

A New Synthesis of Fused Heterocyclic and Carbocyclic Compounds via the Reaction of the Vinylphosphonate with Imide and Ketone Enolate Anions¹⁾

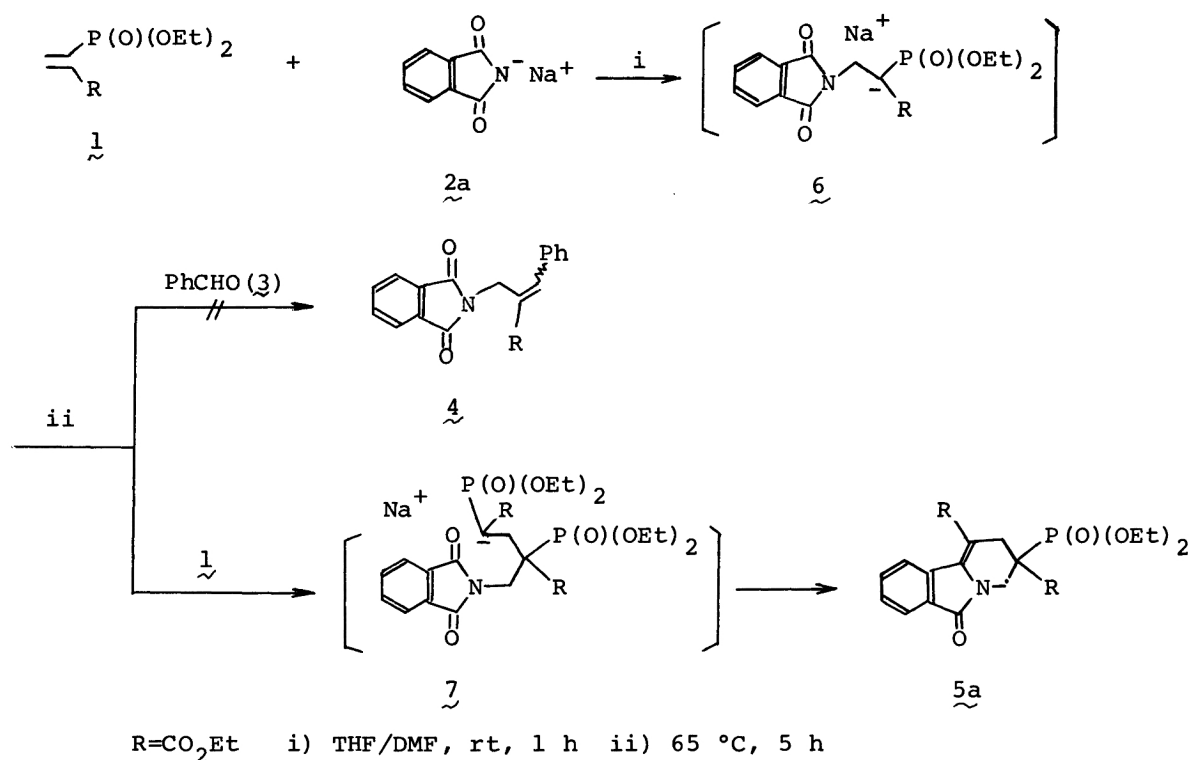
Toru MINAMI,^{*} Kazushi WATANABE, and Kazunari HIRAKAWA

Department of Industrial Chemistry, Kyushu Institute of Technology,
Sensuicho, Tobata, Kitakyushu 804

The reaction of diethyl (α -ethoxycarbonylvinyl)phosphonate with various imide and ketone enolate anions gave functionalized heterocyclic and carbocyclic, and spirocarbocyclic compounds containing the phosphorus residue in good yields.

A variety of allyl amines has been stereoselectively synthesized via the reaction of vinylphosphonium salts and phthalimide with aldehydes, followed by hydrolysis.²⁾ In order to synthesize the N-(2-ethoxycarbonylallyl)phthalimide derivative as a β -amino acid synthon, we have examined similar reactions of diethyl (α -ethoxycarbonylvinyl)phosphonate (1) and sodiophthalimide (2) with aldehydes.

The reaction of the phosphonate carbanion 6, generated from the Michael addition of 2 (2 mmol) to 1 (0.47 g, 2 mmol) in a mixed solvent of THF (10 ml) and DMF (2 ml), with benzaldehyde (3) (0.21 g, 2 mmol) at 65 °C for 5 h gave an annelation product, 1,3-diethoxycarbonyl-3-diethoxyphosphinyl-2,3,4,5-tetrahydropyrido[2,1-a]-isoindolin-6-one (5a) (0.205 g, 44%), but none of the expected phthalimide 4 was formed. The structure of 5a³⁾ was readily assigned on the basis of its spectral data: IR (KBr) 1725 and 1710 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.00-1.49 (12H, m, Me), 2.75-3.27 (2H, dd, $J=9.52, 17.50$ Hz, CH_2), 3.40-3.83 (2H, dd, $J=5.37, 12.94$ Hz, NCH_2), 3.93-5.10 (8H, m, OCH_2), 7.40-8.00 (3H, m), and 8.53-8.80 (1H, br); MS 465 (M^+). As shown in Scheme 1, this result can be explained by the reaction of 6 with a second molecule of 1 to yield the phosphonate carbanion 7, followed by the intramolecular Wittig-Horner reaction to afford 5a. So, when the reaction of 2a was carried out with 2 mol equiv. of 1 in the absence of 3, the compound 5a was obtained in 92% yield.⁴⁾

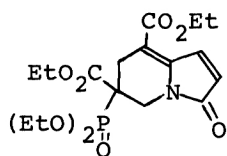
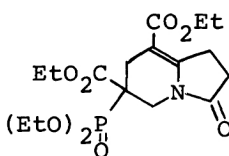
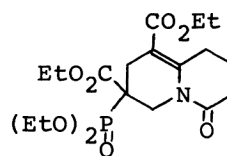


Scheme 1.

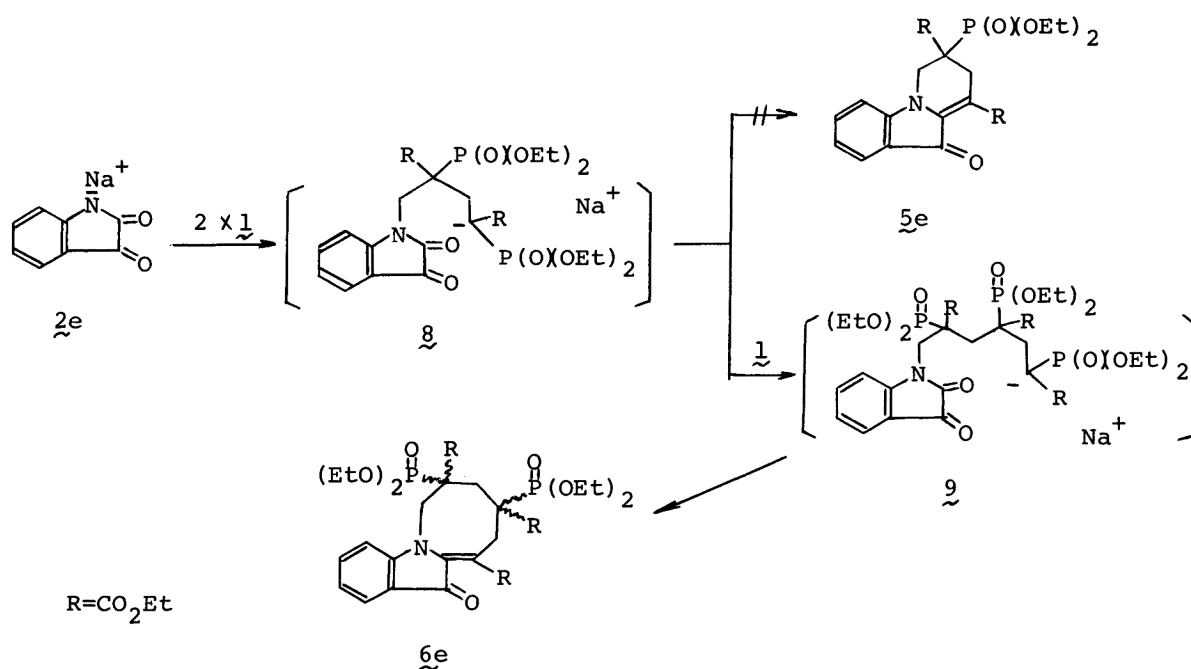
In order to apply this procedure to the synthesis of various fused heterocyclic compounds, similar treatment of 1 with imide anions such as maleimide (2b), succinimide (2c), and glutarimide anions (2d) successfully produced the corresponding indolizine 5b,c and quinolizine derivatives 5d in 19-57% yields.⁵⁾

In contrast, upon similar treatment with 2 equiv. of 1, sodioisatin (2e) afforded no corresponding 1:2 cycloadduct but the unexpected 1:3 cycloadduct 6e albeit in low yield (19%).⁵⁾ The reaction of 2e with a threefold excess of 1 gave 6e in 58% yield. Thus, the yield of 6e was dependent upon the molar ratio of 1 to 2e.

The formation of 6e suggests that the intramolecular Wittig-Horner reaction of the

5b5c5d

carbanion 8 to 5e would be presumably inhibited due to steric strain and 8 undergoes, therefore, the subsequent Michael addition to a third molecule of 1 yielding the carbanion 9, followed by the Wittig olefination (Scheme 2).



Scheme 2.

Also, we have sought to examine the reaction of 1 with ketone enolates.⁶⁾ The reaction of 1 (0.30 g, 1.26 mmol) with cyclopentanone lithium enolate (10a) (0.6 mmol), generated in-situ from cyclopentanone and lithium diisopropylamide (LDA) at -75 °C, in THF for 1 h at -75 °C and for 5 h at reflux produced a functionalized cyclohexenylphosphonate 11a⁷⁾ (0.18 g, 74%) as a 1:1 mixture of two diastereoisomers.

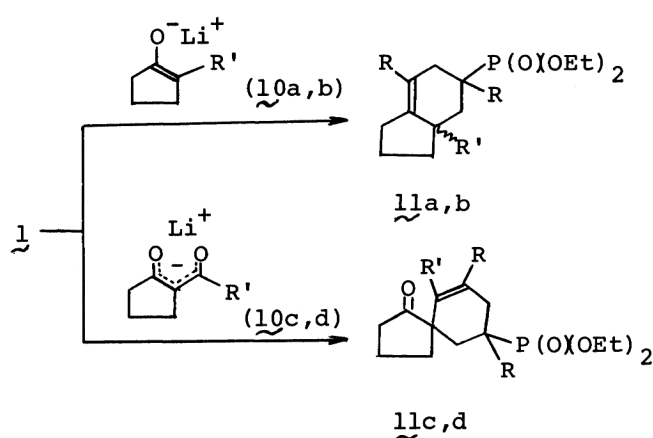


Table 1. Synthesis of Cyclohexenylphosphonates

Product	R	R'	Yield/%
<u>11a</u>	CO ₂ Et	H	74
<u>11b</u>	CO ₂ Et	CO ₂ Et	71
<u>11c</u>	CO ₂ Et	Me	62
<u>11d</u>	CO ₂ Et	Ph	79

Similar treatment of lithium enolates 10b-d of 2-ethoxycarbonyl-, 2-acetyl-, and 2-benzoylcyclopentanones with 1 led to the corresponding cyclohexenylphosphonates 11b-d⁷⁾ in good yields (Table 1).

Thus, the above results show that the vinylphosphonate is a versatile reagent for the synthesis of fused heterocyclic and carbocyclic compounds, which have wide

applicability. Synthetic application of the products is now under investigation.

References

- 1) Reactions of Vinylphosphonates. 4. For the preceding paper in this series, see: T. Minami, S. Tokumasu, and I. Hirao, *Bull. Chem. Soc. Jpn.*, **58**, 2139 (1985).
- 2) A. I. Meyers, J. P. Lawson, and D. R. Carver, *J. Org. Chem.*, **46**, 3119 (1981).
- 3) 5a: mp 75-76 °C. Found: C, 56.67; H, 6.11; N, 3.01%. Calcd for $C_{22}H_{28}NO_3P$: C, 56.77; H, 6.06; N, 3.01%.
- 4) The reaction using 2a and diethyl (α -methylsulfonylvinyl)phosphonate under similar conditions led to only a 1:1 Michael adduct in 70% yield, but no expected annelation product was obtained.
- 5) All new compounds were fully characterized by the IR, 1H NMR, and mass spectra, and gave satisfactory elemental analyses and/or high resolution mass spectra. The physical and spectral data ($CDCl_3$ solutions for 1H and ^{13}C NMR) of the selected compounds are as follows.
5b: 57% yield; oil; IR (neat) 1690-1740 cm^{-1} ; 1H NMR δ 1.08-1.60 (12H, m, Me), 2.52-3.12 (2H, br dd, $J=9.40, 18.31$ Hz, CH_2), 3.28-3.72 (2H, dd, $J=5.71, 13.04$ Hz, NCH_2), 3.90-4.52 (8H, m, OCH_2), 6.27 (1H, d, $J=6.0$ Hz, olefinic H), and 7.90 (1H, d, $J=6.0$ Hz, olefinic H).
5c: 47% yield; oil; 1H NMR δ 1.07-1.52 (12H, m, Me), 2.12-2.80 (4H, m, CH_2CH_2), 2.80-3.60 (4H, m, NCH_2, CH_2), and 3.90-4.40 (8H, m, OCH_2).
5d: 19% yield; oil.
6e: oil; IR (neat) 1725, 1710 cm^{-1} ; 1H NMR δ 0.80-1.60 (21H, m, Me), 2.0-2.92 (4H, m, CH_2), 3.04-4.50 (16H, m, NCH_2, OCH_2), and 6.60-7.68 (4H, m, aromatic H); MS Found: m/z 701.2351. Calcd for $C_{31}H_{45}NO_{13}P_2$: 701.2365.
- 6) Similar reaction using vinyltriphenylphosphonium bromide has recently been reported by Posner and Lu [*J. Am. Chem. Soc.*, **107**, 1424 (1985)].
- 7) 11a: oil; IR (neat) 1700-1730, 1650 cm^{-1} ; 1H NMR δ 1.0-1.52 (12H, m, Me), 1.60-3.40 (11H, m, CH_2, CH), and 3.84-4.48 (8H, m, OCH_2); MS Found: m/z 402.1816. Calcd for $C_{19}H_{31}O_7P$: 402.1807.
11b: oil.
11c: a 2:1 mixture of two diastereoisomers; oil; IR (neat) 1710-1740 cm^{-1} ; 1H NMR δ 1.33 (12H, t, $J=7.03$ Hz, Me), 1.80 (3H, s, Me), 1.90-3.12 (10H, m, CH_2), and 3.80-4.42 (8H, quint, OCH_2); ^{13}C NMR δ 13.8, 14.3, 16.1 (d, $^3J_{P-C}=5.2$ Hz), 16.4 (d, $^3J_{P-C}=5.2$ Hz), 18.2, 18.5, 28.1, 28.2, 31.7, 32.0, 33.4, 33.7, 35.8, 36.5, 38.0, 38.6, 46.3 (d, $^1J_{P-C}=131.5$ Hz), 46.7 (d, $^1J_{P-C}=134.1$ Hz), 54.8 (d, $^3J_{P-C}=11.2$ Hz), 55.6 (d, $^3J_{P-C}=12.0$ Hz), 62.7 (d, $^2J_{P-C}=6.0$ Hz), 63.6 (d, $^2J_{P-C}=6.0$ Hz), 128.5 (d, $^3J_{P-C}=12.9$ Hz), 132.0 (d, $^3J_{P-C}=10.3$ Hz), 141.5, 167.9, 168.4, 168.5 (d, $^2J_{P-C}=4.3$ Hz), 169.9 (d, $^2J_{P-C}=4.3$ Hz), 216.6, and 221.1; MS Found: m/z 444.1877. Calcd for $C_{21}H_{33}O_8P$: 444.1910.
11d: oil.

(Received September 8, 1986)