piperidine derivative by dissolving 50 mg. in 5 ml. of acetone, adding 0.2 ml. of piperidine and heating the mixture on a steam-bath for about five minutes, until the volume was reduced to 2 ml. Addition of water precipitated the nitrolpiperidine derivative, m. p. 173–174° (dec.).[15] Two crystallizations from acetone raised the m. p. to 178–179° (dec.)[15]; melting points taken in the ordinary way were lower. This derivative has been reported to melt at 173°,[17] 179°[16] and 181°,[13] the m. p. depending on the rate of heating.[16]

Recrystallization of 9,10-octalin nitrosochloride from acetone raised the m. p. to 89.5–90.5°. A sample derived from 9,10-octalin prepared from β-decalol[18] melted at 91–92°.

Summary

trans-9-Decalylhydroperoxide (I) has been prepared by the reaction of decalin and oxygen, catalyzed by benzoyl peroxide, and isolated by chromatography on silica gel. 6-Hydroxycyclodecanone has been prepared from I by the route discovered by Criegee, and converted to the *p*-toluenesulfonate (V). The reaction of V with potassium *t*-butoxide resulted in an internal Haller–Bauer type of alkylation and yielded cyclopentanocycloheptanone (VII), while reaction of V with diethylaniline yielded cyclodec-5-en-1-one (VI) containing about 10% of the bridged isomer VII.

Hydrogenation of 6-hydroxycyclodecanone yielded a mixture of two stereoisomers of cyclodecan-1,6-diol, from which two isomeric di-*p*-toluenesulfonates (XI) were prepared. Reaction of these isomeric esters with diethylaniline gave mixtures of 1,9- and 9,10-octalin in quite different ratios, while the reaction of both isomers with potassium *t*-butoxide yielded 9,10-octalin.

CAMBRIDGE, MASSACHUSETTS

RECEIVED DECEMBER 14, 1949

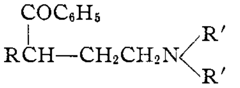
[18] Campbell and Harris, THIS JOURNAL, **63**, 2725 (1941).

[CONTRIBUTION FROM THE CHEMICAL RESEARCH DIVISION OF SCHERING CORPORATION]

Anomalous Alkylation of Desoxybenzoin and Phenacylpyridine with Dialkylaminoalkyl Halides[1]

BY NATHAN SPERBER, ROSEMARIE FRICANO AND DOMENICK PAPA

In the course of the synthesis of several series of compounds in which alkaline condensing agents were employed, we have had an opportunity to investigate the reaction of desoxybenzoin and phenacylpyridine with β-dialkylaminoalkyl halides. Eisleb[2] reported that desoxybenzoin and β-diethylaminoethyl chloride with sodamide yields γ-phenyl-γ-benzoyl-N,N-diethylpropylamine (Ib), a product comparable in structure to the C-alkylated compounds secured from desoxybenzoin and alkyl halides.[3] For the preparation of γ-phenyl-γ-benzoyl-N,N-dimethylpropylamine (I) and γ-(2-pyridyl)-γ-benzoyl-N,N-dimethylpropylamine (II), we employed the reaction conditions described by Eisleb for the synthesis of Ib.



$$\overset{\mathrm{COC_6H_5}}{\overset{|}{\mathrm{RCH}}}\mathrm{—CH_2CH_2N}\left\langle\begin{matrix}\mathrm{R'}\\ \mathrm{R'}\end{matrix}\right.$$

I, R = phenyl, R′ = methyl
Ib, R = phenyl, R′ = ethyl
II, R = 2-pyridyl, R′ = methyl

Our results with this synthesis are at variance with those reported by Eisleb in that the products obtained from desoxybenzoin and β-dimethylaminoethyl chloride (mixture A) or β-diethylaminoethyl chloride (Ib plus IVb) were not homogeneous. The reaction products mixture A and Ib plus IVb, underwent decomposition upon heating in 25% sulfuric acid. The oily product which separated was identified as desoxybenzoin. The ease of regenerating desoxybenzoin from these mixtures indicates that O-alkylation had occurred in the condensation reaction to yield the enol ethers IV and IVb.[4] The remaining acid solutions, after being freed of desoxybenzoin, gave upon neutralization the basic ketones I and Ib, the products of C-alkylation.

Eisleb[2] reported that the amino ketone Ib yielded a hydrochloride melting at 148°. In repeating this experiment, we obtained two hydrochlorides; one melting at 152° and the other at 183°. The former decomposed in warm sulfuric acid solution to give desoxybenzoin, while the latter was stable under these conditions. It is apparent therefore that the hydrochloride, m. p. 148°, obtained by Eisleb was that of the enol ether IVb and not that of the basic ketone Ib as reported.

Only one hydrochloride was obtained from mixture A and this was shown subsequently to be identical with the hydrochloride of an authentic sample of I. Similarly, only one picrate was obtained from mixture A and it was identical with the picrate of an authentic sample of I. Apparently, the hydrochloride and the picrate of the enol ether IV are not isolable under our experimental conditions.

Since the enol ether IV could not be separated from the amino ketone I by distillation or by suitable derivatives, its presence in mixture A was further established by catalytic reduction with Raney nickel in alcohol solution. The reduction products of mixture A were obtained as a low boiling, colorless oil and a high boiling, viscous

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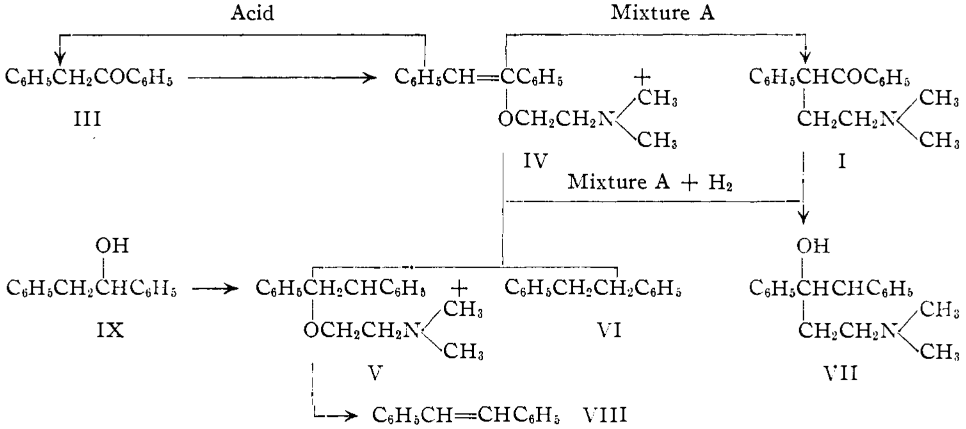
[1] Presented in abstract before the Division of Organic Chemistry of the American Chemical Society at Atlantic City, September 20, 1949.

[2] Eisleb, *Ber.*, **74**, 1437 (1941).

[3] Meyer and Oelkers, *ibid.*, **21**, 1295 (1888).

[4] The susceptibility of enol ethers to acidic reagents has been demonstrated; compare Friedrich, *Ann.*, **219**, 316 (1883), and Schwenk, Fleischer and Whitman, THIS JOURNAL, **60**, 1702 (1938).

FLOW SHEET I



Ib and IVb refer to the homologous diethyl compounds.

liquid which subsequently solidified. The lower boiling fraction formed a picrate and a hydrochloride identical with those prepared from an authentic sample of β-dimethylaminoethyl-1,2-diphenylethyl ether (V),[5] the dihydro derivative of the enol ether IV. The solid fraction was identified as 2-phenyl-2-(β-dimethylaminoethyl)-1-phenylethanol (VII) by comparison with a sample of VII prepared by the reduction of an authentic sample of I. The structure of I, the acid stable fraction of mixture A, was established by independent synthesis. The hydrochloride of the product of α-(β-dimethylaminoethyl)-phenylacetonitrile and phenylmagnesium bromide was identical to that of I, isolated from mixture A, and the mixed melting point of the two hydrochlorides showed no depression.

In another experiment, the reduction products of mixture A were treated with ice cold, 20% hydrochloric acid and a small quantity of an insoluble solid was separated by ether extraction. The latter substance was shown to be dibenzyl (VI) and probably resulted from the hydrogenolysis of IV during the course of the reduction. The presence of dibenzyl escaped detection in the first reduction experiment because the acid extraction had been omitted. The ether V decomposed to stilbene (VIII) when the acid solution was heated. Ether extraction of the acid solution at this stage removed the stilbene and, upon neutralization of the residual acid solution, VII was obtained relatively pure and identical in all respects with VII prepared by the reduction of I.

The yield data for the two alkylation reactions were calculated on the basis of the recovery of desoxybenzoin from the hydrolysis experiments. From β-dimethylaminoethyl chloride and desoxybenzoin with sodamide 79% of total alkylated products were obtained, 56% of which was the enol ether IV and 37% the basic ketone I. With β-diethylaminoethyl chloride, the yields were: total, 85%; enol ether IVb, 61% and basic ketone Ib, 29%.

With sodium methoxide as the condensing agent, O- and C-alkylation also were obtained. In this case, the total yield was 62%, of which 70% was the enol ether IV and 28%, the amino ketone I.

In the alkylation of phenacylpyridine (X) with sodamide and β-dimethylaminoethyl chloride, C- and O-alkylation also occurred to yield the products II and XI (mixture B). When mixture B reacted with hydroxylamine hydrochloride in pyridine–alcohol, an oxime was isolated identical with an authentic sample of phenacylpyridine oxime. The ease of formation of phenacylpyridine oxime established the presence of XI in mixture B. The structure of XI and its presence in mixture B was confirmed further by the isolation of α-stilbazole in low yield by the catalytic reduction of mixture B. It is very probable that α-stilbazole is the cleavage product of the unstable intermediate reduction product, 1-phenyl-1-(β-dimethylaminoethoxy)-2-(2-pyridyl)-ethane.[6]

The presence of amino ketone II in mixture B was established indirectly as follows: When mixture B was heated with 25% sulfuric acid and the acid solution subsequently made alkaline, there was isolated by distillation phenacylpyridine (65%) and a higher boiling yellow liquid in 19% yield. The latter fraction on the basis of the ultraviolet absorption spectrum was assigned structure II.

Ultraviolet Absorption Data.—A comparison of I and IV was made to determine whether the chemical and ultraviolet absorption data were in agreement. It has been reported that in alcohol acetophenone has a maximum at 241–245 mμ and benzophenone at 252 mμ.[7] In our

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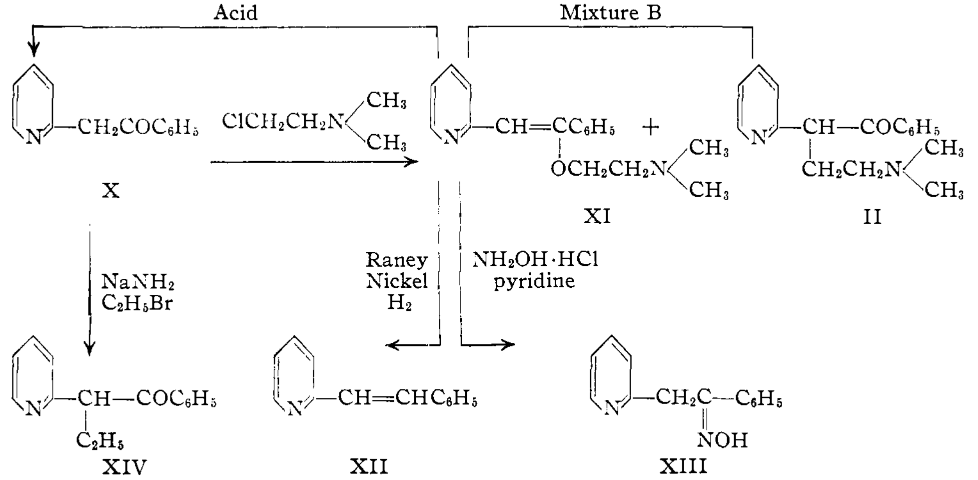
[5] Wright, Kolloff and Hunter, THIS JOURNAL, **70**, 3098 (1948).

[6] Tilford, Shelton and Van Campen (*ibid.*, **70**, 4001 (1948)) prepared this compound in 7% yield by the reaction of phenyl-(2-pyridylmethyl)-carbinol with sodium and β-dimethylaminoethyl chloride.

[7] Scheibe, *Ber.*, **59**, 2617 (1926).

FLOW SHEET II



determinations in alcohol, α-phenacylpyridine had a maximum at 246 mμ, desoxybenzoin at 243 mμ, α-ethyldesoxybenzoin at 245 mμ, and α-ethylphenacylpyridine at 245 mμ with a smaller maximum at 295 mμ (Fig. 1).

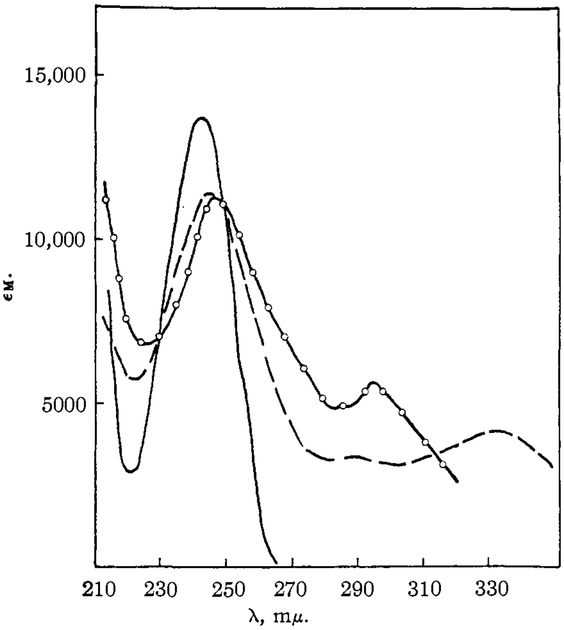


Fig. 1.—Absorption spectra of: — desoxybenzoin (III); – – – 2-phenacylpyridine (X); O—O—O— α-ethylphenacylpyridine (XIV).

If C-alkylation had occurred exclusively in the reaction of desoxybenzoin and β-diethylaminoethyl chloride, the product should have shown a maximum at 240–250 mμ. However, a strong maximum at 290 mμ and a faint maximum at 250 mμ was exhibited by this mixture. Likewise, the corresponding mixtures obtained by alkylating desoxybenzoin and phenacylpyridine with dimethylaminoethyl chloride and sodamide gave maxima at 290 mμ and 305 mμ, respectively. This shift of 15 mμ is in agreement with the shift observed in the maxima of stilbene (294 mμ) and α-stilbazole (310 mμ)[8] (Fig. 2). The enol acetate of desoxybenzoin also exhibits a strong maximum at 295 mμ. These data demonstrate the presence of the $C_6H_5CH{=}\underset{|}{C}{-}$ grouping in all the enol compounds.

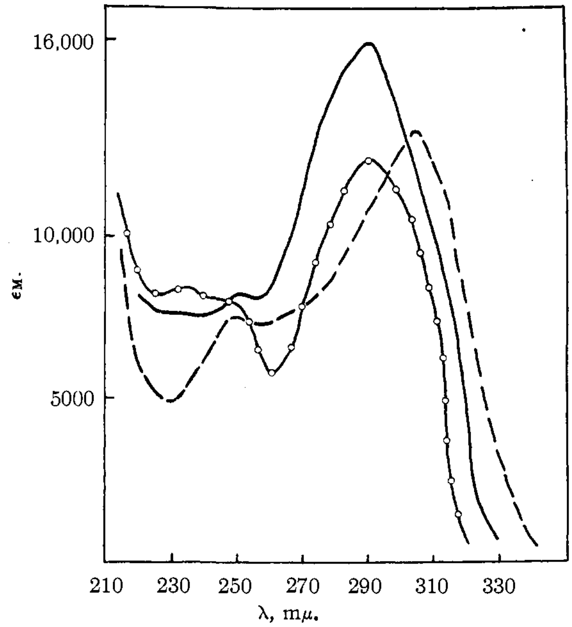


Fig. 2.—Absorption spectra of: — mixture A_b (IVb + Ib); —O—O—O— mixture A (IV + I); – – – mixture B (XI + II).

The acid stable compound I isolated from mixture A showed a maximum at 240 mμ which corresponds to the C_6H_5CO— grouping. Similarly, the acid stable product II isolated from

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[8] Blout and Eager, THIS JOURNAL, 67, 1315 (1945).

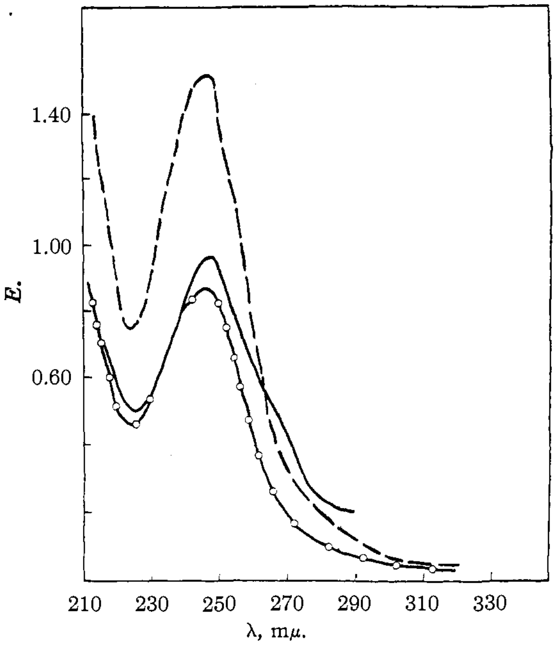

Fig. 3.—Absorption spectra of: — — — γ-phenyl-γ-benzoyl-N,N-dimethylpropylamine (I); — γ-(2-pyridyl)-γ-benzoyl-N,N-dimethylpropylamine (II); —O—O—O— γ-phenyl-γ-benzoyl-N,N-diethylpropylamine (Ib).

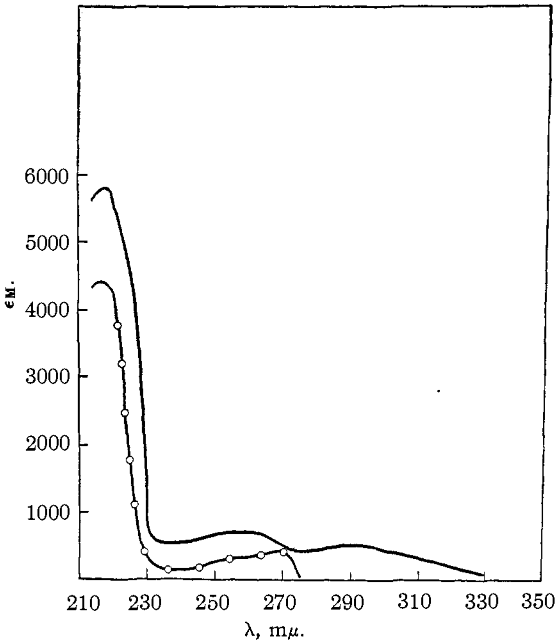

Fig. 4.—Absorption spectra of: — β-dimethylaminoethyl-1,2-diphenylethyl ether (V), authentic sample; O—O—O— V obtained as the lower boiling fraction in the catalytic reduction of Mixture A.

mixture B had a maximum at 247 mμ (Fig. 3). A comparison of the ultraviolet absorption curve of an authentic sample of V with the lower boiling fraction obtained from the catalytic reduction of mixture A showed the same general characteristics (Fig. 4). In contrast, the alkylation product of propiophenone and dimethylaminoethyl chloride showed a strong maximum at 240 mμ indicating essentially C-alkylation.

Experimental

Alkylation of Desoxybenzoin (a) β-Dimethylaminoethyl Chloride and Sodamide (Mixture A).—To a suspension of sodamide (12.5 g., 0.54 mole of sodium) in 300 cc. of toluene was added 98 g. (0.50 mole) of desoxybenzoin. After the mixture had been heated and stirred for three hours on a steam-bath, a solution of 60 g. (0.56 mole) of freshly distilled β-dimethylaminoethyl chloride in 250 cc. of toluene was added slowly and the reaction was allowed to run for an additional 16 hours. The mixture was cooled, decomposed with water, the organic layer separated, washed with water, dried, the solvents removed and the residue fractionated *in vacuo*. After a forerun of 4.5 g., b. p. 70–150° (1 mm.), $n^{23}\text{D}$ 1.5720, mixture A, yield 105.2 g. (79%), boiled at 150–153° (1 mm.), $n^{23}\text{D}$ 1.5837. On redistillation, mixture A was obtained as a viscous, yellow oil and exhibited schlieren; b. p. 147–150° (0.5 mm.), $n^{25}\text{D}$ 1.5812.

Anal. Calcd. for $C_{18}H_{21}ON$: N, 5.24. Found: N, 5.16.

In another experiment, the alkylation product was decomposed with water and the organic layer was extracted with several portions of ice cold, 10% hydrochloric acid. The combined acid extracts were made basic with ammonia, the oil taken up in ether, the ether layer washed with water, dried, the ether removed and the residue fractionated. There was obtained the same viscous yellow oil in a yield of 60% which boiled at 164–166° (2.5 mm.), $n^{26}\text{D}$ 1.5810.

The presence of γ-phenyl-γ-benzoyl-N,N-dimethylpropylamine (I) as one of the components in mixture A was established as follows: A solution of 20 g. (0.075 mole) of mixture A in 100 cc. of ice-cold 25% sulfuric acid was heated slowly on the steam-bath; at 50–60° the solution became turbid, and after heating for two hours, the flask was cooled. The mixture was extracted with ether, the ether layer washed with water, dried and the solvent evaporated. There was obtained 8.2 g. (56%) of desoxybenzoin which melted at 55.2–55.8° after two recrystallizations from alcohol–water. A mixed melting point with an authentic sample of desoxybenzoin showed no depression. The acid layer was made alkaline with ammonia gas and the oil which separated was extracted with benzene. The benzene layer was washed with water, dried, the solvent removed and the residue fractionated; there was obtained 7.3 g. (37%) of I as a faint yellow, viscous oil, b. p. 145–147° (0.3 mm.), $n^{25}\text{D}$ 1.5599.

Anal. Calcd. for $C_{18}H_{21}ON$: C, 80.84; H, 7.91; N, 5.24. Found: C, 81.10; H, 7.88; N, 5.63.

The picrate was recrystallized from alcohol and melted at 148–149°. *Anal.* Calcd. for $C_{24}H_{24}O_8N_4$: N, 11.29. Found: N, 11.48. The hydrochloride melted at 240–241° after two recrystallizations from alcohol–ether. *Anal.* Calcd. for $C_{18}H_{22}ONCl$: C, 71.15; H, 7.30; N, 4.61. Found: C, 71.36; H, 7.24; N, 4.92.

Mixture A formed a crystalline picrate, m. p. 149.5–150.5°, which did not depress the melting point of the picrate of I. Similarly, the hydrochloride, m. p. 240–241°, obtained for mixture A did not depress the melting point of the hydrochloride of I.

When a solution of mixture A (20 g.) in 100 cc. of concentrated hydrochloric acid was heated for four hours on the steam-bath, cooled and extracted with ether 6.6 g. of desoxybenzoin, m. p. 55–56°, was isolated from the ether extracts. Filtration of the acid layer gave 8.7 g. of the insoluble hydrochloride of I which melted at 240–241° after one recrystallization from alcohol–ether.

The independent synthesis of I was effected as follows: To a solution of the Grignard reagent prepared from 39.2 g. (0.25 mole) of bromobenzene and 7.5 g. (0.31 mole) of magnesium in 150 cc. of ether was added dropwise a solution of 22.5 g. (0.12 mole) of γ-dimethylamino-α-phenylbutyronitrile[9] in 50 cc. of benzene over a period of one hour. The ether was distilled off, 100 cc. of benzene added and the mixture refluxed and stirred for five hours. The complex was decomposed with dilute hydrochloric acid and then 50 cc. of concentrated hydrochloric acid was added to the aqueous layer. The insoluble hydrochloride (8.5 g.) was filtered and recrystallized from alcohol–ether, b. p. 239–240°. A mixed melting point with the hydrochloride of I showed no depression.

(b) **β-Dimethylaminoethyl Chloride and Sodium Methoxide.**—A mixture of 13.5 g. (0.25 mole) of sodium methoxide and 43 g. (0.22 mole) of desoxybenzoin in 200 cc. of toluene was allowed to heat for two hours on a steam-bath. A solution of 35 g. (0.326 mole) of β-dimethylaminoethyl chloride in 100 cc. of toluene was then added slowly and the reaction mixture was heated and stirred for 16 hours. Water was added, the organic layer separated, concentrated *in vacuo* and the residue distilled; yield 36.4 g. (62%), b. p. 155–163° (3 mm.), n^{23}D 1.5835.

Thirty-six grams of this mixture in 100 cc. of 25% sulfuric acid was decomposed as described in the previous experiments. There was obtained 18.5 g. (70%) of desoxybenzoin and 10.2 g. (28%) of I, b. p. 148–150° (1.5 mm.), n^{26}D 1.5603.

(c) **β-Diethylaminoethyl Chloride and Sodamide (IVb and Ib).**—Desoxybenzoin (49 g., 0.25 mole) was alkylated with sodamide (from 6 g. of sodium) and 38 g. of β-diethylaminoethyl chloride in toluene. The reaction mixture was processed according to the directions of Eisleb[2] and distilled *in vacuo;* viscous, yellow oil, yield 62 g. (85%), b. p. 190–194° (3.5 mm.), n^{26}D 1.5727 (lit.[2] b. p. 192–193° (3 mm.)). When a solution of this product in dry ether was treated with hydrogen chloride, a crystalline hydrochloride was obtained, m. p. 152–153° (lit.[2] m. p. 148°) after several recrystallizations from isopropyl alcohol. *Anal.* Calcd. for $C_{20}H_{26}ONCl$: N, 4.24. Found: N, 4.47. The hydrochloride decomposed in warm 25% sulfuric acid solution to yield desoxybenzoin.

A solution of 50 g. of the alkylated mixture (Ib and IVb) in 200 cc. of 25% sulfuric acid was heated for four hours on the steam-bath with stirring and the reaction mixture processed as in the previous experiments. There was obtained 21 g. (61%) of desoxybenzoin, m. p. 55–56° and 14.5 g. (29%) of Ib boiling at 172° and 2.5 mm., n^{23}D 1.5518. *Anal.* Calcd. for $C_{20}H_{25}ON$: C, 81.30; H, 8.53; N, 5.42. Found: C, 82.09; H, 8.44; N, 5.51. The hydrochloride of Ib was prepared in ether and recrystallized from isopropyl alcohol, m. p. 183–184°. *Anal.* Calcd. for $C_{20}H_{26}ONCl$: C, 72.38; H, 7.90; N, 4.24. Found: C, 71.63; H, 7.65; N, 4.48. Upon heating the hydrochloride in 25% sulfuric acid solution, no turbidity was observed and Ib was recovered unchanged.

β-Dimethylaminoethyl 1,2-diphenylethyl ether (V) was prepared by the alkylation of benzylphenylcarbinol with sodamide and β-dimethylaminoethyl chloride in toluene[5]; yield 60%, b. p. 152–155° (2 mm.), n^{27}D 1.5391. *Anal.* Calcd. for $C_{18}H_{23}ON$: C, 80.24; H, 8.61; N, 5.20. Found: C, 80.36; H, 9.09; N, 5.88. The hydrochloride melted at 131–132° (lit.,[5] m. p. 132–133°). The picrate, recrystallized from ethanol, melted at 110–111°. *Anal.* Calcd. for $C_{24}H_{26}O_8N_4$: N, 11.25. Found: N, 11.18.

Decomposition of β-Dimethylaminoethyl 1,2-Diphenylethyl Ether (V) with Hydrochloric Acid.—A solution of 5 g. of V in 25 cc. of 20% hydrochloric acid was heated for one hour on the steam-bath. The cooled mixture was extracted with ether, the ether layer washed with water, dried and the ether evaporated. There was obtained 3.34 g. (3.5 g. theory) of crude stilbene (VIII), m. p. 119–121°, which after a recrystallization from alcohol, m. p. 122–123°, did not depress the melting point of an authentic sample.

2-Phenyl-2-(β-dimethylaminoethyl)-1-phenylethanol (VII).—A solution of 16.6 g. (0.067 mole) of I in 200 cc. of methanol was hydrogenated with Raney nickel catalyst at room temperature and a pressure of 50 lb. p. s. i. The catalyst was filtered, washed with water and the filtrate and washings concentrated *in vacuo* to give 16 g. of a viscous oil which solidified rapidly, m. p. 102–103°. A recrystallization from alcohol–water yielded 12.5 g. (75%) of a white powder, m. p. 103.5–104.5°. The analytical sample was recrystallized from acetone and melted at 105.5–106°. *Anal.* Calcd. for $C_{18}H_{23}ON$: C, 80.24; H, 8.61; N, 5.20. Found: C, 80.51; H, 8.49; N, 5.80.

Catalytic Reduction of Mixture A.—A solution of 15 g. of mixture A in 200 cc. of absolute ethanol was hydrogenated in a Parr shaker at room temperature and a pressure of 50 lbs. p. s. i. using an alkaline Raney nickel catalyst. One mole of hydrogen was absorbed rapidly. The catalyst was filtered, washed with hot ethanol, the combined filtrate and washings concentrated *in vacuo* and the residue distilled to give two fractions: (a) β-dimethylaminoethyl 1,2-diphenylethyl ether (V), yield 7 g. (46%), b. p. 146–149° (0.5 mm.), n^{25}D 1.5399. *Anal.* Calcd. for $C_{18}H_{23}ON$: C, 80.24; H, 8.61; N, 5.20. Found: C, 79.92; H, 8.36; N, 5.47. The picrate was prepared in ethyl alcohol by the addition of a small amount of ether, m. p. 107–108°. A recrystallization from acetone raised the melting point to 109–110°. *Anal.* Calcd. for $C_{24}H_{26}O_8N_4$: N, 11.25. Found: N, 11.57. A mixed melting point of this picrate with the authentic sample of the picrate of β-dimethylaminoethyl 1,2-diphenylethyl ether (V) melted at 109–111°.

(b) 2-Phenyl-2-(β-dimethylaminoethyl)-1-phenylethanol (VII), yield 4 g. (27%), b. p. 154–160° (0.5 mm.), viscous oil which solidified upon standing and melted at 104–105° after a recrystallization from alcohol–water. A mixed melting point with the carbinol (VII) obtained by the reduction of I showed no depression, m. p. 104–105°.

Cleavage of the Reduction Products of Mixture A.—A solution of 40 g. (0.15 mole) of mixture A was reduced with Raney nickel catalyst and hydrogen and the colorless oil which remained after the removal of the methanol was dissolved in 150 cc. of ice cold 20% hydrochloric acid. A small quantity of an acid insoluble solid was removed by ether extraction. Upon removal of the ether, there was obtained 2.7 g. of a white solid which was recrystallized from alcohol–water, m. p. 51–52°. A mixed melting point with phenylbenzylcarbinol and desoxybenzoin showed marked depression. However, a mixed melting point with dibenzyl (VI), m. p. 51–52°, showed no depression. The acid solution was heated for one hour on the steam-bath and the clear solution turned milky. The suspension was ether extracted and upon removal of the ether, 15 g. (55%) of white crystals were obtained which melted at 122–123° after a recrystallization from alcohol–water. A mixed melting point with an authentic sample of stilbene (VIII) showed no depression, m. p. 122–123°. The acid fraction was made basic with ammonia and the oil extracted with ether. The ether extracts were washed with water, dried, the solvent evaporated and the residue distilled *in vacuo;* yield 14 g. (35%) of 2-phenyl-2-(β-dimethylaminoethyl)-1-phenylethanol (VII), b. p. 168–170° (2 mm.), viscous colorless liquid. The carbinol solidified and was recrystallized from alcohol–water, m. p. 104–105°.

α-Ethylphenacylpyridine (XIV).—To a cooled sodamide suspension (from 2.53 g. of sodium) in 200 cc. of toluene were added 19.7 g. (0.1 mole) of phenacylpyridine[10] followed by 16.3 g. (0.15 mole) of ethyl bromide. The reaction mixture was heated and stirred for eight hours on a steam-bath, decomposed with water and processed in the usual manner, weight 12.2 g. (54%), b. p. 157–164° (4 mm.), n^{26}D 1.5820. Upon redistillation, the yellow oil boiled at 138–141° (1 mm.), n^{25}D 1.5830. *Anal.* Calcd. for $C_{15}H_{15}ON$: C, 79.96; H, 6.71; N, 6.22. Found: C, 80.00; H, 6.41; N, 6.58. In an attempt to form the oxime, only a gummy product was obtained.

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(9) Kwartler and Lucas, This Journal, **68**, 2395 (1946); see Eisleb, *Ber.*, **74B**, 1433 (1941).

(10) Scheuing and Winterhalder, German Patent 594,849, Marc 15, 1934.

Alkylation of Phenacylpyridine with β-Dimethylaminoethyl Chloride and Sodamide (Mixture B).—To a cooled suspension of sodamide (from 6.3 g. of sodium) in 200 cc. of toluene was added 49.2 g. (0.25 mole) of phenacylpyridine in 250 cc. of toluene. A vigorous evolution of ammonia ensued and the suspension was heated and stirred on the steam-bath for three hours. A solution of 30 g. (0.28 mole) of β-dimethylaminoethyl chloride in 25 cc. of toluene was added dropwise and the mixture heated and stirred for two hours. An additional 15 g. of the halide was added and the reaction was continued for sixteen hours. Water was added and the reaction mixture was processed in the usual manner; yield 56.7 g. (84.5%), b. p. 145–180° (3 mm.), $n^{24}\mathrm{D}$ 1.5908, yellow, viscous oil. The latter was redistilled and obtained as a yellow, viscous oil, yield 52.4 g. (78%), b. p. 155–164° (0.5 mm.), $n^{27}\mathrm{D}$ 1.5920. *Anal.* Calcd. for $C_{17}H_{20}ON_2$: N, 10.45. Found: N, 10.81.

Phenylacylpyridine Oxime.—When one gram of mixture B, one gram of hydroxylamine hydrochloride, five cc. of pyridine and five cc. of absolute alcohol were refluxed for several hours, there was obtained a white solid which melted at 119–120° after a recrystallization from alcohol-water. *Anal.* Calcd. for $C_{13}H_{12}ON_2$: C, 73.55; H, 5.70; N, 13.21. Found: C, 74.20; H, 5.85; N, 13.37. A mixed melting point of this oxime with an authentic sample of phenacylpyridine oxime, m. p. 119.5–120° (lit.[10] m. p. 120) showed no depression.

Catalytic Reduction of Mixture B—α-Stilbazole.—A solution of 13.4 g. (0.05 mole) of mixture B in 150 cc. of methanol was reduced with hydrogen and Raney nickel catalyst at room temperature and atmospheric pressure. The theoretical amount of hydrogen was absorbed rapidly. The catalyst was removed by filtration, the filtrate and washings concentrated *in vacuo* and the residual yellow oil distilled; yield 7.5 g., b. p. 145–152° (0.5 mm.). The oil which partly solidified was dissolved in petroleum ether, cooled and filtered. The white solid was recrystallized from alcohol-water and melted at 90.5–91.5°. A mixed melting point with an authentic sample of α-stilbazole (91–92°) showed no depression.

Decomposition of Mixture B with Sulfuric Acid.—A solution of 43.6 g. of mixture B in 150 cc. of 25% sulfuric acid was heated for one hour on a steam-bath, poured on ice and made basic with ammonia. Both a solid and an oil separated, which were extracted with ether, dried, the ether evaporated and the oily residue distilled. There was obtained 21.2 g. (65%) of a yellow oil boiling at 134–140° (0.3–0.5 mm.) which crystallized upon standing, m. p. 48–50°. Recrystallization from alcohol-water raised the melting point to 55–56° and a mixed melting point with an authentic sample of phenacylpyridine, m. p. 55–56° (lit.[10] m. p. 59°), was not depressed. The second fraction, yield 8.3 g., b. p. 140–149° (0.3 mm.), did not crystallize. Upon redistillation, the fraction boiling at 157–162° (0.1 mm.), $n^{25}\mathrm{D}$ 1.5750, was analyzed and the ultraviolet absorption spectrum was determined. The analysis indicated that this sample was contaminated with phenylacylpyridine. *Anal.* Calcd. for $C_{17}H_{20}ON_2$: C, 76.06; H, 7.51; N, 10.45. Found: C, 77.74; H, 7.18; N, 9.87.

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Summary

In contrast to Eisleb's observation that the alkylation of desoxybenzoin with diethylaminoethyl chloride and sodamide in toluene results in the formation of γ-phenyl-γ-benzoyl-N,N-diethylpropylamine exclusively, we have found that this reaction yields a mixture of the amino ketone and enol ether, the former resulting from C-alkylation and the latter by O-alkylation. Similarly, C- and O-alkylation result when desoxybenzoin is alkylated with dimethylaminoethyl chloride and sodamide or sodium methoxide. Phenacylpyridine reacts similarly but gives higher yields of the O-alkylated product. Only small yields of the C-alkylated amino ketone could be isolated from this experiment. The absorption spectra data support the chemical evidence.

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[CONTRIBUTION FROM THE ROHM & HAAS CO.]

The Behavior of Aliphatic Aldehydes in the Leuckart–Wallach Reaction

BY PETER L. DEBENNEVILLE AND JANE H. MACARTNEY

The reductive alkylation of amines by aldehydes and ketones in the presence of formic acid has been variously called the Leuckart and Wallach reactions. While this reaction has been very extensively investigated[1] very little work has been done with aliphatic aldehydes other than formaldehyde. Wallach[2] carried out a few reactions with valeraldehyde, and obtained the expected products. There is no case reported of the reaction involving an aliphatic aldehyde and a purely aliphatic mono-secondary amine.

We have been studying this reaction as a possible preparative procedure for wholly aliphatic tertiary amines and have obtained some rather interesting results. The Leuckart–Wallach reaction with aliphatic aldehydes and secondary amines is initiated at a generally lower temperature than in the case of ketones and aromatic aldehydes, and gives generally good yields of product. And while we do not propose to offer a mechanism in this report, we have found an additional possible intermediate for this reaction in the form of the enamines, $(\mathrm{R}\overset{|}{\mathrm{C}}{=}\mathrm{CHNR_2})$, a class of compounds which was reported by Mannich and Davidsen in 1936.[3]

It has been pointed out by Moore[1] that secondary amines are more limited as to possible intermediates than ammonia and primary amines since they cannot eliminate water with the formation of a $>\mathrm{C}{=}\mathrm{N}-$ structure. Staples and Wagner[4]

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(1) Moore, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1949, pp. 301-330.

(2) Wallach, *Ann.*, **343**, 54 (1905).

(3) Mannich and Davidsen, *Ber.*, **69B**, 2106 (1936).

(4) Staples and Wagner, *J. Org. Chem.*, **14**, 559 (1949).