



Structure	R	Yield, %	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Amine · HCl M.p., °C.	Amine · HCl Chlorine, % Calcd.	Amine · HCl Chlorine, % Found
A	$CH(CH_3)_2$	70		$C_{15}H_{17}NO$					183–184^{a,b}	13.44	13.40
A	$C(CH_3)_3$	97	75–76^{c}	$C_{16}H_{19}NO$	79.63	79.59	7.94	7.75	204–205^{d}	12.76	12.75
A	$CH(CH_3)C_6H_5$	90	75–76^{e}	$C_{20}H_{19}NO$	83.00	82.84	6.62	6.66	180–182^{b}	10.88	10.82
A	C_6H_{11}	64^{f}	43–44^{c}	$C_{18}H_{21}NO$	80.86	80.90	7.92	8.26	178–179^{l}		
A	*t*-Octyl	85	84–85^{d}	$C_{20}H_{27}NO$	80.76	80.99	9.15	9.07			
B	$CH_2C_6H_5$	94	55–56^{g}	$C_{18}H_{17}NO$	82.10	82.59	6.51	6.65			
B	C_6H_{11}	100	82–84^{g}	$C_{17}H_{21}NO$	79.96	80.00	8.29	8.43	192–193^{m}		
B	$C(CH_3)_3$	90	71–73^{g}	$C_{15}H_{19}NO$	(6.11% N)	(5.92% N)			202–205^{h}	13.34	13.18
B	$CH(CH_3)_2$	90		$C_{14}H_{17}NO$	(4.91% N)	(5.06% N)			180–181^{a,i}	14.08	14.22
B	*t*-Octyl	98	83–84^{c}	$C_{19}H_{27}NO$	79.94	79.95	9.53	9.12	185–187^{j}	11.02	11.05
B	$CH(CH_3)C_6H_5$	100	Oil	$C_{18}H_{19}NO$	81.47	82.15	7.22	7.24	135–137^{k}	11.30	11.11

[a] Isolated and characterized as the hydrochloride. [b] Washed with acetone. [c] Recrystallized from methanol. [d] Recrystallized from 95% ethanol. [e] Recrystallized from dimethylformamide–methanol (1:5). [f] This compound had been reported as an oil. Calcd., for neut. equiv.: 267.4. Found, 270.4. [g] Obtained by treatment of hydrochloride with 2-aminoethanol, not recrystallized. [h] Recrystallized from propanol-1. [i] Recrystallized from ethanol–acetone. [j] Recrystallized from butanol-1–acetone. [k] Recrystallized from acetone containing a trace of water. [l] Lit.[6] m.p. 178–179. [m] Lit.[6] m.p. 192–193.

In view of these results, a study of the stability of other related naphtholic Mannich bases was undertaken. Neutralization of 1-*n*-butylaminomethyl-2-naphthol (IIIb) hydrochloride with 2-aminoethanol at room temperature readily gave the corresponding, previously reported *N*,*N*-bis(2-hydroxy-1-naphthylmethyl)-*n*-butylamine (IIb) in 70% yield. Under similar conditions the Mannich base from methylamine (IIIc) gave an oil which upon treatment with warm methanol deposited the known[6] *N*,*N*-bis(2-hydroxy-1-naphthylmethyl)methylamine (IIc).

1-Cyclohexylaminomethyl-2-naphthol (IIId) was readily obtained in 85% yield upon neutralization of the corresponding hydrochloride at 0°. The product was characterized as the *N*,*O*-diacetyl derivative. When the free base was warmed in ethanol at 35° for several minutes a 65% yield of *N*,*N*-bis(2-hydroxy-1-naphthylmethyl)cyclohexylamine (IId) was obtained along with small amounts of bis(2-hydroxy-1-naphthyl)methane (8%) and 2-cyclohexyl-2,3-dihydro-1*H*-naphth[1,2-*e*]-[1,3]oxazine (18%). The last compound, previously reported[6] as oil, was obtained as a low melting, crystalline solid. Similar results were obtained at 65° except that the yield of the bisamine (IId) was only 37%.

Four new naphthoxazines and the corresponding Mannich base hydrochlorides were prepared by procedures similar to those used earlier[6] in order to study the influence of substituents on the α carbon of the amine on the stability and decomposition path of the free Mannich bases. The condensation of 2-naphthol and formaldehyde with isopropylamine, α-methylbenzylamine, *t*-butylamine, and *t*-octylamine gave the expected naphthoxazines in high yields. These were readily hydrolyzed to the corresponding Mannich base hydrochlorides. Data on these compounds are given in Table I.

Neutralization of 1-isopropylaminomethyl-2-naphthol (IIIe) hydrochloride in the cold led to a low melting solid, which upon treatment with warm ethanol gave an 80% yield of the corresponding tertiary amine (IIe). In another run, addition of concentrated hydrochloric acid to the cold solution shortly after neutralization resulted in a 90% recovery of the Mannich base (IIIe) hydrochloride. This indicates that the low melting solid initially obtained upon neutralization was probably the unstable free Mannich base (IIIe).

In contrast to the results with IIIe, the free base (IIIg) obtained from the neutralization of 1-*t*-octylaminomethyl-2-naphthol hydrochloride was sufficiently stable to withstand several recrystallizations at room temperature from dimethylformamide to which methanol was added. Moreover, when base IIIg was warmed in ethanol for 5 min. at 55°, no *N*,*N*-bis(2-hydroxy-1-naphthylmethyl)-*t*-octylamine (IIg) was isolated. Instead, bis(2-hydroxy-1-naphthyl)methane (73%) and 2-*t*-octyl-1*H*-2,3-dihydronaphth[1,2-*e*][1,3]-oxazine (34%) were obtained in the indicated yields, based on IIIg. The results obtained when the *t*-butyl Mannich base (IIIf) was warmed in ethanol at 55° were analogous to those obtained with the *t*-octyl compound (IIIg) in that bis(2-hydroxy-1-naphthyl)methane and 3-*t*-butyl-2*H*-1,3-dihydronaphth[1,3]oxazine were formed in high yields, and no *N*,*N*-bis(2-hydroxy-1-naphthylmethyl)-*t*-butylamine was isolated. A somewhat smaller amount of oxazine was obtained when IIIg was heated at 50–60° for 24 hr.

When the Mannich base 1-α-methylbenzylaminomethyl-2-naphthol (IIIh) was warmed in ethanol and treated with formaldehyde, the corresponding naphthoxazine and bis(2-hydroxy-1-naphthyl)methane were obtained, but there was no evidence for the formation of *N*,*N*-bis(2-hydroxynaphthylmethyl)-α-methylbenzylamine (IIh).

In carbon alkylations with phenolic Mannich bases derived from secondary amines, methylene quinones have been postulated as intermediates[5] and *o*-quinone methide recently has been prepared.[8] The addition of

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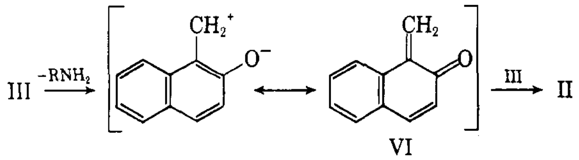
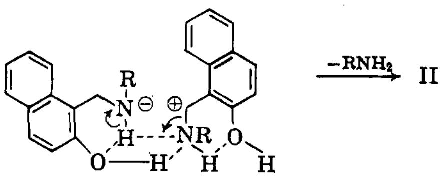
(8) P. D. Gardner, H. Sarrafizadeh, and R. Brandon, *J. Am. Chem. Soc.*, **81**, 5515 (1959).

a Mannich base (III) to an analogous *o*-methylene naphthoquinone intermediate (VI), formed by the elimination of a mole of primary amine from III, would offer a possible route to the formation of *N*,*N*-bis(2-hydroxy-1-naphthylmethyl)amines (II).



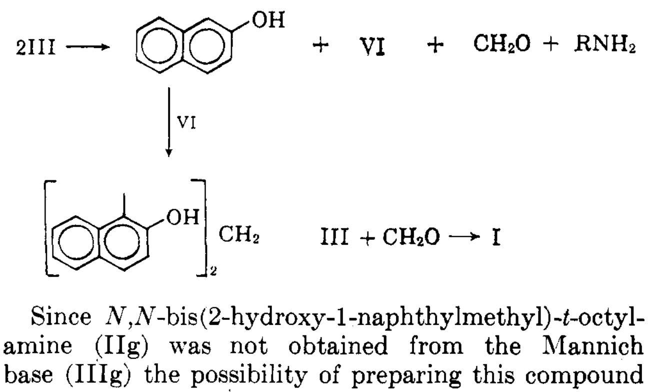
Study of molecular models indicated the excellent opportunities for inter- as well as intramolecular hydrogen bonding of the naphtholic Mannich bases (III). The formation of a dimeric intermediate such as VII would appear to provide an opportunity to facilitate both amine elimination and tertiary amine (II) formation. The possibility of reaction between two molecules of Mannich base with one acting as an acid and another as a base has been pointed out by Brewster and Eliel.[5]



VII

The failure to convert the Mannich bases (III) to the corresponding tertiary amines (II) when R was *t*-butyl, *t*-octyl, or α-methylbenzyl would be consistent with either of the above mechanisms. Bulky R substituents could be expected to discourage either intermolecular hydrogen bonding or the addition of the Mannich base to the *o*-methylene naphthoquinone intermediate (VI).

Phenolic Mannich bases from secondary amines have long been known to undergo self-condensation to form bis(hydroxyaryl)methanes[9] and recently Mannich bases from lawsone were shown to undergo an analogous reaction.[10] It was proposed that the Mannich base reacted first to form lawsone, an *o*-methylene quinone, formaldehyde, and the secondary amine. A similar reaction path with the naphtholic Mannich bases (III) with bulky R substituents would account readily for the formation of bis(2-hydroxy-1-naphthyl)methane and a naphthoxazine.



Since *N*,*N*-bis(2-hydroxy-1-naphthylmethyl)-*t*-octylamine (IIg) was not obtained from the Mannich base (IIIg) the possibility of preparing this compound directly by reaction of *t*-octylamine, formaldehyde, and 2-naphthol in a molar ratio of 1:2:2 at 0° was explored. Even at this low temperature, known to be favorable to the formation of bis(hydroxynaphthyl)amines,[6] a high yield (88%) of the naphthoxazine (I) was obtained. Replacement of *t*-octylamine with *t*-butylamine also led to naphthoxazine formation (47% based on *t*-butylamine), but in addition a high yield of bis(2-hydroxy-1-naphthyl)methane (88% based on available 2-naphthol) was obtained. In neither case was any of the *N*,*N*-bis(hydroxynaphthyl)amine (II) isolated.

Experimental[11]

1-Benzylaminomethyl-2-naphthol (IIIa).—2-Aminoethanol (8 ml.) was added to an agitated suspension of 12.0 g. of IIIa hydrochloride in 200 ml. of water and 300 ml. of ether at 0°. The mixture was stirred at 0° for 10 min. and the small amount of undissolved solid removed by filtration. The ether layer was separated and the aqueous layer extracted with two 100-ml. portions of ether at 0°. The combined ether extracts were concentrated under reduced pressure at 0° and the resulting solid (9.9 g., 94% yield) quickly removed by filtration, washed with ethanol at 0°, and dried at room temperature at 0.1-mm. pressure, m.p. 54–57°

A similar procedure was used to prepare 1-cyclohexylaminomethyl-2-naphthol.

***N*,*N*-Bis(2-hydroxy-1-naphthylmethyl)benzylamine** (IIa). **Procedure A.**—Ethyl ether (300 ml.) and 25 ml. of 2-aminoethanol were added to a suspension of 36 g. of IIIa hydrochloride in 1 l. of water at room temperature. The solid dissolved upon agitation and the ether layer separated. The aqueous layer was extracted twice with ether. Removal of solvent from the combined ether extracts left an oil which was dissolved in 100 ml. of ethanol. Within 15 min. crystallization occurred to yield 14.5 g. (60% yield), m.p. 125–128°; after recrystallization from ethanol, the melting point was 135°.

Procedure B.—1-Benzylaminomethyl-2-naphthol (IIIa, 7 g.) in 75 ml. of 95% ethanol was warmed at 60° for 5 min. and kept at room temperature for 2 days. The white solid (4.52 g., 81% yield) which separated was removed by filtration and washed with cold ethanol, m.p. 131–134°; after recrystallization from ethanol, the melting point was 135–136°.

Procedure C.—Benzyl chloride (2 ml., 0.017 mole) was added to a solution of 2 g. of *N*,*N*-bis(2-hydroxy-1-naphthylmethyl)-amine (0.0057 mole) in 75 ml. of pyridine. After 16 hr. at room temperature the reaction mixture was added with stirring to distilled water. The resulting product (2.5 g., 96% yield) melted at 135–136° after recrystallization from ethanol and did not depress the melting point of the product from procedure A.

***N*,*N*-Bis(2-acetoxy-1-naphthylmethyl)benzylamine.**—Acetic anhydride (2.5 g., 0.03 mole) was added to a solution of 4 g. of IIa (0.013 mole) in 20 ml. of pyridine. After 16 hr. at room temperature, the reaction mixture was poured slowly with agitation into ice and water. The yield of the resulting solid was essentially quantitative; after recrystallization from methanol, the melting point was 170–172°.

Anal. Calcd. for $C_{33}H_{29}NO_4$: C, 78.70; H, 5.80. Found: C, 78.52; H, 5.67.

Treatment of the above ester with a 1% solution of sodium hydroxide in aqueous ethanol at 25° for 3 hr. gave a product which melted at 133–135° and did not depress the melting point of IIa.

***N*,*N*-Bis(2-hydroxy-1-naphthylmethyl)amines** (II).—The following tertiary amines (II) were prepared from the corresponding Mannich bases by a method similar to that described in procedure A for IIa above. The compounds used in the mixture melting point determinations were prepared directly from 2-naphthol as described earlier.[6]

***N*,*N*-Bis(2-hydroxy-1-naphthylmethyl)-*n*-butylamine** (IIb).—The yield was 70%, m.p. and m.m.p. 136–138°, lit.[6] m.p. 137–138°. The **hydrochloride** melted at 135–137°, lit.[6] m.p. 135–137°.

***N*,*N*-Bis(2-hydroxy-1-naphthylmethyl)methylamine** (IIc).—The yield was 59%, m.p. and m.m.p. 146–148°, lit.[6] m.p. 147–

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(9) K. Auwers and A. Dumbrowski, *Ann.*, **344**, 280 (1906).

(10) W. R. Vaughn, M. S. Habib, R. S. McElhinney, N. Takahashi, and J. A. Waters, *J. Org. Chem.*, **26**, 2394 (1961).

(11) All melting points are uncorrected.

148°. The **hydrochloride** melted at 149–151°, lit.[6] m.p. 148–151°.

N,N-**Bis(2-hydroxy-1-naphthylmethyl)isopropylamine** (IIe).—The yield was 83%, m.p. 125–126°, after recrystallization from methanol-1-dimethylformamide (6:1).

Anal. Calcd. for $C_{25}H_{25}NO_2$: C, 80.83; H, 6.75. Found: C, 80.53; H, 6.95.

The **hydrochloride** melted at 163–164°, after recrystallization from methanol.

Anal. Calcd. for $C_{20}H_{26}ClNO_2$: Cl^-, 8.69. Found: Cl^-, 8.73.

Treatment of 1-*t*-Octylaminomethyl-2-naphthol (IIIg) with Hot Ethanol.—1-*t*-Octylaminomethyl-2-naphthol (2.5 g.) was warmed to 50–55° in 30 ml. of 95% ethanol for 5 min. and then kept at room temperature for 2 days. Removal of the solvents under reduced pressure gave an oil which was dissolved in 100 ml. of ether. The resulting solution was extracted with 100 ml. of water containing 2 g. of sodium hydroxide. The ether extract was washed with water and dried over sodium sulfate. Evaporation of the ether gave a solid, m.p. 78–80°. It was recrystallized from 95% ethanol to yield 0.45 g. (34%), m.p. 82–83°; mixture melting point with an authentic sample of 2-*t*-octyl-1*H*-2,3-dihydronaphth[1,2-*e*][1,3]oxazine, m.p. 83–84°, gave no depression.

The aqueous extracts were washed with ether. Upon adding 37% hydrochloric acid to pH 1, a white solid separated. It readily dissolved in ether. Removal of the ether gave 0.95 g. (73% yield) of bis(2-hydroxy-1-naphthyl)methane; melting point and mixture melting point with authentic specimen was 200–202°, lit.[12] m.p. 200°.

The aqueous extracts were neutralized with potassium bicarbonate and extracted with ether. Removal of the ether gave only a trace of oil.

N-**Cyclohexyl**-*N*-**(2-acetoxy-1-naphthylmethyl)acetamide.**—Acetic anhydride (10 g., 0.12 mole) was added to a solution of 4 g. of 1-cyclohexylaminomethyl-2-naphthol (0.016 mole) in 20 ml. of pyridine cooled on an ice bath. After 24 hr. at room temperature, 70 ml. of water was added. Upon cooling 4.8 g. (88% yield) of solid, m.p. 107–108°, separated. The product was recrystallized twice from methanol containing a trace of water, m.p. 108–109°.

Anal. Calcd. for $C_{21}H_{25}NO_3$: C, 74.32; H, 7.42. Found: C, 74.43; H, 7.37.

N-**α-Methylbenzyl**-*N*-**(2-acetoxy-1-naphthylmethyl)acetamide** was prepared from Mannich base by above procedure, 61% yield, m.p. 119–121°, from methanol.

Anal. Calcd. for $C_{23}H_{23}NO_3$: C, 76.43; H, 6.41. Found: C, 76.30; H, 7.00.

N-**α-Methylbenzyl**-*N*-**(2-hydroxy-1-naphthylmethyl)acetamide.**—Hydrolysis of the above ester in 2% potassium hydroxide in 95% ethanol at 25° for 3 hr. gave a product, m.p. 160–160.5°, after two recrystallizations from 95% ethanol.

Anal. Calcd. for $C_{21}H_{21}NO_2$: C, 78.96; H, 6.63. Found: C, 78.77; H, 6.59.

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[12] O. Manasse, *Ber.*, **27**, 2409 (1894).

Amine Exchange Reactions. Mannich Bases from Aromatic Amines[1]

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An exchange reaction occurs readily between tertiary Mannich bases (I) and primary and secondary arylamines, making accessible the monosubstituted arylamine Mannich bases (II and IV) in good yield. The arylamines used include polycyclic and heterocyclic bases as well as diamines. Experiments suggest that the overall amine-exchange reaction may proceed both by a substitution as well as by an elimination–addition mechanism.

A survey of the literature[2] concerning the Mannich reaction, using ketones as the acidic entity, reveals that, although the range of aliphatic amines used is virtually unlimited, the only reported successful condensation using an arylamine is the synthesis, in unstated yield, of 1,2,6-triphenyl-4-piperidone[3] from acetone, benzaldehyde, and aniline. Attempted Mannich reaction[4] between acetophenone, formaldehyde, and aniline hydrochloride failed to give the required β-anilinopropiophenone (IIa), leading instead to the formation of polymeric products derived from the aldehyde and amine.

Only a few isolated examples[5-9] of such condensations have appeared since that observation, and Mannich bases of type II are not readily available and cannot be prepared by the standard Mannich reaction. A number of syntheses of β-arylamino ketones (II) by other routes appear in the literature[10-12] but the methods are usually complex, the starting materials difficultly accessible, and the preparations confined to specific examples and not general in scope.

$R-COCH_2CH_2-NR'_2$	I	a	R = Ph; Ar = Ph
$R-COCH_2CH_2-NHAr$	II	b	R = Me; R′ = Et
$R-COCH_2CH_2-NHR'$	III	c	R = Me; Ar = Ph
		d	R = Ph; R′ = Et
$R-COCH_2CH_2-NMeAr$	IV	e	R = R′ = Me
$Ph-COCHMeCH_2NEt_2$	V	f	R = Ph; Ar = $pClC_6H_4$
$Ph-COCHMeCH_2NHC_6H_4-p-Cl$	VI	g	R = Ph; R′ = Me

It was shown recently[13] that the exchange reaction between tertiary Mannich bases (I) and primary alkyl-

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[1] This work was partially supported by a grant (HE 5881) from the National Institutes of Health, U. S. Public Health Service.

[2] (a) F. F. Blicke, "Organic Reactions," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 303; (b) "Methoden der Organischen Chemie," (Houben-Weyl), Georg Thieme Verlag, Stuttgart, 1957, p. 731; (c) B. Reichert, "Die Mannich Reaktion," Springer Verlag, Berlin, 1960.

[3] P. Petrenko-Kritschenko, *Chem. Ber.*, **42**, 3683 (1909).

[4] F. F. Blicke and J. H. Burckhalter, *J. Am. Chem. Soc.*, **64**, 451 (1942).

[5] L. L. Woods, *ibid.*, **68**, 2744 (1946).

[6] H. G. Johnson, *ibid.*, **68**, 14 (1946).

[7] J. J. Licari, L. W. Hartzel, G. Dougherty, and F. R. Benson, *ibid.*, **77**, 5386 (1955).

[8] K. Bodendorf and M. Raaf, *Ann. Chem.*, **592**, 26 (1955).

[9] R. Maki, Y. Ishida, K. Satake, and R. Oda, *Bull. Inst. Chem. Res. Kyoto Univ.*, **31**, 224 (1953); *Chem. Abstr.*, **48**, 9328 (1954).

[10] A. Collet, *Bull. soc. chim. France*, **17**, 66 (1897).

[11] I. Vavrecka, *Collection Czech. Chem. Commun.*, **14**, 399 (1949).

[12] A. T. Babayan and N. P. Gambaryan, *Izv. Akad. Nauk. Arm. SSR Khim. Nauk*, **3**, 563 (1950).

[13] J. C. Craig, S. R. Johns, and M. Moyle, *J. Org. Chem.*, **28**, 2779 (1963).