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Cyclopentenones from Allylidene Triphenylphosphoranes and α-Halocarbonyl Compounds

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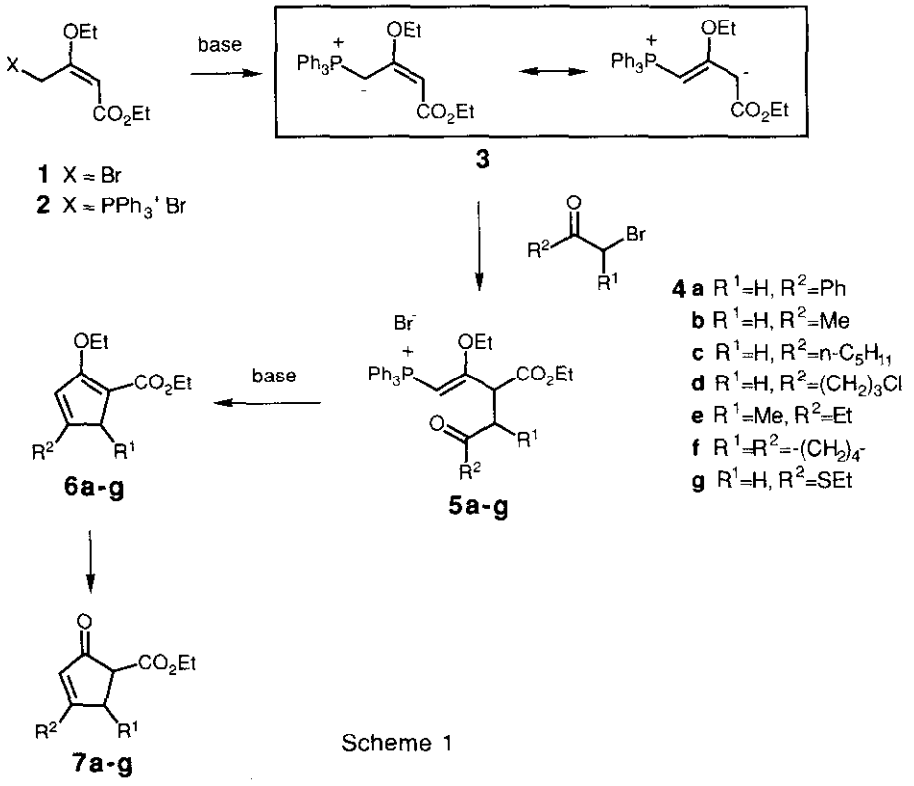
Summary: Allylidene triphenylphosphorane **3** reacted with α-haloketones and α-halothioesters to give 2-ethoxycyclopentadienes *via* a [3+2] annulation process in the presence of base. Mild acid treatment of the 2-ethoxycyclopentadienes provided a new route to cyclopentenones.

The formation of substituted cyclopentenones has been an intensely studied subject for recent years.[1] Many approaches of methodological interest have been reported for their preparation.[2] An intramolecular Aldol condensation of 1,4-diketones is still one of the most potent approaches to cyclopentenones. However, alkylation of ketone enolate with α-haloketone for the preparation of 1,4-diketones does not proceed very well in many cases and hence the halides of the masked ketones were used instead of α-haloketones.[1a, 3] Recently, we have reported that the [3+2] annulation reaction using allylidene triphenylphosphoranes may be used to advantage for the regioselective preparation of cyclopentadienes with a variety of substituents.[4] In this reaction, use of the allylidene phosphorane having an alkoxy group as a substituent would allow to react directly with readily available α-haloketones leading to formation of ethoxycyclopentadienes which would be converted by mild acid treatment into cyclopentenones. Herein, we report a new efficient route to substituted cyclopentenones.

The allylidene triphenylphosphorane **3** has been first prepared by Bestmann et al.[5] However, these methods employ inconvenient procedure. In our hand, the phosphorane **3** was readily prepared in a usual manner from ethyl (*E*)-4-bromo-3-ethoxy-2-butenoate (**1**)[6] in 85% yield by treatment with triphenylphosphine followed by aqueous NaOH solution. When the phosphorane **3** was treated with α-bromoacetophenone in chloroform at room temperature, 2-ethoxycyclopentadiene **6a**[7, 8] was obtained in 19% yield, together with **5a** (31%), **2** (13%) and triphenylphosphine oxide (19%), and recovery of α-bromoacetophenone (22%).

Compound **5a** was quantitatively converted into **6a** on shaking in dichloromethane with aqueous $NaHCO_3$ at room temperature. This indicates that the annulation takes place stepwise as illustrated in Scheme 1. The first step should be alkylation of the carbanion of the 1,4-dipolar resonance form **3** to give **5**, which, after regeneration of the phosphorane by transylidation with **3**, proceeds an intramolecular Wittig reaction to furnish cyclopentadiene **6**.



Scheme 1

The annulation reaction could be carried out in a one-pot reaction starting from the allyl phosphonium bromide **2** in the presence of base. The phosphonium bromide **2** in THF was treated with an equiv of tert-BuOK and then α-bromoacetophenone at room temperature under nitrogen. After disappearance of the yellow color of the phosphorane, the mixture was treated with an additional equiv of tert-BuOK and stirred for 12 h at room temperature to give **6a** in 83% yield (Method A). Alternatively, compound **6a** was more conveniently obtained in 68% yield when **2** was allowed to react with α-bromoacetophenone in dichloromethane in the presence of 2.3 equiv of diisopropylethylamine at room temperature under nitrogen (Method B).

Table 1. 2-Ethoxycyclopentadienes and Cyclopentenones from Allylphosphonium Bromide and α-Bromocarbonyl Compounds

bromide			cyclopentadiene		cyclopentenone	
no.	method[a]	time	no.	yield(%)[b]	no.	yield(%)[b]
4a	A	12 h	**6a**	83	**7a**	99
4a	B	48 h	**6a**	62		
4b	A	12 h	**6b**	90	**7b**	91
4b	B	24 h	**6b**	76		
4c	B	7 days	**6c**	74	**7c**	98
4d	A	12 h	**6d**	74	**7d**	92
4d	B	48 h	**6d**	53		
4e	A	24 h	**6e**	32	**7e**	98
4e	B	48 h	**6e**	26		
4f	B	7 days	**6f**	20	**7f**	92
4f	C	3 days	**6f**	47		
4g	B	18 days	**6g**	60	**7g**	98

[a] For the reaction conditions, see text; method A: tert-BuOK in THF at r.t.; method B: i-Pr_2EtN (2.3 equiv) in CH_2Cl_2 at r.t.; method C: 2 equiv of the phosphorane **3** were used in THF at 40-50 °C.

[b] Isolated yield.

As can be seen from Table 1, this annulation is general for the preparation of a variety of 2-ethoxycyclopentadienes. With primary halides, the reaction proceeded nicely to afford good yields of the corresponding cyclopentadienes. Secondary halides **4e** and **4f** gave moderate yields of **6e** and **6f** with longer reaction times than those necessary for primary halides. α-Bromothioester **4g** also reacted with **3** to afford the 4-ethylthiocyclopentadiene **6g**.

The resulting ethoxycyclopentadienes **6** were converted in exellent yields into the corresponding cyclopentenones **7** upon mild acid treatment (aqueous 2M $HCl/CHCl_3$, room temperature). The cyclopentenones could be also obtained from the phosphonium bromide **2** by a one-flask procedure without isolation of **6** by treating the reaction mixture (Method A) with aqueous HCl solution at room temperature. For instance **7b** was obtained in 65% yield from **2** in this way.

In summary, we have developed a convenient method for the regioselective formation of substituted cyclopentenones from allylidene phosphoranes and α-halocarbonyl compounds. We believe that the

experimental simplicity and the mildness of the reaction conditions should allow the application of this methodology for the preparation of a wide range of useful substituted cyclopentenones. Synthesis of natural cyclopentanoids using this reaction is underway in our laboratories.

References

1. For excellent reviews of methods for the construction of 5-membered carbocycles, see: (a) Ramaiah, M. *Synthesis*, **1984**, 529. (b) Paquette, L. A. *Top. Curr. Chem.* **1984**, *119*, 1.
2. For some leading examples, see: Curran, D. P. *Synthesis* **1988**, 417, 489. Tius, M. A.; Astrab, D. P.; Fauq, A. H.; Ousset., J.-B.; Trehan, S. *J. Am. Chem. Soc.* **1986**, *108*, 3438. Chamberlin, A. R.; Bloom, S. H.; Cervini, L. A.; Fotsch, C. H. *J. Am. Chem. Soc.* **1988**, *110*, 4788. Beak, P; Burg, D. A. *J. Org. Chem.* **1989**, *54*, 1647. Tamao, K.; Kobayashi, K.; Ito, *J. Am. Chem. Soc.* **1988**, *110*, 1286. Y. Buchwald, S. L.; Lum, R. T.; Fisher, R. A.; Davis, W. M. *J. Am. Chem. Soc.* **1989**, *111*, 9113. Negishi, E.; Holmes, S. J.; Tour, J. M.; Miller, J. A.; Cederbaum, F. E.; Swanson, D. R.; Takahashi, T. *J. Am. Chem. Soc.* **1989**, *111*, 3336. Hirst, G. C.; Howard, P. N.; Overman, L. E. *J. Am. Chem. Soc.* **1989**, *111*, 1514. Mathau , J. *J. Chem. Soc., Chem. Commun.* **1990**, 1264. Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081. Trost, B. M. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 1.
3. For a recent example, see: Welch, S. C.; Assercq, J.-M.; Loh, J.-P.; Glase, S. A. *J. Org. Chem.* **1987**, *52*, 1440, and references cited therein.
4. Hatanaka, M.; Himeda, Y.; Ueda, I. *J. Chem. Soc. Chem. Commun.* **1990**, 526.
5. Bestmann, H. J.; Roth, K. *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 575. Bestmann, H. J.; Saalfrank, R. W. *Angew. Chem. Int. Ed. Engl.* **1970**, *9*, 367.
6. Tendil, J.; Verny, M.; Vessiere, R. *Bull. Soc. Chim. France* **1977**, 565. Kochhar, K. S.; Pinnich, H. W. *J. Org. Chem.* **1984**, *49*, 3222.
7. All products gave satisfactorily spectral and/or microanalytical data. Spectral data for **6a**: IR (neat) ν_{max} 1700, 1618 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 1.33 (3H, t, *J*=7.1 Hz), 1.47 (3H, t, *J*=7.0 Hz), 3.69 (2H, d, *J*=0.7 Hz, H5), 4.24 (2H, q, *J*=7.0 Hz), 4.31 (2H, q, *J*=7.1 Hz), 6.90 (1H, br s, H3), 7.30 (5H, m, Ph); UV (MeOH) λ_{max} 342 nm (ε 15,000).
8. The 2-ethoxycyclopentadienes prepared did not proceed a 1,5-sigmatropic migration at least on leaving for several weeks at room temperature, although facile propensity of 1,5-sigmatropic migration of cyclopentadienes has been reported; McLean, S.; Hynes, P. *Tetrahedron*, **1965**, *21*, 2313, 2343.

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