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Photochemical SET Induced 1,4-Conjugate Additions of Silyl Phosphites to Cyclic Enones

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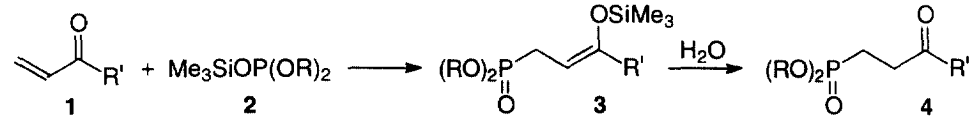
Abstract: Irradiation of cyclic enones **5-8** in the presence of $Me_3SiOP(OMe)_2$ or $Me_3SiOP(OEt)_2$ gives phosphonosilylation products of 1,4-conjugate addition which are hydrolyzed to the phosphonoketones **11-14** in 82-92% isolated yields. An SET process in which the triplet enone accepts an electron from the silyl phosphite is proposed to be the key initiation step in these reactions. © 1999 Elsevier Science Ltd. All rights reserved.

Properly substituted phosphonates can serve as key intermediates for the synthesis of biologically active compounds.[1] The additions of silyl phosphites (**2**) to α,β-unsaturated aldehydes and ketones (**1**) to give the desirable 1,4-adducts of *phosphonosilylation* (**3**), and their β-ketophosphono hydrolysis products (**4**), have been much studied.[2] Unfortunately, unlike their acyclic counterparts, reactions of *cyclic* enones do not occur readily. Thus, reaction of $Me_3SiOP(OEt)_2$ with 2-cyclohexenone (**6**) requires *12 h at 180 °C* to give near-quantitative yields of adducts in 1,4/1,2 ratio of 16/1; i.e., predominantly the 1,4-phosphonosilyl precursor to **12**.[2b] (See Table 1 for structures **5-16**.) The methyl analog, $Me_3SiOP(OMe)_2$, was essentially unreactive.[2b,c]

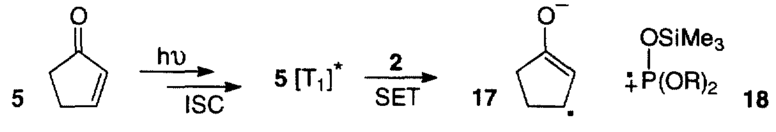
(1)



Continuing interest in these reaction systems is shown by the very recent report of the ability of trimethylsilyl triflate to catalyze, at 0 °C, the nearly exclusive formation of the 1,4-adducts on reaction of cyclic enones, including **5** and **6**, with trimethylsilyl phosphites ($Me_3SiOP(OR)_2$; R = Et, and sometimes Me, $PhCH_2$, Ph).[2a] On hydrolytic workup (eq 1), the cyclic β-ketophosphonates were obtained in 75-98% isolated yields. However, with enone **10** the *1,2-adduct* was the major product (68% 1,2; 20% 1,4).

Our interest in photoinduced single electron transfer (SET) reactions of three-coordinate phosphorus compounds[3] led us to attempt *photochemical* phosphonosilylation by irradiation of cyclic α,β-unsaturated ketones in the presence of $Me_3SiOP(OR)_2$ (R = Me, Et). The envisaged initiation step is electron transfer to the *triplet excited state* of the enone to generate the radical ion pair **17/18**, as illustrated for **5** by eq 2:

(2)



The analogous reduction of triplet excited states of α,β-unsaturated ketones by amines and allylstannanes, to give radical anion intermediates such as **17**, has been extensively studied.[4]

We report here the photochemical phosphonosilylation of the cyclic α,β-unsaturated ketones **5-8** to give high isolated yields of **11-14** (Table 1), formed by hydrolytic workup of the cyclic, 1,4-phosphonosilyl adducts analogous to **3**. Conjugate 1,4-addition occurs essentially exclusively, as shown by GC and ^{31}P NMR analysis of reaction product solutions before workup. Phosphites $Me_3SiOP(OEt)_2$ and $Me_3SiOP(OMe)_2$ work comparably well. The 2-methyl-substituted enone **8** affords ketophosphonate **14** in high yields. However, methyl substitution at C-3 renders phosphite

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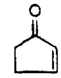
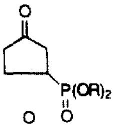
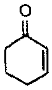
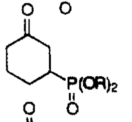
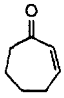
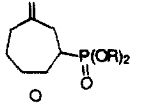
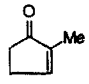
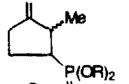
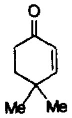
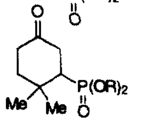
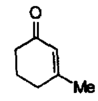
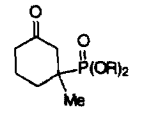
10 resistent to 1,4-addition. The mechanism proposed for formation of phosphonosilylated products involves *hitherto unrecognized reactions of the radical cations of* $Me_3SiOP(OR)_2$. Very significantly, a solution of **5** and $Me_3SiOP(OMe)_2$ that was kept in the dark for 48 h *gave no evidence of reaction (GC).*

Although its scope is not fully defined, the photoinduced SET approach to phosphonosilylation has potential advantages synthetically. As with the Me_3SiOTf-catalyzed phosphonosilylations,[2a] one avoids the high temperatures and long reaction times required in the direct thermal reactions of $Me_3SiOP(OEt)_2$ with enones (180 °C, 12 h for **5**, **6**, and the cyclohexenone analog of **8**).[2b] Moreover, the *absence* of added Me_3SiOTf in the photoinduced SET reactions precludes competing silylation of other sites that could lead to unwanted side reactions in multifunctional molecules. Furthermore, SET-induced phosphonosilylation is successful with a seven-membered ring enone (**7**), Table 1, a reaction not reported for the thermal $Me_3SiOP(OEt)_3$/cyclic enone or triflate-catalyzed phosphonosilylations.

Table 1: Photoinduced SET Reaction of Cyclic Enones with $Me_3SiOP(OR)_2$

enones	product	isolated yields (%) R = Me	R = Et
5 	**11** 	92	82
6 	**12** 	89	91
7 	**13** 	81	78
8 	**14** 	86	87
9 	**15** 	a	c
10 	**16** 	b	c

a) Isolated 57% yield of three products with MS M+ for 1:1 adduct; major product 90% (^{31}P NMR). b) <5%, GC/MS. c) Reaction not run.

The procedure for reaction of 2-cyclopentenone (**5**) with $Me_3SiOP(OMe)_2$ is typical: In a water bath at room temperature, a 50 mL deoxygenated CH_3CN solution, 10.0 mM in **5** and 15 mM in $Me_3SiOP(OMe)_2$, in a septum-capped Pyrex tube was irradiated (450 W medium pressure Hg lamp) to complete consumption of **5** in 4.6 h (GC). The *single new peak* observed in the GC showed by GC/MS an M^+ peak ($m/z = 264$) corresponding to a 1:1 adduct of **5** and $(MeO)_2POSiMe_3$, **22** (R = Me); ^{31}P NMR (C_6D_6) $\delta = 35.9$. Hydrolysate **11** (R = Me, $\delta^{31}P = 33.8$) was absent. Solvent removal under vacuum, dissolution of the residue in stirred ethyl acetate (75 mL), addition of water (5 mL), separation of the organic layer, which was then dried over Na_2SO_4, and removal of solvent left an oil. Silica gel chromatography (2% methanol-ethyl acetate) furnished 0.18 g (92% yield) of product ketophosphonate **11** (R = Me) which was characterized spectroscopically.[5]

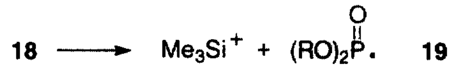
The structures of **11** (R = Et) and **12-14** (R = Me or Et) also are totally supported by their ^{31}P, ^{1}H, ^{13}C NMR and MS/HMRS spectral data. Both diastereomers (cis and trans) of **14** (4/1 ratio, R = Me; 1/1 ratio, R = Et) were observed (^{1}H, ^{13}C, ^{31}P NMR chemical shifts; e.g. for R = Me, $\delta^{31}P = 30.9$ and 30.4, $CDCl_3$).

In a larger scale photoreaction, irradiation of enone **6** (1.25 g, 13.0 mmol) and $Me_3SiOP(OMe)_2$ (3.12 g, 17.1 mmol) in 230 mL of CH_3CN in the jacket of an immersion well (450 W Hg, Pyrex filter) allowed isolation of the initial phosphonosilylation product itself (**21**): 2.8 g (76% yield), 92% pure (GC), bp 89-90 °C (0.005 mmHg), containing 8% of its hydrolysis product (**12**, R = Me).

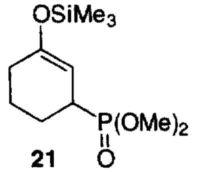
The proposed SET initiation step (eq 2) is estimated for *2-cyclopentenone* (**5**) by the Rehm-Weller equation[6] to be favorable if the oxidation potential ($E_{1/2}^{ox}$) for $Me_3SiOP(OR)_2$ is about 0.6 eV less than $E_{1/2}^{ox}$ for $(MeO)_3P$ (1.6 eV[7]);[8] Indeed, α-Me_3Si substitution reduces the $E_{1/2}^{ox}$ of alkylamines by 0.2-0.5 eV[9]. For 2-cyclopentenone: $E_{1/2}^{red} = -2.16$ eV,[10] $E_T = 3.21$ eV[11].

A probable mechanism for the formation of phosphonosilylation product **21** from *triplet* radical ion pair **17/18**[12] involves the predictably rapid, ***but previously unexploited***, fragmentation of **18** to the trimethylsilyl cation and phosphinoyl radical **19** (eq 3). Scission step 3 is favored thermodynamically by the formation of the phosphoryl bond (P=O) and by the excellent capabilities in acetonitrile of Me_3Si^+ as an electrofuge. Additionally, scission may be assisted *kinetically* by the attack on **18** by the enolate oxygen of **17** (eq 4) to yield directly the pair of neutral radicals **19/20** that rapidly couples to afford product **22** (eq 4):

(3)



$$18 \longrightarrow Me_3Si^+ + (RO)_2\overset{O}{\overset{\|}{P}}\cdot \quad 19$$



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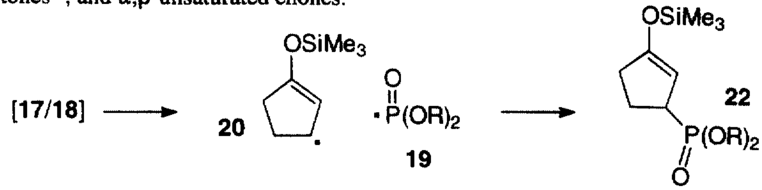
Analogous silylations enolate radical anions such as **17** by cation radicals are proposed in the allyl-stannylations of ketones,[13] α,β-diketones[14], and α,β-unsaturated enones.[4]

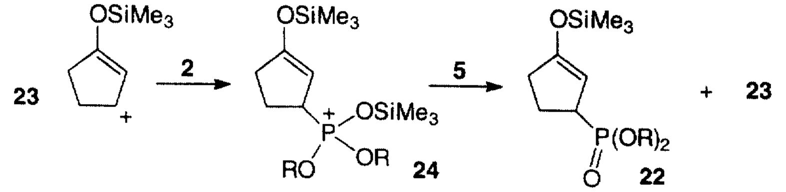
(4)



The above process (eq 4) is in sharp contrast to the well-studied SET, photo-additions in CH_3CN of $Et_2NCH_2SiMe_3$ to enones (e.g. **6** and **9**[15]) in which *silylation of the cyclohexenone radical anion to form the equivalent of 17 does not occur*. Instead, rapid proton transfer to the enolate radical ion from the silyl amine radical cation ensues, followed by coupling of the resultant radical pair. Such a proton transfer step is not available to **17/18**.

A much less likely mechanistic possibility (eq 5) utilizes the silyl cation from **18** (eq 3) *catalytically* to generate **23** which reacts with **2** to give intermediate **24** through which **22** is formed and **23** is regenerated.

(5)



Presumably, this is the pathway by which Me_3SiOTf catalyzes the phosphonosilylation by $Me_3SiOP(OEt)_2$ of **5**, **6** and related enones at 0 °C[2a] and gives *in only 1 h* largely 1,2-phosphono-silylation product (68%) from enone **10**, along with a lesser amount (20%) of the 1,4-product.[2a] However, attempted SET-induced reaction of enone **10** affords (GC/MS) <5% of any product with M^+ corresponding to a 1:1 phosphonosilylation product *in 14 h* (Table 1), a fact *inconsistent* with a mechanism (eq 5) in which radical ion **18** functions as a Me_3SiOTf equivalent.

In the unsuccessful attempted reactions of enones **9** and **10**, $Me_3SiOP(OMe)_2$ is only partially consumed in 14-18 h of irradiation, ***suggesting that SET may be inefficient.*** In fact, a large amount of a dimer of **10** is generated. On extended irradiation, enone **9** and $Me_3SiOP(OMe)_2$ gave a 57% yield of mixture of three products (one very predominant). The GC/MS of each product showed an M^+ peak corresponding to a 1:1 adduct. The possibly marginal energetics of SET (eq 2)[8] also may account for the ***unreactivity we encountered with acyclic enones*** whose more highly twisted, geometrically relaxed triplets should have energies that are lower than those of their cyclic counterparts.[16] Steric problems associated with methyl substitution at carbons 3 and 4 in **9** and **10** also may play a role.

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5. ^{31}P NMR (C_6H_6, 121 MHz) δ 33.8. ^1H NMR (C_6H_6, 300 MHz) δ 3.35 (d, 3 H, J = 10.5 Hz), 3.34 (d, 3 H, J = 10.7 Hz); 1.58-2.34 (m, 7 H). ^{13}C NMR (C_6H_6, 75 mHz) δ 214.5 (d, J = 16 Hz), 52.5 (d, J = 6.5 Hz), 38.9 (d, J = 3.1 Hz), 37.6 (d, J = 7.2 Hz), 32.8 (d, J = 152.2 Hz), 23.9 (d, J = 3.4 Hz). MS (EI) m/z (rel. intensity): 192 (M^+, 11) 164 (20), 151 (21), 137 (100), 111 (54), 110 (59), 109 (15), 83 (26), 82 (19). HRMS (EI), M^+: calcd 192.0551, obsd 192.0553.
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