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Addition Reactions of *tert*-Butylmercury Iodide with Electronegatively Substituted Alkenes: Three- and Four-Component Radical Condensations Based on Control by Polar Effects[1]

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Multicomponent free radical condensations often suffer from a lack of selectivity. We report a group of three- and four-component condensations where selectivity is achieved by utilizing reactions with important polar contributions and by conducting the condensations in a two-stage manner.

Reactions of *t*-BuHgI in Me_2SO with electron-deficient alkenes, e.g., $CH_2{=}CH(EWG)$, with EWG = CO_2R, COR, CN, SO_2Ph, or $P(O)(OEt)_2$, occur readily in the dark at room temperature in the presence of I^- to yield initially the 1:1 adducts observable by ^1H NMR in $Me_2SO\text{-}d_6$, reaction 1.[2] In the presence of NH_4I, the initial adducts with the exception of **1c** are protonolized to give the reductive alkylation products **2a**, Table 1. Electrophilic substitution in **1** in the presence of excess I^- also occurs readily with I_2 or NBS (to yield **2b**) or with iminium cations such as $CH_2{=}N(CH_2)_5^+$ (to yield **2c**).

$$t\text{-BuHgI} + CH_2{=}CH(EWG) \xrightarrow[\text{Me}_2\text{SO}]{\text{I}^-} t\text{-BuCH}_2\text{CH(EWG)HgI} \qquad (1)$$

1

a, EWG = CO_2Me **d**, EWG = CN
b, EWG = SO_2Ph **e**, EWG = $CO_2CH_2CH{=}CH_2$
c, EWG = $P(O)(OEt)_2$ **f**, EWG = $CO_2CH_2CH{=}CHMe$

$$t\text{-BuCH}_2\text{CH(Y)(EWG)}$$

2

a, Y = H **e**, Y = $CH_2CH{=}CH_2$
b, Y = I **f**, Y = $C(Me)_2NO_2$
c, Y = $CH_2N(CH_2)_5$ **g**, Y = SR
d, Y = (*E*)-CH=CHPh **h**, Y = SePh

Reaction 1 occurs more rapidly with sunlamp irradiation, while dark reactions are inhibited for days by 10 mol % $(t\text{-Bu})_2NO^\bullet$. The dark reactions involve thermal initiation by $t\text{-Bu}^\bullet$ formation, possibly from $t\text{-BuHgI}_2^-$ or $(t\text{-Bu})_2Hg$, followed by facile chain-propagating attack of the adduct radicals $[t\text{-BuCH}_2\text{CH(EWG)}^\bullet]$ on $t\text{-BuHgI}_2^-$.[3] Electron transfer to form $t\text{-BuCH}_2\text{CH(EWG)}^-$ does not occur since **1** is also formed in the presence of 10 mol % D_2O or in some cases in the presence of 1 M NH_4^+. The high reactivity of $t\text{-BuHgI}_2^-$ toward electrophilic radicals may involve a transition state in which incipient electron transfer leads in a concerted fashion to the ate complex of **1** and $t\text{-Bu}^\bullet$ in a formally S_H2 substitution on Hg. The iodide-promoted reactions also are observed for *t*-BuHgCl but not for $(t\text{-Bu})_2Hg$. In the absence of added I^-, no significant dark reactions are observed for *t*-BuHgI or $(t\text{-Bu})_2Hg$, while photolysis with $CH_2{=}CHCO_2Me$ or $CH_2{=}CHCN$ leads to a mixture of products derived from radical−radical interactions including oligomers.[4]

The adduct **1** can be utilized without isolation in further photostimulated free radical chain reactions to form products of three- or four-component condensations. Table 1 summarizes some photostimulated reactions of **1a−e** utilizing previously developed reactions of organomercurials with (*E*)-PhCH=CHI (vinyl substitution with retention),[5] $CH_2{=}CHCH_2SPh$ (allylic substitution),[6,7] and $Me_2C{=}NO_2Li$ ($S_{RN}1$ alkylation)[8] to form **2d−f**. Although reactions with disulfides occur readily with alkylmercury halides via steps 2 and 3,[9] electrophilic radicals (e.g., $PhCOCH_2^\bullet$) are very unreactive toward disulfides.[10] Thus, **1a** gives no significant yield of **2g** with dialkyl or diaryl disulfides, although the more reactive PhSeSePh[9] gives a good yield of **2h**. The electronegative radicals generated from **1a−e** also add readily to electron-rich alkenes. However, in the absence of any additional reagent, chain reactions between **1** and the alkene are not feasible. Disulfides, with their low reactivity toward electrophilic radicals but high reactivity toward nucleophilic radicals, allow a chain reaction to occur, thereby converting **1** to **3** for alkenes such as $CH_2{=}CHOEt$, $CH_2{=}CHBu$, and $CH_2{=}CHO_2CCH_3$. Yields in the range of 80% based on starting $CH_2{=}CHCO_2Me$ are observed in these four-component condensations. With use of preformed **1**, excellent yields of **2d−f,h** or **3** can be achieved with *t*-BuHgI and $CH_2{=}CH(EWG)$ in a 1:1 ratio. Photolysis of mixtures of *t*-BuHgI and $CH_2{=}CH(EWG)$ with 4 equiv of the other components required to form **2** or **3** results in a variety of products since the relative reactivities toward $t\text{-Bu}^\bullet$ are PHSeSePh (~8000):$CH_2{=}CHCO_2Et$ (80):$CH_2{=}CHP(O)(OEt)_2$ (10):PhSSPh (43):(*E*)-PhCH=CHI (1.0):$CH_2{=}CHCH_2SPh$ (0.5):$Me_2C{=}NO_2Li$ (0.2).[6,9]

$$R^\bullet + PhSSPh \rightarrow RSPh + PhS^\bullet \qquad (2)$$

$$PhS^\bullet + RHgI \rightarrow PhSHgI + R^\bullet \qquad (3)$$

$$t\text{-BuCH}_2\text{CH(CO}_2\text{Me)CH}_2\text{CH(R)SPh}$$

3

a, R = OEt
b, R = Bu
c, R = O_2CCH_3

Styrene, $CH_2{=}CHSPh$, and 4-vinylpyridine in the presence of PhSSPh fail to form products analogous to **3**. This is perhaps not surprising because the adduct radicals from these alkenes are quite unreactive toward PhSSPh.[11] However, surprisingly, in the presence of these alkenes good yields of $t\text{-BuCH}_2\text{CH(SPh)CO}_2\text{Me}$ (**2g**) are now observed (Table 1), although in their

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[1] Electron Transfer Processes. 58.

[2] The mercurials **1** will slowly undergo comproportionation to form $[t\text{-BuCH}_2\text{CH(EWG)}]_2\text{Hg}$. With EWG = CN or CO_2Me, the diorganomercurial is formed in nearly quantitative yield in a reaction accelerated by *hν*.

[3] Russell, G. A.; Hu, S. S.; Herron, S.; Baik, W.; Ngoviwatchai, P.; Jiang, W.; Nebgen, M.; Wu, Y.-W. *J. Phys. Org. Chem.* **1988**, *1*, 299. K_e is ~1 M^{-1} for the complexation of I^- with *t*-BuHgI at 25 °C in Me_2SO.

[4] The localized adduct radicals with EWG = SO_2Ph or $P(O)(OEt)_2$ will displace $t\text{-Bu}^\bullet$ from *t*-BuHgCl or *t*-BuHgI to give excellent yields of **1** in photostimulated reactions; $(t\text{-Bu})_2Hg/h\nu$ again gives a mixture of products with these substrates. Russell, G. A.; Jiang, W.; Hu, S. S.; Khanna, R. K. *J. Org. Chem.* **1986**, *51*, 5498.

[5] Russell, G. A.; Ngoviwatchai, P. *J. Org. Chem.* **1989**, *54*, 1836.

[6] Russell, G. A.; Ngoviwatchai, P.; Wu, Y. W. *J. Am. Chem. Soc.* **1989**, *111*, 4921.

[7] Allyl bromide is ineffective because of its conversion to allyl iodide, which readily undergoes iodine atom transfer with radicals.[6] However, in PhH or Me_2SO solution, mixtures of *t*-BuHgCl, allyl bromide, and $CH_2{=}CHCN$ or $CH_2{=}CHCO_2Et$ give good yields of $t\text{-BuCH}_2\text{CH(EWG)CH}_2\text{CH}{=}\text{CH}_2$ upon sunlamp irradiation.

[8] Russell, G. A.; Hershberger, J.; Owens, K. *J. Am. Chem. Soc.* **1979**, *101*, 1312. Russell, G. A.; Khanna, R. K. *Tetrahedron* **1985**, *41*, 4133.

[9] Russell, G. A.; Ngoviwatchai, P.; Tashtoush, H. I.; Pla-Dalmau, A.; Khanna, R. K. *J. Am. Chem. Soc.* **1988**, *110*, 3530.

[10] Russell, G. A.; Kulkarni, S. V. *J. Org. Chem.* **1993**, *58*, 2678.

[11] Polystyrenyl radical reacts with PhSSPh with a rate constant of <10 L/mol-s at 60 °C. Pierson, R. M.; Costanza, A. M.; Weinstein, A. H. *J. Polym. Sci.* **1955**, *16*, 471.

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Table 1. Reactions of $CH_2{=}CH(EWG)$ in $Me_2SO^{a,b}$

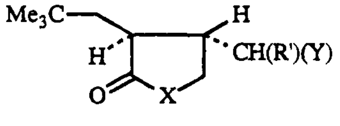
EWG^a	*t*-BuHgI (equiv)	reagent (equiv), conditions^b	product (yield, %)^c
CO_2Me	1.2	KI (2), 1 h	**1a** (96)
CO_2Me	1.2	NH_4I (4), 30 min	**2a** (100)
CO_2All	1.2	KI (3), 20 min	**1b** (91)
CO_2All	2.0	NH_4I (4), 30 min	**2a** (100)
SO_2Ph	2.0	NH_4I (2), 2 h	**1c** (100)
CN	1.2	KI (3), 1 h	**1e** (94)^d
CN	A^e	NBS (2), 12 h	**2b** (77)
CO_2Me	A^e	I_2 (2), 12 h	**2b** (77)
CO_2Me	A^e	I_2 (2), 12 H	**2b** (95)
CO_2Me	A^e	$CH_2{=}N(CH_2)_5^+$ (4), 6 h	**2c** (80)
CO_2Me	A^e	(*E*)-PhCH=CHI (5), *hv*, 6 h	**2d** (65)
CO_2Me	A^e	$CH_2{=}CHCH_2SPh$ (5), *hv*, 1 h	**2e** (63)
CO_2Me	A^e	$Me_2C{=}NO_2Li$ (2), *hv*, 1.5 h	**2f** (68)
SO_2Ph	A^f	(*E*)-PhCH=CHI (5), *hv*, 4 h	**2d** (55)
P	A^f	$Me_2C{=}NO_2Li$ (5), *hv*, 4 h	**2f** (67)
CO_2Me	A^e	PhSSPh (2), *hv*, 1 h	**2g** (not detected)^g
CO_2Me	A^e	$CH_2{=}CHOEt$ (5), PhSSPh (1.5), *hv*, 1 h	**3a** (82)^h
CO_2Me	A^e	$CH_2{=}CHBu$ (5), PhSSPh (1.5), *hv*, 1 h	**3b** (87)^h
CO_2Me	A^e	$CH_2{=}CHO_2CCH_3$ (5), PhSSPh (1.5), *hv*, 1 h	**3c** (70)^h
CO_2Me	A^e	$CH_2{=}CHPh$ (5), PhSSPh (2), *hv*, 1 h	**2g** (77)
CO_2All	A^e	$CH_2{=}CHCH_2SPh$ (3), *hv*, 5 h	**2e** (57)
CO_2All	A^e	(*E*)-PhCH=CHI (5), *hv*, 1.5 h	**2d** (45)
CO_2All	A^e	$Me_2C{=}NO_2Li$ (4), *hv*, 5 h	**2f** (67)
CO_2All	A^e	PhSeSePh (2), *hv*, 5 h	**2h** (75)
CO_2All	A^e	MeSSMe (2), *hv*, 5 h	**4a**, Y = SMe (62)
CO_2All	A^e	PhSSPh (2), *hv*, 5 h	**4a**, Y = SPh (65)

^{a} All = allyl, P = $P(O)(OEt)_2$. ^{b} 25 °C for dark reactions, 35−40 °C upon irradiation with a 275 W fluorescent sunlamp. ^{c} By ^1H NMR in Me_2SO-d_6 with $PhCH_3$ as an internal standard. All yields are based on starting 0.1 M $CH_2{=}CH(EWG)$. ^{d} 6% of $CH_2{=}CHCN$ converted to $[t\text{-}BuCH_2CH(CN)]_2Hg$. ^{e} Condition A: 1.1−1.2 equiv of *t*-BuHgI and 2−3 equiv of KI were first allowed to react in the dark for 1 h. ^{f} The organomercurial **1** was prepared as in A but with sunlamp photolysis for 30 min. ^{g} Photolysis for 17 h (with or without PhSSPh) forms $t\text{-}BuCH_2CH_2CO_2Me$ (20−30%) and $[t\text{-}BuCH_2CH(CO_2Me)]_2$ (45−50%).^{c,h} ^{h} ~1:1 mixture of diastereomers.

absence $t\text{-}BuCH_2CH(CO_2Me)^\bullet$ fails to react with PhSSPh. These alkenes are also quite reactive toward $PhS^\bullet$.[12] Possibly the reversible addition of $PhS^\bullet$ to these alkenes now occurs in competition with reaction 3. This would lead to a situation where $t\text{-}BuCH_2CH(CO_2Me)^\bullet$ would be formed (either photochemically or via reaction 3) in the presence of $PhSCH_2CH(R)^\bullet$ (R = Ph, SPh, 4-pyridinyl). Disproportionation via reaction 4 could lead to the formation of $t\text{-}BuCH_2CH(SPh)CO_2Me$ in a nonchain process. The mercurial derived from allyl acrylate

$$t\text{-}BuCH_2CH(CO_2Me)^\bullet + PhSCH_2CH(R)^\bullet \xrightarrow[c\text{-}C_5H_4N]{R\,=\,Ph,\ SPh} t\text{-}BuCH_2CH(SPh)CO_2Me + CH_2{=}CHR \quad (4)$$

(**1e**) reacts with 4 equiv of (*E*)-PhCH=CHI, $CH_2{=}CHCH_2SPh$, or $Me_2C{=}NO_2Li$ to give the uncyclized products **2d−f**. However, upon photolysis with disulfides, the cyclized lactone **4a** (Y = MeS, PhS) is formed cleanly as a single diastereomer.



4a, X = O, R' = H, Y = SR
b, X = O, R' = Me, Y = SPh
c, X = NR"

From **1f**, **4b** is formed as a mixture of two diastereomers which upon chromatographic separation both demonstrate the trans structure by NOESY spectra (see supplementary material). The trans cyclized product is surprising in view of other radical cyclizations observed for 1,6-dienes.[13,14]

The rate of cyclization of the radicals $t\text{-}BuCH_2{}^\bullet CHC(O)XCH_2CH{=}CH_2$ must increase from X = NH to O to NR″ (R″ = Ph, $CH_2CH{=}CH_2$). Thus, **4c** (R″ = H) is not observed in the reaction of $t\text{-}BuCH_2CH(HgI)C(O)NHCH_2CH{=}CH_2$ with PhSSPh, **2g** being formed in low yield. However, similar reactions of the adduct mercurials from $CH_2{=}CHC(O)N(R'')CH_2CH{=}CH_2$ with R″ = Ph or $CH_2CH{=}CH_2$ yield only the trans diastereomers **4c** (R′ = H, Y = SPh). Moreover, with R″ = Ph, the cyclized products are formed from the reactions of the adduct mercurials with Et_3SiH (**4c**, R′ = Y = H),[15] $BrCCl_3/I^-$ (**4c**, R′ = H, Y = I), or PhSeSePh (**4c**, R′ = H, Y = SePh).[16] Under similar conditions, cyclization is not observed for the radical derived from **1e**. *The adduct radicals formed from N-allylacrylamides in which the second amide hydrogen is substituted by Ph or allyl apparently exist in a conformation more conducive to cyclization than the unsubstituted amide or ester.*

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Supplementary Material Available: Spectroscopic data for **1**, **4b**, and all new compounds listed in Table 1 (11 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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[12] Addition of $PhS^\bullet$ and $p\text{-}ClC_6H_4S^\bullet$ to styrene at 23 °C occurs with rate constants of 2.7×10^7 and 5.2×10^7 L/mol-s, respectively. In the addition of $p\text{-}ClC_6H_4S^\bullet$, styrene is ~300 times as reactive as $i\text{-}BuCH{=}CH_2$. Ito, O.; Matsuda, M. *J. Am. Chem. Soc.* **1979**, *101*, 1815; **1982**, *104*, 1701.

[13] Hanessian, S.; Léger, R. *J. Am. Chem. Soc.* **1992**, *114*, 3115. Ryu, I.; Kurihara, A.; Muraoka, H.; Tsunoi, S.; Kambe, N.; Sonoda, N. *J. Org. Chem.* **1994**, *59*, 7570.

[14] For other examples of preferential radical cyclization to *trans*-α,β-disubstituted γ-butyrolactones, see: Hanessian, S.; Di Fabio, R.; Marcoux, J.-F.; Prud'homme, M. *J. Org. Chem.* **1990**, *55*, 3436.

[15] Russell, G. A.; Shi, B. Z. *Tetrahedron Lett.* **1994**, *35*, 3841.

[16] A mixture of uncyclized and cyclized organomercurials is formed initially since in the presence of NH_4I about equal amounts of **2a** and **4c** (R″ = Ph, R′ = H, Y = HgI) are formed.