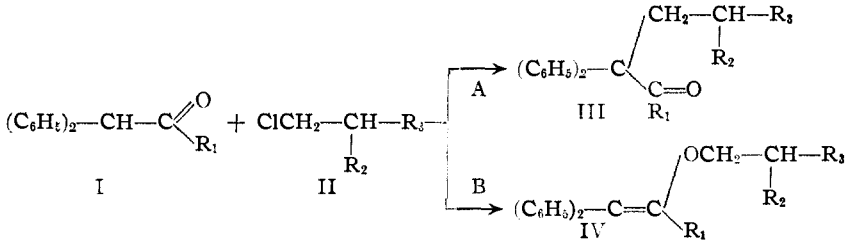
[CONTRIBUTION NO. 1517 FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY]

Some Observations on the Alkylation of Diphenylacetophenone and Diphenylacetone

BY HEINRICH RINDERKNECHT[1]

Alkylation of diphenylacetophenone leads to both C- and O-substitution. The ratio of C- to O-alkylation appears to be governed by steric factors in that methylation gives predominantly the C-substitution product whereas quaternary ethyleneimonium chlorides furnish almost exclusively basic enol-ethers. Other alkyl halides occupy an intermediate position.

In search of a more convenient synthesis of 2-dimethylamino-4,4-diphenylheptan-5-one (III) ($R_1 = C_2H_5$, $R_2 = CH_3$, $R_3 = N(CH_3)_2$, (Amidon)) reaction A was explored



Diphenylacetophenone[2] (I) ($R_1 = C_6H_5$) was chosen as the starting material for model experiments as it is readily prepared in excellent yield from desyl chloride and benzene by a Friedel–Craft condensation. Moreover, compounds of type III, ($R_1 = C_6H_5$, $R_2 = H$, R_3 = secondary amino radical) which would result from C-alkylation of I, ($R_1 = C_6H_5$) with basic alkyl halides such as II, ($R_2 = H$, R_3 = secondary amino radical) are of considerable interest because some of them possess both analgesic and antispasmodic activity to a high degree.[3] The only alkylation of diphenylacetophenone on record was described by Danilow.[4] Using ethyl iodide as alkylating and sodium hydroxide as condensing agent he obtained a product to which he erroneously assigned formula III ($R_1 = C_6H_5$, $R_2 = H$, $R_3 = H$) as will be pointed out later. In the present study the alkylations of diphenylacetophenone were carried out in toluene or *t*-butanol with sodamide or potassium respectively as condensing agents. The reaction products from I ($R_1 = C_6H_5$) and II ($R_2 = H$, R_3 = secondary amino radical) were isolated as hydrochlorides in 50–90% yield. A small amount of a neutral fraction not identical with the starting material was also obtained. This fraction was more substantial in the condensations with sodamide where heating was necessary for the formation of the sodio-derivative of I ($R_1 = C_6H_5$) and consisted presumably of decomposition products of diphenylacetophenone,[5] which were not further investigated. Although elementary analysis indicated the identity of the hydrochlorides with the desired 3,3,4-triphenylbutanones (III) ($R_1 = C_6H_5$, $R_2 = H$, R_3 = secondary amino radical), an authentic sample of the hydrochloride of α,α-diphenyl-γ-N-morpholinobutyrophenone when mixed with the condensation product from I ($R_1 = C_6H_5$) and N-(β-chloroethyl)-morpholine gave a melting point depression. It was thus obvious that the main reaction had not in this case followed path A and the reaction product was tentatively formulated as the enol ether, *i.e.*, IV. This structure was subsequently confirmed in each instance by hydrolysis with dilute hydrochloric acid which led to an almost quantitative regeneration of diphenylacetophenone. The enolic character of these products was further substantiated by spectrographic evidence (Fig. 1) and by hydrogenation of IV ($R_1 = C_6H_5$, $R_2 = H$, $R_3 = C_4H_8NO$) to the dihydro-compound which in contrast to the parent substance was no longer susceptible to hydrolysis by dilute hydrochloric acid. An attempt was made in one instance to isolate the C-alkylated isomer, *i.e.*, III ($R_1 = C_6H_5$, $R_2 = H$, $R_3 = N(CH_3)_2$) which might be formed in a small quantity. However, the only basic material which could be isolated after hydrolysis of the crude reaction product was dimethylaminoethanol. The aqueous mother liquors of the crystalline reaction products obtained in the analogous condensations with β-chloroethylpiperidine and β-chloroethylmorpholine were not further investigated.

When diphenylacetone was substituted for diphenylacetophenone in the condensation with β-chloroethyldimethylamine the reaction product could be isolated only in the absence of acid. It was found to be extremely susceptible to acid hydrolysis, regenerating diphenylacetone quantitatively. No basic ketone could be isolated after hydrolysis of the distilled reaction product. The presence of an enol-ether grouping was thus indicated and the product was formulated as 1,1-diphenyl-2-(β-dimethylaminoethoxy)-propene-1. Since the consideration of resonance structures requires the enolate ion, $\left[(C_6H_5)_2C{=}C\begin{matrix}O\\ \diagdown\\ CH_3\end{matrix}\right]^-$ to be more stable than its isomeric form $\left[\begin{matrix}O\\ \|\\ (C_6H_5)_2CH{-}C{=}CH_2\end{matrix}\right]^-$ the formation of 1,1-diphenyl-2-(β-dimethylaminoethoxy)-propene-2 which would derive from the latter was considered improbable.

In view of the above unexpected results[6] it appeared of interest to investigate the condensation of diphenylacetophenone with non-basic alkyl halides, *i.e.*, methyl, ethyl and *n*-propyl iodide.

(1) Research Associate of the Ciba Company, Schaffhausen, Switzerland.

(2) R. Anschütz and P. Forster, *Ann.*, **368**, 92 (1909).

(3) U. S. A. Office of the Publication Board, Dept. of Commerce, Report No. PB-981, p. 85.

(4) S. Danilow, *Chem. Zentr.*, **94**, III, 761 (1923).

(5) H. Biltz, *Ber.*, **26**, 1958 (1898).

(6) These experiments were carried out in 1948.

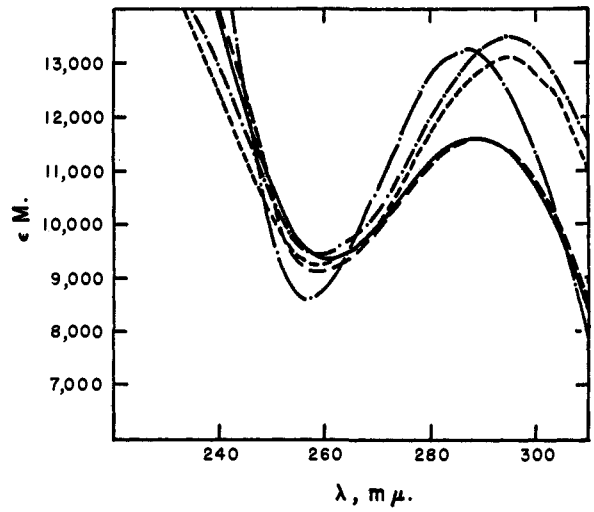


Fig. 1.——·—·—, 1,2,2-triphenyl-1-acetoxyethylene; -·-·-·-, 1,2,2-triphenyl-1-ethoxyethylene; - - - - - - - -, 1,2,2-triphenyl-1-propoxyethylene; ——, 1,2,2-triphenyl-1-(β-N-piperidinoethoxy)-ethylene hydrochloride; — — — — 1,2,2-triphenyl-1-(β-N-morpholinoethoxy)-ethylene hydrochloride.

The identity of the reaction products of this series was established on the basis of their susceptibility to hydrolysis and by spectrographic data.

Methylation of diphenylacetophenone with methyl iodide gave over 60% C-alkylation product. An attempt to isolate the isomeric enol ether was unsuccessful. In the analogous condensation with ethyl iodide the main product had the same melting point, *i.e.*, 120°, as the compound described by Danilow[4] as III (R_1 = C_6H_5, R_2 and R_3 = H). However, the results of hydrolytic experiments and spectrographic data leave no doubt as to the identity of this substance with the enol ether IV (R_1 = C_6H_5, R_2 and R_3 = H). The isomeric ketone which was also isolated melted at 96–98°. Condensation of diphenylacetophenone with propyl iodide yielded, as with ethyl iodide, both C- and O-substitution products.

The absorption spectra of diphenylacetophenone and its enol-acetate have been investigated by Ley and Manecke.[7] In chloroform solution the first compound exhibited a maximum at 244 mμ, the latter at 286 mμ. The determinations in the present study were carried out in alcohol solution and are in close agreement with these data: I (R_1 = C_6H_5) exhibited a maximum at 246–248 mμ, and its enol acetate at 288 mμ. As illustrated in Fig. 1 the ultraviolet absorption curves of the enol ethers follow the general pattern of that of the enol acetate of I (R_1 = C_6H_5). A shift of the maximum from 288 to 295 mμ in the case of the alkyl ethers and from 288 to 290 mμ in the case of the hydrochlorides of the aminoalkyl ethers can be observed. The absorption curves of the ketones (Fig. 2) likewise exhibit the same general characteristics as their parent compound, though with some deviation. No explanation can be offered at present for the seemingly irregular shifts of the maxima or for the low extinction in the case of III (R_1 = C_6H_5, R_2 and R_3 = H) which was reproducible when the determination was repeated with a specially purified sample.

(7) H. Ley and N. Manecke, *Ber.*, **56**, 777 (1923).

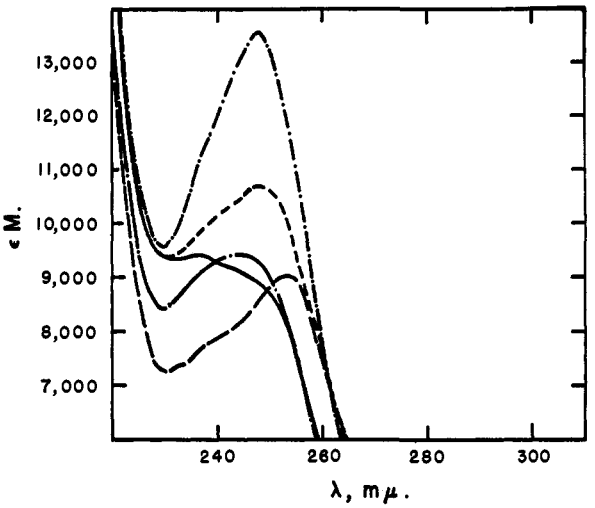


Fig. 2.——·—·—, diphenylacetophenone; - - - -, α,α-diphenylvalerophenone; ———, α,α-diphenylbutyrophenone; —·—·—, α,α-diphenylpropiophenone; — — — —, α,α-diphenyl-γ-N-morpolinobutyrophenone hydrochloride.

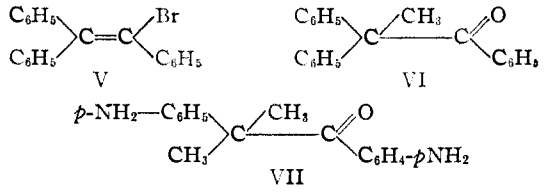
The results of this investigation suggest that the ratio of C- to O-alkylation of diphenylacetophenone depends to a large extent on the size of the alkylating agent. When the small methyl group is introduced C-alkylation is predominant. However, in condensations with the bulkier ethylene-imonium ions with the mesomeric anion of I (R_1 = C_6H_5) steric hindrance is more pronounced and consequently O-alkylation is the preponderant reaction. The other non-basic alkyl halides used in this work occupy an intermediate position, giving rise to both C- and O-substitution products. Similar results have recently been reported[8] for the condensation of desoxybenzoin with β-chloroethylamines. While desoxybenzoin which is sterically less hindered than diphenylacetophenone normally yields only C-substitution products with alkyl halides,[9] it gave rise to C- as well as O-alkyl derivatives on condensation with β-chloroethylamines.[8] The practically unhindered propiophenone, however, gave almost exclusively the C-alkyl derivative when condensed with this reagent. These observations together with the results presented in this paper clearly demonstrate the effect of increasing steric hindrance in a keto–enol system (propiophenone < phenylacetophenone = desoxybenzoin < diphenylacetophenone) on the ratio of C- to O-alkylation.

The enol ethers IV described in this series are structurally related to the synthetic estrogen V, and the ketone VI to compund VII which has progestational properties.[10] They are being investigated for their potential hormone activity. Preliminary results to be reported elsewhere, substantiate such a relationship.

(8) N. Sperber, R. Fricano and D. Papa, THIS JOURNAL, **72**, 3068 (1950).

(9) V. Meyer and L. Oelkers, *Ber.*, **21**, 1295 (1888).

(10) M. J. Allen, R. Hertz and W. W. Tullner, *Proc. Soc. Exp. Biol. Med.*, **74**, 632 (1950).



V VI

VII

Experimental

1,1-Diphenyl-2-(β-dimethylaminoethoxy)-propene-1.—1.3 g. of powdered sodamide was added in several portions to a boiling solution of 6.3 g. of α,α-diphenylacetone in 60 ml. of dry toluene. Crude β-chloroethyldimethylamine which was obtained from 7.3 g. of its hydrochloride by treatment with sodium hydroxide solution and extraction with ether, was added and the reaction mixture refluxed for 2 hours. After cooling, the sodium chloride was removed by filtration and the toluene solution evaporated to dryness. The residue was distilled to give 4.6 g. (55%) of IV (R_1 = CH_3, R_2 = H, R_3 = $N(CH_3)_2$), a yellow oil, boiling at 137–138° (0.1 mm.). When potassium in *t*-butanol was used in this condensation the yield was 71%.

Anal. Calcd. for $C_{19}H_{23}ON$: C, 81.1; H, 8.2; N, 5.0. Found: C, 81.6; H, 8.1; N, 4.9.

Hydrolysis of 1,1-Diphenyl-2-(β-dimethylaminoethoxy)-propene-1.—2.5 g. of IV (R_1 = CH_3, R_2 = H, R_3 = $N(CH_3)_2$) was dissolved in 10 ml. of 2 *N* hydrochloric acid. The solution which became turbid immediately was refluxed for one-half hour. After cooling, the reaction mixture was extracted twice with petroleum ether (60–80°). The extract was washed with water, dried over magnesium sulfate and evaporated to dryness. The light yellow oil when dried *in vacuo* over phosphorus pentoxide and paraffin shavings weighed 1.87 g. (99.5% of the theoretical amount calculated for diphenylacetone). Distillation gave a colorless oil of b.p. 115° (0.25 mm.) which solidified on standing; yield 1.65 g. Recrystallization from benzene–petroleum ether gave colorless crystals, m.p. 45–46.5° which did not depress the m.p. of an authentic sample of diphenylacetone. The aqueous part was evaporated to dryness and dried *in vacuo* over phosphorus pentoxide, when a crystalline deliquescent solid was obtained; yield 1.06 g. (95% of the theoretical amount calculated for dimethylaminoethanol hydrochloride). The chloroaurate melted at 192–194° with decomposition and did not depress the m.p. of an authentic sample.

1,2,2-Triphenyl-1-(β-dimethylaminoethoxy)-ethylene (IV), (R_1 = C_6H_5, R_2 = H, R_3 = $N(CH_3)_2$) was prepared in a similar manner by condensing diphenylacetophenone and β-chloroethyldimethylamine with sodamide in toluene. The cooled reaction mixture was treated with water and the aqueous layer discarded. Addition of excess 2 *N* hydrochloric acid to the toluene solution precipitated an oily hydrochloride which crystallized on standing and melted at 220–222° after recrystallization from ethanol or acetone. The yield was 50%. Hydrolysis gave diphenylacetophenone.

Anal. Calcd. for $C_{24}H_{28}ONCl$: C, 75.9; H, 6.9; N, 3.7; Cl, 9.3. Found: C, 76.0; H, 6.9; N, 3.6; Cl, 9.5.

1,2,2-Triphenyl-1-(β-N-piperidinoethoxy)-ethylene.—The hydrochloride of IV, (R_1 = C_6H_5, R_2 = H, R_3 = $C_5H_{10}N$) was obtained in the same manner; yield 46%, m.p. 222–224° after recrystallization from acetone.

Anal. Calcd. for $C_{27}H_{30}ONCl$: C, 77.2; H, 7.2; N, 3.3. Found: C, 77.2; H, 7.0; N, 3.4.

1,2,2-Triphenyl-1-(β-N-morpholinoethoxy)-ethylene.—To a solution of 0.9 g. of potassium in 50 ml. of *t*-butanol was added 5.4 g. of diphenylacetophenone and 3.5 g. of β-chloroethylmorpholine. The reaction mixture was refluxed for 2 hours, cooled and filtered. The solvent was then removed by distillation under reduced pressure and the residue treated with water and ether. The water layer was discarded. Addition of excess 2 *N* hydrochloric acid precipitated 7.8 g. (93%) of hydrochloride of IV, (R_1 = C_6H_5, R_2 = H, R_3 = C_4H_8NO). After recrystallization from ethanol, the product melted at 245–247°. When sodamide in toluene was used as condensing agent the yield was 45%.

Anal. Calcd. for $C_{26}H_{28}O_2NCl$: C, 74.0; H, 6.7; N, 3.3; Cl, 8.4. Found: C, 73.9; H, 6.7; N, 3.4; Cl, 8.4.

Hydrolysis of 1,2,2-Triphenyl-1-(β-N-morpholinoethoxy)-ethylene.—The hydrochloride (1.5 g.) was suspended in a boiling mixture of 20 ml. of water and 5 ml. of concentrated hydrochloric acid. Enough ethanol was added to give a single phase and refluxing continued for one-half hour. The solvents were then removed by distillation under reduced pressure. The residue was dried and recrystallized from petroleum ether (60–80°) to give 0.8 g. (89%) of crystalline I (R_1 = C_6H_5) melting at 137°. It did not depress the melting point of an authentic sample of diphenylacetophenone.

Hydrogenation of 1,2,2-Triphenyl-1-(β-N-morpholinoethoxy)-ethylene.—The hydrochloride of IV (2.1 g.) (R_1 = C_6H_5, R_2 = H, R_3 = C_4H_8NO) was dissolved in 150 ml. of ethanol and hydrogenated with 1 g. of 5% palladized charcoal. When hydrogen absorption had ceased, the catalyst was filtered off and the residue evaporated to dryness under reduced pressure to give 1.7 g. of 1-(β-N-morpholinoethoxy)-1,2,2-triphenylethane hydrochloride which had m.p. 192–195° after recrystallization from acetone.

Anal. Calcd. for $C_{26}H_{30}O_2NCl$: C, 73.6; H, 7.1; N, 3.3. Found: C, 73.6; H, 7.1; N, 3.4.

α,α-Diphenylpropiophenone.—Diphenylacetophenone (2.7 g.) was condensed with 2.1 g. of methyl iodide by heating for 3 hours in a solution of 0.4 g. of potassium in 40 ml. of *t*-butanol to 80–100° in a sealed tube. The reaction mixture was filtered, the filtrate evaporated to dryness and the residue distilled. A viscous oil was obtained boiling at 195° (2 mm.) (oil-bath temperature). Attempts to separate crystalline reaction products from this oil were unsuccessful. One gram of the distilled product was therefore hydrolyzed by refluxing for 15 min. with 5 ml. of 2 *N* hydrochloric acid and enough ethanol to give a single phase. On cooling, 2 types of crystals separated, long flat needles and bundles of small needles. A sample of each was obtained by mechanical separation. After recrystallization from petroleum ether the first, *i.e.*, diphenylpropiophenone, melted at 88–90°. The latter had m.p. 126–133° and was identified as impure diphenylacetophenone. The total hydrolysate was diluted with water, cooled, and the precipitate (0.8 g.) filtered, dried and dissolved in boiling petroleum ether (60–80°). The solution was seeded with a crystal of diphenylacetophenone. On cooling the latter crystallized. As soon as crystals of α,α-diphenylpropiophenone began to separate which can easily be distinguished from those of diphenylacetophenone, the supernatant was decanted, the impure crystalline diphenylacetophenone set aside, and the remaining solution concentrated to a smaller volume. It was then seeded with a crystal of diphenylpropiophenone. A crop of bead-like crystals of the latter was obtained on gradual cooling. When the formation of crystals of diphenylacetophenone was observed the supernatant was decanted, the crude diphenylpropiophenone saved, and the remaining solution concentrated to a smaller volume. It was again seeded with diphenylacetophenone and the above process repeated. Further crops of diphenylacetophenone and diphenylpropiophenone were thus obtained. They were combined with the respective first crops and recrystallized from petroleum ether. The resulting mother liquors were again subjected to the fractional crystallization process described above. In this way 0.08 g. of diphenylacetophenone, m.p. 135–137° and 0.53 g. of diphenylpropiophenone (*ca.* 66%, based on weight of solid hydrolysate used in this fractionation) m.p. 91–93° were obtained.

Anal. Calcd. for $C_{21}H_{18}O$: C, 88.1; H, 6.3. Found: C, 88.2; H, 6.4.

1,2,2-Triphenyl-1-ethoxyethylene.—Diphenylacetophenone (2.7 g.) was added to a solution of 0.4 g. of potassium in 50 ml. of *t*-butanol and condensed with 3.0 g. of ethyl iodide by refluxing the reaction mixture for 2 hours. The solvent and potassium iodide were removed and the reaction product (2.2 g.) was dissolved in boiling ethanol. On cooling a first crop of crystalline material melting at 116–119° was obtained. After repeated recrystallizations from ethanol the substance (0.5 g.) melted at 120°. It was identified as 1,2,2-triphenyl-1-ethoxyethylene by hydrolysis which gave diphenylacetophenone.

Anal. Calcd. for $C_{22}H_{20}O$: C, 88.0; H, 6.7. Found: C, 88.0; H, 6.8.

α,α-Diphenylbutyrophenone.—Concentration of the original mother liquors of the preceding experiment gave a second crop of material melting unsharply at 79°. It was dissolved in boiling petroleum ether and the α,α-diphenylbutyrophen-

one separated from triphenylethoxyethylene and diphenylacetophenone by the process of fractional crystallization employed for the isolation of diphenylpropiophenone. The pure diphenylbutyrophenone thus isolated (0.35 g.) melted at 97–98° and was not hydrolyzed by 2 *N* hydrochloric acid.

Anal. Calcd. for $C_{22}H_{20}O$: C, 88.0; H, 6.7. Found: C, 88.2; H, 6.7.

1,2,2-Triphenyl-1-propoxyethylene.—Diphenylacetophenone (2.7 g.) was condensed with 2.1 g. of propyl iodide as described above. The crude reaction product (1.6 g.) was recrystallized from ethanol to give crystalline material melting at 84–85°. Fractional crystallization from petroleum ether (60–80°) as outlined above gave 0.5 g. of pure triphenylpropoxyethylene melting at 92–93° and 0.15 g. of diphenylacetophenone.

Anal. Calcd. $C_{23}H_{22}O$: C, 87.9; H, 7.1. Found: C, 87.9; H, 7.1.

α,α-Diphenylvalerophenone.—As the alcoholic mother liquors of the preceding experiment did not furnish a crystalline product on concentration, the material was subjected to hydrolysis by dilute aqueous alcoholic hydrochloric acid. Addition of water and cooling of the reaction mixture gave 0.2 g. of diphenylacetophenone. The filtrate was evaporated to dryness under reduced pressure and the residue distilled to give 0.2 g. of a yellow oil which boiled at 195° (2.5 mm.) (oil-bath temperature). Attempts to crystallize this material from petroleum ether or alcohol failed.

Anal. Calcd. for $C_{23}H_{22}O$: C, 87.9; H, 7.1. Found: C, 87.8; H, 7.0.

α,α-Diphenyl-γ-N-morpholino-butyrophenone.—A benzene solution of Grignard reagent prepared from 9.5 g. of bromobenzene and 1.44 g. of magnesium was added to a solution of 6.15 g. of α,α-diphenyl-γ-N-morpholino-butyronitrile.[11] After refluxing for 18 hours, the reaction mixture was poured onto a mixture of cracked ice and concentrated hydrochloric acid. The benzene layer was separated and the aqueous part heated on the water-bath for 3 hours. On cooling 7 g. (83%) of crystalline hydrochloride of III ($R_1 = C_6H_5$, $R_2 = H$, $R_3 = C_4H_8NO$) was obtained. After recrystallization from acetone, it melted at 235–237°.

Anal. Calcd. for $C_{26}H_{28}O_2NCl$: C, 74.0; H, 6.7; N, 3.3. Found: C, 74.1; H, 6.6; N, 3.2.

Acknowledgment.—I wish to express my gratitude to Mr. H. Schubert of the Forsanose Fabrik in Switzerland for the laboratory facilities and hospitality extended to me during the first stages of this investigation and to Dr. C. Niemann of the California Institute of Technology for his helpful criticism and encouragement in this work.

(11) D. J. Dupre, J. Elks, B. A. Hems, K. N. Speyer and R. M. Evans, *J. Chem. Soc.*, 500 (1949).

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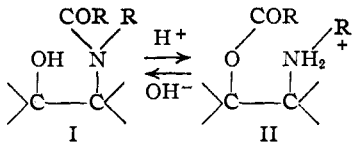
[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Mechanism of Nitrogen–Oxygen Acyl Migrations

BY EUGENE E. VAN TAMELEN

Both *cis*- and *trans*-N-(*p*-nitrobenzoyl)-2-aminocyclopentanol have been converted by means of hydrogen chloride to the hydrochloride of *cis*-2-aminocyclopentyl *p*-nitrobenzoate. The latter result is attributed to the suppressed formation of a *trans*-fused, bicyclic intermediate and constitutes strong evidence for a cyclic intermediate in nitrogen–oxygen acyl migrations which proceed with retention of configuration.

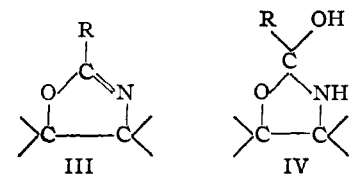
Nitrogen to oxygen (N→O) and oxygen to nitrogen (O→N) acyl migrations, which may be represented generally as

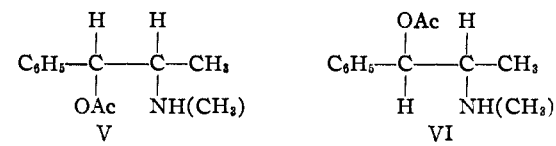


have been critically investigated in several laboratories during recent years. Ordinarily the former rearrangement is effected by treatment of an N-acyl-1,2-aminoalcohol (I) with mineral acid. The resulting salt of the O-acyl-1,2-aminoalcohol (II) can be reconverted, *via* the free O-acylamino-alcohol,[1] to I through the agency of aqueous alkali.

It is the purpose of this study to gain some insight into the nature of the intermediates involved in this type of interconversion.

Evidence bearing on the mechanism of acyl migrations has been brought out in several investigations. Phillips and Baltzly[2] rejected an oxazoline (III) as a possible intermediate, because an oxazoline, which should ordinarily be stable in neutral or alkaline medium, could not be isolated in the O→N reaction. Alternately, a cyclic, hemiacetal-like structure (IV) was suggested.[3] Welsh[4] has demonstrated that the initial products resulting from the acyl migration involving N-acetylephedrine are O-acetylephedrine (V)—arising through retention of configuration—and a greater amount of its epimer, O-acetyl-Ψ-ephedrine (VI), the product of inversion at the benzylic position. N-Acetyl-Ψ-ephedrine, on the other hand, gave rise to only O-acetyl-ψ-ephedrine—reaction with exclusive retention. Welsh[5] correlated these results with the probable conformations of the diastereo-





(1) G. Fodor and J. Kiss, THIS JOURNAL, 73, 3495 (1950).
(2) A. P. Phillips and R. Baltzly, *ibid.*, 69, 202 (1947).
(3) There still remains the possibility of an oxazoline intermediate in the N → O migration, which might well form through dehydration with cyclization; cleavage with strong acid to 1,2-amino ester salts (II) is a reaction characteristic of oxazolines. The isolation of some 2-phenyloxazoline[2] in the N → O migration with N-(2-hydroxyethyl)-benzamide supports this formulation. However, it seems likely that—at least in the retention mechanism (*vide infra*)—cyclization of I to an oxazoline should proceed *via* IV and that IV would also intermediate the conversion of III to II; thus the formation of an oxazoline does not preclude the presence of IV nor invalidate the retention mechanism.
(4) L. H. Welsh, THIS JOURNAL, 69, 128 (1947).
(5) L. H. Welsh, *ibid.*, 71, 3500 (1949).