A New Approach to Cyclopentane Annulated Compounds *via* 1-(Cyclopent-1-enylcarbonyl)vinylphosphonates

Toru Minami,* Minoru Nakayama, Kouichi Fujimoto and Shingo Matsuo

Department of Applied Chemistry, Kyushu Institute of Technology, Sensuicho 1-1, Tobata, Kitakyushu 804, Japan

Fused ring systems, containing two or three five-membered rings, were constructed by utilizing 1-(cyclopent-1-enylcarbonyl)vinylphosphonates which function as versatile annulating reagents.

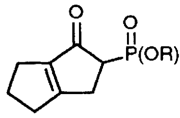
Development of convenient synthetic routes to cyclopentanoid frameworks has been a challenging theme to synthetic chemists, since many naturally occurring diquinane and triquinane terpenoids have been shown to have useful antibiotic or antitumour properties.[1]

Reported herein is the synthesis of versatile cyclopentane annulating reagents, 1-(cyclopent-1-enylcarbonyl)vinylphosphonates **4**† and their synthetic applications to the preparation of functionalized cyclopentanoids.

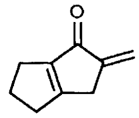
As shown in Scheme 1, methylation of 1-(cyclopent-1-enylcarbonyl)methylphosphonates **1** and phenylselenenylation of the resulting 1-(cyclopent-1-enylcarbonyl)ethylphosphonates **2** into the selenides **3** followed by oxidation led to the corresponding 1-(cyclopent-1-enylcarbonyl)vinylphosphonates **4** (method A).[2a] The vinylphosphonate **4a** was alternatively synthesized by the condensation of **1a** with paraformaldehyde (method B).[2b]

The Nazarov cyclization of the 1-(cyclopent-1-enylcarbonyl)vinylphosphonates **4a** or **4b** was carried out in the presence of 1.1–3.0 equiv. of $SnCl_4$ or $FeCl_3$ at room temperature for 12–30 h in CH_2Cl_2, which produced 2-(dialkoxyphosphoryl)-2,3,4,5,6-pentahydropentalen-1-ones **6a** in 25–40% or **6b** in 35–37% yields, respectively. The low yields of the products **6a,b** in these reactions were due to the formation of unidentified polymeric materials. The use of $AlCl_3$, $TiCl_4$ or polyphosphoric acid as a catalyst did not result in the expected Nazarov cyclization products **6**, and only unidentified polymeric products were obtained. In addition, the vinylphosphonate **4b** easily underwent the intramolecular double Michael addition of diethyl sodiomalonate to give the 3-diethoxyphosphorylbicyclo[4.3.0]nonan-2-one **8** in 83% yield. As one of the synthetic applications of the thus synthesized β-ketophosphonates **6** and **8**, the Horner–Wittig reaction with paraformaldehyde was performed to afford the corresponding enones **7** and **9** in 48 and 44% yields, respectively.

Furthermore, by making use of the α-ketovinylphosphonate moiety in **4** as a cyclopentene annulation reagent,[3] we have been able to achieve the synthesis of dicyclopent-1-enyl ketones which when treated with acids lead to Nazarov cyclization products. Thus, the Michael addition of (1,3-dioxolan-2-yl)ethylmagnesium bromide to **4** to provide **10** (76–84%), followed by acidic hydrolysis to the aldehydes **11** (85–94%) and the intramolecular Horner–Wittig reaction gave the desired dicyclopent-1-enyl ketones **12** (51–70%) (Scheme 2). A polyphosphoric acid-catalysed cyclization of



6a: R = Me
6b: R = Et



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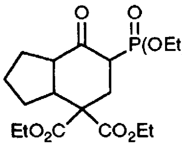

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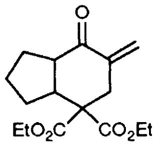

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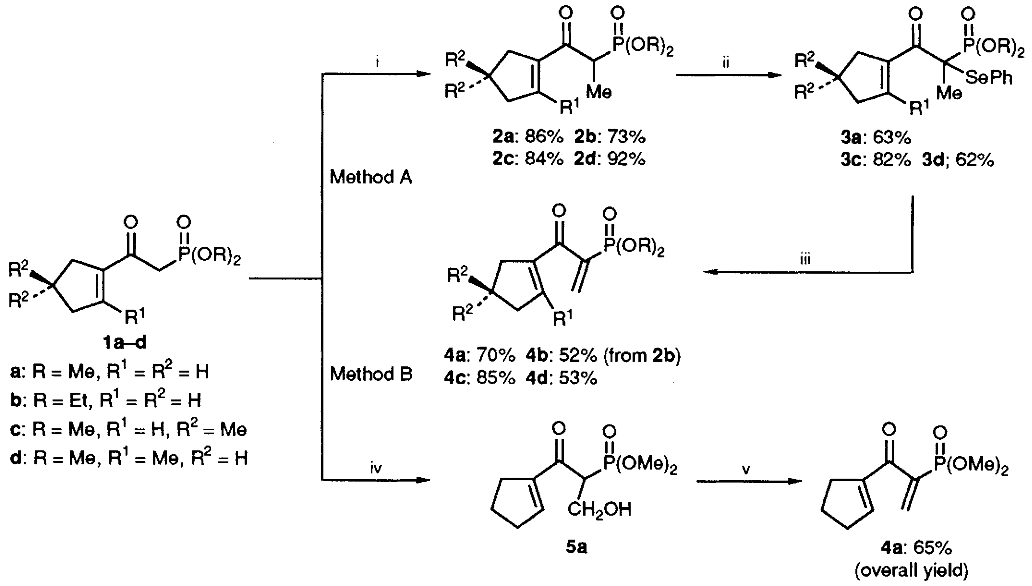
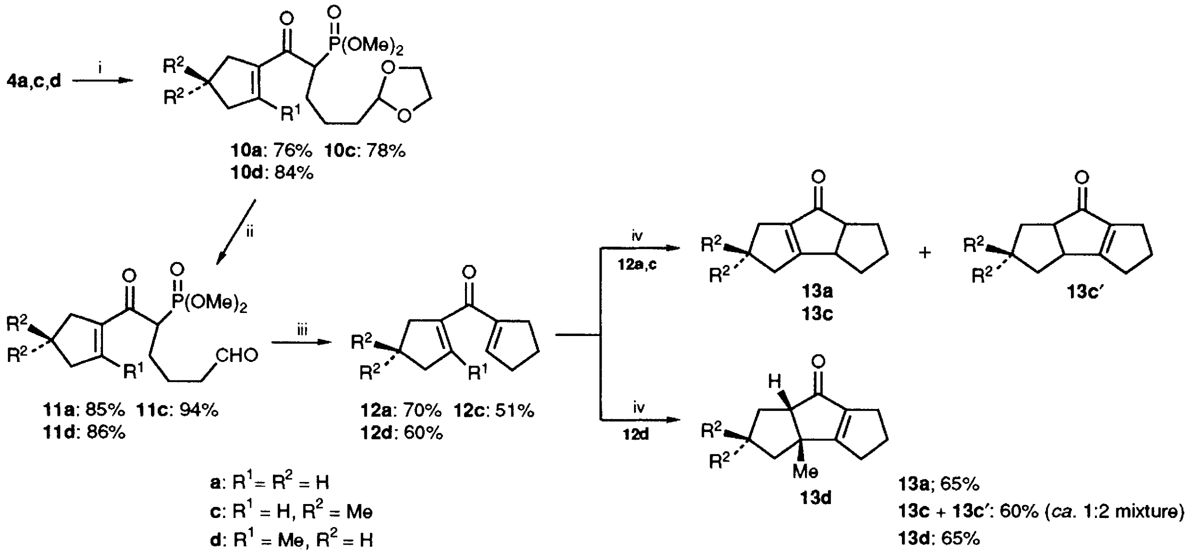
† All new compounds were characterized by ^1H and ^{13}C NMR spectroscopy and by high-resolution mass spectrometry and/or combustion analysis. Selected physical data **4a**; b.p. 130 °C at 2 mmHg; ^1H NMR (60 MHz, $CDCl_3$): δ 1.60–2.30 (m, 2H, CH_2), 2.30–2.90 (m, 4H, CH_2), 3.80 (d, $^3J_{H-P}$ 11.3 Hz, 6H, OMe), 6.19 (dd, J_{gem} 1.3, $^3J_{H-P}$ 28.4 Hz, 1H, *E*-vinylic H), 6.73 (br s, 1H, alkenic H) and 6.77 (dd, J_{gem} 1.3, $^3J_{H-P}$ 6.6 Hz, 1H, *Z*-vinylic H). **6a**; Oil; ^1H NMR: δ 1.50–3.00 (br, 8H, CH_2), 3.00–3.30 [m, 1H, COCHP(O)], 3.80 (d, $^3J_{H-P}$ 11.0 Hz, 3H, OMe) and 3.83 (d, $^3J_{H-P}$ 11.0 Hz, 3H, OMe). **13d**; Oil; ^1H NMR: δ 1.30 (s, 3H, Me), 1.35–2.03 (m, 6H, CH_2) and 2.10–2.80 (m, 7H, CH_2, CH); ^{13}C NMR: δ 23.9, 24.6, 25.4, 27.4, 27.9, 29.4, 35.7, 49.0, 64.5, 147.9, 191.7 and 205.5. 2,4-Dinitrophenylhydrazone derivative m.p. 151 °C (EtOH).



Scheme 1 *Reagents and conditions*: i, $Bu_4N^+Br^-$, NaOH, MeI, CH_2Cl_2–H_2O, room temp., 10 h; ii, NaH, PhSeBr, tetrahydrofuran (THF), −78 °C, 2 h; iii, H_2O_2, CH_2Cl_2–H_2O, 0 °C, 1 h; iv, piperidine, $(HCHO)_n$, EtOH, reflux, 5 h; v, p-$MeC_6H_4SO_3H$, benzene, 80 °C, 3 h



Scheme 2 *Reagents and conditions*: i, $\overline{\mathrm{OCH_2CH_2OC}}\mathrm{HCH_2CH_2MgBr}$, THF, −78 °C, 2 h; ii, HCl (1 mol dm^{-3}), THF, reflux, 5 h; iii, NaH, THF, room temp., 10 h; iv, polyphosphoric acid, 100 °C, 0.5 h

the resulting divinyl ketones **12** produced the expected tricyclo[6.3.0.0^{3,7}]undecenone system **13**.[4]

Thus, 1-(cyclopent-1-enylcarbonyl)vinylphosphonates have been proved to be useful for the construction of triquinane ring systems *via* a sequence of Michael addition, intramolecular Horner–Wittig reaction, and the Nazarov reaction.

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References

1 L. A. Paquette and A. M. Doherty, *Polyquinane Chemistry*, Springer-Verlag, 1987 and references cited therein; for recent reviews, see, M. Ramaiah, *Synthesis*, 1984, 529; T. Hudlicky and J.D. Price, *Chem. Rev.*, 1989, **89** 1467.

2 See, (*a*) W. A. Kleschick and C. H. Heathcock, *J. Org. Chem.*, 1978, **43**, 1256; (*b*) A. N. Pudovik, G. E. Yastrebova and V. I. Nikitina, *Zh. Obshch. Khim.*, 1966, **36**, 1232; *Chem. Abstr.*, 1966, **65**, 15418.

3 T. Minami, K. Watanabe, T. Chikugo and Y. Kitajima, *Chem. Lett.*, 1987, 2369; for a review, see, T. Minami and J. Motoyoshiya, *Synthesis*, in the press.

4 P. E. Eaton, C. Giordano, G. Schloemer and U. Vogel, *J. Org. Chem.*, 1976, **41**, 2238.