the aqueous phase filtered to remove dicyclohexylurea. Samples were spotted onto Whatman No. 40 paper along with standards of thymidylic acid (R_f 0.12), dithymidine pyrophosphate (R_f 0.24), and β-cyanoethylthymidine-5′ phosphate (R_f 0.55) and chromatographed in isopropyl alcohol–water–concentrated ammonium hydroxide (7:2:1). The products were visualized under ultraviolet light and the areas containing the products cut out and eluted with 5 ml. of water. Not more than three components were found in each aliquot. Quantititive data (Table I) were obtained by comparing the ultraviolet absorption of each of these solutions at 267 mμ and the results expressed as the per cent of the component (in terms of its absorption) in the aliquot.

B. **From Dithymidine Pyrophosphate.**—Similar esterification reactions were carried out using 0.013 mmole of dithymidine pyrophosphate, 5.75 mmoles of hydracrylonitrile, 5 ml. of anhydrous pyridine, and either 146 mg. or 1460 mg. of DCC. The reaction was treated as in A with the results shown in Table II.

Condensation of Aromatic Aldehydes with Acetone-1,3-bis(triphenylphosphonium) Chloride in the Presence of Base[1]

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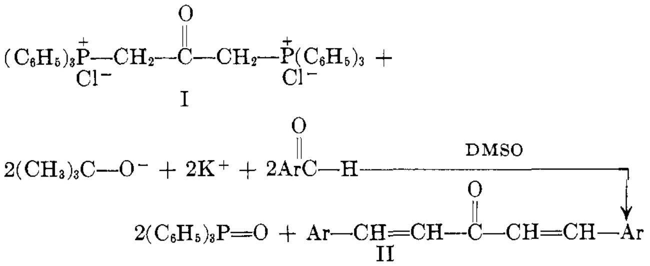
Recently Ford and Wilson[4] have reported that acetone-1,3-bis(triphenylphosphonium) chloride (I) does not give a stable mono- or diylide derived directly from I when treated with aqueous sodium carbonate, but rather undergoes hydrolysis to give triphenylphosphine oxide and acetylmethylenetriphenylphosphorane.

As part of other studies in this laboratory, I was prepared and allowed to react with butyllithium in ether. Reaction of the deeply colored solution with benzaldehyde gave dibenzalacetone.[5] These results indicated that ylide formation from I was possible and that a Wittig reaction could be effected.



$$\underset{\text{Cl}^-}{(C_6H_5)_3\overset{+}{P}}\text{—}CH_2\text{—}\overset{O}{\overset{\|}{C}}\text{—}CH_2\text{—}\underset{\text{Cl}^-}{\overset{+}{P}(C_6H_5)_3} +$$

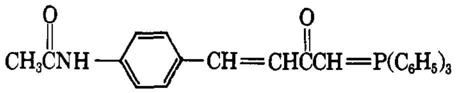
I

$$2(CH_3)_3C\text{—}O^- + 2K^+ + 2Ar\overset{O}{\overset{\|}{C}}\text{—}H \xrightarrow{\text{DMSO}} 2(C_6H_5)_3P{=}O + Ar\text{—}CH{=}CH\text{—}\overset{O}{\overset{\|}{C}}\text{—}CH{=}CH\text{—}Ar$$

II

It has now been found that I (1 mole) will react with aromatic aldehydes (2 moles) and 2 moles of potassium *t*-butoxide in dimethyl sulfoxide or 2 moles of sodium ethoxide in ethanol to give substituted dibenzalacetones (II). The potassium *t*-butoxide–dimethyl sulfoxide system was found to be the most synthetically useful. The yields of symmetrically substituted dibenzalacetones were di-*m*-nitro, 48%, di-*p*-chloro, 76%, and di-*p*-methoxy, 37%. It also was found that unsymmetrically substituted dibenzalacetones could be prepared if 1 mole of potassium *t*-butoxide and 1 mole of aldehyde were allowed to react with I followed by addition of another mole of base and a mole of another aldehyde. By this technique the mono-*m*-nitro compound was prepared in 57% yield and the *p*-chloro-*m*-nitro compound was prepared in 67% yield.

An attempt to condense I with 2 moles of *p*-acetamidobenzaldehyde and 2 moles of potassium *t*-butoxide gave no compound corresponding to II. There was isolated the phosphorane (III). Attempts to effect the reaction under more strenuous conditions were not undertaken.



III

Experimental[6]

Preparation of Acetone-1,3-bis(triphenylphosphonium) Chloride (I).—A mixture of 21.3 g. (0.168 mole) of 1,3-dichloroacetone, 112.5 g. (0.43 mole) of triphenylphosphine, and 225 ml. of chloroform was stirred under reflux for 20 hr. The cooled reaction mixture was treated with 150 ml. of dry ether. The precipitate was washed with 100 ml. of ether–chloroform (1:1.5) and dried *in vacuo* to give 103 g. of product. This material was further purified by dissolving it in 400 ml. of warm chloroform followed by precipitation with 300 ml. of dry ether. There was obtained 98 g. (86%) of I, m.p. 260–261, lit.[4] m.p. 266–267°.

Preparation of 1,5-Bis(*m*-nitrophenyl)penta-1,4-dien-3-one.—Sodium ethoxide solution (1.37 *N*, 14.5 ml., 0.02 mole) was added with stirring to a mixture of 5.98 g. (0.01 mole) of I and 3.02 g. (0.02 mole) of *m*-nitrobenzaldehyde. After stirring for 3 hr. at 30°, the precipitate was collected, washed with two 15-ml. portions of ethanol and water, and dried to give 1.4 g. (43%) of bis-*m*-nitrobenzalacetone, m.p. 238–241°, lit.[7] m.p. 238°. The infrared spectrum was commensurate with the assigned structure.

Preparation of 1,5-Bis(*p*-chlorophenyl)penta-1,4-dien-3-one.—A mixture of 2.24 g. (0.02 mole) of potassium *t*-butoxide, 5.98 g. (0.01 mole) of I, and 40 ml. of dimethyl sulfoxide was stirred under nitrogen at room temperature for 1 hr. The resulting solution was treated with 2.81 g. (0.02 mole) of *p*-chlorobenzaldehyde in 10 ml. of dimethyl sulfoxide. The mixture was warmed at 40° for 7 hr. The precipitate which formed after cooling was collected and washed with 5-ml. portions of ethanol and water. There was obtained 2.3 g. (76%) of material, m.p. 193–195°, lit.[8] m.p. 193–194°. The infrared spectrum was commensurate with the assigned structure.

Similarly 1,5-bis(*p*-methoxyphenyl)-1,4-dien-3-one was prepared in 37% yield, m.p. 123–125°, lit.[9] m.p. 125°. The infrared spectrum of this compound agreed with that predicted.

Preparation of 1-*m*-Nitrophenyl-5-phenylpenta-1,4-dien-3-one.—A mixture of 1.12 g. (0.01 mole) of potassium *t*-butoxide, 5.89 g. (0.01 mole) of I in 25 ml. of dimethyl sulfoxide was stirred for 1 hr. under nitrogen. There was added 1.06 g. (0.01 mole) of benzaldehyde and the mixture was warmed at 45° for 2 hr. This mixture was cooled and treated with 1.12 g. (0.01 mole) of potassium *t*-butoxide, and after stirring at 45° for 15 min. 1.51 g. (0.01 mole) of *m*-nitrobenzaldehyde in 15 ml. of dimethyl sulfoxide was added. The mixture was heated at 50° for 3 hr. and then cooled. The precipitate (inorganic salt) which formed on cooling was filtered and discarded. The filtrate was treated with 30 ml. of water and the crystals were collected to give 1.6 g. (57%) of material, m.p. 138–141°. A portion was recrystallized twice from ethanol, m.p. 142–143°, lit.[10] m.p. 140°.

Anal. Calcd. for $C_{17}H_{13}O_3N$: C, 73.20; H, 4.67. Found: C, 72.99; H, 4.89.

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[1] Research supported by the National Science Foundation.

[2] Rutgers Research Council Faculty Fellow, 1963–1964.

[3] Recipient of an American Cyanamid Junior Educational Award, 1961–1963.

[4] J. A. Ford and C. V. Wilson, *J. Org. Chem.*, **26**, 1433 (1961).

[5] Unpublished results of C. Dennis Hall.

[6] All melting points are uncorrected. Analyses were by G. Robertson, Florham Park, N. J.

[7] P. Pfeiffer and B. Segal, *Ann.*, **460**, 131 (1928).

[8] R. E. Lutz and T. A. Martin, *J. Org. Chem.*, **14**, 286 (1949).

[9] G. V. Austerweil and R. Polland, *J. Appl. Chem.* (London), **5**, 213 (1955).

[10] H. Kauffmann and H. Burkhardt, *Ber.*, **46**, 3808 (1914).

Similarly 1-*p*-chlorophenyl-5-*m*-nitrophenylpenta-1,4-dien-3-one was prepared in 67% yield, m.p. 160°.

Anal. Calcd. for $C_{17}H_{12}NO_3Cl$: C, 65.00; H, 3.82. Found: C, 65.31; H, 4.05.

The infrared spectrum was in accord with the assigned structure.

Preparation of *p*-Acetamidocinnamoylmethylenetriphenylphosphorane (III).—A mixture of 2.24 g. (0.02 mole) of potassium *t*-butoxide, 5.89 g. (0.01 mole) of I, and 40 ml. of dimethyl sulfoxide was stirred under nitrogen at 40° for 2 hr. There was added 3.60 g. (0.022 mole) of *p*-acetamidebenzaldehyde in 13 ml. of dimethyl sulfoxide. The mixture was heated at *ca.* 46° for 8 hr. After cooling, the precipitate was collected to give 3.0 g. of material, m.p. 269–271. Titration with perchloric acid gave equiv. wt., 487; calculated for III, 476.[11] Two crystallizations from acetic acid gave material, m.p. 273–274°.

Anal. Calcd. for $C_{30}H_{26}O_2NP$: C, 77.75; H, 5.62; N, 3.10. Found: C, 77.32; H, 5.86; N, 2.98.

The infrared spectrum had N-H and amide carbonyl absorptions. The material gave a positive test for phosphorus.[12]

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(11) S. T. Ross and D. B. Denney, *Anal. Chem.*, **32**, 1896 (1960).

(12) A Vogel, "A Textbook of Practical Organic Chemistry," 3rd Ed., Longmans Green and Co., London, 1957, p. 1043.

The Cyclization of N-Phenylcinnamamides to 3,4-Dihydro-4-phenylcarbostyrils with Polyphosphoric Acid[1]

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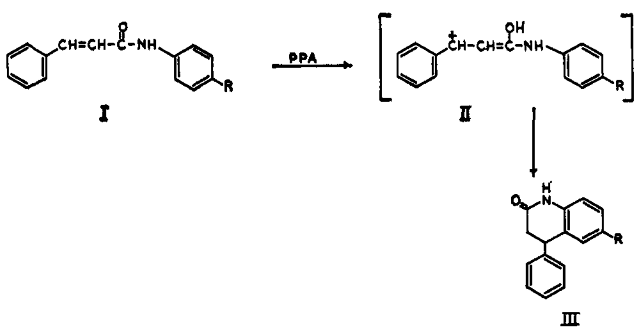
Recently, Koo[2] has reported the cyclization of 3-anilinopropionic acids to 4-keto-1,2,3,4-tetrahydroquinolines using polyphosphoric acid. A convenient preparation of 2-keto-1,2,3,4-tetrahydroquinolines (3,4-dihydrocarbostyrils) was observed by us sometime ago in the preparation of a series of substituted materials for pharmacological evaluation. The procedure reported here is analogous to the cyclization of 3-halopropionanilides[3] to 3,4-dihydrocarbostyrils in which typical Friedel–Crafts conditions using aluminum chloride were employed.

It was reasoned that N-phenylcinnamamide (I) should readily protonate in hot polyphosphoric acid to give an intermediate (II) capable of undergoing a Friedel–Crafts cyclization to 3,4-dihydro-4-phenylcarbostyril (III). In an effort to confirm this proposal and to evaluate the synthetic value and general applicability of the reaction, a series of N-(4-substituted) phenylcinnamamides were prepared. It was found that the amides could readily be cyclized with polyphosphoric acid to 3,4-dihydro-4-phenyl-6-substituted carbostyrils. N-(*p*-Nitrophenyl)cinnamamide could not be cyclized in polyphosphoric acid at reaction temperatures as high as 180°. In this case, the starting amide was recovered almost quantitatively. The parent amide and the *p*-substituted amides were prepared in benzene solution by reacting cinnamoyl chloride with the desired aniline derivative. The cyclization procedure described in the Experimental was typical and appears quite general for amides which do not have strong electron-deactivating groups on the aromatic ring. The structure of the lactams was confirmed in each case by examination of the infrared spectral characteristics, namely, by the absence of the α,β-unsaturated linkages in conjugation with the amide carbonyl and the amide II linkage of secondary amides which is generally absent in lactams. In the case of the known parent compound of the series, 3,4-dihydro-4-phenylcarbostyril, identity was established by both its characteristic spectrum and mixture melting point determination. The yields and physical properties of the substituted dihydrocarbostyrils are summarized in Table I.



It also should be noted that both N-phenylcrotonamide and N-(*p*-methoxyphenyl)crotonamide could not be cyclized to the 3,4-dihydro-4-methylcarbostyrils by this technique, thus presently limiting the synthetic applicability of this method to 4-phenyl-substituted carbostyrils. Apparently this failure is due to the instability of the intermediate alkyl carbonium ion.

TABLE I

SUMMARY OF N-PHENYL-α,β-UNSATURATED AMIDE CYCLIZATIONS

			Analysis, %					
			Calcd.			Found		
R	Yield, %	M.p., °C.	C	H	N	C	H	N
H	94	177–178[a]						
Br	83	188–190	59.62	4.00	4.63	59.40	3.79	4.50
CH_3	83	164–165	80.98	6.37	5.90	81.22	6.51	5.93
OCH_3	90	110–111	75.86	5.96	5.53	75.84	5.72	5.29

[a] Ref. 4 reports 177–178°.

Experimental

All melting points are corrected. The infrared comparisons were determined on the solid samples in potassium bromide wafers using a Beckman IR-5A infrared spectrophotometer.

3,4-Dihydro-4-phenylcarbostyril.—A mixture of 1.00 g. of N-phenylcinnamamide and 20 g. of polyphosphoric acid was heated to 120°. After 10 min., the reaction mixture was cooled and hydrolyzed over crushed ice. The reaction products were ex-

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(1) This work was supported by the Division of Neurological Disease and Blindness, National Institutes of Health under Grant No. NB-03628.

(2) J. Koo, *J. Org. Chem.*, **28**, 1134 (1963).

(3) F. Mayer, L. van Zutphen, and M. Philipps, *Ber.*, **60**, 858 (1927).