Fraction (3) was shown to be 2,5-dicarbethoxycyclopentanone by its boiling point, the melting point (194–195°) of its dianilide[9] and the fact that it also yielded cyclopentanone on hydrolysis. The yield of this product was 31% of the theoretical.

Fraction (5) was unchanged starting material.

(b) Ethyl α-Ethyl-α,α'-Dicarbethoxyadipate.—A mixture of 46.3 g. (0.125 mole) of this ester and 8.5 g. (0.125 mole) of sodium ethoxide was treated in the same manner as described under (a) above, except that the reaction was run and completed in two and one-half hours at 115°. The distillate was found by refractive index to consist of 4.5 g. (0.093 mole) of alcohol and 11.1 g. (0.096 mole) of ethyl carbonate. Fractionation of the other reaction products gave the following fractions under 8 mm. of pressure: (1) 125–147°, 2.6 g.; (2) 147–154°, 23.9 g.; (3) 154–185°, 1.1 g.; (4) 185–195°, 3.8 g.; (5) undistillable residue, 5 g.

Fraction (2) was shown to be 2-ethyl-2,5-dicarbethoxycyclopentanone by analyses and the fact that it yielded 2-ethylcyclopentanone, b. p. 160–161°; semicarbazone, m. p. 189–190°.[10] The yield of this material amounted to 74.3% of the theoretical.

Anal. Calcd. for $C_{13}H_{20}O_5$: C, 60.93; H, 7.81%. Found: C, 60.75; H, 7.91.

Fraction (4) represented 8.1% of the starting material.

(c) Ethyl α,α'-Diethyl-α,α'-dicarbethoxyadipate.—A mixture of 100 g. (0.25 mole) of this ester, m. p. 94–95°, and 17 g. (0.25 mole) of sodium ethoxide was heated under diminished pressure, as described under (a) above, for two and one-half hours at 115° and for half-hour periods at 125, 150, 200 and 250°. Only 2.75 g. of distillate came over. This distillate consisted of 1.13 g. of alcohol and 1.62 g. of ethyl carbonate as estimated from its refractive index. The reaction mixture was acidified with dilute acetic acid and the insoluble solid material recrystallized from petroleum ether. In this way 52.3 g. of starting material, m. p. 92–93°, and 34.2 g., m. p. 85–86°, were recovered.

Summary

A study of the reaction of certain ethylenedimalonic esters with sodium ethoxide is reported. It has been found that those esters which have α- and α'-hydrogens or even a single α-hydrogen are cyclicized to cyclopentanone derivatives with the elimination of ethyl carbonate. When no α-hydrogen is present the ester shows no appreciable reaction with sodium ethoxide. These facts suggest that the same intermediate, as previously proposed for the acetoacetic ester condensation, is also involved in this condensation.

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[10] Case and Reid, THIS JOURNAL, **50**, 3062 (1928).

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Relative Reactivities of Certain 2- and 2,6-Substituted Piperidines

BY ALVIN W. SINGER AND S. M. MCELVAIN

In the preparation of various substituted piperidino-alkyl benzoates by the condensation of a chloro-alkyl benzoate with the substituted piperidine, it was noticed[1] that those piperidines containing a substituent in the 2-position were very much less reactive than both the unsubstituted piperidine and those piperidines substituted in the 3-position. This observation suggested a study of the effect of various groups in the 2-position on the reactivity of the piperidine with an organic halide.

This paper presents the results obtained with a representative halide, *n*-butyl bromide, and nine different 2- and 2,6-substituted piperidines. The general procedure which has been previously reported,[2] consisted of heating 2 moles of the amine with one mole of the bromide in petroleum naphtha (b. p. 95–150°) solution and determining, after a given time, the amount of precipitated secondary amine hydrobromide.

Exploratory experiments showed that the reaction temperature (90°) which was used[2] for the rate determinations with piperidine was too low to give a sufficient amount of reaction in a reasonable time with these substituted piperidines. For example, while piperidine was found to react with *n*-butyl bromide to the extent of 88.4% in forty-eight hours at 90°, 2-methylpiperidine, 2-phenylethylpiperidine and 2,6-dimethylpiperidine showed 52.7, 57.2, and 4.9% reaction, respectively, in the same time. It was decided, therefore, in order to get more complete reaction with the substituted piperidines, to carry out the reactions at 150–155°.

Table I shows the rates at which the various substituted piperidines react with *n*-butyl bromide. Each value in this table represents the average of at least two determinations, the variations of which were less than 3%.

The most significant feature of the data shown in Table I is the depressing effect of the

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[1] McElvain, THIS JOURNAL, **49**, 2837 (1927).

[2] Semb and McElvain, *ibid.*, **53**, 692 (1931).

TABLE I

RATE OF REACTION OF *n*-BUTYL BROMIDE AND CERTAIN SUBSTITUTED PIPERIDINES AT 150–155°

Piperidine substituent	% Reaction in hrs. 6	12	24	48
2-Methyl	87.8	96.0	100	
2-Benzyl	89.4	95.7		
2-Phenylethyl	90.2	92.1		
2-Carbethoxy	87.6	91.1		
2,6-Dimethyl	14.5	37.6	52.6	65.2
2,6-Diphenyl		49.0	67.4	
2,6-Diphenylethyl	49.2	64.9	68.7	72.0
2,6-Dicarbethoxy	40.9	58.9	72.3	
2-Methyl-6-phenyl	32.0	43.6	62.7	

methyl group in the 2-position on the reactivity of the piperidine with the bromide. In the case of a single substituent, the methyl group is just as effective in this respect as the larger benzyl, phenylethyl and carbethoxy groups. When substituents are present in both the 2- and 6-positions, the methyl group is even more effective, when compared with the larger groups, in diminishing the reactivity of the piperidine. This is evident from the fact that 2,6-dimethylpiperidine shows the lowest and 2-methyl-6-phenylpiperidine the next lowest reactivity of the group of piperidines studied.

Materials Used

Substituted Pyridines.—Commercial α-picoline was dried over lime and carefully fractionated. The fraction boiling at 128–132° was used. 2-Benzylpyridine was prepared from benzyl chloride and pyridine.[3] 2-Stilbazole was prepared from α-picoline and benzaldehyde.[4] 2,6-Dimethylpyridine was prepared according to the procedure described in "Organic Syntheses."[5] Diphenylpyridine was obtained by the dry distillation of cinnamylacetophenone oxime.[6] 2,6-Distilbazole was prepared from 2,6-dimethylpyridine and benzaldehyde by an adaptation of the method of Shaw and Wagstaff.[4] 2-Methyl-6-phenylpyridine was prepared by the dry distillation of cinnamylacetone oxime.[7]

Picolinic Acid Hydrochloride.—To 2500 cc. of water in a 5-liter 2-necked flask carrying a reflux condenser in one neck and a stopper in the other were added 50 g. of α-picoline, b. p. 128–132°, and 90 g. of potassium permanganate. The resulting solution was heated on a steam-bath until the permanganate color had practically disappeared. Then another 90-g. portion of potassium permanganate was added to the reaction mixture, followed by 500 cc. of water and the heating continued until the permanganate was entirely destroyed (two to two and one-half hours). The reaction mixture was then allowed to cool, the manganese dioxide filtered off with suction and washed well by stirring in 1 liter of hot water and again filtering. The combined filtrates were concentrated to 150–200 cc. by distillation under diminished pressure from a steam-bath. The resulting solution was filtered hot to remove any manganese dioxide, washed with a little water, and made acid to congo red with concentrated hydrochloric acid (65–70 cc., sp. gr. 1.19). This acid solution was then evaporated to dryness under diminished pressure. The remaining solid residue was heated under a reflux for one hour with 250 cc. of 95% alcohol and filtered. The salt residue was again extracted with another 150-cc. portion of alcohol and filtered. The combined alcoholic filtrates were treated with dry hydrogen chloride until crystals began to separate out, whereupon the alcoholic solution was cooled to about 10° in an ice-bath and the addition of hydrogen chloride continued until the solution was saturated. The crystals of picolinic acid hydrochloride which separated out were filtered by suction and dried. The yield was 52 g. (61%).

This hydrochloride may contain traces of potassium chloride which may be removed by dissolving it in hot absolute alcohol (50 g. of hydrochloride requires about 1 liter of alcohol for solution) and filtering to remove any insoluble material. An equal volume of dry ether is then added to the alcoholic solution and, after cooling, the precipitated picolinic acid hydrochloride filtered off. From 50 g. of the hydrochloride 46 g. of recrystallized product of m. p. 210–212° is obtained.

Dipicolinic Acid (Pyridine 2,6-Dicarboxylic Acid).—In a 3-liter flask fitted with a reflux condenser were placed 1500 cc. of water, 80 g. of potassium permanganate and 25 g. of 2,6-dimethylpyridine. The contents of the flask were heated sufficiently to produce gentle refluxing. When the color of the permanganate was nearly destroyed (about one-half hour), another 80-g. portion of potassium permanganate was added through the condenser and washed into the flask with 300 cc. of water. The heating was continued until the permanganate color completely disappeared (one and one-half hours). The flask and contents were allowed to cool sufficiently for handling, the manganese dioxide filtered through a suction filter, and washed well by suspending in 1 liter of hot water and filtering. The combined filtrates were concentrated to 300–350 cc. by distillation from a steam-bath under diminished pressure. The concentrated solution was filtered directly to remove any manganese dioxide and then acidified while still hot with 50 cc. of 70% sulfuric acid. After the solution was cooled to room temperature the precipitated dipicolinic acid was filtered off and dried. The yield was 25 g. (64%); m. p. 227–228°.

2,6-Dicarbethoxypyridine.—Thirty grams of 2,6-dipicolinic acid and 240 g. of thionyl chloride were placed in a 2-necked flask fitted with a dropping funnel and reflux condenser, and refluxed on a steam-bath until complete solution took place (four to six hours). The excess thionyl chloride was then removed by distillation from a steam-bath, the last traces being removed under diminished pressure. The flask containing the acid chloride hydrochloride was again fitted with a reflux condenser and 300 cc. of absolute alcohol added in small portions through the dropping funnel. The alcoholic solution was refluxed for one hour and the excess alcohol removed by distilla-

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(3) Crook and McElvain, THIS JOURNAL, **52**, 4006 (1930).

(4) Shaw and Wagstaff, *J. Chem. Soc.*, 77 (1933).

(5) "Organic Syntheses," Vol. XIV, p. 30.

(6) Scholtz, *Ber.*, **28**, 1730 (1895).

(7) Meisenheimer, Stratmann and Theilacker, *ibid.*, **65**, 423 (1932).

TABLE II

2- AND 2,6-SUBSTITUTED PIPERIDINES

Piperidine substituent	B. p. °C.	B. p. Mm.	d^{25}_4	$n^{25}D$	M_D Calcd.	M_D Found	Acetyl value[a]
2-Methyl	117–119		0.8341	1.4426	31.32	31.47	..
2-Benzyl[b]	268–269	738	.9660	1.5272	55.65	55.76	1.00
2-Phenylethyl[c]	131–132	6	.9540	1.5213	60.25	60.41	..
2-Carbethoxy[d]	93–94	11	1.0065	1.4547	42.39	42.33	1.00
2,6-Dimethyl[e]	127–129	742	0.8158	1.4366	36.20	35.92	1.00
2,6-Diphenyl[f]	193–194	10	.9507	1.5168	75.38	75.45	0.97
2,6-Diphenylethyl[g]	238–239	11	1.0063	1.5587	93.79	93.82	1.01
2,6-Dicarbethoxy[h]	155–156	11	1.0748	1.4581	58.06	58.18	1.04
2-Methyl-6-phenyl[i]	112–114	12	0.9096	1.4882	55.64	55.50	0.98

[a] Crook and McElvain, THIS JOURNAL, **52**, 4010 (1930). [b] *Cf.* Bailey and McElvain, *ibid.*, **52**, 1637 (1930). [c] *Cf.* Ref. 8. [d] *Cf.* Willstätter, *Ber.*, **29**, 390 (1896). [e] *Cf.* Marcuse and Wolffenstein, *ibid.*, **32**, 2528 (1899). [f] *Cf.* Scholtz, *ibid.*, **34**, 1621 (1901). [g] Shaw, *J. Chem. Soc.*, **125**, 2364 (1923), reports the boiling point of this compound as 290–295° (20 mm.). The compound used in the present work gave the following analyses. Calcd. for $C_{21}H_{27}N$: C, 85.94; H, 9.28. Found: C, 85.87; H, 8.98. [h] This compound does not appear to have been described previously. *Anal.* Calcd. for $C_{11}H_{19}O_4N$: C, 57.60, H, 8.35. Found: 57.70; 8.22. [i] *Cf.* Ref. 7.

tion. The residue was cooled in an ice-bath, covered with a layer of ether, and sufficient of a solution of 20% sodium carbonate added to make the water layer alkaline. The water layer was separated and extracted twice with small portions of ether. The ether was removed from the combined extracts by distillation. The remaining residue on distillation yielded 36 g. (90%) of 2,6-dipicolinic ester which boiled at 188–188.5° (12 mm.) and melted at 42–43°. This compound does not appear to have been described previously in the literature.

Anal. Calcd. for $C_{11}H_{13}O_4N$: C, 59.17; H, 5.87. Found: C, 59.20; H, 6.05.

Substituted Piperidines.—With the exception of 2-carbethoxypiperidine the substituted piperidines used were prepared by catalytic reduction of the corresponding pyridines as described in a recent paper by Adkins, Kuick, Farlow and Wojcik.[8] 2-Carbethoxypiperidine was prepared from picolinic acid hydrochloride by the same procedure as that previously used for ethyl nipecotate.[9] The properties of these various piperidines are listed in Table II.

Summary

The relative rates at which a number of 2- and 2,6-substituted piperidines react with *n*-butyl bromide have been determined.

[8] Adkins, Kuick, Farlow and Wojcik, THIS JOURNAL, **56**, 2425 (1934).

[9] McElvain and Adams, *ibid.*, **45**, 2745 (1923).

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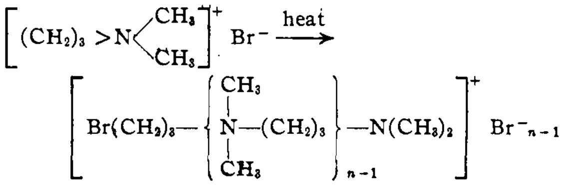
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

Quaternary Ammonium Salts from Bromopropyldialkylamines. V. Conversion of Cyclic Ammonium Salts to Linear Polymers

BY C. F. GIBBS AND C. S. MARVEL

Previous work[1] has shown that when an amine of the type Br—$(CH_2)_3$—NR_2 condenses with itself the course of the reaction is determined by the nature of the R groups. If R is a methyl group, linear polymerization occurs. If R is ethyl, *n*-propyl or *n*-butyl a four-membered ring is formed.

In the present investigation it has been observed that in very dilute solution (approximately 0.01 molar) gamma-bromopropyldimethylamine will react intramolecularly to give a cyclic quaternary ammonium salt.[2] This cyclic salt is quite different in physical properties from the polymeric salt which is formed when bromopropyldimethylamine is allowed to stand without a solvent or in concentrated solution. This cyclic salt is much less stable than are those in which the alkyl groups on the nitrogen are larger than methyl. When the monomeric salt is heated to 200° for a short time it is transformed into a linear polymeric salt with a molecular weight of about 3600.



$$n\left[(CH_2)_3 > N\begin{matrix}CH_3\\ CH_3\end{matrix}\right]^+ Br^- \xrightarrow{\text{heat}} \left[Br(CH_2)_3—\left\{\begin{matrix}CH_3\\ |\\ N—(CH_2)_3\\ |\\ CH_3\end{matrix}\right\}_{n-1}—N(CH_3)_2\right]^+ Br^-_{n-1}$$

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[1] (a) Gibbs, Littmann and Marvel, THIS JOURNAL, **55** 753 (1933); (b) Gibbs and Marvel, *ibid.*, **56** 725 (1934).

[2] Ruzicka, Salomon and Meyer, *Helv. Chim. Acta*, **17**, 882 (1934), have used the high dilution method to obtain hexadecamethyleneimine