SOME STUDIES ON 6,7-UNSATURATED CARBONYL RADICAL CYCLIZATIONS

David Crich* and Simon M. Fortt

Department of Chemistry, University College London,

20 Gordon Street, London WC1H OAJ

Abstract: 6,7-Unsaturated carbonyl radicals, generated by the action of
tri-*n*-butylstannane on the corresponding selenol esters, cyclize to give
either cyclohexanones or cycloheptanones depending on the nature and
position of the substituents in the hydrocarbon chain.

In connection with a project aimed at the preparation of oxygenated
cyclohexanones we have been studying the cyclization of functionalized
6,7-unsaturated carbonyl radicals[1,2] and wish to report the results of our
work here.

Thus treatment of the selenol ester (1)[3,4] with tri-*n*-butylstannane and
azoisobutyronitrile(AIBN) in benzene at reflux resulted in formation of
aldehyde (2) and cycloheptanone (15), but not cyclohexanone (10) (Table,
entry 1). Reinvestigation of our earlier work[5] showed that under similar
conditions the ester (3) gave cycloheptanone (16) and not cyclohexanone (11),
together with aldehyde (4) (Table, entry 2). Removal of the oxygen
functionality from the 5 to 3 position, as in selenol esters (5) and (7) led
to higher overall cyclization yields but with the predominant products now
being cyclohexanones (Table, entries 3 and 4). The inclusion of oxygen
functionality at both the 3 and 5 positions, as in (9), again resulted in a
good yield of cyclized material consisting mainly of cyclohexanone (Table,
entry 5).

Treatment of the selenocarbonate (20) with tri-*n*-butylstannane and AIBN
under the standard conditions gave no cyclized product[6] and only a low yield
of formate (21) was isolated. This result cannot be attributed to
δ-hydrogen abstraction competing with cyclization as the use of tri-*n*-
butylstannyl deuteride in place of the hydride gave, almost exclusively, the

deuterioformate (<u>22</u>). The selenide (<u>23</u>) gave, under standard conditions, six and seven membered heterocycles (<u>24</u>) and (<u>25</u>) in a 1:2 ratio (Table, entry 6). Finally the selenol ester (<u>26</u>), on irradiation with tri-*n*-butylstannane and AIBN in benzene at room temperature, gave (<u>27</u>) and (<u>28</u>); the product of decarbonylation followed by 5-*exo-trig* cyclization (Table, entry 7). No evidence for cyclization in the 6-*exo-trig* mode was observed in this latter reaction.

Table

Entry	Substrate	Products (% Yield)
1	(<u>1</u>)	(<u>2</u>)(35) + (<u>15</u>)(27)
2	(<u>3</u>)	(<u>4</u>)(55) + (<u>16</u>)(32)
3	(<u>5</u>)	(<u>6</u>)(10) + [(<u>12</u>) + (<u>17</u>)] (86)†
4	(<u>7</u>)	(<u>8</u>)(10) + (<u>13</u>)(54) + (<u>18</u>)(17)
5	(<u>9</u>)	(<u>14</u>)(72) + (<u>19</u>)(24)
6	(<u>23</u>)	(<u>24</u>)(12) + (<u>25</u>)(25)
7	(<u>26</u>)	(<u>27</u>)(25) + (<u>28</u>)(32)

† Isolated as a mixture; ratio (<u>12</u>):(<u>17</u>) = 6:1 by ^{1}H nmr.
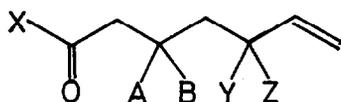
(<u>1</u>) X = SePh, A = B = H, Y = OEt, Z = H
(<u>2</u>) X = H, A = B = H, Y = OEt, Z = H
(<u>3</u>) X = SePh, A = B = H, Y-Z = OCH_2CH_2O
(<u>4</u>) X = H, A = B = H, Y-Z = OCH_2CH_2O
(<u>5</u>) X = SePh, A-B = OCH_2CH_2O, Y = Z = H
(<u>6</u>) X = H, A-B = OCH_2CH_2O, Y = Z = H
(<u>7</u>) X = SePh, A = OSi^{t}BuPh$_2$, B = Y = Z = H
(<u>8</u>) X = H, A = OSi^{t}BuPh$_2$, B = Y = Z = H
(<u>9</u>) X = SePh, A-B = OCH_2CH_2O, Y = OSi^{t}BuMe$_2$, Z = H
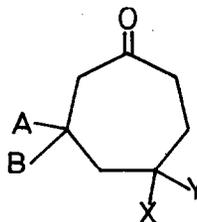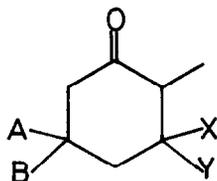
(**10**) A = B = H,X = OEt,Y = H

(**11**) A = B = H,X-Y = OCH$_2$CH$_2$O

(**12**) A-B = OCH$_2$CH$_2$O, X = Y = H

(**13**) A = OSi^{t}BuPh$_2$,B = X = Y = H

(**14**) A-B = OCH$_2$CH$_2$O,X = OSi^{t}BuMe$_2$,Y = H

(**15**) A = B = H,X = OEt,Y = H

(**16**) A = B = H,X-Y = OCH$_2$CH$_2$O

(**17**) A-B = OCH$_2$CH$_2$O,X = Y = H

(**18**) A = OSi^{t}BuPh$_2$,B = X = Y = H

(**19**) A-B = OCH$_2$CH$_2$O,X = OSi^{t}BuMe$_2$,
Y = H
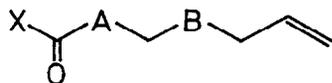
(**20**) X = SePh,A = O,B = CH$_2$

(**21**) X = H,A = O,B = CH$_2$

(**22**) X = D,A = O,B = CH$_2$

(**23**) X = SePh,A = CH$_2$,B = O
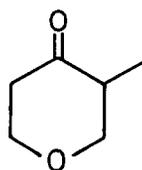
(**24**)
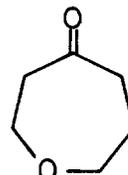
(**25**)

(**26**)

(**27**)

(**28**)
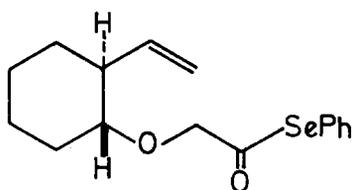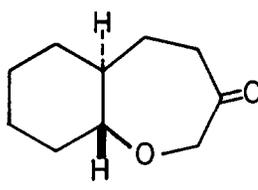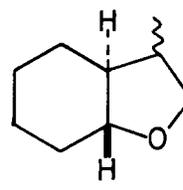
The prefered formation of seven membered rings in several of the examples described above (Table, entries 1,2,6 and 7) could be the result of kinetic cyclization in the *exo*-mode followed by rapid rearrangement to the overall *endo*-mode cyclization product or the result of direct *endo*-mode cyclization. Recent papers have drawn attention[7] to the fact that closely related vinyl radicals undergo cyclization almost exclusively in the *exo*-mode and that at low stannane concentrations rearrangement to the overall

endo-mode product is rapid; it is suggested that such rearrangements proceed *via* cyclopropylmethyl radicals. Related work involving 3-oxoalkyl radicals indicates[8] that a similar rearrangement may be possible in carbonyl radical cyclizations of the type described here. Supportive evidence for the attack of alkyl radicals onto carbonyl groups, as required by such a rearrangement, is provided[9] by the recent work of Fraser-Reid. We are currently attempting to differentiate between the two mechanistic possibilities and to determine the effect of ring substituents and heteroatoms on the overall mode of cyclization.

References

(1)   For earlier isolated examples of such cyclizations see: M. Chatzopoulos and J.P. Montheard, *Compt. Rendu C,* 280, 29 (1975); Z. Cekovic, *Tetrahedron Lett.,* 749 (1972)

(2)   For recent work involving carbonyl radicals see: D.J. Coveney, V.F. Patel and G. Pattenden, *Tetrahedron Lett.,* 28, 5949 (1987); V.F. Patel and G. Pattenden, *ibid,* 29, 707 (1988); P. Delduc, C. Tailhan and S.Z. Zard, *J. Chem. Soc., Chem. Commun.,* 308 (1988).

(3)   Cyclization substrates were prepared by a variety of standard techniques to be described in full subsequently.

(4)   All new compounds gave satisfactory spectroscopic and microanalytical or high resolution mass data.

(5)   D. Crich and S.M. Fortt, *Tetrahedron Lett.,* 28 2895 (1987).

(6)   For the formation of five membered rings by alkoxycarbonyl radical cyclizations see: M.D. Bachi and E. Bosch, *Tetrahedron Lett.,* 27, 641 (1986); D.H.R. Barton and D. Crich, *J. Chem. Soc., Perkin Trans. 1,* 1603 (1986).

(7)   A.L.J. Beckwith and D.M. O'Shea, *Tetrahedron Lett.,* 27, 4525 (1986); G. Stork and R. Mook, *ibid,* 27, 4529 (1986).

(8)   H. Riemann, A.S. Capomaggi, T. Strauss, E.P. Olivetto and D.H.R. Barton, *J. Am. Chem. Soc.,* 83, 4481 (1961); A.L.J. Beckwith, D.M. O'Shea, S. Gerba and S.W. Westwood, *J. Chem. Soc., Chem. Commun.,* 666 (1987); P. Dowd and S.C. Choi, *J. Am. Chem. Soc.,* 109, 3493 (1987).

(9)   R. Tsang and B. Fraser-Reid, *J. Am. Chem. Soc.,* 108, 2116, 8102 (1986); R. Tsang, J.K. Dickson, H. Pak, R. Walton and B. Fraser-Reid, *ibid,* 109, 3484 (1987); also see; F. Flies, R. Lalande and B. Maillard, *Tetrahedron Lett.,* 439 (1976).