tion of 10.4 g. of the glycol in 32.2 ml. of dry pyridine was cooled to 20° while a solution of 19 g. of *p*-toluenesulfonyl chloride in 50 ml. of dry ether was added over a period of 0.5 hr. After the mixture had been stirred for 3 hours at room temperature, the pyridine was removed by neutralizing with 30 ml. of concentrated hydrochloric acid and washing the ether solution with water. The ether was displaced with methanol on the steam-bath and water was added to the point of cloudiness. Chilling deposited 5.4 g. of oily crystals of the di-*p*-toluenesulfonate (unaffected by acetic anhydride) which was recrystallized from aqueous acetone, m.p. 116–120°. Addition of more water to the mother liquor gave the mono-*p*-toluenesulfonate as an oil which was used directly in the next step.

The oil was dissolved in 65 ml. of 95% ethanol and a solution of 7.9 g. of potassium cyanide in 21 ml. of water was added. After a 14-hour reflux period, the mixture was extracted with benzene and the solution was distilled at the aspirator. No volatile material passed over at the expected temperature of 100°, and at a bath temperature of 200°, pyrolysis of the unchanged *p*-toluenesulfonate commenced.

2,2-Dimethyl-3-methoxypropanol.—Sodium (11.5 g.) was dissolved in a solution of 57.3 g. of 2,2-dimethylpropanediol in 300 ml. of absolute *t*-amyl alcohol. The solution was cooled and 46 ml. of methyl iodide was added and the mixture was stirred for 3 hours at room temperature. Water was added and the organic layer was separated and dried. Distillation gave 30.3 g. (73% conv.) of product, b.p. 150–160°, and 14.2 g. of unreacted glycol.

4-Methoxy-3,3-dimethylbutyronitrile.—A solution of 49 g. of *p*-toluenesulfonyl chloride was added to a solution of 30.3 g. of the methoxy alcohol in 129 ml. of pyridine and after 1 hour on the steam-bath, the mixture was treated with water and 75 ml. of concentrated hydrochloric acid and extracted with petroleum hexane. The solvent was removed on the steam-bath and the 32 g. of residue was taken up in 200 ml. of ethylene glycol. After the addition of 11.8 g. of potassium cyanide, the solution was distilled until the distillate was no longer cloudy. The 2-phase distillate was partitioned between water and petroleum pentane. The organic solution was separated and distilled, giving 3.1 g. (10%) of oil, b.p. 165–175°.

4-Methoxy-3,3-dimethylbutylamine.—The total quantity of nitrile, plus forerun and residue in 20 ml. of 2-butanol was added to a stirred slurry of 4 g. of molten sodium in 20 ml. of toluene. After decomposition with ethanol, water and 20 ml. of concentrated hydrochloric acid were added and the solvent was distilled. After treatment with charcoal, the solution was made basic and the amine extracted with benzene. The benzene solution was extracted with dilute hydrobromic acid and the extract was evaporated *in vacuo*, giving about 5 g. (60%) of very hygroscopic crystals of the hydrobromide. The nickel tests were positive for a primary amine and negative for a secondary amine.[2] The Hinsberg test gave a base-soluble oil, which resisted crystallization. Concentrated hydrobromic acid was distilled from the salt to give a hygroscopic solid resembling the original salt. A small portion was treated with the nickel reagent after prior neutralization with sodium bicarbonate and gave a strong test for a primary amine. Therefore, not much I was formed, if any. The methoxyamine salt was boiled with anhydrous hydrogen bromide in acetic acid for 16 hours and, after removal of the solvent *in vacuo*, the dark residue was treated with benzenesulfonyl chloride and aqueous base to give a black oil insoluble in base. (Acidification of the reaction mixture precipitated nothing, so no primary amine had survived the hydrolysis.) The black oil was chromatographed on alumina from 3:7 carbon tetrachloride and petroleum hexane to give a crude yellowish solid, which was fractionally oiled from carbon tetrachloride and petroleum hexane to give a colorless but still impure solid, m.p. 52–64°. This material liquefied when mixed with authentic 1-phenylsulfonyl-3,3-dimethylpyrrolidine.

LOS ANGELES 7, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

The Formation of 3,3,5-Trimethyl-2-pyrrolidone by the Cleavage of 5-Ethoxy-2,2-dimethylvalerophenone with Sodamide[1]

BY RONALD F. BROWN AND NORMAN M. VAN GULICK

RECEIVED JULY 13, 1954

In an attempt to prepare 5-ethoxy-2,2-dimethylvaleramide, the cleavage with sodamide of 5-ethoxy-2,2-dimethylvalerophenone was tried, but the unexpected product proved to be the lactam of 4-amino-2,2-dimethylvaleric acid. Presumably, the reaction proceeds by elimination of ethanol as well as benzene to give 2,2-dimethyl-4-pentenamide which then cyclizes in the basic media. The sensitivity of the ether to cleavage may be due to the nascent phenyl anion which is very close to the hydrogen which is beta to the ethoxy group, leading to a concerted cleavage and E_2 type elimination.

In the course of attempts to prepare the hydrobromide of 4-bromo-1,1-dimethylbutylamine,[2] an attractive route appeared to be the cleavage with sodamide of 5-ethoxy-2,2-dimethylvalerophenone (I) to give 5-ethoxy-2,2-dimethylvaleramide, which, by the Hofmann rearrangement, should yield 4-ethoxy-1,1-dimethylbutylamine, the precursor of the desired product.

$$\mathrm{EtOCH_2CH_2CH_2CMe_2COC_6H_5} \xrightarrow{\mathrm{NaNH_2}}$$

$$\mathrm{EtOCH_2CH_2CH_2CMe_2CONH_2} \xrightarrow{\mathrm{Br_2 + NaOH}}$$

$$\mathrm{EtOCH_2CH_2CH_2CMe_2NH_2} \xrightarrow{\mathrm{HBr}}$$

$$\mathrm{BrCH_2CH_2CH_2CMe_2NH_2{\cdot}HBr}$$

Compound I was prepared readily by the alkylation of isobutyrophenone with 3-ethoxypropyl bromide, but subsequent cleavage with sodamide gave a partially crystalline product which was subjected to conditions for rearrangement. To our surprise, only a trace of crude amine was formed, primary as determined by the Duke test[3] and this could not be the required amine which does not give a positive primary amine test.[2] The main product was recovered starting material, which proved to be 3,3,5-trimethyl-2-pyrrolidone (II), the properties of which were identical with those reported by Haller and Bauer[4] for authentic material from the cleavage of allyldimethylacetophenone with sodamide and from an independent synthesis. These workers proposed, but did not prove, that their cleavage proceeded normally to give 2,2-dimethyl-4-pentenamide (III), which then cyclized under the basic conditions.

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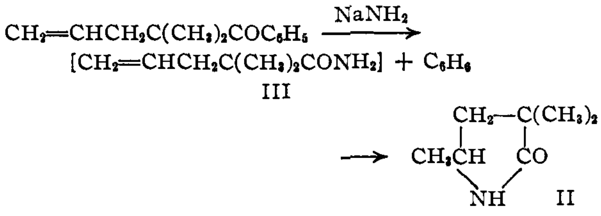
[1] Generously supported in part by the Office of Naval Research under Contract No. Nonr-723(00).

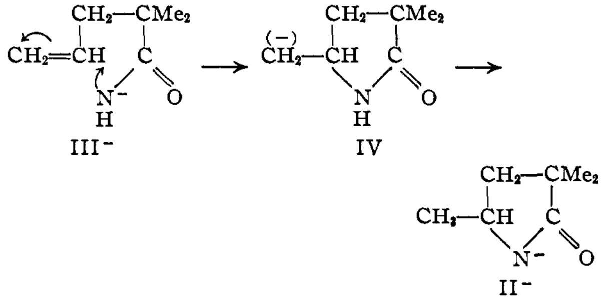
[2] R. F. Brown and N. M. van Gulick, THIS JOURNAL, **77**, 1079 (1955).

[3] F. R. Duke, *Ind. Eng. Chem., Anal. Ed.*, **17**, 196 (1945).

[4] A. Haller and E. Bauer, *Compt. rend.*, **158**, 1086 (1914).



In order to establish the possibility that III was an intermediate, it was prepared from the corresponding nitrile, which was available by alkylation of isobutyronitrile with allyl chloride. It was found that III was converted smoothly to II upon boiling in a toluene suspension of sodamide. The addition of bases to isolated double bonds is a relatively unknown phenomenon. Except for a few examples of addition of bases to double bonds activated by aromatic rings,[5] the only recorded case of the addition of a base to an unactivated olefin seems to be a report by Bartlett, who succeeded in adding isopropyllithium and *t*-butyllithium to ethylene.[6] Hence, the cyclization of the comparatively weakly basic anion of III is unusual if one considers the reaction to be stepwise, since even with the driving force of the *gem*-dimethyl group toward cyclization, the weak base of the amide group must add uphill energywise to produce the highly basic carbanion IV. This would indicate some concerted scheme which would give rise to II$^{(-)}$ directly. In order to remove the possibility that amide ion or toluene might furnish protons, the cyclization of the amide was carried out with sodium hydride in Skellysolve E and found to be quite facile. It would seem that the remaining hydrogen in III$^{(-)}$ is involved. To test this idea the N-benzyl amide was prepared and subjected to the same conditions. It did not form a pyrrolidone and was recovered in good yield. While this lends some support to the hypothesis, the steric effect of the benzyl group might have been such as to prevent the attainment of a transition state similar to that of the unsubstituted amide. Otherwise the presence of the group prevents the formation of the ion II$^{(-)}$, which might be essential to the process. In turn, it is of interest that the benzyl group did not migrate.



Returning again to the formation of II from the sodamide treatment of I, the facile cleavage of the ether function is of interest. Although many examples are known of ether cleavages which, from inspection of the products, probably involve S$_N$2 mechanisms,[7] there are not many authentic examples of the E$_2$ cleavage of unactivated ethers, and these have only been observed under the influence of organometallic reagents.[8] Apparently, there are no recorded examples of E$_2$ cleavage resulting from the action of sodamide. Accordingly, the cleavage of an ordinary ether was attempted, but after boiling a suspension of sodamide in dibutyl ether for 16 hours, only a trace of the cleavage product, 1-butene, was formed. These conditions were appreciably more drastic than those required for the facile cleavage of I. Whether the nascent phenyl anion acts to remove the hydrogen β to the ether, or whether the amide function is involved subsequent to the departure of the phenyl must await the preparation and study of 5-ethoxy-2,3-dimethylvaleramide.

Experimental[9]

5-Ethoxy-2,2-dimethylvalerophenone (I).—Sodamide was prepared from 16.8 g. of sodium and 560 ml. of liquid ammonia. Toluene (560 ml.) was added and the ammonia was removed by warming. Next, 106 ml. of isobutyrophenone was added all at once and the mixture was heated under reflux for one hour. 3-Ethoxypropyl bromide[3] (117 g.) was added over a period of 1.5 hours. After a reflux period of 10 hours, the mixture was decomposed with water and the toluene solution was distilled to give 129.5 g. (79%) of crude product, b.p. 70–112° (1 mm.).

The crude ketone (0.55 mole) was added to a suspension of 1.1 moles of sodamide in 800 ml. of toluene. After a reflux period of 4 hours, ammonia evolution had ceased, and the mixture was decomposed with aqueous acetic acid. The toluene solution was distilled to give 57 g. of product, b.p. 110–160° (15 mm.), which soon deposited crystals upon chilling. The crystals went into solution at room temperature and were not collected.

A solution of 14.4 g. of sodium in 300 ml. of absolute methanol was added to 54 g. of the above cleavage product in 250 ml. of absolute methanol. Next, 16.0 ml. of bromine in 100 ml. of absolute methanol was added with swirling. After heating for 15 minutes on the steam-bath, 40 g. of sodium hydroxide in 100 ml. of water was added. After 8 hours of refluxing, the mixture was distilled to remove the methanol and volatile product. The distillate was acidified and extracted to remove 31 g. of high boiling liquid which could not be distilled, even at reduced pressure, because of serious foaming. The solution was rendered basic and extracted with chloroform. The extract was fractionally distilled to give 4 g. of crude amine, b.p. 160–190°, and 10 g. of a fraction, b.p. 240°, which solidified on standing. The nickel reagents[3] showed the amine to be primary. The solid, m.p. 90–91°, lit.[4] m.p. 92°, after several crystallizations from petroleum hexane and a sublimation, was analyzed.

Anal. Calcd. for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.02; mol. wt., 127. Found: C, 66.18; H, 10.38; N, 10.92; mol. wt. (Rast), 160.

The solid showed no melting point depression when mixed with II from the original cleavage with sodamide.

A mixture of 200 ml. of dry dibutyl ether and 0.25 mole of sodamide was heated under reflux for 16 hours, the exit gases being collected in a Dry Ice trap filled with toluene. The toluene solution was washed successively with cold dilute hydrochloric acid and cold water and then dried. An acetic acid solution of 1 g. of 2,4-dinitrobenzenesulfenyl chloride was added and, after standing for four days, the solution was poured into water and the toluene evaporated in a current of air. The gummy solid was chromatographed twice to give *ca.* 0.1 g. of yellow crystals, m.p. 77–80°. A sample of authentic 1-butene adduct, kindly supplied by

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[5] R. C. Fuson and F. E. Mumford, *J. Org. Chem.*, **17**, 255 (1952); W. C. E. Higginson and N. S. Wooding, *J. Chem. Soc.*, 744, 760 (1952).

[6] P. D. Bartlett, S. Friedman and M. Stiles, THIS JOURNAL, **75**, 1771 (1953).

[7] For example see V. Grignard, *Compt. rend.*, **151**, 322 (1910).

[8] Beside Ref. 6, see A. Luttringhaus, *Ann.*, **557**, 51, 59 (1945). E. Späth, *Monatsh. Chem.*, **35**, 319 (1914), D. H. Gould, K. H. Schaaf and W. L. Ruigh, THIS JOURNAL, **73**, 1263 (1951), and R. L. Letsinger, A. W. Schnizer and E. Bobko, *ibid.*, **73**, 5708 (1951).

[9] All m.p.'s and b.p.'s are uncorrected. Analyses by Mr. W. J. Schenck of this department.

Dr. N. Kharasch, gave m.p. 75–78°. The mixed melting point was 75–76°.

4-Amino-2,2-dimethylvaleric Acid Hydrochloride.—Two grams of II and 20 ml. of concentrated hydrochloric acid were heated under reflux for 24 hours. The solution was decolorized and evaporated to dryness *in vacuo*. The product was washed with acetone and recrystallized several times from ethanol and acetone to give 1.5 g., m.p. 156–157°, lit.[4] m.p. 164°.

Anal. Calcd. for $C_7H_{16}ClNO_2$: C, 46.28; H, 8.88. Found: C, 46.12; H, 8.54.

The pyrrolidone was regenerated easily by neutralization of the hydrochloride.

2,2-Dimethyl-4-pentenamide (III).—The corresponding nitrile was prepared in 61% yield by alkylation of lithium isobutyronitrile with allyl chloride according to Ziegler.[10] The nitrile was hydrolyzed by heating 5 g. under reflux for 6 hours with a solution of 15 g. of potassium hydroxide in 100 ml. of ethylene glycol and 5 ml. of water. After the addition of 100 ml. of saturated salt solution and 20 ml. of concentrated hydrochloric acid, the solution was extracted with methylene chloride. Distillation gave 5.3 g. (90%) of the acid, b.p. 104–108° (20 mm.). The amide, m.p. 80–81°, prepared from the acid *via* the acid chloride sublimes readily at 70° (20 mm.) to give large sheets which are invisibly thin and show strong interference colors.

Anal. Calcd. for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.02. Found: C, 66.40; H, 10.35; N, 10.94.

A solution of 2 g. of III in 15 ml. of toluene was added (vigorous ammonia evolution) to 0.031 mole of sodamide in 20 ml. of toluene. After heating under reflux for 4 hours, the solution was cooled, treated with 5 ml. of acetic acid and extracted with saturated salt solution. The toluene solution was evaporated to small volume and decolorized. The addition of petroleum pentane and chilling gave 1.5 g. (75%) of II, m.p. 90–91°. The m.p. of a mixture with authentic material was undepressed.

Alternatively, 1.00 g. of III in 5 ml. of hot ligroin, b.p. 115–135°, was added to 0.38 g. of sodium hydride in 5 ml. of ligroin at 80°. After the vigorous hydrogen evolution subsided, the mixture was heated under reflux for 1 hour, during which time a gummy sodium salt went into solution, leaving about one-half of the original sodium hydride on the bottom. The mixture was cooled and decomposed by the portionwise addition of 1 ml. of acetic acid. The mixture was filtered and heated to boiling to codistil traces of acetic acid. Cooling deposited 0.72 g. (72%) of II.

N-Benzyl-2,2-dimethyl-4-pentenamide.—A solution of 2,2-dimethyl-4-pentenoyl chloride (from 2.56 g. of the acid and 4 ml. of thionyl chloride) in 5 ml. of ether was added portionwise to a solution of 10 ml. of benzylamine and 20 ml. of water maintained in an ice-bath. The product, 3.5 g. (81%), was recrystallized from petroleum hexane and again from 70% methanol giving 3.2 g. of material, m.p. 55–56°. Sublimation at the water-pump (100°) raised the m.p. to 56–57°.

Anal. Calcd. for $C_{14}H_{19}NO$: C, 77.38; H, 8.81. Found: C, 77.50; H, 8.71.

Treatment with sodium hydride in either ligroin or toluene according to the procedure for 2,2-dimethyl-4-pentenamide gave the sodium salt as a gum. The benzyl amide was recovered unchanged to the extent of 77%. No other product was isolated.

LOS ANGELES 7, CALIFORNIA

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[10] K. Ziegler and H. Ohlinger, *Ann.*, **495**, 84 (1932).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

The Beckmann Rearrangement of the Oximes of Alkyl Phenyl Ketones[1,2]

BY RONALD F. BROWN, NORMAN M. VAN GULICK AND GEORGE H. SCHMID

RECEIVED JULY 26, 1954

The rearrangement of the oximes of pivalophenone and of 5-phenoxy-2,2-dimethylvalerophenone in alkaline solution with benzenesulfonyl chloride results in alkyl group migration, in contrast to aryl migration with hydrogen chloride in acetic acid. Aceto-, propio- and isobutyrophenoximes (both *syn-* and *anti*-forms of the last) behave normally with phosphorus pentachloride or with benzenesulfonyl chloride, but the *syn-* and *anti*-isobutyrophenoxime react alike with hydrogen chloride in acetic acid. The sensitivity of the acyl derivatives of *t*-carbinamines to cleavage by acids is noted.

While attempting to prepare the hydrobromide of 4-bromo-1,1-dimethylbutylamine,[3] a synthetic route which involved the rearrangement of the oxime of 5-phenoxy-2,2-dimethylvalerophenone appeared to be of utility if the alkyl group migrated instead of the phenyl. It had been reported that pivalophenoxime (I), a model compound, gave benzonitrile exclusively upon treatment with phosphorus pentachloride, but that treatment with a solution of hydrogen chloride in acetic acid gave pivalanilide.[4] In spite of these discouraging facts, pivalophenoxime was prepared and subjected to rearrangement under various conditions. The rearrangement with phosphorus pentachloride, even under the mildest conditions, led to the exclusive formation of benzonitrile, and the rearrangement with hydrogen chloride in acetic acid to give pivalanilide was confirmed also. It seemed possible that the benzenesulfonyl chloride method of rearranging oximes[5] might produce the desired result, since the rearrangement occurs in an alkaline environment. The rearrangement was carried out in the usual manner, the unstable benzenesulfonyl ester rearranged *in situ*, giving N-*t*-butylbenzamide in 72% yield. The rearrangement under these conditions followed two competing paths since the odor of benzonitrile was evident at the end of the reaction.

Because of the success of the model rearrangement, 2,2-dimethyl-5-phenoxyvalerophenone was prepared and the crude liquid ketone was converted into the oxime directly. Rearrangement of the oxime produced an 84% yield of N-benzoyl-1,1-dimethyl-4-phenoxybutylamine. This amide proved extremely resistant to basic hydrolysis. After treatment with sodium butoxide in refluxing butanol, the amine was obtained in only 25% yield, 47% of the amide being recovered unchanged. Potassium hydroxide in boiling ethylene glycol like-

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[1] Abstracted in part from the Ph.D. Dissertation of N. M. van Gulick, 1953.

[2] Generously supported in part by the Office of Naval Research under Contract No. Nonr-723(00).

[3] R. F. Brown and N. M. van Gulick, THIS JOURNAL, **77**, 1079 (1955).

[4] G. Schroeter, *Ber.*, **44**, 1201 (1911).

[5] H. Wege, *ibid.*, **24**, 3537 (1891); A. Werner and A. Piguet, *ibid.*, **37**, 4295 (1904); and see P. Oxley and W. F. Short, *J. Chem. Soc.*, 1514 (1948), for recent work.