interpreted as evidence of the formation of a β-glycoside. Since the acetal eventually became hydrolyzed to mannose as shown by the final rotation, it was concluded that the intermediate must have been β-methylmannofuranoside or a mixture of this substance and its α-form. The formation of these intermediates from the acetal proceeded about twenty times faster than the hydrolysis of these intermediates into mannose and methyl alcohol.

Acknowledgment is made to Mr. Richard C. Johnson, a student at the Union Junior College, Roselle, New Jersey, for making the drawings of the models.

Summary

1. By application of the general method of Pacsu and Green to mannosediethylmercaptal prepared directly from α-methylmannopyranoside, crystalline β-methyl, α-ethyl, α-*n*-propyl and α-isopropyl mannofuranosides have been obtained. The β-methylmannofuranoside has been isolated from its crystalline calcium chloride addition compound, $C_6H_{11}O_5OCH_3 \cdot CaCl_2 \cdot 3H_2O$, which was obtained from the mother liquor of the α-methylmannofuranoside. The same calcium chloride compound also has been obtained directly from the reaction products of mannose and methyl alcoholic hydrogen chloride and from the mother liquor of α-methylmannofuranoside prepared according to Haworth and co-workers.

2. It has been found that calcium chloride has a perturbing effect upon the rotation of the β-methylmannofuranoside with which it is combined and therefore it is unsafe to calculate the rotation of a sugar or a sugar derivative from the rotation of its calcium chloride compound by multiplying by a formula weight ratio.

3. Crystalline mannosedimethylacetal has been prepared and its hydrolysis has been studied.

4. It has been shown that Hudson's rules of isorotation hold closely in the mannofuranose series provided that a factor *F* is introduced in the equations. The numerical value of *F* has been determined to be 2725 for the furanoid derivatives of mannose in water solution.

5. It has been suggested that the factor *F* probably represents the disturbing optical effect of the different orientation of the hydroxyl groups in the α- and β-isomers of certain sugars and their pyranoid or furanoid derivatives.

PRINCETON, NEW JERSEY RECEIVED JANUARY 16, 1940

[CONTRIBUTION NO. 185 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

Disubstituted Aminoacetones Containing Two Unlike Substituents[1]

BY J. WM. MAGEE[2] WITH HENRY R. HENZE

Continuing our attempts to prepare compounds possessing satisfactory activity as soporifics, we reported[3] recently our synthesis of ten disubstituted aminoacetones which subsequently were converted into disubstituted aminohydantoins. The ketones thus employed were all of the simple type $CH_3COCH_2NR_2$ in which the two substituents are identical and are either alkyl or allyl. We have now been interested in obtaining examples of the less well-known type CH_3COCH_2NRR', in which the two substituents are different, since these compounds present greater opportunity for variation in the combination of the groups most usually present in useful sedatives.

We have completed the synthesis of ten disubstituted aminoacetones, six of which had not been reported previously, by interaction of bromoacetone and the appropriate mixed secondary amine.[3] Most of the amines employed were produced in almost quantitative yield by catalytic reduction of the appropriate Schiff base by high pressure hydrogenation in the presence of Raney nickel catalyst.

Experimental

Preparation of the Mixed Secondary Amines.—The monomethylaniline and monoethylaniline were redistilled immediately before use. Cyclohexylmethylamine was obtained by heating one mole of methylaniline for eight hours at 200° in the presence of Raney nickel catalyst and an initial hydrogen pressure of 3500 lb. (233 atm.). The product was of such purity as to permit use immediately upon filtration from the catalyst. In the other instances, one mole of benzaldehyde, or a derivative, was warmed on a steam cone with one mole of a primary amine for fifteen minutes. After cooling to room temperature and separating the water formed from the unsaturated base, the latter was reduced in thirty minutes at 75° under initial hydrogen pressure of 2000 lb. (133 atm.). Here, too, the mixed amines were obtained in excellent yield and in a state of practical purity.

---

[1] From the Ph.D. dissertation of J. Wm. Magee, June, 1938.

[2] Present address, Federal Bureau of Investigation, United States Department of Justice, Washington, D. C.

[3] Magee with Henze, THIS JOURNAL, **60**, 2148 (1938).

TABLE I

DISUBSTITUTED AMINOACETONES, RR'NCH_2COCH_3

	-R	-R'	Yield, %	B. p. (cor.), °C.	Mm.	Density, d^{20}_4	Ref. index n^{20}_D	Surface tension γ^{20}, dynes/cm.	Free surface energy $\gamma(m/d)^{2/3}$
1	$—C_6H_5$	$—CH_3$	46	110.7[a]	3.0	1.0490	1.5578	40.21	1163.2
2	$—C_6H_5$	$—CH_2CH_3$	50	123.5[b]	3.0	1.0275	1.5488	38.27	1186.0
3	$—CH_2C_6H_5$	$—C_6H_5$	28	187.9[c]	4.5	1.0971	1.5961	42.37	1534.6
4	$—CH_2C_6H_5$	$—CH_3$	45	129.5	16.0	0.9899	1.5108	36.17	1149.2
5	$—CH_2C_6H_5$	$—CH_2CH_3$	47	113.8	3.0	.9759	1.5060	34.90	1177.5
6	$—CH_2C_6H_5$	$—CH_2CH_2CH_3$	53	130.0	6.0	.9670	1.5030	32.81	1167.6
7	$—CH_2C_6H_5$	$—CH_2CH_2CH_2CH_3$	51	147.5	8.0	.9551	1.4994	31.77	1191.3
8	$—CH_2C_6H_4(CH_3)$-*o*	$—CH_3$	54	137.3	10.0	.9769	1.5092	33.62	1133.6
9	$—CH_2C_6H_4(CH_3)$-*p*	$—CH_3$	51	132.3	9.0	.9769	1.5090	33.48	1128.9
10	$—C_6H_{11}$	$—CH_3$	46	93.2[d]	4.0	.9387	1.4673	32.54	1038.6

Compound	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Molecular refraction Calcd.	Molecular refraction Found	Δ*MR*	Parachor Calcd.	Parachor found	Δ*P*
1	73.58	73.86	8.03	7.92	50.25	50.15	−0.10	401.7	382.9	−18.8
2	74.52	74.67	8.53	8.72	54.87	54.90	+ .04	440.7	428.3	−12.4
3	80.32	80.47	7.16	7.14	74.37	74.31	− .06	574.7	556.1	−18.6
4	74.52	74.69	8.53	8.47	53.35	53.57	+ .22	440.7	439.3	− 1.4
5	75.35	75.53	8.96	8.90	57.97	58.23	+ .26	479.7	476.4	− 3.3
6	76.05	76.22	9.33	9.17	62.58	62.76	+ .16	518.7	508.1	−10.6
7	76.66	76.89	10.36	10.33	67.20	67.46	+ .26	557.7	545.2	−12.5
8	75.35	75.51	8.96	8.86	57.97	58.46	+ .49	479.7	471.5	− 8.2
9	75.35	75.78	8.96	8.92	57.97	58.46	+ .49	479.7	471.0	− 8.7
10	70.96	71.12	11.32	11.41	50.13	50.06	− .07	434.7	430.7	− 4.0

[a] Meisenheimer, Angerman, Finn and Vieweg [*Ber.*, **57B**, 1744 (1924)] reported b. p. 119–120° (7 mm.).

[b] Stevens, Cowan and MacKinnon [*J. Chem. Soc.*, 2570 (1931)] reported b. p. 143° (11 mm.).

[c] Bauer and Bühler [*Arch. Pharm.*, **262**, 128 (1924)] reported b. p. 320–334° (atm. pres.) with slight decomposition.

[d] Reference *a*, reported b. p. 106° (11 mm.).

Preparation of Disubstituted Aminoacetones.—The two general procedures previously described[3] for preparing dialkylaminoacetones were employed in this investigation. Thus 0.4 mole of methylaniline, ethylaniline, benzylmethylamine or benzylphenylamine, diluted with 400 cc. of ether was added to 0.2 mole of bromoacetone in 50 cc. of ether and cooled to aid in the separation of the hydrobromide of the secondary amine. After evaporation of the ether, it was found desirable to dissolve 90–95% of the keto amine by addition of 6 *N* hydrochloric acid, to extract the acid solution with ether before neutralizing with alkali and again extracting with ether. Upon distillation the aminoacetones were obtained in yields of 45–50% of the theoretical.

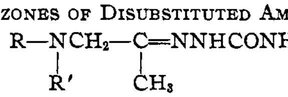
For the aminoacetones derived from the more expensive mixed secondary amines, slightly higher yields of product were obtained by suspending 0.2 mole of the amine in 150 cc. of water containing 0.2 mole of sodium carbonate and adding 0.2 mole of bromoacetone dropwise with efficient stirring. The sodium bicarbonate separating from solution was removed by suction filtration. A small amount of unreacted bromoacetone could be removed efficiently from the keto amine by extraction with 1 *N* hydrochloric acid. Fractionation under diminished pressure yielded these aminoacetones in about 50% yield.

The substituted aminoacetones prepared in this study are colorless oils when first prepared but develop a dark color quite quickly. But sparingly soluble in water, the keto amines are readily soluble in 6 *N* acid solutions and in the usual organic solvents. Data obtained by analysis or measurement of the physical properties of these ten compounds are listed in Table I. The surface tensions were measured by means of Cassel's[4] precision capillarimeter at 20°. In calculating the parachors, the atomic parachor values of Sugden[5] were used.

Preparation of Semicarbazones from the Substituted Aminoacetones.—Solid, crystalline semicarbazones were obtained readily and in good yield from each of the ten substituted aminoacetones, best by dissolving the ketone in dilute alcohol, adding slightly more than the equivalent quantity of semicarbazide hydrochloride and making the solution barely alkaline with sodium hydroxide solution. The derivatives were recrystallized from dilute alcohol.

TABLE II

SEMICARBAZONES OF DISUBSTITUTED AMINOACETONES



$$R—N(R')CH_2—C(CH_3)=NNHCONH_2$$

	-R	-R'	M. p., °C. (cor.)	Nitrogen, % Calcd.	Nitrogen, % Found
1	$—C_6H_5$	$—CH_3$	158	25.46	25.77
2	$—C_6H_5$	$—CH_2CH_3$	140	23.92	23.96
3	$—CH_2C_6H_5$	$—C_6H_5$	141	18.91	19.05
4	$—CH_2C_6H_5$	$—CH_3$	132	23.92	24.02
5	$—CH_2C_6H_5$	$—CH_2CH_3$	135	22.56	22.68
6	$—CH_2C_6H_5$	$—CH_2CH_2CH_3$	125	21.36	21.47
7	$—CH_2C_6H_5$	$—CH_2CH_2CH_2CH_3$	113	20.27	20.34
8	$—CH_2C_6H_4(CH_3)$-*o*	$—CH_3$	134	22.56	22.68
9	$—CH_2C_6H_4(CH_3)$-*p*	$—CH_3$	133	22.56	22.61
10	$—C_6H_{11}$	$—CH_3$	171	24.76	24.85

---

(4) Cassel, *Chem. Ztg.*, **53**, 479 (1929).

(5) Sugden, *J. Chem. Soc.*, **125**, 1180 (1924).

The corrected melting points and the analytical data of the ten semicarbazones are to be found in Table II.

Summary

1. Ten disubstituted aminoacetones, CH_3COCH_2NRR', have been prepared from mixed secondary amines, this being the initial report of the synthesis of six of the amino ketones.

2. Catalytic hydrogenation of seven Schiff bases, derived from benzaldehyde, by the use of Raney nickel and hydrogen under pressure afforded an easy and convenient method of preparing the corresponding mixed secondary amines in good yield.

AUSTIN, TEXAS RECEIVED JANUARY 29, 1940

[CONTRIBUTION NO. 187 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

5,5-Dimethylhydantoins Containing a –NRR′ Substituent[1]

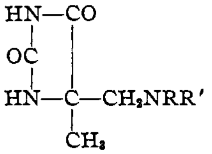
BY HENRY R. HENZE AND J. WM. MAGEE[2]

Recently we reported[3] the synthesis of ten 5,5-dimethylhydantoins containing a dialkylamino constituent. This synthesis was accomplished by adaptation of Bucherer's[4] procedure to the utilization of aminoacetone derivatives of the type $CH_3COCH_2NR_2$. In this manner, for example, we were able to convert dimethylaminoacetone into 5-dimethylamino-5-methylhydantoin despite the fact that this conversion had not been obtained by other investigators[5] using the closely related method of Bergs.[6]

It has been possible now to extend our investigation to the preparation of hydantoins from substituted aminoacetones of the type CH_3COCH_2NRR' in which R— and R′— represent different groupings. Further, since phenyl and benzyl groups are present in the structure of many anticonvulsants[7] and antispasmodics, one or both of these are present in all but one of the mixed secondary amines from which the substituted aminoacetones were prepared.

TABLE I

DISUBSTITUTED AMINODIMETHYLHYDANTOINS,



–R	–R′	Yield, %	M. p., °C. (cor.)	Nitrogen, % Calcd.	Nitrogen, % Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
$—C_6H_5$	$—CH_3$	90	190	18.02	17.96	61.78	61.94	6.49	6.55
$—C_6H_5$	$—C_2H_5$	80	171	16.99	17.02	63.14	63.35	6.93	6.99
$—CH_2C_6H_5$	$—C_6H_5$	91	213	13.85	13.90	69.88	70.07	6.19	6.65
$—CH_2C_6H_5$	$—CH_3$	77	204	16.99	17.08	63.14	63.37	6.93	7.17
$—CH_2C_6H_5$	$—C_2H_5$	92	165	16.08	16.22	64.34	64.51	7.33	7.61
$—CH_2C_6H_5$	$—C_3H_7$-*n*	91	157	15.26	15.40	65.43	65.59	7.69	7.86
$—CH_2C_6H_5$	$—C_4H_9$-*n*	96	169	14.46	14.61	66.40	66.61	8.01	8.14
$—CH_2C_6H_4CH_3$(*o*)	$—CH_3$	90	177	16.08	16.19	64.34	64.51	7.33	7.59
$—CH_2C_6H_4CH_3$(*p*)	$—CH_3$	91	178	16.08	16.19	64.34	64.48	7.33	7.62
$—C_6H_{11}$	$—CH_3$	68	199	16.96	17.09	58.18	58.30	10.92	10.98

Experimental

For the preparation of the ten hydantoins included in this investigation, 0.1 mole of the appropriate substituted aminoacetone, whose synthesis has been reported previously,[8] 0.15 mole of potassium cyanide, 0.3 mole of ammonium carbonate and 7–8 volumes of 50% alcohol were warmed under a reflux condenser for about ten hours at 55–65°. After concentration of the solution to about one-half volume, cooling in an ice-bath caused separation of most of the hydantoin and only an additional small quantity was obtained upon neutralization of the filtrate with con-

---

(1) From the Ph.D. dissertation of J. Wm. Magee, June, 1938.

(2) Present address, Federal Bureau of Investigation, United States Department of Justice, Washington, D. C.

(3) Magee with Henze, THIS JOURNAL, **60**, 2148 (1938).

(4) Bucherer and Lieb, *J. prakt. Chem.*, [2] **141**, 5 (1934).

(5) Slotta, Behnisch and Szyszka, *Ber.*, **67B**, 1529 (1934).

(6) Bergs, German Patent 566,094 (1932).

(7) Through the courtesy of Eli Lilly and Company the 5-(di-*n*-butylaminomethyl)-5-methylhydantoin and the 5-(diethylaminomethyl)-5-methylhydantoin have been shown to possess approximately 50% and 40%, respectively, of the anticonvulsant value of 5,5-diphenylhydantoin.

(8) Magee with Henze, THIS JOURNAL, **62**, 910 (1940).