A reaction took place immediately with the formation of a heavy pale-yellow precipitate and the evolution of heat. The mixture was heated on a steam-bath for one hour with shaking. The precipitate was filtered, washed with dioxane and ether, and dried in a vacuum desiccator. The yield was 13.6 g. (10%) of pale-yellow crystals melting at 214.5–215.5° dec.

N-*p*-Acetylsulfanilyl-N′-phenylhydrazine.—Four and five-tenths grams of phenylhydrazine was placed in a beaker containing 5 g. of sodium carbonate dissolved in 100 ml. of cold water. To this was added slowly with stirring 10 g. of *p*-acetylaminobenzenesulfonyl chloride. The mixture was removed from the ice-bath after all the chloride had been added and stirred for an additional thirty minutes. The tan precipitate was removed by filtration, washed with water, and dried in a vacuum desiccator. It weighed 11 g. (76% yield). Three recrystallizations from an alcohol–water mixture, using Norit, gave a white crystalline product melting at 157–9° dec.

N-(N-Thiazolyl)-*p*-sulfonamidophenyl-N′-methylthiourea.—Seventeen and seven-tenths grams of sulfathiazole was placed in a small flask with a ground glass joint. To this was added 150 ml. of absolute ethanol and 5 g. of methyl isothiocyanate. The mixture was refluxed on the steam-bath for twenty-two hours. At the end of this time there was a slight residue in the flask. The reaction mixture was cooled in an ice-bath and the crystalline precipitate filtered, washed with ethanol, and dried. The yield was 17 g. (75%). The product was thoroughly ground up and treated with dilute hydrochloric acid to remove any unreacted sulfathiazole. It was then recrystallized from boiling water using Norit. White needles melting at 190–193° were obtained.

Summary

1. Twelve sulfanilamide derivatives containing a substituted urea or thiourea grouping in the N^4 position and fourteen containing a urea or thiourea grouping in the N′ position were prepared and described.

2. The preparation of acetylsulfanilylhydrazine and N-*p*-acetylsulfanilyl-N′-3-nitrophenylhydrazine is described.

3. Methyl isothiocyanate was found to react with sulfathiazole to give N-(N-thiazolyl)-*p*-sulfonamidophenyl-N′-methylthiourea.

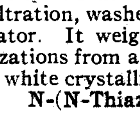
LAFAYETTE, IND. RECEIVED JUNE 22, 1944

[CONTRIBUTION FROM DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CHICAGO]

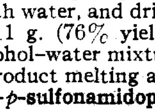
Factors Influencing the Course and Mechanism of Grignard Reactions. XVI. An Isomer of Isophorone—$\Delta^{3,4}$-3,5,5-Trimethylcyclohexenone

BY M. S. KHARASCH AND P. O. TAWNEY

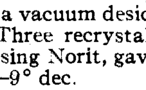
In a previous paper[1] it was shown that methylmagnesium bromide, in the presence of a small amount of ferric chloride, converts isophorone into an isomeric substance for which the structures (II) and (III) were considered.



Isophorone (I)



Enol (II)



Keto (III)

The following facts favor the enol structure (II): (a) The compound is easily reconverted into isophorone, especially in the presence of acid. (b) The new compound yields a semicarbazone which is identical with that of isophorone, since the two do not depress each other's melting points. The following facts favor the keto structure (III): (a) The molar refraction of the new compound checks with that calculated for a compound with structure (III). (b) Cyclohexylidineacetic acid and cyclohexenylacetic acid are easily converted into one another as are cyclohexylidine acetone and cyclohexenylacetone.[2] By analogy, similar behavior might be expected of the two ketones (I) and (III).

At the time the aforementioned paper was published, the available data were insufficient to warrant a decision between structures (II) and (III). Structure (III) was favored, inasmuch as no stable enol of a cyclic ketone (saturated or unsaturated) has ever been isolated. The absorption spectra of the two compounds in question have, however, since been determined. They indicate conclusively that the new isomer has the keto structure (III). That is to say, when methylmagnesium bromide reacts upon isophorone in the presence of small amounts of ferric chloride, it shifts the double bond from the α-β to the β-γ position.

The ultraviolet absorption curves for isophorone I and $\Delta^{3,4}$-3,5,5-trimethylcyclohexenone (III) are given in Fig. 1. These curves (as well as the infrared absorption curves in Fig. 2) were obtained through the courtesy of the Stamford Research Laboratories of the American Cyanamide Company, to whom sincere thanks are here expressed. These investigators have also kindly provided an analysis of their findings, from which some of the following statements are taken.

The ultraviolet absorption curve for isophorone exhibits an intense broad absorption band with maxima near 2845, 2975, 3070 and 3700 mm.$^{-1}$. The band at 4450 mm.$^{-1}$ indicates the presence of conjugated unsaturation; the absorption near 3700 mm.$^{-1}$ may possibly represent approximately 0.5% of a substance such as compound (II) with two conjugated double bonds in the ring. Cooke and Macbeth[3] have examined the ultraviolet absorption spectra of a number of unsaturated aldehydes and ketones. The curve they obtained for piperitone (IV) in hexane very closely approximates that of isophorone (I) in

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(1) Kharasch and Tawney, THIS JOURNAL, **63**, 2308 (1941).

(2) Linstead, *J. Chem. Soc.*, 1603 (1930).

(3) Cooke and Macbeth, *J. Chem. Soc.*, 1408 (1938).

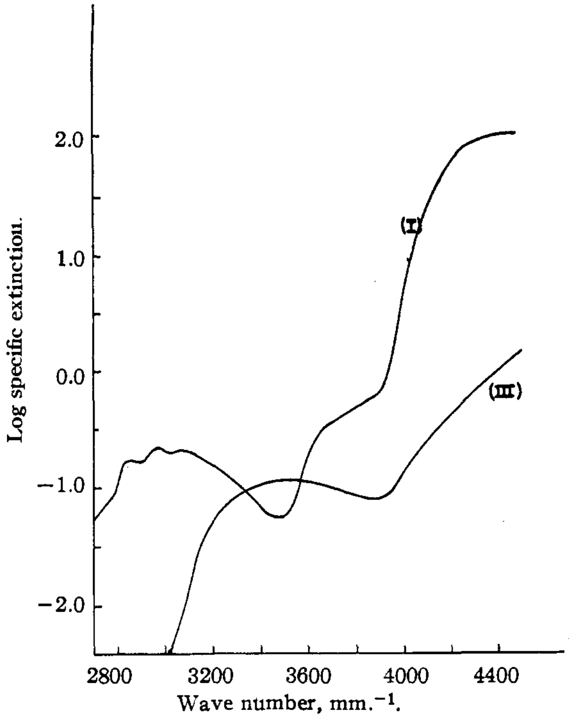
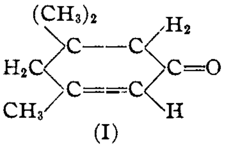


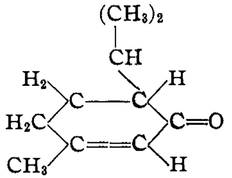
Fig. 1.—Ultraviolet absorption curves for cyclohexane solutions of isophorone (I), and $\Delta^{3,4}$-3,5,5-trimethylhexenone (III).

cyclohexane, as may be seen from the following data.



(I)

$K_{4450} = 106.2$
$K_{2975} = 0.228$



(IV)

$K_{4438} = 118$
$K_{3000} = 0.228$

The ultraviolet absorption curve of the new isomer shows no evidence for any conjugated double bonds, but it does show carbonyl absorption in the broad band near 3500 mm.⁻¹. A double bond in the ring, when not conjugated, has a very small effect on the absorption. The spectrum for compound (III) may be compared with that of menthone (V) given by Cooke and Macbeth[3]

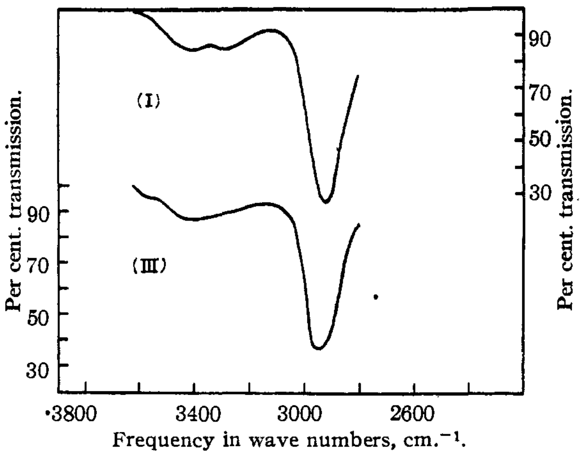


Fig. 2a.—Infrared absorption spectra (thickness 0.02 mm.).

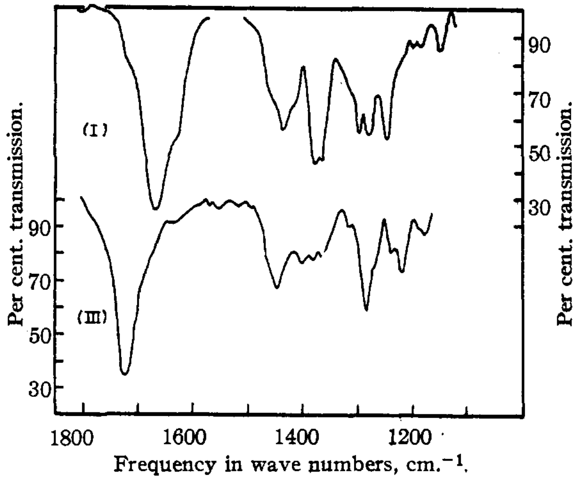


Fig. 2b.—Infrared absorption spectra (thickness 0.01 mm.)

Isophorone shows an infrared absorption band at 1670 cm.⁻¹ which is characteristic of a carbonyl group conjugated with an olefin double bond. The spectrum observed is quite parallel to that of mesityl oxide. The new isomer shows no infrared

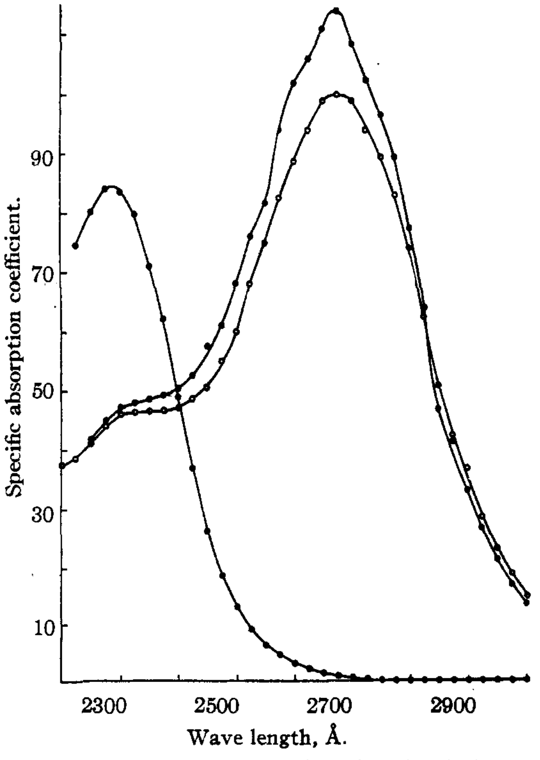
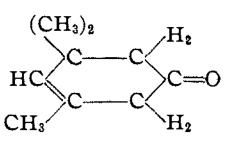
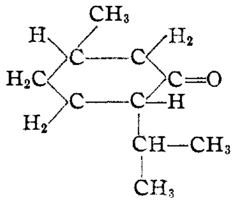


Fig. 3.—Absorption spectra in ethanol solution: ● cyclohexanone semicarbazone; ⊙, isophorone semicarbazone; ○, tautomer (III) semicarbazone.



(III)

$K_{3500} = 0.117$



(V)

$K_{3390} = 0.126$

absorption for hydroxyl, either associated or unassociated. The carbonyl absorption is that of a normal ketone.

These data indicate that both the infrared and ultraviolet absorption spectra of the new compound are in accord with the keto structure (III).

Structure of the Semicarbazone Formed from Compounds (I) and (III).—Compounds (I) and (III) each yields a semicarbazone which melts at 186–187°.[1] Since these semicarbazones do not depress each other's melting points, they may be concluded to be identical. This conclusion is supported by their ultraviolet absorption curves (Fig. 3).

The chemical data do not warrant the assignment of a definite structure to the semicarbazone in question, but a comparison of its ultraviolet absorption curve with that of cyclohexanone semicarbazone (Fig. 3) suggests that the semicarbazone in question is derived from isophorone (I) rather than from its isomer (III). If such is the fact, then when the semicarbazone is formed from (III), the double bond is shifted, during the process of formation, from the β,γ to the α,β position.

Summary

1. Ultraviolet and infrared absorption spectra indicate that when isophorone is treated with methylmagnesium bromide in the presence of small amounts of ferric chloride, the double bond in the ring is shifted from the α,β to the β,γ position.

2. In the formation of the semicarbazone of $\Delta^{3,4}$-3,5,5-trimethylcyclohexenone, the double bond is shifted back to the α,β position and the semicarbazone of isophorone is obtained.

CHICAGO, ILLINOIS RECEIVED AUGUST 28, 1944

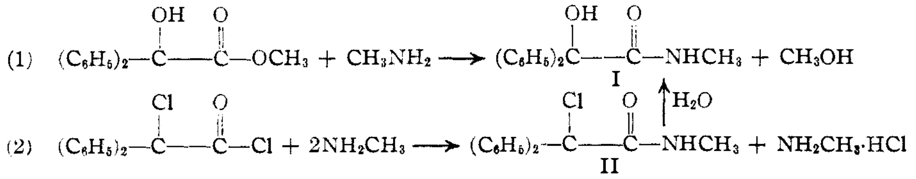
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF INDIANA UNIVERSITY]

Antispasmodics and Anticonvulsants. IV. N,N'-Substituted α-Aminodiphenylacetamides

BY JOHN H. BILLMAN, THELMA G. WARD[1] AND PHIL HARTER HIDY[2]

In an earlier publication[3] it was shown that certain α-aminodiphenylacetamides having identical radicals attached to both of the nitrogen atoms, possessed anticonvulsant as well as antispasmodic acitivity. It was decided, therefore, to synthesize a number of derivatives having dissimilar groups attached to the nitrogens by using α-chlorodiphenylacetyl chloride and two different amines.

The α-chlorine atom of an α-chloroacyl chloride is normally much less reactive than the chlorine atom attached to the carbonyl group. Klinger[4] has done some work which indicates that α-chlorodiphenylacetyl chloride when treated with two moles of aniline produces N-phenyl-α-chlorodiphenylacetamide. However, to verify this the following reactions were run



$$(1)\quad (C_6H_5)_2-\overset{OH}{\overset{|}{C}}-\overset{O}{\overset{\|}{C}}-OCH_3 + CH_3NH_2 \longrightarrow \underset{I}{(C_6H_5)_2\overset{OH}{\overset{|}{C}}-\overset{O}{\overset{\|}{C}}-NHCH_3} + CH_3OH$$

$$\uparrow H_2O$$

$$(2)\quad (C_6H_5)_2-\overset{Cl}{\overset{|}{C}}-\overset{O}{\overset{\|}{C}}-Cl + 2NH_2CH_3 \longrightarrow \underset{II}{(C_6H_5)_2-\overset{Cl}{\overset{|}{C}}-\overset{O}{\overset{\|}{C}}-NHCH_3} + NH_2CH_3\cdot HCl$$

The diphenylacetic acid derivatives (I) formed in reactions (1) and (2) were found to be identical. Both products melted at 146–147° and gave no depression in melting point when fused together. This temperature is approximately 60° below the melting point of the isomeric α-methylaminodiphenylacetic acid.[5] Neither product was soluble in alkali or hydrochloric acid. Thus the structure of Compound II is established. These results along with the fact that the α-chloroacetamides were obtained in yields of better than seventy per cent. confirm the order and relative ease of replacement of the chlorine atoms in α-chlorodiphenylacetyl chloride. It is this appreciable difference in reactivity which made possible the synthesis of α-aminodiphenylacetamides, with unlike radicals attached to each nitrogen atom, according to the reactions

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(1) Submitted to the Faculty of the Graduate School in partial fulfillment of the requirements for the degree, Doctor of Philosophy, in the Department of Chemistry, Indiana University.

(2) Eli Lilly Fellow.

(3) Billman and Hidy, THIS JOURNAL, **65**, 760 (1943).

(4) Klinger, *Ann.*, **389**, 255 (1912).

(5) Biltz and Seydel, *Ann.*, **391**, 227 (1912).