Pergamon

Tetrahedron Letters, Vol. 35, No. 23, pp. 3841-3844, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)E0695-T

Reductive Alkylations Involving 2°- and 3°-Enolyl Adduct Radicals

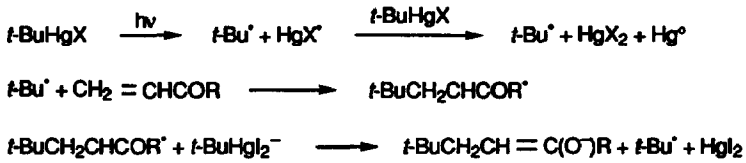
Glen A. Russell* and Bing Zhi Shi

Department of Chemistry, Iowa State University, Ames, Iowa 50011

Summary: *Reductive tert-butylation of electronegatively substituted alkenes is readily achieved in Me_2SO by reaction with excess t-BuHgCl/Et_3SiH. Reactivity studies indicate that towards t-Bu* s-cis enones are more reactive than the s-trans conformers.*

Photolysis of *t*-BuHgCl with CH_2=CHP(O)(OEt)$_2$ or CH_2=$CHSO_2Ph$ in PhH forms the adducts *t*-$BuCH_2CH(HgCl)(EWG)$ by a radical chain mechanism.[1] Although α,β-unsaturated carbonyls fail to form these adducts in PhH or Me_2SO (e.g. CH_2=$CHCO_2Et$ undergoes polymerization) many unsaturated ketones, esters, lactones or amides which form 2°-enolyl radicals as intermediates, yield the reductive alkylation products (e.g., *t*-$BuCH_2CH_2COR$, *t*-$BuCH(CO_2Et)CH_2CO_2Et$, *t*-$BuCH(CN)CH_2CN$) upon photolysis with *t*-BuHgCl/KI in Me_2SO by the process of Scheme 1.[2,3] The enolate anion formed by electron transfer from the ate-complex can be protonated by traces of water in the solvent, by the use of protic cosolvents such as MeOH, or upon workup with aq. $Na_2S_2O_3$ to remove mercury compounds. However, 3°-enolyl radicals are inefficiently reduced. Thus,

Scheme 1



ethyl methacrylate upon photolysis with 4 equiv. each of *t*-BuHgCl and KI in Me_2SO yields a mixture of **1** and **2** (Table 1). Compound **2** apparently arises from disproportionation of the 3°-enolyl radical to form **1** and

1 **2**

t-$BuCH_2C(=CH_2)CO_2Et$ which adds a second *t*-Bu* to form a new 3°-enolyl radical converted to **2**. Dimethyl itaconate reacts in a similar fashion upon photolysis with 4 equiv. each of *t*-BuHgI and KI to form *t*-$BuCH_2CH(CO_2Me)CH_2CO_2Me$ and *t*-$BuCH_2C(CO_2Me)$=$CHCO_2Me$. The adduct radical (*t*-$BuCH_2C(CO_2Me)CH_2CO_2Me$*) must undergo competing reduction and chain-terminating disproportionation reactions. Since the adduct radical now contains an easily abstractable proton, the reaction in the presence of DABCO leads to oxidative alkylation products via the radical anion *t*-$BuCH_2C(CO_2Me)$=$CHCO_2Me^{\bullet-}$ which

Table 1. *tert*-Butylation products of ethyl methacrylate in Me_2SO at 35 °C.[a]

mercurial	other reagent (equiv.)	1 (%)	2 (%)
t-BuHgI	-	10	10
t-BuHgCl	KI (4)	18	13
t-BuHgCl	KI (4), DABCO (4)	19	10
t-BuHgCl	KI (8)	28	6
$(t\text{-Bu})_2Hg$	-	14	12
$(t\text{-Bu})_2Hg$	Et_3SiH (4)	18	13
$(t\text{-Bu})_2Hg$	$PhSiH_3$ (4)	35	4
t-BuHgCl	Et_3SiH (4)	90	-
t-BuHgCl	$PhSiH_3$ (4)	54	-

[a]Four equiv. of the mercurial with 0.05 M methacrylate; photolysis by a 275 W fluorescent sunlamp for 11 h.

readily transfers an electron to *t*-BuHgI.[3] Photolysis with 1 equiv. each of *t*-BuHgI and DABCO yields 56% of *t*-$BuC(CO_2Me)$=$CHCO_2Me$ and 6% of *t*-$BuCH_2CH(CO_2Me)CH(t\text{-Bu})CO_2Me$. The di-*tert*-butylated product is formed by attack of *t*-Bu$^\bullet$ upon the initially-formed oxidative alkylation product since with 4 equiv. each of *t*-BuHgI and DABCO the final products are *t*-$BuCH_2CH(CO_2Me)CH(t\text{-Bu})CO_2Me$ (53%) and *t*-$BuCH$=$C(CO_2Me)CH(t\text{-Bu})CO_2Me$ (13%).

To obtain the reductive monoalkylation products in Me_2SO we have developed a technique employing mixtures of *t*-BuHgCl and Et_3SiH, a system which efficiently alkylates ethyl methacrylate or dimethyl itaconate in yields of 93 and 88%, respectively when using a 3-fold excess of both reagents.[4] The reactions occur in ~10 h in the dark, are inhibited by $(t\text{-Bu})_2NO^\bullet$ (the initial kinetic chain length for 0.1 M ethyl methacrylate is ~10), form the cyclopentylcarbinyl product (52%) in the alkylation of ethyl acrylate with 5-hexenylmercury chloride, and fail to occur in solvents such as CH_2Cl_2, THF or DMF. This reductive alkylation is similar to the Giese technique employing $NaBH_4/OH^-/CH_2Cl_2$ or Bu_3SnH.[5] Although the reactions are faster with Bu_3SnH in Me_2SO or with $NaBH_4/OH^-$ in CH_2Cl_2, the yields are often lower, particularly when the alkene is the limiting reagent or has a low reactivity towards *t*-Bu$^\bullet$, see Table 2.

Table 2. Reductive alkylation of ethyl methacrylate with *t*-BuHgX in Me_2SO.[a]

X	hydride	conditions[b]	1 (%)
Cl	Bu_3SnH	hv, 10 min	45
Cl	Bu_3SnH	dark, 10 min	50
I	Bu_3SnH	hv, 10 min	67
I	Bu_3SnH	dark, 10 min	63
Cl	Et_3SiH	dark, 11 h	93
Cl	$PhSiH_3$	dark, 1 h	54[c]
Cl	$NaBH_4$	CH_2Cl_2/NaOH, 20 min	60

[a]0.25 mmol of methacrylate with 2 equiv. each of *t*-BuHgX and the hydride in 5 mL of Me_2SO. [b]Under N_2 with deoxygenated solvent; hv, irradiation with a 275 W fluorescent sunlamp, ~35 °C; dark, 25 °C. [c]Reaction complete as evidenced by the cessation of Hg° precipitation.

Stannyl hydrides are known to react with RHgCl to form RHgH,[6] and apparently hydrogen-halogen exchange occurs with silanes in Me_2SO solution, reaction 1. The consumption of the silane, which can be

$$Et_3SiH + t\text{-BuHgCl} \rightleftharpoons t\text{-BuHgH} + Et_3SiCl \xrightarrow{Me_2SO} Et_3SiOSiEt_3 \qquad (1)$$

followed by ^1H NMR in Me_2SO-d_6 in the absence of the alkene, is not influenced by sunlamp irradiation or by the presence of t-$Bu_2NO^{\bullet}$. As in the Giese process, RHgH serves as a free radical initiator and as a hydrogen atom donor in the propagation step leading to the alkylation product. Because reaction 1 occurs slowly, only a low steady state concentration of RHgH is formed. This is advantageous when the alkene is not used in excess since it minimizes the trapping of $R^{\bullet}$ by RHgH and maximizes the yield of the reductive alkylation product. Giese had previously discounted the use of simple trialkylsilanes in such processes on the basis of their low reactivity in hydrogen atom transfer.[5b] However Et_3SiH clearly does not react in this manner in Me_2SO. This was demonstrated by an examination of the effect of silanes in reactions involving t-Bu$^{\bullet}$ generated by the photolysis of $(t\text{-Bu})_2Hg$. Table 1 shows that Et_3SiH is ineffective in trapping the adduct radical since the disproportionation derived **1** and **2** are formed in the same ~1:1 ratio in the presence and absence of the silane. With $PhSiH_3$ the data suggest that hydrogen atom transfer may be involved. With more reactive alkenes, (e.g., CH_2=C(Cl)CO_2Et) Et_3SiH or $PhSiH_3$ and t-BuHgCl give about the same yield (90-95%) of the reductive alkylation product (in ~1 h for $PhSiH_3$ and ~12 h for Et_3SiH). $PhSiH_3$ apparently forms RHgH more rapidly and thus creates a higher steady state concentration of RHgH. Trapping of t-Bu$^{\bullet}$ by RHgH is a serious limitation when the alkene reacts slowly with t-Bu$^{\bullet}$. Thus, with CH_2=C(Me)CO_2Et a much better yield of the reductive *tert*-butylate on product is observed with Et_3SiH.

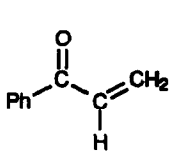
The system t-BuHgCl/Et_3SiH is a convenient one for measuring reactivities towards t-Bu$^{\bullet}$ in Me_2SO at 25 °C (Table 3). Competitive reactions of CH_2=CHCO_2Et, CH_2=CHP(O)$(OEt)_2$, CH_2=CHSO_2Ph and (*E*)-PhCH=CHI (to yield (*E*)-PhCH=CHBu-t)[7] give the relative reactivities of 80:20:100:1.0. Since the value of $k_{add.}$ of t-Bu$^{\bullet}$ to CH_2=CHP(O)$(OEt)_2$ has been measured at 233 K,[8] the absolute rate constant for attack of t-Bu$^{\bullet}$ upon (*E*)-PhCH=CHI at 25 °C can be estimated as between 5.0×10^3 and 2.6×10^4 L/mol-s based upon log A = 7.5 ± 0.5, a value observed in the addition of t-Bu$^{\bullet}$ to a variety of 1-alkenes.[9]

Table 3. Reactivities towards t-Bu$^{\bullet}$ at 25 °C in Me_2SO relative to (*E*)-PhCH=CHI.

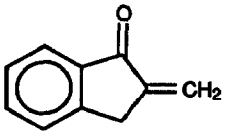
R	CH_2=C(R)CO_2Et	CH_2=C(R)COPh	CH_2=C(R)CN
H	80 ± 10	470 ± 20	220 ± 10
Me	50 ± 10	70 ± 10	55 ± 5
Ph	310 ± 10	175 ± 10	-
Cl	1300 ± 200	700 ± 100	950 ± 50

The reactivities of the three series in Table 3 are controlled mainly by polar effects with the reactivity increasing from R = Me < H < Cl for the nucleophilic t-Bu$^{\bullet}$.[10] However, the relative reactivities of the ketones and esters show a puzzling variation with the nature of R. We believe this reflects mainly a variation in the preferred conformation of the enones where CH_2=CHCOPh is known to exist in the *s-cis* conformation (3, 84%) but α-substituted derivatives prefer the *s-trans* structure.[11] Thus, t-BuCOCH=CH_2 (100% of *s-cis*)[12] has a reactivity

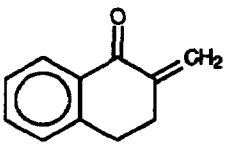
towards *t*-Bu• 2.3-times that of $CH_3COCH{=}CH_2$ (29% *s-cis*,[12] reactivity 90). The reactivities of **4-7** confirm the high reactivities of *s-cis* enones in radical additions (reactivities are given in parentheses under each structure). The dramatic decrease in reactivity of $CH_2{=}C(Me)COPh$ compared to $CH_2{=}CHCOPh$ reflects partially the inductive effect of the methyl group but mainly the switch in preferred conformation from *s-cis* to *s-trans*. The high reactivity of the *s-cis* enones is apparently connected with a favorable SOMO-LUMO overlap in the rather polar transition state for *t*-Bu• addition.[10] α,β-Unsaturated aliphatic ketones and esters (or lactones) with the same preferred conformations have nearly the same reactivity towards *t*-Bu•, e.g. **6** vs. **7** while benzoyl derivatives are considerably more reactive than their aliphatic analogues, e.g., $PhCOCH{=}CH_2$ vs. *t*-$BuCOCH{=}CH_2$ or **4** vs. **6**.



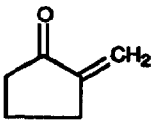
3 (470)



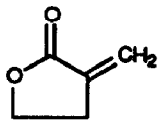
4 (780)



5 (370)



6 (180)



7 (150)

Acknowledgment. This work was supported by grants CHE-8717871 and CHE-9220639 from the National Science Foundation.

References and Notes

(1) Russell, G. A.; Jiang, W.; Hu, S. S.; Khanna, R. K. *J. Org. Chem.* **1986**, *51*, 5498.

(2) Russell, G. A.; Hu, S.; Herron, S.; Baik, W. Ngoviwatchai, P.; Jiang, W.; Nebgen, M.; Yu, Y.-W. *J. Phys. Org. Chem.* **1988**, *1*, 299.

(3) Russell, G. A.; Kim, B. H. *Tetrahedron Lett.* **1990**, *31*, 6273. Russell, G. A.; Kim, B. H.; Kulkarni, S. V. *J. Org. Chem.* **1989**, *54*, 3768.

(4) Russell, G. A.; Shi, B. Z. *Synlett* **1993**, 701.

(5) (a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*, Pergamon: Oxford, 1986. (b) Giese, B., *loc. cit.* p. 68.

(6) Quirk, R. P. *J. Org. Chem.* **1972**, *37*, 3554.

(7) Russell, G. A.; Tashtoush, H.; Ngoviwatchai, P. *J. Am. Chem. Soc.* **1984**, *106*, 4622.

(8) Baban, J. A.; Roberts, B. P. *J. Chem. Soc. Perkin Trans. II* **1981**, 161.

(9) Fischer, H. in *Substituent Effects in Radical Chemistry*; Viehe, H. G.; Janovsek, Z.; Merenyi, R., Eds.; Reidel: Dordrecht, 1988, p. 123.

(10) Mayo, F. R.; Walling, C. *Chem. Rev.* **1950**, *46*, 191. Giese, B.; He, J.; Mehl, W. *Chem. Ber.* **1988**, *121*, 2063.

(11) Gottlieb, H. in *The Chemistry of Enones*, Part 1; Patai, S.; Rappoport, Z., Eds.; Wiley: New York, 1989, Chapter 5.

(12) Hayes, W. P.; Timmons, C. J. *Spectrochim. Acta* **1968**, *24A*, 323.

(*Received in USA* 17 *August* 1993; *revised* 6 *April* 1994; *accepted* 8 *April* 1994)