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ORGANOPHOSPHORUS ENAMINES V. ENAMINE PHOSPHINE OXIDES. A NEW SYNTHETIC ROUTE TO CYCLOPROPYL KETIMINES AND THE CORRESPONDING KETONES

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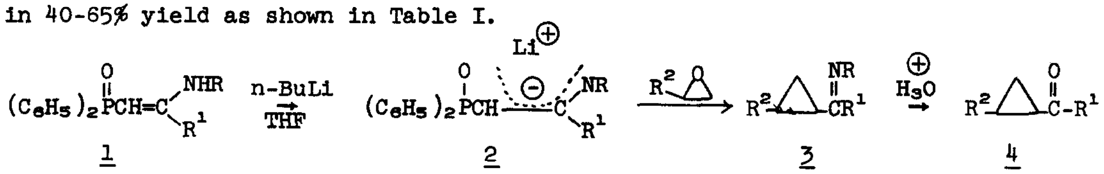
The reaction of Wittig type reagents with epoxides to yield cyclopropanes is well recorded in the chemical literature.[1] We have been investigating the chemistry of organophosphorus enamines 1 with particular interest in their ability to undergo ylid type reactions. These enamines are conveniently prepared by the nucleophilic addition of a primary amine to the appropriate 1-alkynylphosphine oxide.[2]

We wish here to report that the lithio salt 2 of these enamine phosphine oxides reacts cleanly with epoxides in refluxing THF to provide the cyclopropyl ketimines 3. The presence of the C=N bond is evident from the strong infrared absorption at 1640 cm^{-1}. Two-layer hydrolysis of an ethereal/chloroform solution of the crude ketimines 3 with 5-10% aqueous oxalic acid followed by vacuum distillation of the crude hydrolysis product provides the pure ketones 4 in 40-65% yield as shown in Table I.



Although generally the crude ketimines 3 are hydrolyzed to the ketones 4, they can easily be purified by reduced pressure distillation after workup of the reaction mixture as shown in Table I. The cyclopropyl ketimine 3 ($R = n\text{-}C_4H_9$, $R^1 = R^2 = C_6H_5$) thus obtained provides the corresponding ketone 4 [$R^1 = R^2 = C_6H_5$, bp 132-134° (0.05 mm)] in 85% yield after hydrolysis.

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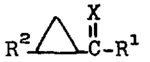
TABLE I

The Cyclopropyl Ketimines 3 and Ketones 4



3. X = NR
4. X = O

R^1	R^2	X	Bp °C/mm Hg	% Yield
C_6H_5	C_6H_5	NC_4H_9-n	137-139/0.03	56
C_6H_5	C_6H_5	NC_4H_9-t	136-138/0.05	60
t-C_4H_9	C_6H_5	NC_4H_9-n	102-104/0.05	70
C_6H_5	C_6H_5	O	117-124/0.05[a]	58
n-C_3H_7	C_6H_5	O	88-90/0.08	58[b]
n-C_3H_7	CH_3	O	57-62/42[c]	40
t-C_4H_9	C_6H_5	O	78-83/0.10	65[b]

a. This ketone, prepared by our method (mp 39-44°), had spectral properties identical to those reported previously by E. J. Corey et al., J. Amer. Chem. Soc., 87, 1353-64 (1965), mp 45-50° (isomers).

b. The crude hydrolysis product was obtained in >90% yield and exhibited the identical richly detailed infrared spectrum as the purified material.

c. S. Julia, M. Julia and L. Brasseur, Bull. Soc. Chim., Fr., 1634-8 (1962), bp 45° (25 mm).

This is the first report on the use of organophosphorus enamines as intermediates in the synthesis of cyclopropyl ketimines and ketones. In contrast to the older methods, most of which involve insertion of a single methylene into a preformed α,β-unsaturated moiety, this synthesis allows the union of two variable small carbon fragments. Moreover, the crystalline enamine phosphine oxides 1 are indefinitely stable at room temperature and form the anions quantitatively on addition of n-butyllithium.

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REFERENCES

1. A. William Johnson, "Ylid Chemistry," Academic Press, New York and London, 1966, pp. 111-113, and references cited therein.

2. N. A. Portnoy, C. J. Morrow, M. S. Chattha, J. C. Williams, Jr. and A. M. Aguiar, "Organophosphorus Enamines I and II," Tetrahedron Lett., in press.

3. All yields herein reported are based on the 1-alkynylphosphine oxide. Yields are for purified material. All compounds exhibited the expected infrared and nmr spectra and the molecular weight of all cyclopropyl ketones was correct as determined by mass spectrometry.