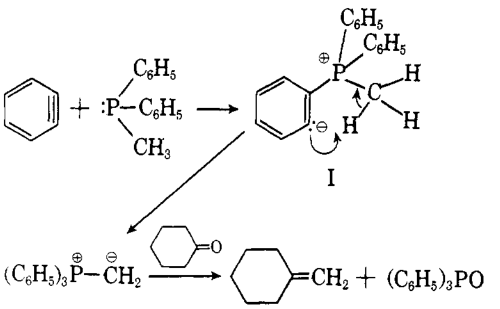

reaction. In order to obtain more information concerning this question, benzyne was generated in the presence of an equimolar amount of methyldiphenylphosphine using the *o*-bromofluorobenzene–lithium amalgam procedure.[7] Again, the yield of methylenecyclohexane obtained on treating the reaction mixture with cyclohexanone was low (21%). Since the deactivation of I by lithium bromide does not seem too likely, we tend toward the conclusion that it is a reaction between benzyne and triphenylphosphinemethylene which serves to complicate matters. Further evidence favoring this view was obtained in an experiment in which methyldiphenylphosphine was allowed to compete more effectively for the benzyne (generated by the lithium amalgam procedure) by having the phosphine present in large excess (methyldiphenylphosphine to *o*-bromofluorobenzene ratio = 11). In this case methylenecyclohexane was obtained in 52% yield.

The reaction of phosphinealkylidenes with benzyne is receiving further attention in these laboratories.

Experimental

Preparation of Methyldiphenylphosphine.—To a stirred solution of 75 g. (0.33 mole) of diphenylchlorophosphine in 100 ml. of ether at 0° (under nitrogen) was added 245 ml. (0.33 mole) of 1.35 *N* methyllithium in ether over a period of 2 hr. The ice bath was removed and the mixture stirred for an additional 30 min. The organic layer was decanted and fractionally distilled to give 52 g. (78%) of methyldiphenylphosphine, b.p. 108–110° (0.15 mm.); lit.[8] b.p. 120–122° (0.15 mm.). The product was characterized by conversion to dimethyldiphenylphosphonium iodide, m.p. 253–255° (lit.[8] m.p. 242–243°); a mixture melting point with an authentic sample was undepressed.

The Reaction of Benzyne (*via* the Magnesium Route) with Methyldiphenylphosphine.—Into a 200 ml., three-necked flask equipped with a mechanical stirrer, an addition funnel, and a reflux condenser, all maintained under an atmosphere of dry nitrogen, were placed 1.46 g. (0.06-g.-atom) of magnesium turnings and 50 ml. of tetrahydrofuran, freshly distilled from lithium aluminum hydride. The magnesium was activated with 3 drops of 1,2-dibromoethane, and then 12.0 g. (0.06 mole) of methyldiphenylphosphine was added with a syringe. The mixture was heated to 60°, and a solution of 8.95 g. (0.05 mole) of *o*-bromofluorobenzene in 30 ml. of anhydrous tetrahydrofuran was added, dropwise with stirring, over a period of 1 hr. The resulting burgundy red solution was stirred at reflux for 30 min.; it gave a negative Gilman Color Test I. The reaction mixture was cooled to room temperature, and 9.1 g. (0.1 mole) of cyclohexanone was added during 15 min. The mixture refluxed slightly and a tan precipitate formed, but the red color was not discharged. The reaction mixture was stirred while a gentle reflux was maintained for 3 hr., then was filtered under nitrogen. The tan residue was washed with tetrahydrofuran. All volatile material was removed from the combined filtrate and washings by trap-to-trap distillation at 85° (0.3 mm.). Analysis of the distillate by gas chromatography, using xylene as an internal standard, showed that 6.93 mmoles (13.8%) of methylenecyclohexane and 1.13 mmoles of cyclohexanone were present. Methylenecyclohexane was identified by its retention time and infrared spectrum. Three similar reactions with reaction times of 1.5, 2.5, and 15 hr. gave methylenecyclohexane in yields of 13.8, 10.8, and 14.2%, respectively.

The Reaction of Benzyne (*via* the Lithium Amalgam Route) with Methyldiphenylphosphine.—Lithium amalgam, from 0.31 g. (0.045 g.-atom) of lithium and 125 g. of mercury, was prepared in a Schlenk tube under an argon atmosphere using the method of Wittig and Pohmer.[7] To this was added a solution of 2.68 g. (0.015 mole) of *o*-bromofluorobenzene and 3.40 g. (0.017 mole) of methyldiphenylphosphine in 15 ml. of freshly distilled ether. The tube was sealed at atmospheric pressure (argon atmosphere) and shaken at room temperature for 24 hr. During this time the solution became dark red, and a very small amount of light-colored solid precipitated. The solution was decanted into a 100-ml. flask equipped with a reflux condenser and a side-arm inlet tube, maintained under an argon atmosphere. After the amalgam had been washed with 10 ml. of anhydrous ether and the washings combined with the solution, 2.94 g. (0.03 mole) of cyclohexanone in 5 ml. of ether was added and the mixture stirred at reflux under argon overnight. The resulting dark red solution was decanted from a cream-colored solid and separated into low [25–50°(0.3 mm.)] and high [50–85° (0.05 mm.)] boiling fractions by trap-to-trap distillation. Gas chromatographic analysis of the first fraction, using toluene as an internal standard, showed that 3.16 mmoles of methylenecyclohexane (21% based on the completely consumed *o*-bromofluorobenzene) had been formed. Analysis of the second fraction, 1.95 g., showed it to contain methyldiphenylphosphine, a minor amount of cyclohexanone, and another high boiling component which showed absorption in the infrared spectrum at 1725 cm.$^{-1}$; this suggests that it is a product of the base-catalyzed condensation of cyclohexanone itself.

Another experiment was carried out in the same manner in which the same quantities of lithium amalgam and *o*-bromofluorobenzene were allowed to react in the presence of 33.0 g. (0.165 mole) of methyldiphenylphosphine in 25 ml. of ether. Addition of 0.03 mole of cyclohexanone resulted in 7.85 mmoles (by gas chromatography) (52.4%) of methylenecyclohexane.

Acknowledgment.—The authors are grateful to the U. S. Army Research Office (Durham) for generous support of this work and to the Victor Chemical Works Division of the Stauffer Chemical Company for a gift of diphenylchlorophosphine.

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[7] G. Wittig and L. Pohmer, *Chem. Ber.*, **89**, 1334 (1956).

[8] S. T. D. Gough and S. Trippett, *J. Chem. Soc.*, 4263 (1961).

A Novel Synthesis of 1,2,3-Triphenylisoindole

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The synthesis of the remarkably stable *o*-quinoid compound 1,2,3-triphenylisoindole (I) has been achieved only by the reaction of phenyllithium with 2,3-diphenylisoindolone (II).[1] We have now prepared this isoindole by a novel one-step process starting from the readily available 1,3-diphenylisobenzofuran (III).[2]

When furan III was mixed with an approximately equimolar amount of thionylaniline (IV) in benzene, a red color appeared immediately, indicative of a charge-transfer complex. After refluxing the mixture for thirty-six hours, none of the expected adduct (V) was obtained,[3] and most of the furan was recovered

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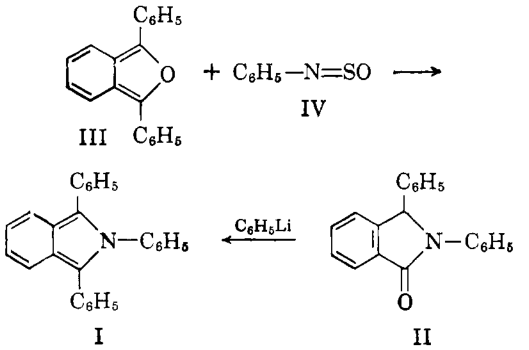
[1] W. Theilacker and W. Schmidt, *Ann.*, **605**, 43 (1957).

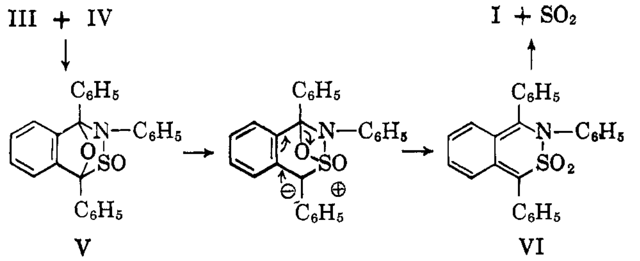
[2] M. S. Newman, *J. Org. Chem.*, **26**, 2630 (1961), and earlier references cited therein.

[3] For a recent review of the Diels-Alder addition of dienes to thionylamines, see: G. Kresze, A. Maschke, R. Albrecht, K. Bederke, H. P. Patzschke, H. Smalla, and A. Trede, *Angew. Chem.*, **74**, 135 (1962).

unchanged. Since Diels–Alder reactions can be greatly accelerated by Lewis acid catalysts,[4] the addition of III to IV was attempted in refluxing benzene in the presence of boron trifluoride etherate. Under these conditions, after thirteen hours heating, there was isolated directly 1,2,3-triphenylisoindole in 78% yield. The isoindole I was obtained also in 46% yield when compounds III and IV were heated together without a solvent at 84° for thirty-six hours.



The exact mechanism of the conversion of furan III to isoindole I is somewhat obscure. We propose that the normal Diels–Alder adduct (V) is first formed. Rearrangement of adduct V, as illustrated, could lead to an *o*-quinoid δ-sultam (VI), which then collapses to 1,2,3-triphenylisoindole by thermal extrusion of sulfur dioxide. The loss of sulfur dioxide in this manner from both unsaturated δ-sultones and unsaturated δ-sultams has ample analogy.[5,6]



Experimental

Reaction of 1,3-Diphenylisobenzofuran (III) with Thionylaniline (IV). A. In the Presence of Boron Trifluoride.—Boron trifluoride etherate (3.0 ml.) was added to a solution of furan III (1.00 g., 4.1 mmoles) and thionylaniline[7] (0.62 g., 4.4 mmoles) in benzene (50 ml.). After refluxing for 13 hr., the brown reaction solution was washed well with water (two 150-ml. lots), dried over magnesium sulfate, and evaporated. The dark residue was dissolved in benzene (10 ml.) and chromatographed on Woelm neutral alumina (grade II, 60 g.). The column was eluted with benzene (250 ml.), and the eluate was evaporated to yield isoindole I, which was crystallized from ethanol as fine pale yellow needles (1.10 g., 78%), m.p. 234–235° (lit.[1] m.p. 234.5°). The infrared and ultraviolet spectra of this material corresponded exactly to the reported spectral data[1] for compound I.

Anal. Calcd. for $C_{26}H_{19}N$: C, 90.40; H, 5.54; N, 4.06. Found: C, 90.48; H, 5.36; N, 4.22.

B. Reaction of III and IV in the Absence of Catalyst.—The reaction described before was repeated a number of times with minor variations in the absence of boron trifluoride; furan III was recovered in all cases in at least 80% yield. The variations included the use of refluxing toluene in place of benzene as solvent, increasing the heating time to 36 hr. and using a 4-equiv. excess of thionylaniline. Isoindole I was formed in moderate yield, however, in the following reaction in which solvent was omitted.

A mixture of furan III (1.00 g., 4.1 mmoles) and thionylaniline (2.0 ml., 17.7 mmoles) was heated for 36 hr. at 84° (water bath) in a test tube fitted with a loose cotton plug. The resulting brown mass was dissolved in benzene (20 ml.), and the solution was diluted with ethanol (80 ml.). The solution was concentrated by boiling to 35 ml. and allowed to cool, when isoindole I (0.650 g., 46%), m.p. 233°, separated as pale yellow needles.

Acknowledgment.—We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

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[4] P. Yates and P. Eaton, *J. Am. Chem. Soc.*, **82**, 4436 (1960).

[5] Th. Morel and P. E. Verkade, *Rec. trav. chim.*, **70**, 35 (1951), and earlier references cited therein.

[6] B. Helferich and W. Klebert, *Ann.*, **657**, 79 (1962).

[7] A. Michaelis and R. Herz, *Ber.*, **23**, 3481 (1890).

Acetylenic Amines. VI. Amides of Secondary Acetylenic Amines

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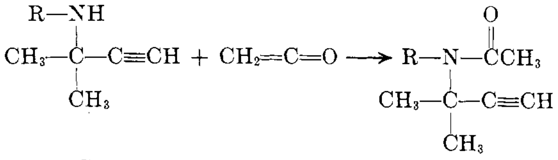
Received October 23, 1962

The availability[1,2] of many substituted propargylamines and the notable activity of some of these as hypotensive agents[3a,b] suggested the preparation of assorted derivatives. The preparation and reactions of some of the amides derived from secondary propargylamines (I) are discussed in this paper.



Ia, R = CH_3
b, R = C_2H_5
c, R = $CH(CH_3)_2$
d, R = $C(CH_3)_3$

II

When the N-methyl-1,1-dimethylpropargylamine (Ia) was dissolved in dry ether and treated with ketene, the desired amide (IIa) was obtained and could be isolated by distillation. Similar products were obtained with Ib and Ic, but no derivative of Id could be obtained even after a twelve-hour treatment with ketene. It was found that these amides could be prepared by the usual treatment with acetic anhydride followed by treatment with water, if the water solutions were made basic. However, when solutions of these amides in dilute hydrochloric acid were neutralized, the acetylenic amides (II) were not recovered and, instead, the keto amides (V) were isolated.

Treatment of the amide II in dry ether with anhydrous hydrogen chloride gave a solid material III. Elemental analyses indicated only the addition of hydrogen chloride. The infrared spectrum showed the absence of both the acetylene C—H absorption band at 3.05 μ and the carbonyl absorption at 6.2 μ. However, two new bands in the 6-μ region were present;

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[1] (a) G. F. Hennion and R. S. Hanzel, *J. Am. Chem. Soc.*, **82**, 4908 (1960); (b) N. R. Easton, R. D. Dillard, W. J. Doran, M. Livezey, and D. E. Morrison, *J. Org. Chem.*, **26**, 3772 (1961).

[2] C. Ainsworth and N. R. Easton, *ibid.*, **26**, 3776 (1961).

[3] (a) Abstracts 46–50, 138th National Meeting of the American Chemical Society, New York, N. Y., September, 1960; (b) C. W. Ryan, N. R. Easton, R. D. Dillard, and F. G. Henderson, *J. Med. Pharm. Chem.*, **5**, 780 (1962).