A New One-Step Synthesis of Functionalized Fulvenes

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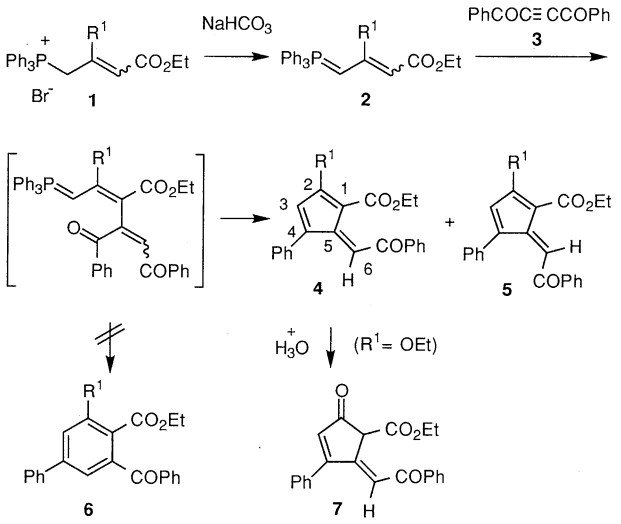
Functionalized fulvenes were prepared in a single operation by condensation of allylidenetriphenylphosphoranes and 1,2-diacylacetylenes

Fulvene can serve as versatile synthetic intermediates for the construction of various ring systems through inter- or intramolecular [6 + 2]-, [6 + 4]- and [4 + 2]-cycloadditions.[1] However, utility of fulvenes is limited due to general inaccessibility of substituted fulvenes. Although fulvene ring is readily derived from cyclopentadiene by base-catalyzed condensation with ketones, application of this approach to substituted cyclopentadienes usually resulted in the formation of a mixture of regioisomers.[2] We have demonstrated that [3 + 2] annulation of allylidenetriphenylphosphorane is a powerful tool for the preparation of 5-membered carbocycles.[3] The recent publication has described the reaction of the phosphorane with 1,2-diacylethylenes undergoes [3 + 2] annulation to provide tri- and tetra-substituted cyclopentadienes exclusively as a mixture of the double-bond isomers without the attendant formation of another possible [3 + 3] annulation product.[4] In this context, we investigated reactions of the phosphorane with 1,2-diacylacetylenes which would provide substituted fulvenes in a single operation. This paper describes preliminarily outcomes of regioselective synthesis and the properties of polyfunctionalized fulvenes.



Scheme 1. For R^1, see Table 1.

When the phosphonium bromide **1a** was allowed to react with dibenzoylacetylene (**3**) in a heterogeneous medium of dichloromethane and saturated aqueous $NaHCO_3$ solution at room temp under nitrogen, the fulvene **4a** was produced as crystals in 88% yield (Scheme 1, Table 1, entry 1). The formation of the [3 + 3] annulation product **6** was not detected. Structure of **4a** was confirmed by a combination of CH-COSY and HMBC spectra and the ^{13}C and ^1H chemical shifts in the NMR spectra are shown in Table 2. Geometry of the exocyclic double bond was assigned to be *Z*-configuration on the basis of the C-6 proton chemical shift (6.94 ppm) as described later. The phosphonium salt **1b** having no substituent at the C-2 position also reacted with **3** in a similar manner to give geometrical isomers of the fulvenes **4b** and **5b**[5] in 38 and 28% yields, respectively (entry 2). In the ^1H NMR spectra, the exocyclic C-6 proton of the *E*-isomer **5b** absorbed at 8.37 ppm, while that of the *Z*-isomer **4b** centered at 7.08 ppm. It appears that the downfield shift observed for the *E*-isomer **5b** is attributable to the anisotropy of the ester carbonyl group.[1b]

Table 1. Fulvenes from allylidenetriphenylphosphorane and dibenzoylacetylene

Entry	Phosphorus Compound No.	R^1	Method[a]	Yield(%) of Fulvene[b] *Z*-isomer **4**	*E*-isomer **5**
1	**1a**	Me	A	88	-
2	**1b**	H	A	38	28
3	**2c**	OEt	B	92	-

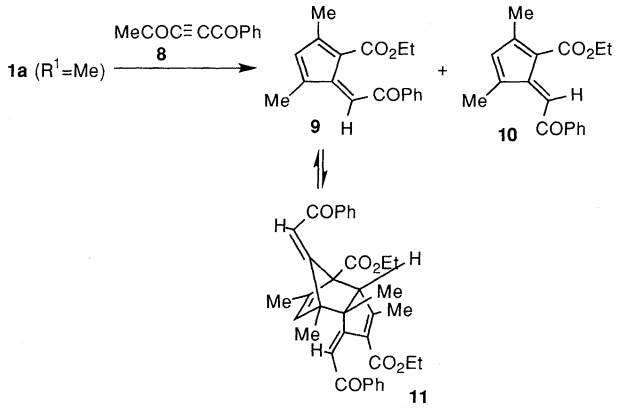
[a]Method A: reaction was carried out at room temp for 12 h in a heterogeneous medium of CH_2Cl_2 and aqueous $NaHCO_3$; Method B: reaction was carried out in THF at -20 °C to room temp for 48 h. [b]Isolated yield based on **3**.

Table 2. ^{13}C and ^1H Chemical Shifts of **4a**

Position	^{13}C Chemical Shift (ppm)	^1H Chemical Shift (ppm)
1	120.02	-
2	157.01	-
3	133.45	6.44
4	145.13	-
5	143.96	-
6	134.71	6.94

The reaction of the ethoxyphosphorane **2c** with **3** was carried out in THF at -20 °C to room temp for 48 h to give the fulvene **4c** as a single *Z*-isomer (entry 3), which showed the peak due to the C-6 proton at 6.76 ppm. Mild acid treatment (aqueous 2M HCl-$CHCl_3$, room temp) of **4c** gave **7** in 97% yield, providing an access to exomethylene cyclopentenones. Thus, annulation with dibenzoylacetylene gave the *Z*-isomers from the phosphoranes **2a** and **2c** and the mixture of *Z*- and *E*-isomers from the phosphorane **2b** having no substituent at the C-2 position. The product distribution in each case may depend on the thermodynamic stability of their isomers.[6]

Next, the diacylacetylene **8** was examined as an unsymmetrical substrate. When **8** was allowed to react with **1a** in the heterogeneous medium at room temp, chromatographic analysis showed the presence of two products, one of which the *E*-isomer **10** was isolated in 16% yield in a pure form. The *Z*-isomer **9** (34% yield) was very unstable and transformed readily into the dimer **11**[7] in a condensed state. Other possible regioisomers were not detected in the reaction mixture, indicating that annulation of unsymmetrical diacylacetylene **8** with **1a** proceeded via highly regioselective Michael addition at the 3-position of **8**.[4b] Interestingly, when a solution of the dimer **11** in $CDCl_3$ was left at room temp overnight, ^1H NMR spectra showed the formation of a 1:3 mixture of **9** and **11**. Evaporation of the $CDCl_3$ *in vacuo* gave the dimer **11** exclusively.



Scheme 2.

In a sharp contrast, the *E*-isomer **10** was stable against dimerization and unchanged upon leaving at room temp for a month. This may suggest that approach of the two molecules of **10** is inhibited by steric hindrance due to the benzoyl group at the same side with the 3-position. In addition, comparison of the behavior of **9** with that of **4a-c** indicates that replacement of the 4-phenylsubstituent by the methyl group makes dimerization easy. Further study on the annulation and its application to synthesis of carbocycles is underway.

References and Notes

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5 Spectral data for **4b**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.94 (2H, bd, *J* = 8.4 Hz), 7.57-7.41 (9H, m, 2-H), 7.08 (1H, bs, 6-H), 6.44 (1H, d, *J* = 3.0 Hz, 3-H), 3.91 (2H, q, *J* = 7.1 Hz), 1.00 (3H, t, *J* = 7.1 Hz); IR(neat) 1705, 1669, 1597 cm^{-1}; UV λmax (MeOH) 458.0 (2600), 424.0 (2800), 243.0 nm (26600).

5b: ^1H NMR (300 MHz, $CDCl_3$) δ 8.37 (1H, dd, *J* = 0.8, 1.3 Hz, 6-H), 8.07 (2H, bd, *J* = 8.4 Hz), 7.65-6.93 (8H, m), 7.49 (1H, dd, *J* = 0.8, 2.6 Hz, 2-H), 6.46 (1H, dd, *J* = 1.3, 2.6 Hz, 3-H), 4.36 (2H, q, *J* = 7.1 Hz), 1.41 (3H, t, *J* = 7.1 Hz); IR(neat) 1701, 1659, 1597 cm^{-1}; UV λmax (MeOH) 458.0 (2400), 424.0 (2500), 242.5 nm (27100).

6 The ester carbonyl frequencies in the IR spectra might suggest conformational difference of the ester moieties between 3-substituted and 3-unsubstituted *Z*-isomers. The *Z*-isomers **4a** and **4c** showed the ester carbonyl absorption at 1715 and 1717 cm^{-1}, whilst **4b** at 1705cm^{-1}.

7 Structure of the dimer **11** was confirmed by a combination of CH-COSY and NOESY spectra. Stereochemical evidence was obtained from the observation of NOEs between C2-H and C3-Me and between C5'-vinyl proton and C7-Me. Spectral data for **11**: IR(neat) 1732, 1657, 1599 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.96-7.90 (4H, m), 7.60-7.42 (6H, m), 6.51 (1H, s, C5'-vinyl H), 6.21 (1H, s, C10'-vinyl H), 5.72 (1H, q, *J* = 1.6 Hz, 8-H), 4.25-3.94 (4H, m), 3.54 (1H, bs, 2-H), 2.13 (3H, s, 3-Me), 1.74 (3H, d, *J* = 1.6 Hz, 9-Me), 1.46 (3H, s, 7-Me), 1.36 (3H, s, 6-Me), 1.11 (3H, t, *J* = 7.1 Hz); 1.01 (3H, t, *J* = 7.1 Hz); HRMS Found 564.2504, Calcd. for $C_{36}H_{36}O_6$ 564.2510.