

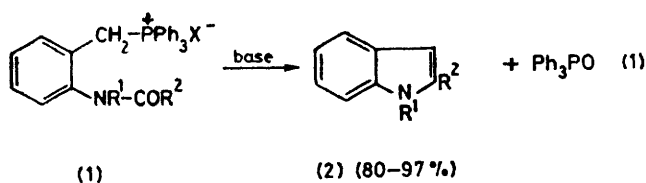
## New Synthesis of Indoles from *o*-Acylaminobenzyltriphenylphosphonium Salts

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**Summary** The action of bases on *o*-acylaminobenzyltriphenylphosphonium salts gives indoles in high yields.

MADDELUNG synthesis of indoles<sup>1</sup> by cyclization of *o*-methyl-anilides is initiated only by strong bases at elevated temperatures and the useful scope of this synthesis is therefore limited to molecules which can survive these very drastic conditions. We report herein a new general synthetic procedure for the synthesis of indoles which is based on the intramolecular reaction of amides with alkylidene-phosphoranes.† The synthetic approach is outlined in reaction (1).



A typical procedure is as follows: 1.1 equiv. of a suitable base (MeONa, Bu<sup>t</sup>OK, or sodium t-pentoxide) was added (10–15 min) to a stirred suspension of 1 equiv. of dry

phosphonium salt (1) in boiling toluene. The solution was stirred for 10 min, filtered, and evaporated to dryness. The crude material was essentially the desired indole, contaminated with triphenylphosphine oxide. The yields (Table) for reaction (1) are for isolated pure products (2) obtained by preparative layer chromatography on silica gel (1:1 ether–benzene), or by crystallisation from ethanol.

The examples in the Table demonstrate the generality of the synthesis. Not only is this reaction compatible with a wide variety of substituents at the 2 position, but our procedure can also be used to prepare 1-substituted indoles.

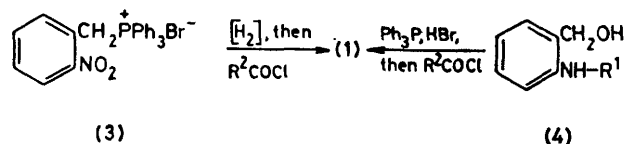
TABLE. Preparation of indoles (2).

R <sup>1</sup>	R <sup>2</sup>	Yield/%	Mp./°C
H	Me	96	61 <sup>a</sup>
H	CH <sub>2</sub> =C(Me)	93	118–120
H	Ph	97	189–190 <sup>b</sup>
H	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	93	249–251 <sup>c</sup>
H	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	85	228–230 <sup>d</sup>
Ph	Me	80	Oil

<sup>a</sup> Lit., m.p. 62 °C; L. Marion and C. W. Oldfield, *Can. J. Res.*, 1947, 25B, 1. <sup>b</sup> Lit., m.p. 188–189 °C; J. I. G. Cadogan and M. Cameron-Wood, *Proc. Chem. Soc.*, 1962, 361. <sup>c</sup> Lit., m.p. 251–252 °C, and <sup>d</sup> lit., m.p. 230–230.5 °C; C. E. Blades and A. L. Wilds, *J. Org. Chem.*, 1956, 21, 1031.

† To our knowledge, amides failed to react with phosphorus ylides; the only published exception is the reaction of Ph<sub>3</sub>P=CHCO<sub>2</sub>Et with a lactam (W. Flitsch and H. Peters, *Tetrahedron Lett.*, 1969, 1161).

The requisite *o*-acylaminobenzylphosphonium salts (1) are available from either (i) *o*-nitrobenzylphosphonium salts<sup>2</sup> (3) *via* reduction with zinc in hydrobromic acid-ethanol ( $R^1 = H$ ; yield 95%) (the reductive cleavage of the carbon-phosphorus bond<sup>3</sup> can be avoided by using only 2 equiv. of reagent), or (ii) anthranilic alcohols (4) *via* condensation with triphenylphosphine hydrobromide ( $R^1 = Ph$ ; yield 76%). In the presence of 2 equiv. of triethylamine or pyridine, acyl chlorides (1.25 equiv.) react in toluene-dichloromethane (1:1) with the *o*-aminobenzylphosphonium salts formed by either of the above methods



to give 85—96% yields of the required salts (1) [reaction (2)].

(Received, 22nd September 1980; Com. 1042.)

<sup>1</sup> W. Madelung, *Chem. Ber.*, 1912, **25**, 1128.

<sup>2</sup> A. A. Ardanaki, N. Maleki, and M. R. Saadein, *J. Org. Chem.*, 1978, **43**, 4128.

<sup>3</sup> A. Schönberg, K. H. Brosowski, and E. Singer, *Chem. Ber.*, 1962, **95**, 2984.