Deoxygenation of Nitro Groups by Trivalent Phosphorus. Indoles from *o*-Nitrostyrenes

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A convenient synthesis of β-alkyl-*o*-nitrostyrenes employing the phosphonate modification of the Wittig reaction is described. β-Alkyl-*o*-nitrostyrenes react with triethyl phosphite to give 2-alkylindoles in about 50% yield. β-Acyl-*o*-nitrostyrenes react similarly to give 2-acylindoles, but in lower yield. Several by-products of these reactions have been characterized. The possibility that 1-hydroxy-2-phenylindole is an intermediate in the reduction of *o*-nitrostilbene to 2-phenylindole is considered. *o*-Nitroethylbenzene gives triethyl N-(*o*-ethylphenyl)phosphorimidate when heated with triethyl phosphite.

In the course of their investigations concerning the chemistry of triethyl phosphite, Cadogan and co-workers discovered that certain aromatic nitro compounds react with triethyl phosphite in such a way that the nitrogen atom is deoxygenated and a heterocyclic ring is formed. For example, Cadogan and Cameron-Wood isolated carbazole in high yield when *o*-nitrobiphenyl was heated with triethyl phosphite.[1] In the same communication these workers reported briefly on the formation of 2-phenylindole (**8**) from the reaction of triethyl phosphite with both *trans*- and *cis*-*o*-nitrostilbene (**1** and **2**, respectively).[1] Interest in employing a similar indole ring closure in a projected synthetic sequence led us to investigate the applicability of the reaction to other β-substituted *o*-nitrostyrenes, in particular some β-alkyl and β-acyl derivatives.

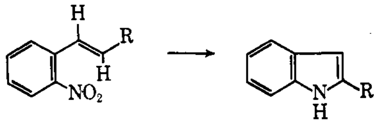
Synthesis and Reductive Cyclization of *o*-Nitrostyrenes.—1-(*o*-Nitrophenyl)propene (**3**) and 1-(*o*-nitrophenyl)-1-pentene (**4**) were chosen as representative β-alkyl-*o*-nitrostyrenes. The nitrostyrene **3** is formed along with the *para* isomer during the nitration of β-methylstyrene but has not been characterized as a pure compound.[2] Compound **4** is new. The phosphonate modification[3] of the Wittig reaction was employed for the synthesis of the *o*-nitrostyrenes **3** and **4**. The reaction also was a convenient method of obtaining *trans*-*o*-nitrostilbene. The required diethyl *o*-nitrobenzylphosphonate was prepared from *o*-nitrobenzyl bromide by means of the Michaelis–Arbuzov reaction. It has been reported[4] that the Michaelis–Arbuzov reaction is unsatisfactory with nitro-substituted halides and nitration of diethyl benzylphosphonate is the standard route to esters of *p*-nitrobenzylphosphonic acid.[5] It has now been found that *o*-nitrobenzyl bromide can be converted to the phosphonate in fair yield if the maximum reaction temperature is kept below about 110°. An attempt to use the less reactive chloride gave unsatisfactory results. The phosphonate, when treated with sodium methoxide and then an aldehyde in dimethylformamide,[6] gave the expected *trans* olefins in 30–60% yields. The *trans* stereochemistry of **3** and **4** was indicated by strong absorption in the infrared near 960 cm.$^{-1}$[7] and by the n.m.r. spectra which, in each case, revealed a coupling of 16 c.p.s. between the two vinyl protons.[8] The n.m.r. spectra gave no indication of contamination by the *cis* isomers. Similarly, the *trans*-*o*-nitrostilbene prepared was identical with a sample prepared by thermal isomerization[9] of *cis*-*o*-nitrostilbene, and the infrared spectrum of the product of the Wittig reaction gave no evidence of the presence of any *cis* isomer. These findings are in accord with the results reported by Wadsworth and co-workers in their recent study on the stereochemistry of the phosphonate modification of the Wittig reaction.[10] Several by-products were formed during the nitrostyrene syntheses. Among those which were identified are 2,2′-dinitrobibenzyl and *trans*-2,2′-dinitrostilbene.

The β-acyl-*o*-nitrostyrenes **5** and **6**, both of which are known, were obtained readily by condensation of the appropriate methyl ketone with *o*-nitrobenzaldehyde, followed in the case of **5** by dehydration of the intermediate ketol. The synthetic routes to the β-alkyl- and β-acyl-*o*-nitrostyrenes both involve reactions which proceed readily and should be capable of extension to considerably more complex *o*-nitrostyrenes.

Each of the nitrostyrenes **1**–**7**, when heated with triethyl phosphite, gave the corresponding indole **8**–**13**. Yields are tabulated in Table I. Triethyl

TABLE I

YIELDS OF 2-SUBSTITUTED INDOLES FROM REDUCTIVE CYCLIZATION OF β-SUBSTITUTED *o*-NITROSTYRENES WITH TRIETHYL PHOSPHITE



Nitrostyrene	R	Indole	% yield
1	C_6H_5 (*trans*)	8	71
2	C_6H_5 (*cis*)	8	[a]
3	CH_3	9	51
4	$CH_3CH_2CH_2$	10	60
5	CH_3CO	11	16
6	C_6H_5CO	12	16
7	C_2H_5OCO	13[b]	19[b]

[a] Not determined under usual conditions. [b] Isolated as the carboxylic acid.

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(1) J. I. G. Cadogan and M. Cameron-Wood, *Proc. Chem. Soc.*, 361 (1962).

(2) (a) F. G. Bordwell and E. W. Garbisch, Jr., *J. Org. Chem.*, **27**, 2322 (1962); (b) G. Drefhal, H. Crahmer, and W. Thomas, *Chem. Ber.*, **91**, 282 (1958).

(3) W. S. Wadsworth and W. D. Emmons, *J. Am. Chem. Soc.*, **83**, 1733 (1960).

(4) G. M. Kosolapoff, "Organophosphorus Compounds," 1st Ed., John Wiley and Sons, Inc., New York, N. Y., 1950, p. 122.

(5) A. Meisters and J. M. Swan, *Australian J. Chem.*, **16**, 725 (1963); G. M. Kosolapoff, *J. Am. Chem. Soc.*, **71**, 1876 (1949).

(6) E. J. Seus and C. V. Wilson, *J. Org. Chem.*, **26**, 5243 (1961); L. F. Fieser and M. J. Haddadin, *J. Am. Chem. Soc.*, **86**, 2392 (1964).

(7) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, p. 34.

(8) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959, p. 85.

(9) P. Ruggli and A. Staub, *Helv. Chim. Acta*, **20**, 37 (1937).

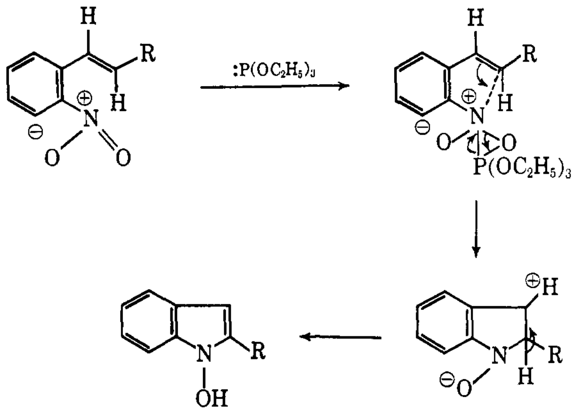
(10) D. H. Wadsworth, O. E. Schupp, III, E. J. Seus, and J. A. Ford, Jr., *J. Org. Chem.*, **30**, 680 (1965).

phosphate was also obtained and, in most cases, by-products were isolated. The structures of several of these by-products are discussed below.

All of the indoles except **11** are known compounds and were identified by comparison of melting points and ultraviolet spectral data (except for **12**) with literature values. Direct comparison with an authentic sample was made in the case of **9**. Few syntheses of 2-acylindoles have been reported, so the formation of **11** and **12** is of particular interest. The infrared spectra of **11** and **12** show strong absorption in the NH and C=O stretching regions, and the ultraviolet spectra (see Experimental Section) are consistent with the presence of 2-acylindole chromophores.[11]

Mechanistic Considerations.—The reductive cyclization of *o*-nitrostyrenes could conceivably proceed *via* the corresponding nitroso compound. Bunyan and Cadogan[12a] have shown that nitroso compounds are rapidly deoxygenated by triethyl phosphite, with heterocyclic ring formation occurring in suitably constituted molecules. It has been suggested[12a] that imido intermediates (monovalent, electron-deficient nitrogens)[12b] are involved in such reactions. It has been very tentatively suggested[12b] that the reductive cyclization of nitro compounds might also proceed through imido intermediates. An alternative path could involve ring closure prior to total deoxygenation of the nitrogen atom. Such a reaction path, involving formation of the new C–N bond concurrently with or immediately after the first deoxygenation step and implying the intermediacy of 1-hydroxyindoles, is shown in Chart I.

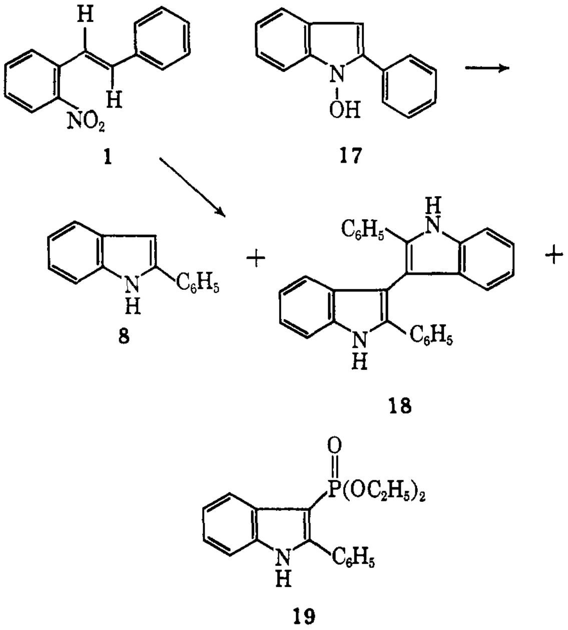
CHART I



1-Hydroxy-2-phenylindole (**17**) was synthesized as described by Fischer and Hütz.[13a] When heated with triethyl phosphite (4 hr., 160°), **17** was converted to 2-phenylindole (**8**) in 79% yield, demonstrating that, if **17** were formed from *o*-nitrostilbene under the conditions of the reductive cyclization, it would be converted mainly to **8**. Small amounts of 2,2′-diphenyl-3,3′-biindole (**18**) and diethyl 2-phenyl-3-indolylphosphonate (**19**) were formed along with **8** in this reaction. Evidence for the structures of **18** and **19** is presented below.

When the crude product from a typical reductive cyclization of *trans*-*o*-nitrostilbene was chromatographed, three products were characterized. 2-Phenylindole was isolated in 71% yield, and **18** (7% yield) and **19** (1.6% yield) were also formed. Thus, the two by-products, **18** and **19**, which are formed when **17** reacts with triethyl phosphite are also formed during the reductive cyclization of *o*-nitrostilbene (see Chart II).

CHART II



Elemental analysis and the n.m.r. spectrum suggested the structure assigned to **18**. In dimethyl-d_6 sulfoxide **18** exhibits a broad singlet at 11.6 p.p.m. (NH protons)[14] and a multiplet in the aromatic region. There is no indication of the singlet to be expected from a proton at the 3-position. The melting point and ultraviolet spectrum of **18** are in agreement with values reported[15] for a substance assigned the 2,2′-diphenyl-3,3′-biindole structure. Colonna and Monti[15] obtained **18** by iron–acetic acid reduction of 2,2′-diphenyl-$\Delta^{3,3'}$-bi-3H-indole 1,1′-dioxide, which had in turn been obtained from **17** by oxidation with *p*-benzoquinone.

The structure assigned **19** rests on elemental analysis and the n.m.r. spectrum, which shows signals consistent with the presence of two ethoxy groups attached to phosphorus and a signal at 12.2 p.p.m. (NH). The other features of the n.m.r., infrared, and ultraviolet spectra (see Experimental Section) are consistent with the assigned structure.[16]

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[11] U. Renner, D. A. Prins, A. L. Burlingame, and K. Biemann, *Helv. Chim. Acta*, **46**, 2186 (1963); E. Leete, *J. Am. Chem. Soc.*, **83**, 3645 (1961).

[12] (a) P. J. Bunyan and J. I. G. Cadogan, *J. Chem. Soc.*, 42 (1963); (b) R. A. Abramovitch and B. A. Davis, *Chem. Rev.*, **64**, 149 (1964).

[13] (a) E. Fischer and H. Hütz, *Ber.*, **28**, 585 (1895); E. Fischer, *ibid.*, **29**, 2062 (1896); (b) J. D. Loudon and G. Tennant, *J. Chem. Soc.*, 3466 (1960).

[14] The position of the NH signal is downfield from the region where such signals are observed in carbon tetrachloride or chloroform solutions. Similar downfield shifts in diethyl sulfoxide have been observed in the spectra of simpler indoles. See, for example, R. V. Jardine and R. K. Brown, *Can. J. Chem.*, **41**, 2067 (1963).

[15] M. Colonna and A. Monti, *Gazz. chim. ital.*, **92**, 1401 (1962). While this synthetic route is not unambiguous, our spectral data support the structure assigned to the final product.

[16] Simple derivatives of indolylphosphonic acids are apparently rare. The only examples which have come to our attention are 2-methyl-3-indolylphosphonic dichloride and some derivatives of 1-indolylphosphonic acid. The former is briefly mentioned in a preliminary communication [J. C. Powers, *Tetrahedron Letters*, 655 (1965)], but details of its properties and preparation are not given. The diethyl ester and N,N,N′,N′-tetramethyldiamide of the latter are reported in the patent literature [J. Meltzer, K. Wellinga, and B. G. van den Bos, U. S. Patent 3,111,525 (1963); *Chem. Abstr.*, **60**, 9285 (1964); British Patent 940,921 (1963); *Chem. Abstr.*, **60**, 2951 (1964)].

A series of experiments was carried out in which the concentration of triethyl phosphite was reduced by solvent in the hope that the rate of reduction of any intermediate **17** might be diminished and the thermally unstable **17** thereby might be diverted to other products. The results of these experiments are summarized in Table II.

TABLE II

PRODUCT DISTRIBUTION IN REDUCTION OF *o*-NITROSTILBENES AND 1-HYDROXY-2-PHENYLINDOLE AT 163 ± 2°

Compound reduced	Reaction medium[a]	% yield of products **8**	**18**	**19**
1	A	71	7	1.6
17	A	79[b]	Trace[b]	2[b]
1	B	32, 32	16, 20	5, *c*
2	B	30	16	7
17	B	44, 48	11, 11	9, 10
1	C	36,[d] 36	20,[d] 24	Trace,[d] 1.8
17	C	70	2.7	0.5

[a] Reduction media: A, triethyl phosphite (6 moles); B, triethyl phosphite (2 moles) and triethyl phosphate (4 moles); C, triethyl phosphite (2 moles) and *p*-cymene (4 moles). [b] 160°, 4 hr. [c] Yield not determined. [d] Temperature 170–173°.

When the reduction of **1** or **2** was run in reaction media in which triethyl phosphite concentration was reduced by using either triethyl phosphate or *p*-cymene as solvent, the yield of **8** dropped to about 30%, while the yield of **18** isolated rose to about 20%. Appropriate control experiments showed that **1** does not react with triethyl phosphate at 160° and that **8** is not converted to **18** by triethyl phosphite–triethyl phosphate mixtures at 160°. These results show that, as expected, some substance formed from the reaction of *o*-nitrostilbene with triethyl phosphite can be diverted to biindole **18** when the concentration of triethyl phosphite is diminished. The yields of characterizable products are not high enough for it to be unequivocably stated that the substance diverted to biindole is converted to **8** in excess triethyl phosphite, although it seems likely that this is the case. As can be seen from Table II, it has been shown that the by-products of the *o*-nitrostyrene reductions in the various solvent systems can be obtained directly from **17** under comparable conditions.[17]

Some component of the various reaction mixtures may catalyze the formation of biindole **18** from **17**, for in pure triethyl phosphate substantial amounts of **17** can be recovered after 16 hr. at 170–175° and **18** is only a minor product. In refluxing *p*-cymene, on the other hand, **17** is very cleanly converted to **18** (~90% yield after 5 hr.).

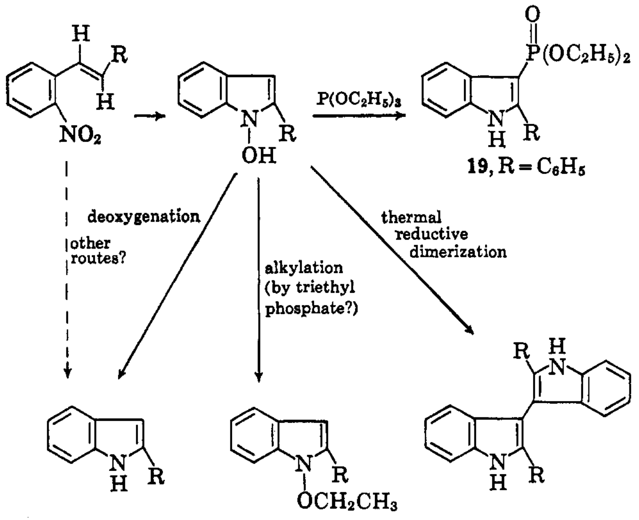
Biindoles analogous to **18** were formed during deoxygenations of the *β*-alkyl-*o*-nitrostyrenes **3** and **4**. The biindole from **3**, 2,2′-dimethyl-3,3′-biindole (**20**), is a known compound.[18] It has been prepared from the potassium salt of 2-methylindole by the action of iodine. A sample prepared by this procedure[18] had an infrared spectrum identical with that of the biindole formed from **3**. The structure of the biindole **21** from the deoxygenation of **4** is assigned by analogy and is fully supported by analytical and spectral data reported in the Experimental Section.

1-Ethoxyindoles were isolated as by-products in some of the nitrostyrene reductive cyclizations. In one experiment (see Experimental Section) a 3% yield of 1-ethoxy-2-propylindole (**14**) was isolated, along with **10**, from the nitrostyrene **4**. Similarly, 1-ethoxy-2-indolyl phenyl ketone (**15**, characterized in the Experimental Section) was consistently isolated as a by-product when 2-nitrochalcone (**6**) was converted to **12**. In the case most thoroughly studied, the *o*-nitrostilbenes, the 1-ethoxy derivative was never isolated. The compound was prepared independently but never detected as a by-product, even by thin layer chromatography.

When the reactions that involved *trans*-*o*-nitrostilbene and triethyl phosphite were interrupted after 1 hr. at 163 ± 2°, it was possible to isolate **17** in about 15% yield. Separation of **17** from other components of such reaction mixtures was facilitated by its solubility in aqueous sodium hydroxide.

These various observations can be rationalized by a generalized reaction scheme which includes 2-substituted 1-hydroxyindoles as intermediates in the reductive cyclization of *β*-substituted *o*-nitrostyrenes. Such a scheme is shown in Chart III. These results can not rule out the possibility that there may be other reaction paths from *o*-nitrostyrenes to indoles in the presence of triethyl phosphite, but all of the data at hand are consistent with invoking 1-hydroxyindoles as intermediates.

CHART III



19, $R = C_6H_5$

all R groups studied

14, $R = CH_3CH_2CH_2$
15, $R = C_6H_5CO$

18, $R = C_6H_5$
20, $R = CH_3$
21, $R = CH_3CH_2CH_2$

No information about the electronic details of the reaction between **17** and triethyl phosphite has been obtained as yet. The reaction is at least formally related to other reactions which effect cleavage of N–O bonds by the action of trivalent phosphorus[19] and to the reduction of hydroperoxides and peroxides by trivalent

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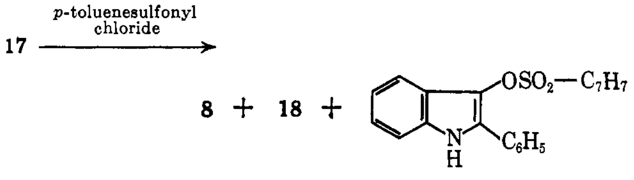
[17] It will be noted in Table II that the ratio of **8**:**18** is higher in the experiments when **17** is the starting material. This effect is probably caused by two factors. (1) None of the triethyl phosphite is used up in the first deoxygenation step when **17** is the starting material. (2) It is probable that impurities arising from the nitrostilbene may catalyze the conversion of **17** to **18**.

[18] B. Witkop and J. B. Patrick, *J. Am. Chem. Soc.*, **73**, 713 (1951).

[19] (a) J. I. G. Cadogan, *Quart. Rev.* (London), 208 (1962); (b) L. Horner and H. Hoffmann, *Angew. Chem.*, **68**, 473 (1956); (c) H. H. Wasserman and R. C. Koch, *Chem. Ind.* (London), 1014 (1956).

compounds of phosphorus.[20] The formation of the indolylphosphonate **19** is reminiscent of the formation of diethyl phenylphosphonate from dibenzoyl peroxide and triethyl phosphite under apparent radical conditions[20c] and therefore suggests a homolytic path for the formation of **19**. Likewise, the mechanistic details of the interesting, medium-sensitive, thermal conversion of **17** to **18** remain obscure. In this connection, the biindole **18** is also formed from **17** when it is treated with *p*-toluenesulfonyl chloride in pyridine–methylene chloride. After 20 hr. at room temperature, the products are 2-phenylindole (trace), **18** (14% yield), and a third product which is apparently the *p*-toluenesulfonate of 2-phenyl-3-indolol (**22**, 22% yield). The structural assignment rests on spectral data reported in the Experimental Section. It would seem that the N–O bond cleavage would be heterolytic under these conditions, since N–O bonds cleave heterolytically under similar conditions, for instance in the Beckmann rearrangement,[21] and tosyl derivatives of hydroperoxides are known to cleave heterolytically in solution.[22]



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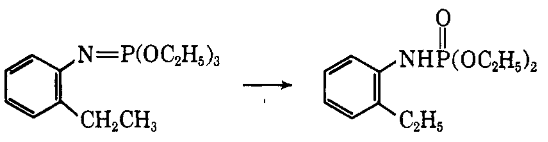
Since the present study tended to indicate the involvement of the olefinic bond in an early stage of the deoxygenation reaction, it became of interest to test the reactivity of a saturated analog. *o*-Nitroethylbenzene was found to react with triethyl phosphite to give mainly triethyl N-(*o*-ethylphenyl)phosphorimidate (**23**), a liquid which can be readily vacuum distilled. The structure is assigned on the basis of analytical and spectral data (see Experimental Section). Compound **23** is converted to diethyl N-(*o*-ethylphenyl)phosphoramidate (**24**) on alumina or silicic acid columns. Triethyl N-(*p*-dimethylaminophenyl)phosphorimidate has been reported[12a] to undergo a similar transformation on alumina.



23 **24**

Other trivalent phosphorus compounds deoxygenate nitrostyrenes to indoles. Triphenylphosphine and tributylphosphine react in this manner, but product isolation was not as convenient as when triethyl phosphite was employed as the deoxygenating agent.

Experimental Section[23]

Materials.—Commercial triethyl phosphite samples were distilled through a short Vigreux column (reduced pressure) or through a 40-cm. spinning-band column (atmospheric pressure, under nitrogen) at approximately 3-week intervals and stored in tightly closed bottles in a desiccator in the interim. Triethyl phosphate was vacuum distilled through a 40-cm. spinning-band column. *p*-Cymene was washed with aqueous ferrous sulfate, dried over magnesium sulfate, passed through an alumina column, distilled, and then fractionated through a 40-cm. spinning-band column. A minute impurity was present in such material as indicated by gas–liquid partition chromatography. All reactions involving triethyl phosphite, triethyl phosphate, or indoles were run under nitrogen.

***trans*-1-(*o*-Nitrophenyl)propene (3).**—*o*-Nitrobenzyl bromide[24] (10.80 g., 0.0500 mole), triethyl phosphite (8.4 g., 0.050 mole), and toluene (10 ml.) were mixed in an apparatus equipped with a nitrogen inlet placed so that nitrogen bubbled through the solution. The reaction mixture was heated to 110° in an oil bath and maintained at that temperature for 0.5–1.0 hr. The nitrogen swept volatile material, presumably ethyl bromide, into a cold trap as the reaction proceeded. The reaction flask was allowed to cool to room temperature, and dry dimethylformamide (20 ml.) was added. Powdered sodium methoxide was added in small portions until a deep violet color persisted. Additional sodium methoxide (2.7 g., 0.050 mole) was added and the resulting solution placed in an ice bath. Acetaldehyde (2.2 g., 0.050 mole) in dimethylformamide (5 ml.) was added. After stirring at 0° for 10 min. and 25° for 5 min. the reaction mixture was diluted with water and extracted with hexane (four 50-ml. portions). The extract was dried over magnesium sulfate, filtered, and concentrated on a rotary evaporator. Distillation of the residual oil gave **3** (2.62 g., 0.016 mole, 32%), b.p. 76–80° (0.5 mm.). The analytical sample was prepared by rapid chromatography on alumina and redistillation: ν_{NO_2} 1525, 1350 cm.$^{-1}$, $\nu_{CH=CH\,(trans)}$ 962 cm.$^{-1}$; λ_{max}, mμ (log ϵ) in 95% ethanol, 323 (3.33), 239 (4.16). The n.m.r. spectrum (CCl_4) showed a doublet at 1.9 p.p.m. (CH_3), two overlapping quartets at 5.9–6.5 p.p.m., a doublet with further fine splitting at 6.8 p.p.m. (CH=CH), and the aromatic multiplet at 7.1–7.9 p.p.m.

Anal. Calcd. for $C_9H_9NO_2$ (163.17): C, 66.24; H, 5.56. Found: C, 65.75; H, 5.79.

***trans*-1-(*o*-Nitrophenyl)-1-pentene (4).**—The nitrostyrene **4** was prepared from butyraldehyde by the procedure described for **3** except that butyraldehyde was added as the pure liquid. Yields varied from 28 to 63%. The analytical sample was prepared by chromatography and redistillation: b.p. 108–110° (0.8 mm.); ν_{NO_2} 1525, 1375 cm.$^{-1}$, $\nu_{CH=CH\,(trans)}$ 962 cm.$^{-1}$; λ_{max}, mμ (log ϵ) in 95% ethanol, 323 (3.35), 239 (4.18). The n.m.r. spectrum (CCl_4) showed a triplet at 1.0 p.p.m. (CH_3), a sextet centered on 1.55 p.p.m. (CH_2), a quartet centered on 2.28 p.p.m. (CH_2), two triplets at 6.1 and 6.38 p.p.m., a doublet with further fine splitting centered on 6.94 p.p.m. (CH=CH), and the aromatic multiplet at 7.2–7.8 p.p.m.

Anal. Calcd. for $C_{11}H_{13}NO_2$ (191.22): C, 69.09; H, 6.84. Found: C, 69.07; H, 6.81.

***trans*-2-Nitrostilbene (1).**—The procedure was essentially that described for **3**. The crude product was isolated by filtration of the reaction mixture after dilution with water. Recrystallization from ethanol–water gave **1** in 53% yield, m.p. 71–73° (lit.[9] m.p. 73°).

Diethyl *o*-Nitrobenzylphosphonate.—The phosphonate was routinely used without purification. It did not crystallize, and attempted distillation resulted in decomposition. The infrared spectrum of the crude oil showed ν_{NO_2} 1540, 1360 cm.$^{-1}$, $\nu_{P=O}$ 1255 cm.$^{-1}$, ν_{P-O-C} 1050, 1030, 970 cm.$^{-1}$. The n.m.r. spectrum (CCl_4) showed a triplet at 1.18 p.p.m. (CH_3), a doublet (J = 22 c.p.s.) centered on 3.57 p.p.m. (PCH_2), two overlapping quartets centered on 3.83 and 4.03 p.p.m. ($POCH_2$), and an aromatic multiplet at 7.2–8.0 p.p.m.

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[20] (a) C. Walling and R. Rabinowitz, *J. Am. Chem. Soc.*, **81**, 1243 (1959); (b) D. B. Denney, W. F. Goodyear, and B. Goldstein, *ibid.*, **82**, 1393 (1960); (c) A. J. Burn, J. I. G. Cadogan, and P. J. Bunyan, *J. Chem. Soc.*, 1527 (1963).

[21] L. G. Donaruma and W. Z. Heldt, *Org. Reactions*, **11**, 1 (1960).

[22] P. D. Bartlett and B. T. Storey, *J. Am. Chem. Soc.*, **80**, 4954 (1958).

[23] Melting points were taken in a calibrated liquid bath. Thin layer chromatograms were obtained using silica gel H (Brinkmann Instruments). Spots were developed by iodine vapor. Column chromatography was carried out using Fischer Scientific absorption alumina or Baker and Adamson silicic acid. Unless otherwise stated, infrared spectra of solids were run in KBr pellets and oils as thin films using a Perkin-Elmer Model 337 spectrophotometer. Ultraviolet spectra were determined with a Beckman DK-2 spectrophotometer, and n.m.r. spectra were obtained with a Varian Model A-60 instrument. Microanalyses were performed by Geller Laboratories, Charleston, W. Va.

[24] N. Kornblum and D. C. Iffland, *J. Am. Chem. Soc.*, **71**, 2137 (1949); G. H. Daub and R. C. Castle, *J. Org. Chem.*, **19**, 1571 (1954).

By-products from *o*-Nitrostyrene Syntheses.—The crude reaction products usually contained several impurities, some of which were isolated as crystalline solids either from the concentrated hexane extracts or from distillation residues. One was identified as 2,2′-dinitrobibenzyl, m.p. 121–122° (lit.[25] m.p. 121–122.5°). A second by-product was *trans*-2,2′-dinitrostilbene, m.p. 195–196° (lit.[2a] m.p. 194–195°).

***cis*-2-Nitrostilbene** (2).—The method of DeTar and Chu[26] was followed except that the crude **2** which was isolated by continuous extraction was not distilled but was directly recrystallized.

1-Hydroxy-2-phenylindole (17).—The procedure of Fischer and Hütz[13a] was used. The crude product was recrystallized from ethanol and then from benzene giving fine yellow needles, m.p. 173° with gas evolution (lit.[13b] m.p. 172°), ν_{NOH} 2430 cm.$^{-1}$ (very broad).

1-Ethoxy-2-phenylindole.—Ethyl iodide (excess) was added to a solution of 1-hydroxy-2-phenylindole (0.70 g., 3.4 mmoles) in methanol (20 ml.) containing potassium hydroxide (0.2 g.). The resulting solution was refluxed for 2 hr. and then diluted with water and extracted with ether. The extract was dried over magnesium sulfate, filtered, and concentrated. The product was homogeneous (thin layer chromatography), but it could not be crystallized. Distillation (160°, 0.8 mm.) resulted in partial decomposition. Chromatography on alumina using 1:1 hexane–benzene as the eluent followed by vacuum drying gave the product (0.40 g., 1.7 mmoles, 50%) as a golden oil: $\nu_{NH,OH}$ none. The n.m.r. spectrum (CCl_4) showed a triplet at 1.16 p.p.m. (CH_3), a quartet at 3.89 p.p.m. (CH_2), a singlet at 6.45 p.p.m. (indole-3 H), and the aromatic multiplet at 6.9–8.0 p.p.m.

Anal. Calcd. for $C_{16}H_{15}NO$ (237.29): C, 80.99; H, 6.37; N, 5.90. Found: C, 80.70; H, 6.42; N, 5.85.

Standardized Procedure for Experiments Listed in Table II.—The starting material (5.0 mmoles) was heated with the triethyl phosphite-solvent system indicated in Table II. In each case the total amount of triethyl phosphite and solvent used was 30 mmoles. The reaction solutions were kept at 163 ± 2° in an electrically heated oil bath for 18 hr. The reaction solution was then cooled and transferred to a small distillation apparatus. Most of the triethyl phosphate (b.p. 54–56° at 0.6–0.8 mm.) and more volatile components were distilled off. An oil bath (kept below 110°) was used as the heat source. The residue was dissolved in ether (20–25 ml.) and extracted with three 20-ml. portions of water and saturated salt solution (20 ml.). The ether solution was dried over magnesium sulfate, filtered, and concentrated on a rotary evaporator. The residue was dissolved in benzene and chromatographed on a column (4.5 × 10 cm.) of silicic acid (60–90 g., packed as a slurry in 1:4 hexane–benzene) using 1:4 hexane–benzene, benzene, ether–benzene mixtures, ether, and ether–methanol mixtures as the solvents. The course of the chromatography was followed by thin layer chromatography. The yields of isolated products are listed in Table II. These products were routinely identified by infrared spectra and melting points. All experiments listed in Table II were carried out in this manner except the reaction of **17** with medium A and the first run of the reaction of **1** with medium B. These two experiments differed as follows. In the reduction of **17**, products **8** and **19** were separated by fractional crystallization and trace amounts of **18** were identified by thin layer chromatography. In the reaction between **1** and medium B (first run only), a mixed fraction of **8** and **18**, as well as pure **8** and **18**, was obtained on chromatography. The composition of the mixed fraction was estimated by comparing the absorbance at 564 mμ of a sample treated with Ehrlich's reagent with the absorbance shown by a series of known mixtures of **8** and **18**. Compound **18** does not give a color with Ehrlich's reagent.

An analytical sample of **2,2′-diphenyl-3,3′-biindole** (**18**, eluted by benzene), m.p. 278° (lit.[15] m.p. 276°) was prepared by three recrystallizations from benzene–hexane: ν_{NH} 3360, 3400 cm.$^{-1}$; λ_{max}, mμ (log ε) in 95% ethanol, 306 (4.54), 239 (4.62). The n.m.r. spectrum (dimethyl-d_6 sulfoxide) showed an aromatic multiplet at 6.8–7.8 p.p.m. and a broad singlet at 11.6 p.p.m. (NH).

Anal. Calcd. for $C_{22}H_{20}N_2$ (384.46): C, 87.47; H, 5.25; N, 7.29. Found: C, 87.60; H, 5.34; N, 7.23.

Ether eluted **diethyl 2-phenyl-3-indolylphosphonate** (19). An analytical sample was prepared by two recrystallizations from chloroform–hexane: m.p. 175–176°; ν_{NH} 2700–3200 cm.$^{-1}$ (very broad), $\nu_{P=O}$ 1205 cm.$^{-1}$, ν_{POC} 1030 cm.$^{-1}$, ν_{NH} 3410 cm.$^{-1}$ in chloroform solution; λ_{max}, mμ (log ε) in 95% ethanol, 293 (4.25), 230 infl. (4.36). The n.m.r. spectrum (dimethyl-d_6 sulfoxide) showed a triplet at 1.12 p.p.m. (CH_3), a five-line pattern centered at 3.96 p.p.m. arising from overlapping quartets ($POCH_2$), the aromatic multiplet at 7.0–8.2 p.p.m., and a broad peak at 12.2 p.p.m. (NH).

Anal. Calcd. for $C_{18}H_{20}NO_3P$ (329.32): C, 65.64; H, 6.12; N, 4.25; P, 9.40. Found: C, 65.88; H, 6.13; N, 4.21; P, 9.23.

Ether and ether–methanol usually eluted several oily fractions from which no well-defined products could be isolated.

Reaction of 1-Hydroxy-2-phenylindole (17) **with Triethyl Phosphate.**—A solution of **17** (1.04 g., 5.0 mmoles) in triethyl phosphate (5.5 g., 30 mmoles) was maintained at 170–175° for 20 hr. The triethyl phosphate was removed by distillation and the dark residue was dissolved in ether and extracted successively with water (three 20-ml. portions) and cold 2% sodium hydroxide (four 20-ml. portions). The cold alkaline extracts were immediately acidified with concentrated hydrochloric acid and extracted with ether. The original ether layer containing neutral material was dried over magnesium sulfate, filtered, and concentrated. The residue was chromatographed on silicic acid giving **8** (28 mg., 0.14 mmole, 3%) and **18** (15 mg., 0.04 mmole, 1.6%).

The ether extract containing base-soluble material was dried over sodium sulfate and concentrated. The residue was dried *in vacuo* for several hours, giving recovered **17** (0.47 g., 45% recovery), identified by its infrared spectrum, m.p. 155° dec., m.p. 161° dec. after a single recrystallization from benzene.

Reductive Dimerization of 1-Hydroxy-2-phenylindole (17) **in *p*-Cymene.**—A suspension of **17** (2.09 g., 10.0 mmoles) in *p*-cymene (15.0 g.) was heated to the reflux temperature.[27] The indole dissolved as the solvent became hot. The resulting solution was refluxed for 5 hr. and then allowed to cool to room temperature. Filtration gave **18** (1.62 g., 4.2 mmoles, 84%), m.p. 278°. Distillation of the filtrate gave *p*-cymene (13.97 g.) which had an infrared spectrum identical with that of the original solvent. No new contamination by volatile products was indicated by g.l.p.c. Chromatography of the distillation residue gave only additional small amounts of *p*-cymene and **18**.

Control Experiment.—A solution of **8** (0.48 g., 2.5 mmoles) in triethyl phosphite (0.83 g., 5.0 mmoles) and triethyl phosphate (1.8 g., 10 mmoles) was maintained at 160–165° for 18 hr. and then processed in the standard manner. Thin layer chromatography indicated the absence of **18**. Crystallization of the product from benzene–hexane gave recovered **8** (0.431 g., 90%).

Isolation of 1-Hydroxy-2-phenylindole (17) **from an Interrupted Reductive Cyclization.**—A solution of **1** (0.56 g., 2.5 mmoles) in triethyl phosphite (1.7 g., 10 mmoles) was maintained at 163 ± 2° for 1 hr. Unreacted triethyl phosphite was removed by vacuum distillation and the yellow residue was dissolved in ether (20 ml.) and washed several times with water and then with saturated sodium chloride solution. Thin layer chromatography at this point indicated the presence of **1**, **8**, **17**, **18**, and other trace components. The ether solution was extracted with ice-cold 5% aqueous sodium hydroxide (two 10-ml. portions), and the aqueous layer was separated and immediately acidified with concentrated hydrochloric acid in the presence of ether. The ether layer was separated, dried over sodium sulfate, and concentrated. The dried residue was slightly impure **17**. Recrystallization from benzene gave **17** (0.073 g., 0.35 mmole, 14%), m.p. 150–152° dec.[28] The identity of the product was established by comparison of its infrared spectrum with that of authentic **17**. Thin layer chromatographic comparison with authentic **17** in three solvent systems confirmed the identification.

Reaction of 1-Hydroxy-2-phenylindole (17) **with *p*-Toluenesulfonyl Chloride.**—A solution of **17** (1.00 g., 4.8 mmoles) in methylene chloride (18 ml.) and pyridine (2 ml.) was cooled to 0° and added to a cooled solution of *p*-toluenesulfonyl chloride (1.4 g.) in pyridine (4 ml.). The resulting solution was stirred at 0° for 45 min. and then at room temperature for 20 hr. Ice (~10 g.) was added, and the resulting mixture was stirred at

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(26) D. F. DeTar and Y.-W. Chu, *J. Am. Chem. Soc.*, **76**, 1686 (1954).

(27) The over-all results are the same at 163–165°, but at this temperature the reaction is heterogeneous during the early stages.

(28) As is stated in the original report[13a] of the synthesis of 1-hydroxy-2-phenylindole (**17**), its melting point is rather variable. The substance melts with decomposition to a black tar. Once such decomposition sets in, it proceeds rapidly. Except for the very purest samples of **17**, this decomposition temperature was generally observed to be in the range of 155–165°.

room temperature for 6 hr. Methylene chloride (20 ml.) was added, and the resulting two-phase system was extracted with cold 4% hydrochloric acid (two 20-ml. portions) and 5% sodium carbonate (two 20-ml. portions). The dark organic layer was dried over magnesium sulfate, filtered, diluted with benzene, and treated with charcoal. Evaporation of the filtrate left a brown oil shown by thin layer chromatography to contain **8** (trace only), **18**, and a new product ($R_f \sim 0.3$ with 1:4 chloroform–benzene). The crude product was chromatographed on silicic acid (60 g.). Benzene eluted **18** (0.135 g., 0.35 mmole, 14%) and then the ***p*-toluenesulfonate ester of 2-phenyl-3-indolol** (**22**, 0.380 g., 1.05 mmoles, 22%), m.p. 152–155° dec. Three recrystallizations from benzene–hexane gave the analytical sample: m.p. 149–150° dec.; ν_{NH} 3345, 3370 cm.$^{-1}$, ν_{OSO_2} 1360, 1180 cm.$^{-1}$; λ_{max}, mμ (log ϵ) in 95% ethanol, 303 (4.31), 225 (4.50). The n.m.r. spectrum (dimethyl-d_6 sulfoxide) showed a singlet at 2.25 p.p.m. (CH_3), the aromatic multiplet at 7.0–7.8 p.p.m., and a broad singlet at 11.8 p.p.m. (NH).

Anal. Calcd. for $C_{21}H_{17}NO_3S$ (363.35): C, 69.41; H, 4.71; N, 3.86; S, 8.80. Found: C, 69.37; H, 4.76; N, 3.73; S, 8.62.

2-Methylindole (9) and 2,2′-Dimethyl-3,3′-biindole (20).—A solution of **3** (0.82 g., 5.0 mmoles) and triethyl phosphite (5.0 g., 30 mmoles) was maintained at 160° for 18 hr. The crude product obtained by the standard work-up was chromatographed on silicic acid (60 g.) using benzene as the eluent. The products characterized were **9** (0.331 g., 2.52 mmoles, 51%), m.p. 59–60°, and **20** (0.072 g., 0.27 mmole, 11%), m.p. 232–235° (lit.[18] m.p. 234°). The n.m.r. spectrum of **20** (dimethyl-d_6 sulfoxide) showed a singlet (CH_3) at 2.26 p.p.m., the aromatic multiplet at 6.6–7.6 p.p.m., and a singlet (NH) at 10.90 p.p.m. The infrared spectrum of this sample of **20** was identical with that of a sample which was prepared by the method of Witkop and Patrick.[18]

2-Propylindole (10) and 2,2′-Dipropyl-3,3′-biindole (21).—A solution of **4** (0.96 g., 5.0 mmoles) in triethyl phosphite (5.0 g., 30 mmoles) was maintained at 160° for 18 hr. Work-up in the usual manner followed by chromatography on silicic acid (60 g.) gave **10** (0.48 g., 3.0 mmoles, 60%), m.p. 32–34° (lit.[29] m.p 34°), and **21** (0.036 g., 0.11 mmole, 4.5%), m.p. 165–170°. Two recrystallizations of **21** from benzene–hexane gave the analytical sample: m.p. 172–173°; ν_{NH} 3360 cm.$^{-1}$; λ_{max}, mμ (log ϵ) in 95% ethanol, 290 (4.15), 283 (4.17), 230 (4.71). The n.m.r. spectrum showed a triplet at 0.82 p.p.m. (CH_3), a sextet at 1.59 p.p.m., a triplet at 2.63 p.p.m. (CH_2CH_2), the aromatic multiplet at 7.0–7.5 p.p.m., and a broad singlet at 7.9 p.p.m. (NH).

Anal. Calcd. for $C_{22}H_{24}N_2$ (316.24): C, 83.50; H, 7.65; N, 8.86. Found: C, 83.83; H, 7.82; N, 8.97.

1-Ethoxy-2-propylindole (14).—A solution of **4** (3.00 g., 15.7 mmoles) in triethyl phosphite (10.4 g., 63 mmoles) was stirred at room temperature for 4 hr. and then at 145° for 10 hr. The resulting solution was diluted with hexane and washed successively with water (two 20-ml. portions), 3% sodium carbonate (three 30-ml. portions), and saturated sodium chloride solution. The concentrated residue was washed through a short alumina column with 1:3 benzene–hexane without achieving any purification (substantial amounts of triethyl phosphate in the crude product resulted in elution of most of the material with the solvent front). The yellow eluate was concentrated, evacuated at 0.5 mm. for 12 hr., dissolved in hexane, and washed with water. The product was then chromatographed on alumina. Hexane eluted a 1:2 mixture of unreacted **4** and **14** (0.244 g.). Hexane–benzene and benzene eluted **9** (0.557 g., 3.5 mmoles, 22%), m.p. 33–35°.

Compound **14** (0.105 g., 0.51 mmole, 3%) was separated from **4** by rechromatography on alumina. Distillation at 0.5 mm. gave a colorless oil: ν_{NH} none; λ_{max}, mμ (log ϵ) in 95% ethanol, 292 infl. (3.7), 282 (3.8), 274 (3.8). The n.m.r. spectrum (CCl_4) showed triplets at 1.01 and 1.31 p.p.m. (two CH_3 groups), an apparent sextet at 1.78 p.p.m., a triplet at 2.71 p.p.m. (CH_2CH_2), a quartet at 4.08 p.p.m. (OCH_2), a singlet at 5.98 p.p.m. (indole-3 H), and the aromatic multiplet at 6.8–7.5 p.p.m.

Anal. Calcd. for $C_{13}H_{17}NO$ (203.28): C, 76.85; H, 8.43; N, 6.89. Found: C, 77.07; H, 8.71; N, 6.99.

2-Indolyl Phenyl Ketone (12) and 1-Ethoxy-2-indolyl Phenyl Ketone (15).—A solution of 2-nitrochalcone[30] (2.53 g., 10.0 mmoles) in triethyl phosphite (13.3 g., 80 mmoles) was heated at 160° for 65 min. Triethyl phosphite and triethyl phosphate were removed by vacuum distillation, and the dark residue was dissolved in ether (40 ml.), washed with water (three 20-ml. portions) and salt solution, dried over magnesium sulfate, and concentrated. Chromatography on silicic acid (80 g.) gave, on elution with benzene, first a trace (17 mg.) of **1-ethyl-2-indolyl phenyl ketone**, identified by comparison with an authentic sample (see below). Benzene next eluted **15** (0.097 g., 0.37 mmole, 4%). Rechromatography on alumina gave a yellow oil: ν_{NH} none, $\nu_{C=O}$ 1645 cm.$^{-1}$; λ_{max}, mμ (log ϵ) in 95% ethanol, 314 (4.30), 250 (4.12). The n.m.r. spectrum ($CDCl_3$) showed a triplet at 1.45 p.p.m. (CH_3), a quartet at 4.58 p.p.m. (OCH_2), a singlet at 6.82 p.p.m. (indole-3 H), and the aromatic multiplet at 7.0–8.0 p.p.m.

Anal. Calcd. for $C_{17}H_{15}NO_2$ (265.30): C, 76.96; H, 5.70; O, 12.06. Found: C, 76.99; H, 5.60; O, 12.40.

Benzene–ether (10:1) eluted **12** (0.345 g., 1.56 mmoles, 16%), m.p. 146–148° (lit.[31] m.p. 146–148°). Three recrystallizations from chloroform–hexane gave needles: m.p. 151–152°; ν_{NH} 3285 cm.$^{-1}$, $\nu_{C=O}$ 1625 cm.$^{-1}$; λ_{max}, mμ (log ϵ) in 95% ethanol, 322 (4.33), 245 (4.12). The n.m.r. spectrum ($CDCl_3$) showed a multiplet at 7.0–8.2 p.p.m. and a broad singlet (NH) at 10.2 p.p.m.

Anal. Calcd. for $C_{15}H_{11}NO$ (221.25): C, 81.42; H, 5.01; N, 6.33. Found: C, 81.44; H, 5.18; N, 6.40.

1-Ethyl-2-indolyl Phenyl Ketone.—2-Indolyl phenyl ketone (0.20 g., 0.91 mmole) was dissolved in dry dimethylformamide (4 ml.). Sodium methoxide (0.05 g., 1 mmole) and ethyl iodide (0.2 ml.) were added, and the reaction mixture was stirred at room temperature for 12 hr. Additional sodium methoxide (0.05 g.) and ethyl iodide (0.2 ml.) were added and the mixture was refluxed for 40 min. Dilution with water and extraction with ether gave, on concentration, a brown oil which crystallized from hexane in a Dry Ice–acetone bath giving 1-ethyl-2-indolyl phenyl ketone (0.145 g., 0.58 mmole, 64%), m.p. 62–64°. Three recrystallizations from hexane gave the analytical sample: m.p. 69–70°; ν_{NH} none, $\nu_{C=O}$ 1640 cm.$^{-1}$; λ_{max}, mμ (log ϵ) in 95% ethanol, 319 (4.33), 247 (4.13).

Anal. Calcd. for $C_{17}H_{15}NO$ (249.30): C, 81.90; H, 6.06. Found: C, 82.30; H, 6.32.

4-(*o*-Nitrophenyl)-3-buten-2-one (5).—Acetone (100 ml.) and *o*-nitrobenzaldehyde (7.0 g., 46 mmoles) were condensed and the resulting ketol was dehydrated according to the procedure described for 1-(*p*-nitrophenyl)-1-penten-3-one.[32] Compound **5** (7.55 g., 39.6 mmoles, 87%), m.p. 53° (lit.[33] m.p. 53°), was obtained as dull yellow needles.

2-Indolyl Methyl Ketone (11).—A solution of **5** (1.91 g., 10.0 mmoles) in triethyl phosphite (6.3 g., 38 mmoles) was refluxed for 1.5 hr. The dark solution was diluted with ether (40 ml.) and washed with 10% aqueous sodium hydroxide (three 20-ml. portions) and with saturated sodium chloride solution. The ether layer was dried over sodium sulfate, concentrated, and vacuum distilled to remove triethyl phosphite and triethyl phosphate. The residue was dissolved in benzene and diluted with warm hexane. The gummy solid which precipitated was crystallized from benzene–hexane giving **11** (0.26 g., 1.6 mmoles, 16%), m.p. 153–154°. Three recrystallizations from benzene–hexane gave the analytical sample: m.p. 154–155°; ν_{NH} 3270, $\nu_{C=O}$ 1645; λ_{max}, mμ (log ϵ) in 95% ethanol, 305 (4.33), 225 (4.10). The n.m.r. spectrum ($CDCl_3$) showed a singlet at 2.58 p.p.m. (CH_3) and a series of multiplets at 7.1–7.8 p.p.m.

Anal. Calcd. for $C_{10}H_9NO$ (159.20): C, 75.45; H, 5.70; N, 8.80. Found: C, 75.85; H, 5.80; N, 8.57.

Indole-2-carboxylic Acid (13).—A solution of ethyl *o*-nitrocinnamate (2.21 g., 10.0 mmoles) in triethyl phosphite was kept at 150–160° for 10 hr. The solution was diluted with 1:1 benzene–hexane (30 ml.) and washed with sodium carbonate solution. The organic layer was dried, concentrated, and washed through an alumina column with benzene, but sufficient triethyl phosphate was present to prevent any separation being achieved. The dark eluate was concentrated and stirred overnight with 30% aqueous potassium hydroxide. The solution was washed with ether and acidified. Extraction with ether followed by drying and evaporation gave the crude acidic product (0.7 g.)

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(31) See reference in footnote 14.

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(33) J. H. Burckhalter and S. H. Johnston, *ibid.*, **73**, 4835 (1951).

which was recrystallized from benzene, giving **13** (0.30 g., 0.19 mmole, 19%), m.p. 204–205° (lit.[34] m.p. 203–204°).

Triethyl N-(*o*-Ethylphenyl)phosphorimidate (23) and Diethyl N-(*o*-Ethylphenyl)phosphoramidate (24).—A solution of *o*-nitroethylbenzene (3.02 g., 20 mmoles) in triethyl phosphite (13.4 g., 81 mmoles) was refluxed for 14 hr. and then vacuum distilled, giving first unreacted triethyl phosphite and then triethyl phosphate (7.0 g., 38 mmoles, 96%), b.p. 52–54° (0.4 mm.). The cooled distillation residue was diluted with ether (30 ml.) and extracted successively with dilute hydrochloric acid (two 20-ml. portions) and 1% sodium hydroxide (two 20-ml. portions). The ether layer was dried over magnesium sulfate, filtered, and concentrated, leaving a brown oil. The oil crystallized from hexane, giving **24** (0.13 g., 0.51 mmole, 2.5%), m.p. 105°. Recrystallization from hexane gave the analytical sample: m.p. 105°; ν_{NH} 3200 cm.$^{-1}$, $\nu_{C=O}$ 1240 cm.$^{-1}$, ν_{POC} 1025, 980 cm.$^{-1}$. The n.m.r. spectrum showed two overlapping triplets, the weaker one at 1.23 p.p.m. (CH_3) and a stronger triplet at 1.29 p.p.m. (CH_3), a quartet at 2.60 p.p.m. (CH_2), a five-line pattern (overlapping quartets) at 4.15 p.p.m. (OCH_2), a broad doublet at 5.2 p.p.m. (NH?), and the aromatic multiplet at 6.9–7.4 p.p.m.

Anal. Calcd. for $C_{12}H_{20}NO_3P$ (257.26): C, 56.02; H, 7.84. Found: C, 55.85; H, 7.55.

When the acidic extract of the distillation residue was made alkaline with solid sodium hydroxide, a dark oil separated. The oil was dissolved in ether and the solution was dried over sodium sulfate, filtered, and concentrated. Simple vacuum distillation gave **23** (2.236 g., 8.8 mmoles, 44%), b.p. 110–130° (0.45 mm.). Redistillation through a short Vigreux column gave the product as a yellow oil: b.p. 108–111° (0.6 mm.); ν_{NH} none, ν_{POC} 1035, 970 cm.$^{-1}$. The n.m.r. spectrum (CCl_4) showed overlapping triplets at 1.20 p.p.m. (weaker, ethyl CH_3) and 1.32 p.p.m. (stronger, ethoxy CH_3), an irregular quintet apparently containing a quartet from the benzyl CH_2 at 2.63 p.p.m., a quintet at 4.20 p.p.m. (OCH_2), and a multiplet at 6.7–7.2 p.p.m.

Anal. Calcd. for $C_{14}H_{24}NO_3P$ (285.31): C, 58.93; H, 8.48; P, 10.86. Found: C, 58.93; H, 8.30; P, 10.74.

Conversion of Triethyl N-(*o*-Ethylphenyl)phosphorimidate (23) into Diethyl N-(*o*-Ethylphenyl)phosphoramidate (24).—A solution of **23** (1.00 g., 3.5 mmoles) in hexane (~10 ml.) was placed on a column of silicic acid (30 g.) and kept at room temperature for 16 hr. Elution with ether, evaporation, and crystallization of the residue from hexane gave **24** (0.67 g., 2.6 mmoles, 87%), m.p. 103–104°. A similar transformation was effected in lower yield using alumina and a 3-day reaction period

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Alkoxyoxindoles. A Convenient Method for the Reduction of Isatins

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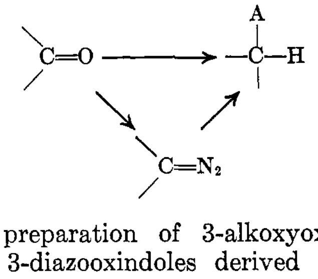
The treatment of 3-diazooxindoles in methanol solution with a suitable Lewis acid provided a preparative source of 3-methoxyoxindoles. Alcohols other than methanol yielded 3-alkoxyoxindoles. This sequence constitutes a useful technique for the reduction of isatins from which the 3-diazooxindoles were derived.

Most conventional methods for the preparation of dioxindoles from readily available isatins lack convenience or satisfactory yields or both.[1,2] Attempts to employ several selective metal hydrides for this reduction resulted in the formation of complexes or bimolecular products from which no dioxindole could be isolated when isatin was used as starting material.[3] As an alternative, several reactions were explored which involve over-all a change in hybridization and thus result in reduction (eq. 1). This communication reports the preparation of 3-alkoxyoxindoles from intermediate 3-diazooxindoles derived in turn from isatins. While the reaction of diazo compounds with acids in the presence of various nucleophiles is familiar,[4,5] this sequence has been used less frequently as a specific method for the reduction of carbonyl groups from which the diazo function was generated.[6–8] The sequence possesses synthetic utility in this special example because the 3-diazooxindoles are relatively stable and easily prepared.



(1)

3-Diazooxindole (IIa) has been prepared by mercuric oxide oxidation of isatin hydrazone[9] and by treatment of isatin *p*-toluenesulfonylhydrazone (Ia) with aqueous base.[10] More recently 1-methyl-3-diazooxindole has been prepared by treatment of the corresponding isatoxime with chloramine in addition to preparation from 1-methylisatin hydrazone and 1-methylisatin *p*-toluenesulfonylhydrazone.[11] Few reactions of 3-diazooxindole have been recorded other than to observe its decomposition on treatment with sulfuric acid[9] and to observe the formation of an isomeric indigo

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