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(23) Chambers, R. W., and Kurkov, V., *J. Am. Chem. Soc.*, **85**, 2160(1963).
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(25) Wang, S., *J. Am. Chem. Soc.*, **81**, 3786(1959).
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(27) Fox, J. J., Miller, N. C., and Cushley, R. J., *Tetrahedron Letters*, No. 40, 4927(1966).
(28) Sander, E., personal communication.
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(31) Izatt, R. M., Christensen, J. J., Hansen, L. D., and Watt, G. D., *ibid.*, **87**, 2760(1965).

Keyphrases

5-Halouridines, related nucleosides—solvolysis
Solvolysis—halogen-substituted uridines
UV spectrophotometry—solvolysis monitoring
Paper chromatography—separation
UV light—nucleoside visualization
Bromide ion measurement—bromide ion activity electrode

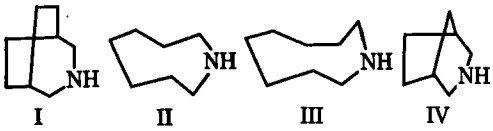
Use of 3-Azabicyclo[3.2.1]octane in the Mannich Reaction

By N. D. POTTI* and W. LEWIS NOBLES

The preparation of a group of ketonic Mannich bases utilizing 3-azabicyclo(3.2.1)-octane as the amine component is described. Also reported are the syntheses of several γ-amino secondary and tertiary alcohols obtained from these Mannich bases by sodium borohydride reduction and the Grignard reaction, respectively. These compounds are being screened for possible pharmacodynamic and chemotherapeutic activity.

AZABICYCLIC RING SYSTEMS are often found in alkaloids, many of which are medicinally useful, *e.g.*, morphine, atropine, *etc.* During the past two decades numerous 3-azabicyclic compounds were synthesized and tested for useful therapeutic activities (1–12). Many of them possessed hypotensive and antibacterial activities.

Nobles and his associates found interesting pharmacological activities associated with derivatives of complex amines like 3-azabicyclo[3.2.2]nonane I (6–8, 12); heptamethyleneimine II (13); and octamethyleneimine III (14).



I II III IV

Certain ketonic Mannich bases derived from such complex amines possessed an unexpected high order of antibacterial activity (15). The object of the present investigation was to extend the study with the complex amine, 3-azabicyclo-[3.2.1]octane (IV). A convenient laboratory method of preparation of this amine is reported elsewhere (16).

Promising pharmacological properties of β-aminoketones prompted several groups of workers to continue their studies with several of the derivatives of β-aminoketones (7–8, 13, 14, 17–19). Among these derivatives were included several γ-amino secondary and tertiary alcohols. In general, these alcohols were reported to be more

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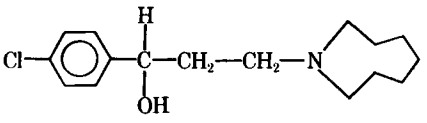
* Present address: Roswell Park Memorial Institute, Buffalo, NY 14203

stable than the corresponding ketones and some of them more active, exhibiting additional pharmacological properties. Luts and Nobles (13) reported remarkable analgesic activity for 1-(*p*-chlorophenyl)-3-(1-heptamethyleneimino)-1-propanol (V), the corresponding ketone having no such activity.



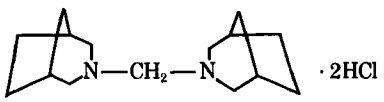
V

In this paper the preparation of a number of β-aminoketones and several γ-aminoalcohols is reported.

DISCUSSION

The β-aminoketones synthesized in this study are listed in Table I. These compounds have been prepared by the well-known Mannich reaction (20). The appropriately substituted aromatic ketone, paraformaldehyde, and 3-azabicyclo[3.2.1]octane hydrochloride reacted to give very good yields of the desired product.

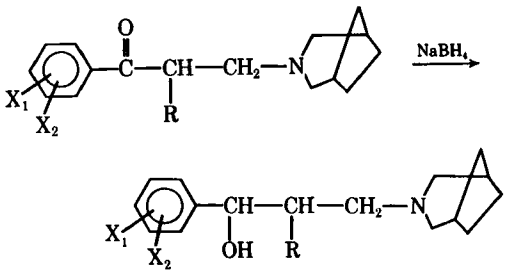
Under the general conditions described in the experimental section, 4-methylpropiophenone did not give the expected β-aminoketone, but resulted in the formation of the methylenebisamine dihydrochloride (VI). Similar observation was reported by Varma and Nobles (21) while attempting the Mannich reaction of indan-1,3-dione using 3-azabicyclo[3.2.2]nonane.



VI

Despite the extensive studies, the mechanism of this reaction is not conclusive. The mechanistic aspect has been dealt with in a recent report (22).

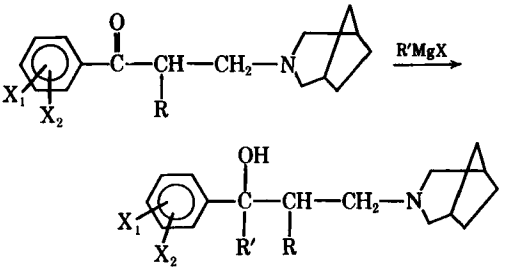
A selected group of β-aminoketones in Table I was reduced to the corresponding γ-amino secondary alcohol. The reduction was effected by treating a methanolic solution of the β-aminoketone with a 6% solution of sodium borohydride in methanol (Scheme I).



Scheme I

These compounds were characterized as hydrochlorides and are listed in Table II.

The third group of compounds described in this paper are the γ-amino tertiary alcohols (Table III). These alcohols were synthesized by the Grignard reaction on selected β-aminoketones, using three different Grignard reagents. (Scheme II.)



Scheme II

The reaction has been carried out in anhydrous ether. The compounds were purified as hydrochlorides. In general the yields are fairly good.

EXPERIMENTAL[1]

The β-aminoketones (Table I)—These compounds were prepared by following the method of Nobles and associates (6–8, 13, 14). All of the ketones in this investigation are commercially available.

A mixture of 0.02 mole of the appropriate ketone, 2.95 g. (0.02 mole) of 3-azabicyclo[3.2.1]octane hydrochloride, 0.9 g. (0.03 mole) of paraformaldehyde, and 5 ml. of ethanol (95%) containing a drop of concentrated hydrochloric acid was refluxed for 3 hr. After refluxing, the volume of the mixture was reduced to one half, using the water aspirator. The residue was cooled and stirred with 30 ml. of acetone. The solid thus separated was filtered and recrystallized from ethanol–acetone mixture. The properties are described in Table I.

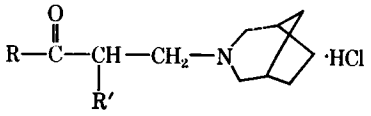
γ-Amino Secondary Alcohol Hydrochlorides (Table II)—The γ-amino secondary alcohols were prepared by the following general method. The appropriate β-aminoketone (0.02 mole) was dissolved in 40 ml. of methanol in a 200-ml. three-necked flask fitted with a condenser, thermometer, dropping funnel, and magnetic stirrer. A solution of 1.52 g. (0.04 mole) of sodium borohydride in 20 ml. of methanol was added to the above with stirring. The temperature of the reaction mixture was maintained between 24–40°, while the stirring was continued for 2 hr. The methanol was removed using water vacuum, and the residue, after the addition of 30 ml. of distilled water, was extracted with three 50-ml. portions of ether. The combined ether extract was washed with 10 ml. of distilled water and dried over anhydrous sodium sulfate. Anhydrous hydrogen chloride was passed through the ether solution to precipitate the aminoalcohol hydrochloride.[2] The precipitate was filtered and recrystallized for ethanol–acetone mixture.

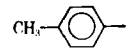
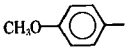
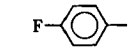
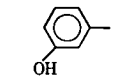
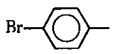
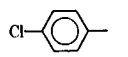
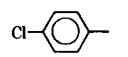
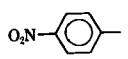
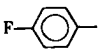
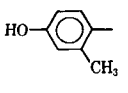
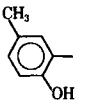
γ-Amino Tertiary Alcohol Hydrochlorides (Table III)—Following the method of Pohland and Sullivan (23), these alcohols were prepared. The com-

[1] All melting points are uncorrected. Melting points were determined on a Thomas-Hoover capillary melting-point apparatus. Infrared spectra were determined on a Perkin-Elmer Infracord spectrophotometer.

[2] Sometimes the precipitate might form a sticky mass, but could be recrystallized from ethanol–acetone mixture.

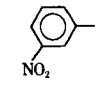
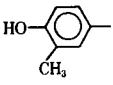
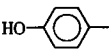
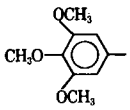
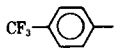
TABLE I—MANNICH BASES (β-AMINO KETONE HYDROCHLORIDES)



No.	R	R′	Yield, %	M.p., °C.[b]	Formula	Anal.[a] Calcd.	Found
1		H	40	198–199	$C_{17}H_{23}NO \cdot HCl$[c]	C, 69.49 H, 8.23 N, 4.77	C, 69.36 H, 8.42 N, 4.66
2		CH_3	77	187–188	$C_{18}H_{25}NO_2 \cdot HCl$[c]	C, 66.75 H, 8.09 N, 4.33	C, 66.74 H, 8.21 N, 4.10
3		CH_3	56	178–179	$C_{17}H_{22}FNO \cdot HCl$[c]	C, 65.48 H, 7.43 N, 4.49	C, 65.56 H, 7.56 N, 4.46
4		H	63	213–214	$C_{16}H_{21}NO_2 \cdot HCl$[c]	C, 64.96 H, 7.50 N, 4.79	C, 64.83 H, 7.49 N, 4.63
5		H	70	198–199	$C_{16}H_{20}BrNO \cdot HCl$[d]	C, 53.50 H, 5.88 N, 3.90	C, 53.58 H, 5.94 N, 3.84
6		CH_3	35	180–181	$C_{17}H_{22}ClNO \cdot HCl$[e]	C, 62.15 H, 7.06 N, 4.27	C, 62.33 H, 7.09 N, 4.08
7		H	48	202–203	$C_{16}H_{20}ClNO \cdot HCl$[c]	C, 61.22 H, 6.74 N, 4.46	C, 61.21 H, 6.70 N, 4.31
8		H	49	177–178	$C_{16}H_{21}NO_2 \cdot HCl$[c]	C, 64.96 H, 7.50 N, 4.74	C, 63.49 H, 7.42 N, 4.50
9		H	51.5	171–172	$C_{17}H_{23}NO_2 \cdot HCl$[e]	C, 65.90 H, 7.81 N, 4.52	C, 66.08 H, 7.79 N, 4.46
10		H	50	200–201	$C_{16}H_{20}BrNO \cdot HCl$[e]	C, 53.57 H, 5.90 N, 3.90	C, 53.78 H, 5.56 N, 3.75
11		H	53	195–196	$C_{16}H_{20}N_2O_3 \cdot HCl$[c]	C, 59.16 H, 6.52 N, 8.63	C, 59.14 H, 6.52 N, 8.39
12		H	52	195–196	$C_{16}H_{20}FNO \cdot HCl$[c]	C, 64.51 H, 7.11 N, 4.71	C, 63.54 H, 7.14 N, 4.81
13		H	53	168–169	$C_{17}H_{23}NO \cdot HCl$[e]	C, 69.50 H, 8.25 N, 4.78	C, 69.70 H, 8.21 N, 4.55
14		H	60	212–213	$C_{17}H_{23}NO_2 \cdot HCl$[c]	C, 65.91 H, 7.75 N, 4.52	C, 65.67 H, 7.77 N, 4.77
15		H	58	188–189	$C_{16}H_{20}N_2O_3 \cdot HCl$[e]	C, 59.16 H, 6.52 N, 8.63	C, 58.94 H, 6.49 N, 8.26
16		H	53	173–174	$C_{14}H_{19}NOS \cdot HCl$[c]	C, 58.82 H, 7.13 N, 4.90	C, 58.80 H, 7.18 N, 4.57
17		H	48	201–202	$C_{17}H_{23}NO_2 \cdot HCl$[c]	C, 65.91 H, 7.75 N, 4.52	C, 65.47 H, 7.85 N, 4.69

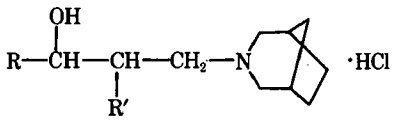
(*Continued on next page.*)

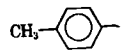
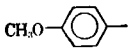
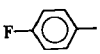
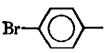
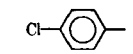
TABLE I (*Continued.*)

No.	R	R′	Yield, %	M.p., °C.[b]	Formula	Anal.[a] Calcd.	Anal.[a] Found
18		H	65	215–216	$C_{16}H_{23}N_2O_3 \cdot HCl$[f]	C, 59.10 H, 6.52 N, 8.62	C, 59.06 H, 6.49 N, 8.55
19		H	55	205–206	$C_{17}H_{23}NO_2 \cdot HCl$[c]	C 65.91 H, 7.75 N, 4.52	C, 65.53 H, 7.88 N, 4.37
20		H	55	195–196	$C_{16}H_{21}NO \cdot HCl$[c]	C, 68.54 H, 7.92 N, 5.0	C, 68.69 H, 8.01 N, 4.88
21		CH_3	48	193–194	$C_{17}H_{23}NO_2 \cdot HCl$[c]	C, 65.91 H, 7.75 N, 4.52	C, 65.93 H, 7.95 N, 4.51
22		H	68	211–212	$C_{19}H_{27}NO_4 \cdot HCl$[d]	C, 61.60 H, 7.63 N, 3.79	C, 60.94 H, 7.44 N, 3.24
23		H	53	204–205	$C_{17}H_{20}F_3NO \cdot HCl$[c]	C, 58.62 H, 6.09 N, 4.03	C, 58.52 H, 6.09 N, 4.31
24		H	50	206–207	$C_{17}H_{20}F_3NO \cdot HCl$[c]	C, 58.62 H, 6.09 N, 4.03	C, 58.45 H, 6.19 N, 3.94
25		H	48	177–178	$C_{17}H_{20}F_3NO \cdot HCl$[e]	C, 58.62 H, 6.09 N, 4.03	C, 58.71 H, 6.07 N, 3.88

[a] Carbon, hydrogen, and nitrogen analyses are through the courtesy of Dr. Paul Craig of Smith Kline & French Laboratories, Philadelphia, Pa. [b] Melting points are uncorrected. [c] Recrystallized from ethanol–acetone mixture. [d] Recrystallized from ethanol. [e] Recrystallized from ethanol–benzene mixture. [f] Recrystallized from ethanol–water mixture.

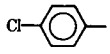
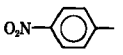
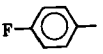
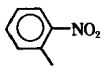
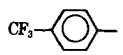
TABLE II—γ-AMINO SECONDARY ALCOHOLS (HYDROCHLORIDE SALTS)[a]



No.[a]	R	R′	Yield, %	M.p., °C.[b]	Formula	Anal.[c] Calcd.	Anal.[c] Found
1		H	68	201–202	$C_{17}H_{25}NO \cdot HCl$	C, 69.02 H, 8.86 N, 4.74	C, 69.08 H, 8.69 N, 4.81
2		CH_3	62	206–207	$C_{18}H_{27}NO_2 \cdot HCl$	C, 66.34 H, 8.66 N, 4.30	C, 66.48 H, 8.63 N, 4.18
3		CH_3	61	227–228	$C_{17}H_{24}FNO \cdot HCl$	C, 65.06 H, 8.03 N, 4.46	C, 65.10 H, 7.91 N, 4.27
4		H	62	209–210	$C_{16}H_{22}BrNO \cdot HCl$	C, 53.27 H, 6.43 N, 3.88	C, 53.17 H, 6.47 N, 3.88
5		H	45	169–170	$C_{16}H_{23}NO_2 \cdot HCl$	C, 64.53 H, 8.12 N, 4.70	C, 64.42 H, 8.02 N, 4.60
6		CH_3	58	254–255	$C_{17}H_{24}ClNO \cdot HCl$	C, 61.51 H, 7.63 N, 4.24	C, 61.52 H, 7.54 N, 6.14

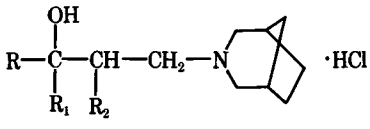
(*Continued on next page.*)

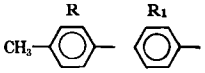
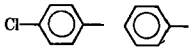
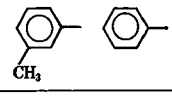
TABLE II (*Continued.*)

No.[a]	R	R′	Yield, %	M.p., °C.[b]	Formula	Anal.[c] Calcd.	Found
7		H	60	195–196	$C_{16}H_{22}ClNO \cdot HCl$	C, 60.76 H, 7.33 N, 4.43	C, 60.75 H, 7.26 N, 4.34
8		H	55	195–196	$C_{17}H_{25}NO_2 \cdot HCl$	C, 65.50 H, 8.41 N, 4.50	C, 65.55 H, 8.33 N, 4.66
9		H	65	177–178	$C_{16}H_{22}BrNO \cdot HCl$	C, 53.27 H, 6.41 N, 3.88	C, 53.39 H, 6.46 N, 4.13
10		H	62	223–224	$C_{16}H_{22}N_2O_3 \cdot HCl$	C, 58.70 H, 7.09 N, 8.56	C, 59.31 H, 7.75 N, 8.47
11		H	58	173–174	$C_{16}H_{22}FNO \cdot HCl$	C, 64.02 H, 7.72 N, 4.67	C, 63.84 H, 7.65 N, 5.05
12		H	69	204–205	$C_{17}H_{25}NO \cdot HCl$	C, 69.02 H, 8.86 N, 4.74	C, 68.91 H, 8.71 N, 4.97
13		H	61	209–210	$C_{16}H_{22}N_2O_3 \cdot HCl$	C, 58.80 H, 7.09 N, 8.56	C, 58.80 H, 6.85 N, 8.46
14		H	70	192–193	$C_{16}H_{23}NO \cdot HCl$	C, 68.19 H, 8.58 N, 4.97	C, 68.07 H, 8.70 N, 5.04
15		H	52	164–165	$C_{17}H_{22}F_3NO \cdot HCl$	C, 58.37 H, 6.62 N, 4.01	C, 58.43 H, 6.60 N, 4.26
16		H	53	221–222	$C_{17}H_{22}F_3NO \cdot HCl$	C, 58.37 H, 6.62 N, 4.01	C, 58.40 H, 6.68 N, 4.07
17		H	48	198–199	$C_{17}H_{22}F_3NO \cdot HCl$	C, 58.37 H, 6.62 N, 4.01	C, 58.12 H, 6.63 N, 4.14

[a] All of these γ-amino secondary alcohol hydrochlorides were crystallized from an alcohol–acetone mixture. [b] Melting points are uncorrected. [c] Carbon, hydrogen, and nitrogen analyses are through the courtesy of Dr. Paul Craig of Smith Kline & French Laboratories, Philadelphia, Pa.

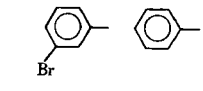
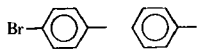
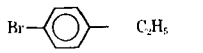
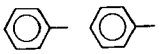
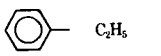
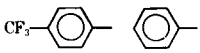
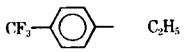
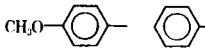
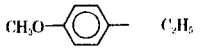
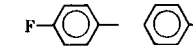
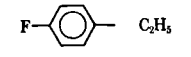
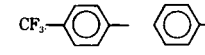
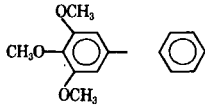
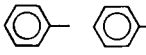
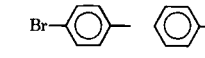
TABLE III—γ-AMINO TERTIARY ALCOHOLS (HYDROCHLORIDE SALTS)[a]



No.[a]	R	R_1	R_2	Yield, %	M.p., °C.[b]	Formula	Anal.[c] Calcd.	Found
1			H	32	247–248	$C_{23}H_{29}NO \cdot HCl$	C, 74.27 H, 8.13 N, 3.76	C, 74.21 H, 8.07 N, 3.75
2			H	43	258–259	$C_{22}H_{26}ClNO \cdot HCl$	C, 67.36 H, 6.94 N, 3.57	C, 66.96 H, 7.16 N, 3.59
3			H	50	229–230	$C_{23}H_{29}NO \cdot HCl$	C, 74.26 H, 8.13 N, 3.76	C, 74.16 H, 8.04 N, 3.78

(*Continued on next page.*)

TABLE III (*Continued.*)

No.[a]	R	R_1	R_2	Yield, %	M.p., °C.[b]	Formula	Anal.[c] Calcd.	Found
4			H	48	241–242	$C_{22}H_{26}BrNO \cdot HCl$	C, 60.48 H, 6.23 N, 3.20	C, 60.30 H, 6.42 N, 3.21
5			H	44	267–268	$C_{22}H_{26}BrNO \cdot HCl$	C, 60.48 H, 6.23 N, 3.20	C, 60.62 H, 6.42 N, 3.04
6			H	43	226–227	$C_{18}H_{26}BrNO \cdot HCl$	C, 55.61 H, 7.00 N, 3.60	C, 55.77 H, 7.20 N, 3.60
7			H	68	247–248	$C_{22}H_{27}NO \cdot HCl$	C, 73.81 H, 7.89 N, 3.91	C, 73.75 H, 8.08 N, 3.93
8			H	72	196–197	$C_{18}H_{27}NO \cdot HCl$	C, 69.78 H, 9.10 N, 4.51	C, 69.65 H, 9.20 N, 4.47
9			H	40	265–266	$C_{23}H_{26}F_3NO \cdot HCl$	C, 64.60 H, 6.39 N, 3.29	C, 64.91 H, 6.59 N, 3.55
10			H	49	225–226	$C_{19}H_{26}F_3NO \cdot HCl$	C, 60.40 H, 7.20 N, 3.70	C, 59.86 H, 7.44 N, 3.46
11			CH_3	51	196–197	$C_{24}H_{31}NO_2 \cdot HCl$	C, 71.70 H, 8.02 N, 3.48	C, 70.12 H, 7.98 N, 3.21
12			CH_3	55	185–186	$C_{20}H_{31}NO_2 \cdot HCl$	C, 67.88 H, 9.11 N, 3.95	C, 68.18 H, 9.20 N, 4.02
13			CH_3	48	228–229	$C_{23}H_{28}FNO \cdot HCl$	C, 70.84 H, 7.49 N, 3.59	C, 70.66 H, 7.56 N, 3.54
14			CH_3	58	207–208	$C_{19}H_{28}FNO \cdot HCl$	C, 66.74 H, 8.55 N, 4.09	C, 66.50 H, 8.56 N, 4.15
15			H	57	240–241	$C_{24}H_{28}F_3NO \cdot HCl$	C, 65.52 H, 6.64 N, 3.18	C, 65.74 H, 6.65 N, 3.30
16			H	28	256–257	$C_{26}H_{35}NO_4 \cdot HCl$	C, 67.60 H, 7.85 N, 3.03	C, 69.52 H, 7.68 N, 2.95
17			H	63	214–215	$C_{23}H_{29}NO \cdot HCl$	C, 74.27 H, 8.13 N, 3.76	C, 74.05 H, 8.04 N, 4.04
18			H	58	247–248	$C_{23}H_{28}BrNO \cdot HCl$	C, 61.26 H, 6.48 N, 3.10	C, 61.08 H, 6.38 N, 2.78

[a] All the aminoalcohol hydrochlorides are crystallized from ethanol–acetone mixture. [b] Melting points are uncorrected. [c] Carbon, hydrogen, nitrogen analyses are through the courtesy of Dr. Paul Craig, Smith Kline & French Laboratories, Philadelphia, Pa.

mercially available "anhydrous" ether was redried by stirring for 5–10 min. with anhydrous magnesium sulfate (one heaping tablespoon per liter) in a stoppered container, using a magnetic stirrer. The anhydrous ether was decanted quickly into the reaction vessel provided with a drying tube containing a mixture of calcium chloride and soda lime.

While phenyl magnesium bromide and ethyl magnesium bromide are available commercially, benzyl magnesium chloride was prepared by following the method of Gilman and Catlin (24). In a 300-ml. dry three-necked flask, fitted with a dropping funnel, a condenser having a drying tube carrying a mixture of calcium chloride and soda lime at the upper end, and a magnetic stirrer, was placed 4.86 g. (0.02 g. atom) of magnesium turnings. To this was added 10 ml. of dry ether. In 100 ml. of dry ether, 25.3 ml. (0.2 mole) of pure benzyl chloride was dissolved.

Five milliliters of this solution was added to the above magnesium turnings-ether mixture. To induce the reaction to begin, a small crystal of iodine was added. The reaction proceeded with development of heat and decolorization of the iodine. The mixture was stirred by means of a magnetic stirrer, and the remainder of the benzyl chloride was added gradually over a period of 30 min., regulating the temperature of the reaction with the aid of an ice water bath. The reagent was used as described in the case of phenyl magnesium bromide.

All of the compounds listed in Table III were prepared by the following general method.

In a 200-ml. round-bottom flask, 0.02 mole of the appropriate aminoketone was dissolved in 75 ml. of anhydrous ether, and the solution was dried with anhydrous magnesium sulfate. Meanwhile, in a dry 300-ml. three-necked flask equipped with dropping funnel, magnetic stirrer, and condenser with drying tube on the upper end, 13.5 ml. of a 3 *M* solution (0.04 mole) of phenyl magnesium bromide and 30 ml. of anhydrous ether was placed. To this, a dry ether solution of the Mannich base as previously prepared, was dropped little by little with vigorous stirring. Stirring was continued for 2 hr., and the mixture was allowed to stand overnight. The reaction flask was cooled in an ice bath. A saturated solution of ammonium chloride was added to decompose the complex. The ether solution was decanted into a separator and washed with 10 ml. of amino-alcohol–ether solution, was filtered, cooled in an ice bath, and dry hydrogen chloride gas was passed through it. The hydrochloride was collected and recrystallized from the alcohol–acetone mixture.

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Keyphrases

Mannich reaction
β-Aminoketones—synthesis
γ-Aminoalcohols—synthesis
3-Azabicyclo[3.2.1]octane—amine component, Mannich reaction

Effect of Sodium Deoxycholate on Gastric Emptying in the Rat

By STUART FELDMAN*, RALPH J. WYNN, and MILO GIBALDI

Sodium deoxycholate delays considerably the gastric emptying of phenol red in rats. Gastric emptying of phenol red in control animals proceeds by apparent first-order kinetics, but a very different kinetic pattern emerges upon administration of the bile salt. Sodium deoxycholate also produces a large net secretion of fluids into the gastric pouch. It is proposed that the resulting increase in gastric volume is the immediate cause for the decreased rate of gastric emptying.

THE EFFECTS of orally administered bile salts on the gastrointestinal absorption of riboflavin (1) and other drugs are currently being investigated in this laboratory. These studies have prompted a consideration of the influence of bile salts on gastric emptying since the rate of passage of drug through the pylorus may have a profound influence on the overall rate and extent of drug absorption (2, 3).

Previous studies (4) have shown that the oral administration of sodium taurodeoxycholate and

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