Table II

Preparation of Alkyl-glyoxalidines

	Ethylenediamine deriv.	Wt. used	Metal	Wt.	T., °C.	Press., mm.	Time, hours	Wt. of product, g.	Yield
I	Diacetyl	30	Mg	5	270	at.	1.25	12.7	68
II	Dipropionyl	20	Mg	1.5	300	at.	5	5.2	46
III	Dibutyryl	20	Mg	1.2	330	at.	1.25	5.5	49
IV	Divaleryl	10	Mg	0.5	290	125	2.5	1.5	27
V	Dicaproyl	4	Mg	.2	190	75	1.75	0.7	34
VI	Diheptoyl	12	Mg	.5	300	at.	7	.1	1.7
VII	Dicaprylyl	1.7	Na	.1	270	at.	1	.4	47
VIII	Dipelargonyl	0.7	Na	.2	250	2	..	.08	21
IX	Dicapryl	5.5	Mg	.5	300	at.	6	.015	5.6
X	Diundecylyl	0.9	Na	..	300	10	..	.10	22
XI	Dilauroyl	1.6	Na	..	300	2	0.5	.20	24

Reactions of Methyl-glyoxalidine.—To 5 g. of the base dissolved in chloroform was added a solution of bromine in the same solvent, with shaking and cooling, until the color remained. The heavy yellow precipitate was filtered off, washed with chloroform and dried in a vacuum desiccator. The yield was 11.9 g. or 82%. Analysis gave 65.23% of bromine; calculated for $C_4H_7N_2Br \cdot HBr$, 65.53. The product appears to be the hydrobromide of the brominated base.

Summary

The method of preparing methyl-glyoxalidine has been improved. Its homologs with normal alkyls have been made up to the undecyl. Their pharmacological properties have been determined.

Baltimore, Maryland Received September 30, 1935

[Contribution from the Hall Laboratory of Chemistry, Wesleyan University]

The Omega-Benzyl Derivatives of Acetophenone and their Reduction Products

By G. Albert Hill and A. J. Cofrancesco

Although Haller and Bauer were not the first to prepare omega benzylated acetophenones, no earlier investigator produced these substances by the use of sodamide.[1,2] They did not, however, make tribenzylacetophenone. From our experience[3] with omega benzylated pinacolones, it was believed that tribenzylacetophenone could be synthesized by the sodamide method. As a consequence, it was decided that the preparation of the series of omega, mono-, di- and tri-benzyl acetophenones should be undertaken. Furthermore, it was decided to parallel our earlier investigation of the benzylpinacolone derivatives and to prepare, in addition to the ketones, their oximes, the corresponding carbinols and their phenylurethans, and also the hydrocarbons resulting from the replacement of each of the ketone oxygen atoms by two atoms of hydrogen.

Some trouble was experienced because the solvents employed in the ketone syntheses, ether, benzene, and toluene, seemed to form additive compounds with the first products of the reactions, the sodium derivatives of acetophenone, of monobenzylacetophenone, and of dibenzylacetophenone, respectively. This effect increased the viscosity of the systems to an extraordinary degree, making thorough mixing and temperature control difficult. These factors markedly affect the success of a given synthesis and may lead to the decomposition of the desired product when that has been formed.

Monobenzylacetophenone was prepared from sodamide, acetophenone, and benzyl chloride, in toluene, since the above-mentioned difficulties were minimized in this medium. Though odorless at first, the ketone developed fragrance on standing. This was probably caused by oxidation and splitting, an effect which is known to occur with dibenzyl ketone.[4] No attempt was made to isolate or to identify the odorous substances. With hydroxylamine, the ketone yielded a crystalline oxime.[5]

The secondary alcohol derived from monobenzylacetophenone had already been prepared

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[1] Haller and Bauer, *Ann. chim.*, [8] **28**, 398 (1931).

[2] Haller and Bauer, *Bull. soc. chim.*, **31**, 1077 (1922).

[3] Hill and Bruce, This Journal, **52**, 347 (1930).

[4] Fortey, *J. Chem. Soc.*, **75**, 871 (1899).

[5] Perkin and Stenhouse, *ibid.*, **59**, 1008 (1891).

by reduction with sodium and alcohol,[6] and also catalytically.[7] The ketone was reduced in this Laboratory by the older methods and by Hartung's[8] which had not been reported previously. Contrary to expectations, this method did not yield the hydrocarbon, for reduction stopped at the alcohol stage. The phenylurethan obtained from this product melted at 86°. Straus and Grindel reported a melting point of 83—84°.

Monobenzylacetophenone, previously reduced to 1,3-diphenylpropane, only by catalytic means,[7] in this investigation was reduced by the action of red phosphorus and hydriodic acid in a heated sealed tube.[9] It is significant that neither Clemmensen's[10] nor Hartung's method accomplished the desired result.

Dibenzylacetophenone was formed simultaneously with the monobenzyl compound. Its purification was complicated by a tendency to yield intractable condensation products if the temperature were too high or if the vacuum were not sufficiently low. Although the earlier investigators were unable to prepare its oxime, this compound was finally obtained.

The corresponding alcohol, 1,3-diphenyl-2-benzylpropanol-1,[11] had not been prepared before by the reduction of this ketone. Sodium and alcohol sufficed to bring about the desired transformation. This alcohol readily yielded a phenylurethan.

Dibenzylacetophenone was reduced to a hydrocarbon by the method involving hydriodic acid and red phosphorus. The product, so synthesized, has already been reported.[12] In the reduction of dibenzylacetophenone, as in the case of the monobenzyl ketone, Clemmensen's method failed completely; Hartung's gave only the secondary alcohol.

Tribenzylacetophenone was prepared from dibenzylacetophenone. Despite strenuous efforts, all attempts to isolate its oxime were uniformly unsuccessful. It is believed that steric hindrance is the cause of these negative results.

The corresponding carbinol, 1,3-diphenyl-2,2-dibenzylpropanol-1, was easily formed from the ketone by the use of sodium and absolute alcohol. Attempts to purify the product, a gummy mass, by vacuum distillation, always failed because of resinification. The carbinol was separated from the unchanged ketone by taking advantage of its greater solubility in ethyl alcohol. All efforts to prepare a phenylurethan invariably came to nought.

Tribenzylacetophenone was not affected when subjected to the reducing action of Hartung's or of Clemmensen's method. Heating in a sealed tube with red phosphorus and hydriodic acid brought about the desired result, the formation of 1,3-diphenyl-2,2-dibenzylpropane, tetrabenzylmethane. This hydrocarbon had previously been prepared by treating appropriate Grignard reagents with certain organic halides.[13,14] However, the yields never approached those obtained in this investigation.

The consistent failure of the Clemmensen method to reduce the ketones of this series, and the analogous derivatives of pinacolone, previously reported, seems sufficiently interesting to merit further study.

In the experimental part only the reactions leading to new products or to considerably improved yields of known compounds will be reported.

It is a pleasure to acknowledge the assistance given us by W. F. Bruce and R. W. Ehlers in certain preliminary work in the synthesis of tribenzylacetophenone. Without the financial aid afforded by the Atwater Fund this investigation could not have been undertaken.

Experimental

Dibenzylacetophenone Oxime.—Five grams of ketone was dissolved in 75 cc. of 95% ethyl alcohol. An excess (3 g.) of hydroxylamine hydrochloride and 2 g. of potassium hydroxide in 3 cc. of water were added. The system was refluxed vigorously for ninety-six hours. Water, sufficient to dissolve the potassium salt, was added and the solution extracted with ether. After drying with anhydrous sodium sulfate, the ether solution was distilled. The white crystalline residue was recrystallized from 95% ethyl alcohol, in which any unchanged ketone dissolved readily. The oxime melted at 157°.

Anal. Calcd. for $C_{22}H_{21}ON$: N, 4.45. Found: N, 4.50.

Phenylurethan of 1,3-Diphenyl-2-benzylpropanol-1.—Three grams of the alcohol was dissolved in 3 cc. of dry toluene; 2 g. of phenyl isocyanate was added and the solution kept at 40° for fourteen hours. The white, crystalline solid which settled out was recrystallized from 95% ethyl alcohol. The melting point was 185°.

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(6) Dieckmann and Kämmerer, *Ber.*, **39**, 3049 (1906).

(7) Straus and Grindel, *Ann.*, **439**, 294 (1924).

(8) Hartung, THIS JOURNAL, **53**, 2248 (1931).

(9) Lautemann, *Ann.*, **310**, 322 (1863).

(10) Clemmensen, *Ber.*, **46**, 1841 (1913).

(11) Tiffeneau and Lévy, *Bull. soc. chim.*, [4] **39**, 780 (1926).

(12) Hill, Little, Wray, Jr., and Trimbey, THIS JOURNAL, **56**, 911 (1934).

(13) Schmerda, *Monatsh.*, **30**, 387 (1909).

(14) Trotman, *J. Chem. Soc.*, **127**, 88 (1925).

Anal. Calcd. for $C_{29}H_{27}O_2N$: N, 3.32. Found: N, 3.35.

Tribenzylacetophenone.—160 g. of dibenzylacetophenone was dissolved in twice its volume of toluene, 400 cc. Cooling occurred as solution progressed. Twenty-three grams of sodamide of the necessary high quality was finely pulverized and placed in a three-necked flask equipped with a condenser, a mercury-seal stirrer, and a dropping funnel. The ketone solution was introduced dropwise during two hours while the mixture was stirred and refluxed. At the end of the two-hour period, the system became purple and ammonia was evolved very rapidly. The reaction was continued for eighteen hours. Seventy-four grams of benzyl chloride, b. p. 176–178°, was then introduced at a rate of three or four drops a second. Heating and stirring were continued for twenty-four hours more. By the end of this period the purple color had given place to yellowish-brown. The flask was cooled, 250 cc. of water was added and the toluene layer separated. It was washed with water, dilute hydrochloric acid, and again with water, dried with calcium chloride and distilled on a steam-bath under slightly reduced pressure. The crude ketone which crystallized was filtered and washed with 50 cc. of methyl alcohol in which tribenzylacetophenone is but very slightly soluble, whereas the dibenzyl compound is soluble. The product, recrystallized from toluene, melted at 127–128°. The average yield of crude crystals was 135–140 g., about 68%. The unused dibenzylacetophenone was recovered. Neither the use of a larger proportion of sodamide nor longer heating had a material effect in increasing the output.

Anal. Calcd. for $C_{29}H_{26}O$: C, 89.23; H, 6.67; mol. wt., 390. Found: C, 89.24, 89.17; H, 6.74, 6.77; mol. wt. (ebullioscopic method with benzene), 383, 380.

1,3-Diphenyl-2,2-dibenzylpropanol-1.—Five grams of tribenzylacetophenone was dissolved in 400 cc. of absolute alcohol. As rapidly as possible, 50 g. of sodium was added to the solution. When the vigor of the reaction had abated, the system was heated and refluxed for half an hour, then 200 cc. of water was added to the cooled contents of the flask. The gummy organic product was heated repeatedly with portions of hot ethyl alcohol which removed the carbinol, but had little effect on any unchanged ketone. Evaporation of the alcohol yielded 2 g. of a very viscous, light yellow liquid which decomposed when heated even under a low pressure. Two grams of ketone was recovered.

When a similar experiment was conducted with isoamyl alcohol as the medium, there resulted in addition to the oil, mentioned above, a solid which, after treatment with acetone and finally with toluene, was found to be tetrabenzylmethane.

Anal. Calcd. for $C_{29}H_{28}O$: C, 88.77; H, 7.14; mol. wt., 392. Found: C, 88.73, 88.75; H, 7.06, 7.08; mol. wt. (Rast method), 383, 384.

Tetrabenzylmethane.—Four grams of tribenzylacetophenone was heated for twenty-four hours at 200° in a sealed tube with 4 g. of red phosphorus and 80 cc. of 47% hydriodic acid. The cooled tube was opened and the contents extracted with toluene. This solution was washed with aqueous potassium hydroxide and with water, and then dried with calcium chloride. Removal of the toluene left a gummy white mass which upon repeated crystallization from ethyl alcohol gave 0.5 g. of large diamond-shaped crystals melting at 164°. The yield is 13%.

Anal. Calcd. for $C_{29}H_{28}$: C, 92.55; H, 7.45; mol. wt., 376. Found: C, 92.50; H, 7.38; mol. wt. (Rast method), 374.

Summary

1. Tribenzylacetophenone has been produced by a sodamide synthesis.

2. Certain derivatives of the omega-benzylacetophenones, analogous to a series of omega-benzylpinacolone derivatives, have also been prepared.

Middletown, Conn. Received October 2, 1935

[Contribution from the Research Laboratory, United States Steel Corporation]

A Useful Integrated Form of the Equation for Calculating Change of Equilibrium with Temperature

By J. B. Austin

There are a number of thermodynamic equations expressing the change of equilibrium with temperature which have the general form

$$d \ln f/dT = \Delta H/RT^2 \qquad \text{I}$$

where f is the equilibrium constant, vapor pressure, solubility, or some other similar quantity which characterizes a state of equilibrium, ΔH is the molar heat effect for the reaction in question at the absolute temperature T, and R is the gas constant. If ΔH is assumed constant with T, this equation integrated between T' and T gives

$$\ln f'/f = \frac{\Delta H}{R}\left(\frac{T'-T}{T'T}\right) \qquad \text{II}$$

This relation, according to which $\ln f'/f$ is a linear function of $1/T$, has proved very useful as an aid in the critical examination of experimental observations, and even as a basis for estimating values of f'/f from ΔH (or conversely) when no direct measurement is available. The ease with which it can be applied, however, can be considerably increased in a number of cases, particularly in condensed systems, by a simple trans-