Novel Synthesis of 3-Alkyl-2-phenoxychromones involving an Intramolecular Wittig Reaction of Carbonates

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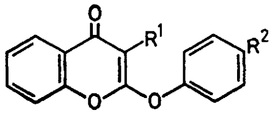
Summary The intramolecular Wittig reaction between phosphorus ylides and carbonates provides a simple, convenient method for preparing cyclic keten-acetal structures.

The Wittig reaction provides an important and often employed method for the construction of various carbon frameworks in synthetic natural chemistry, but is usually limited to the carbonyl groups of aldehydes and ketones.[1] We report herein the first application of the intramolecular Wittig reaction between phosphorus ylides and carbonates to constructing a cyclic keten-acetal function. This function is the basic framework of 2-phenoxychromone (**1a**) whose derivatives have recently emerged as a new class of naturally occurring chromones.[2]



(1)

a; $R^1 = R^2 = H$
b; $R^1 = Me$, $R^2 = H$
c; $R^1 = Me$, $R^2 = OMe$

As an initial experiment, we examined the intramolecular cyclization of the ylide (**3a**), whose corresponding phosphonium bromide (**2a**) was readily prepared from *o*-(phenoxycarbonyloxy)acetophenone† by bromination ($CuBr_2$–AcOEt–$CHCl_3$, reflux, 3 h), followed by treatment with triphenylphosphine (CH_2Cl_2, room temp., 1 h). When (**2a**) was heated under reflux in the presence of *NN*-di-isopropylethylamine (1 mol. equiv.) in toluene for 2 h, the sole product isolated was (**6**) [m.p. 205—207 °C, M^+ *m/e*

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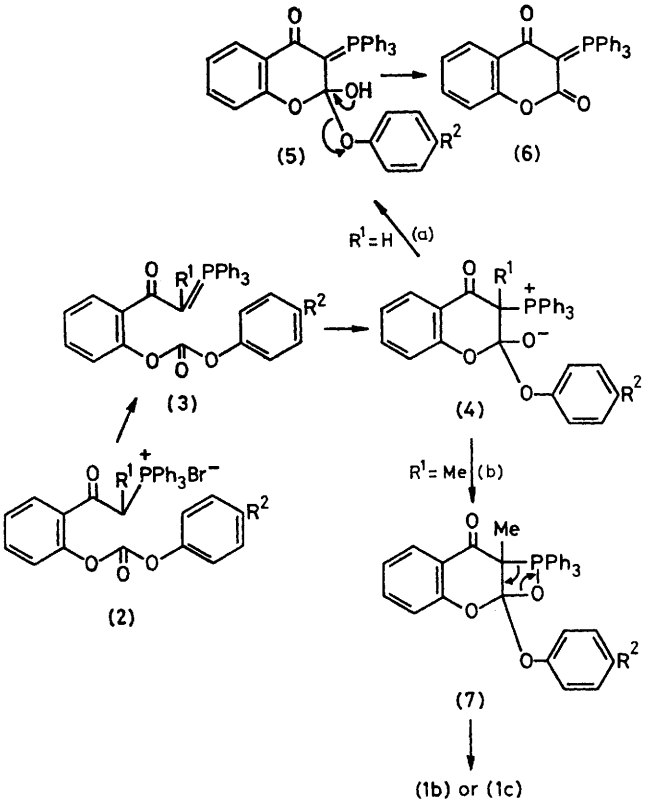
† Prepared from *o*-hydroxy-acetophenone or -propiophenone by acylation with phenyl chloroformate or *p*-methoxyphenyl chloroformate.



SCHEME. **a**; $R^1 = R^2 = H$
b; $R^1 = Me, R^2 = H$
c; $R^1 = Me, R^2 = OMe$

422, λ_{max} (EtOH) 270 nm (ϵ 10,500), 276 (10,800), 287 (10,300)]. As a rationalization for the formation of (**6**), we assume that, after cyclization of the ylide (3a) to the intermediate (**4**), an intramolecular proton transfer took place in (**4**) giving the intermediate (**5**) which then eliminated phenol to yield (**6**) [pathway (a), Scheme].

This result suggested that, if suitably substituted ylides [*e.g.* (**3b**)] were chosen, then a similar cyclization to (**4**) would be followed by elimination of phosphine oxide to produce the desired 2-phenoxychromones [*e.g.* (**1b**)]. To test this idea, the phosphonium bromide (**2b**) was prepared, starting from *o*-(phenoxycarbonyloxy)propiophenone† ($CuBr_2$–AcOEt–$CHCl_3$, reflux, 3 h, followed by PPh_3–$CHCl_3$, reflux, 22 h). Heating the ylide (**3b**), prepared *in situ* in a manner similar to that for (**3a**), in toluene for 1·5 h, afforded, as expected, the chromone (**1b**) [m.p. 61—64 °C, M^+ *m/e* 252, λ_{max} (EtOH) 273 nm (ϵ 11,000), 293 (11,200)] in 36% yield from the starting material. This reaction apparently proceeded by pathway (b), Scheme.

Similarly, the phosphonium bromide (**2c**), prepared from *o*-[*p*-(methoxy)phenoxycarbonyloxy]propiophenone† by a method similar to that used for (**2b**), was converted *in situ* into the ylide (**3c**) and heated in toluene for 2 h to produce the chromone (**1c**) [m.p. 115—116 °C, M^+ *m/e* 282, λ_{max} (EtOH) 290 nm (ϵ 13,800)] in 25% total yield.

In conclusion, the intramolecular Wittig reaction of the carbonates provides a simple, convenient method for producing cyclic keten-acetal structures.

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[1] For reviews on the Wittig reaction, see *e.g.* S. Trippet, *Adv. Org. Chem.*, 1960, **1**, 83; H. O. House, 'Modern Synthetic Reactions,' W. A. Benjamin Inc., California, 1972, p. 682; D. J. H. Smith, 'Comprehensive Organic Chemistry,' vol. 2, eds. D. Barton and W. D. Ollis, Pergamon Press, Oxford, 1979, p. 1316.

[2] T. Komiya, M. Tsukui, and H. Oshio, *Chem. Pharm. Bull.*, 1974, **23**, 1387; E. K. Adesogan and A. L. Okunade, *J. Chem. Soc., Chem. Commun.*, 1978, 152; H. Kikuchi, Y. Koma, and H. Hoirai, unpublished result.