EFFECTS OF IODIDE ION AND AMINES ON THE FREE RADICAL ALKYLATION OF 1,4-ENEDIONES BY ALKYLMERCURY HALIDES¹

Glen A. Russell* and Byeong Hyo Kim

Department of Chemistry, Iowa State University, Ames, Iowa 50010

Summary: lodide ion promotes the photostimulated reductive alkylation of α , β -unsaturated ketones by electron transfer from RHgI₂⁻ to the adduct enolyl radicals. Amines such as Dabco can promote oxidative alkylation by removal of a proton from the adduct radicals.

The conversion of α , β -unsaturated carbonyl compounds into saturated β -alkylated derivatives in a free radical chain reaction with alkylmercury chlorides is dramatically promoted by the presence of iodide salts² or other complexing anions.³ It has been suggested that iodide functions by formation of the ate-complex (RHgl₂⁻) which reduces the adduct enolyl radical, Scheme 1. However, the conversion of the enolyl radical to the enolate product could also be formulated to involve electron transfer from free I⁻ or to an enhanced reactivity of RHgI in the

Scheme 1

R• + >C=CHC(O)R¹ -------> >C(R)ĊHC(O)R¹

>C(R) $^{\circ}$ HC(O)R¹ + RHgX₂ ------ >C(R)CH=C(O)R¹ + R• + HgX₂

process, enolyl• + RHgX \rightarrow enolyl⁻HgX⁺ + R•. The thrust of this communication is to demonstrate that the iodide ion effect depends upon the structure of R and that *t*-BuHgX/KI is more effective than *t*-BuHgI alone.

Acceptor radicals such as I· or > \dot{C} (EWG) react with RHgCl in the presence or absence of I⁻ to form alkyl radicals with a significant rate increase from R = *n*-Bu to *i*-Pr to *t*-Bu.⁴ Thus, the reaction of *N*-methylmaleimide with a 1:1 mixture of *t*-BuHgCl and *n*-BuHgCl in the presence of excess I⁻ forms only the 3-*tert*-butyl-1-methyl-1*H*-pyrrole-2,5-dione. However, this selectivity fails to distinguish between electron transfer (from I⁻ or RHgI₂⁻) and S_H2 (with RHgI) reactions of the adduct enolyl radical. To separate the effects due to I⁻, RHgI and RHgI₂⁻, we have studied the competition between Reactions 1 and 2 for enolyl radicals derived from diethyl fumarate (Table 1) and *N*-methylmaleimide (Table 2).³ In a reaction incorporating both I⁻ and Dabco, product formation will be controlled by competing bimolecular reactions of the enolyl intermediate as shown in Scheme 2. Using diethyl fumarate as the substrate (Table 1) and varying the nature of the alkyl group in RHgCl/I⁻systems clearly demonstrates that the competition between Reactions 1 and 2 is a function of the alkyl group (compare entries 9 and 14). Table 1 also shows that in the



absence of I⁻ the competing reactions leading to the saturated and unsaturated products increasingly favors the saturated product in going from Bu unsaturated products increasingly favors the saturated product in going from BuHgCl to *i*-PrHgCl to *t*-BuHgCl (entries 15, 10 and 5).⁴

entry	R	molar equivalents	% yield (time, h) ^b
		RHgCI:KI:Dabco:K2S2O8	ECH(R)CH2E:EC(R)=CHE ^c
1	t-Bu	4:0:0:0	39:0 (14)
2	⊁Bu	4:4:0:0	52:0 (3)
3	t-Bu	4:4:0:2	62:0 (3)
4	t-Bu	4:4:4:0	87:0 (10)
5	t-Bu	4:0:4:0	37:0(24)
6	i∕Pr	4:0:0:0	26:0 (22)
7	₽Pr	4:4:0:0	83:0 (3)
8	i⊦Pr	4:4:0:2	100:0 (3)
9	i⊦Pr	4:4:4:0	89:0 (11)
10	i⊦Pr	4:0:4:0	36:58 (23)
11	⊬Pr	2:0:8:0	12:72 (23)
12	<i>n</i> -Bu	4:4:0:0	46:0 (4)
13	<i>n</i> -Bu	4:4:0:2	38:0 (4)
14	<i>n</i> -Bu	4:4:4:0	5:53 (10)
15	n-Bu	4:0:8:0	0:44 (24)

 Table 1. Photostimulated Reactions of RHgCl with Diethyl Fumarate (ECH=CHE) in the

 Presence of KI or Dabco in Me2SO^a

42.0 mmol of RHgCl in 10 mL of Me₂SO irradiated at 35-40 °C with a 275 W GE sunlamp.

bBy GC with an internal standard after hydrolysis and extraction.

Cone stereoisomer with $\delta = 6.4$ (*i*-Pr), 6.8 (*n*-Bu) for the vinyl hydrogen atoms. The (*Z*) stereochemistry can be assigned for R = i-Pr.

If the effect of the structure of R in the adduct radicals can be ignored in Reactions 1 and 2, it follows from the data of Table 1 that the agent responsible for the enolyi to enolate conversion

must be RHgI or RHgI₂⁻ and not I⁻. However, it is difficult to estimate the effect of the structure of R upon the reactions of the adduct radicals, particularly upon the deprotonation step of Reaction 2. Additional evidence against the enolyl to enolate reduction by I⁻ is available from reduction potentials. Thus, in water it is easier to reduce I⁺ than CH₃COCH₂⁺ [E^o = 1.2V(I⁺); 0.6V(CH₃COCH₂⁺)]⁵ while in non-aqueous solvents I⁺ is more easily reduced than (EtO₂C)₂CH⁺ or (CH₃CO)₂CH⁺ by ~0.2V.⁶

X	molar equivalents	% yield (time) ^b	
	f-BuHgX:KI:Dabco:K2S2O8	1a (sat)	2a (unsat)
CI	4:0:0:0	37 (4 h)	0
CI	4:4:0:2	99 (20 min)	0
CI	4:0:8:0	tr	95 (6 h)
CI	4:8:4:0	99 (20 min)	0
1	4:0:0:0	95 (4 h)	0
I .	4:0:4:0	35 (5 h)	53 (5 h)
I.	4:8:4:0	58 (10 min)	0

 Table 2.
 Alkylation of N-methylmaleimide by t-BuHgX in the Presence of KI and Dabco in Me₂SO^a

^aSee a, Table 1. ^b By GC with an internal standard after hydrolysis and extraction.

Table 2 presents data with *N*-methylmaleimide as the substrate which demonstrate that *t*-BuHgX/KI systems are more effective than *t*-BuHgI alone in the conversion of enolyl radicals to the saturated alkylation product. With *t*-BuHgCI/Dabco the unsaturated product **2a** is formed in up



to 95% yield (diethyl fumarate gave only the saturated product) while t-BuHgl/Dabco

(4 equiv each) gives a mixture of 1a (35%) and 2a (53%). However, a mixture of *t*-BuHgCl(4)/KI(8)/Dabco(4) gives 1a in a yield of 99%. Although *t*-BuHgI is more effective than *t*-BuHgCl for the 3a to 1a conversion, it is also obvious that either *t*-BuHgCl/2KI or *t*-BuHgl/2KI is more effective than *t*-BuHgI alone. Workup of the iodide ion promoted reactions with D₂O gave > 70% of monodeuterated 1a consistent with the formation of an enolate salt.

Dialkylation can also occur in the presence of Dabco. In the reaction of *N*-methylmaleimide with *t*-BuHgCl/Dabco in the absence of 1⁻, 2a is formed with only a trace of 4a (5a not detected). However, with *i*-PrHgCl/Dabco and catalysis by Kl/K₂S₂O₈,⁷ the first formed 2b is converted to 5b (4b not detected) in 57% yield. Photolysis of 2a with *t*-BuHgCl(4)/Kl(8) forms only the

saturated product 4a (71% in 3h) as a 2.5 : 1 ratio of cis and trans isomers. *Cis*-4a does not isomerize to *trans*-4a under the reaction conditions but isomerization is observed in MeOH/OAc⁻ to give a cis/trans ratio of ~ 1 : 100. The results suggest that the formation of 4a from 2a even in the presence of KI now involves hydrogen atom transfer to the least hindered side of the adduct radical, possibly from R•. This is supported by the observations that workup with D₂O incorporates no more than 10% of deuterium in the isolated 4a.

Competition between Reactions 1 and 2 of Scheme 2 depends upon the structure of the substrate as well as the nature of R in RHgCl. With PhCOCH=CHCO₂Et a mixture of the saturated and unsaturated alkylation products is observed with *t*-BuHgCl or *i*-PrHgCl in the presence of Kl and Dabco. In the absence of Dabco only saturated alkylation products are formed in 70-75% yield (4 equiv. each of RHgCl and Kl) but the radical addition is not regiospecific giving a ratio of PhCOCH₂CH(R)CO₂Et to PhCOCH(R)CH₂CO₂Et of 8:1 for R = *t*-Bu and 2.5:1 for R = *i*-Pr. With 4 equiv. of Dabco added the ratio of PhCOCH₂CH(R)CO₂Et to PhCOCH₂CH(R)CO₂Et is 61:24% for R = *t*-Bu and 31:37% for R = *i*-Pr. Again the *tert*-butylmecurial is more effective in trapping the adduct radical⁴ but deprotonation of the adduct radical by Dabco can be detected even in the presence of Kl in contrast to the exclusive reductive alkylation observed for diethyl fumarate or *N*-methylmaleimide. Independent experiments in the three substrate systems demonstrated that the unsaturated products observed in the presence of Dabco were not formed by a dehydrogenation of the initially formed saturated alkylation product.

Acknowledgment. This work was supported by the National Science Foundation. (Grant CHE 8717871) and by donors to the Petroleum Research Fund administered by the American Chemical Society.

References and Notes

- (1) Electron Transfer Processes. 51.
- Russell, G.A.; Hu, S.; Herron, S.; Baik, W.; Ngoviwatchai, P.; Jiang, W.; Nebgen, M.; Wu, Y. W. J. Phys. Org. Chem. 1988, 1, 299.
- (3) Reaction 2 has been previously described by Russell, G. A.; Kim, B. H.; Kulkarni, S. V.; J. Org. Chem. 1989, 54, 3768; Russell, G. A.; Kim, B. H. Synlett, 1990, 1, 87.
- (4) Russell, G. A.; Jiang, W.; Hu, S. S.; Khanna, R. K. J. Org. Chem. 1986, 51, 5498.
- (5) Pearson, R. G. J. Am. Chem. Soc. 1986, 108, 6109.
- (6) Eberson, L. "*Electron Transfer Reactions in Organic Chemistry*", Springer-Verlag, New York, 1987, Chapter IV.
- (7) Radical formation by I⁻/S₂O₈⁻² involves, I⁺ + S₂O₈⁻² → I⁺ + SO₄⁻²; I⁺ + RHgX → R⁺ + IHgX; SO₄^{-*} + RHgX → R⁺ + ⁻O₃SOHgX; Russell, G.A.; Guo, D.; Baik, W.; Herron, S.J. *Heterocycles* 1989, *28*, 143.

(Received in USA 6 December 1989; accepted 17 July 1990)