Electron Transfer Chain Reactions in the Alkylation of Isonitriles by Alkylmercury Halides

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Dedicated to Professor Lennart Eberson on the occasion of his 65th birthday


Isonitriles are known to be potent radicaliphiles,1–5 which yield imidoyl radicals (RN=CR′) that readily undergo β-elimination when R=alkyl.1–3 Because of the ease of oxidation of imidoyl radicals to the nitrium ion (RN+=CR), we have investigated the participation of isonitriles in electron transfer chain (ETC) reactions involving secondary or tertiary alkylmercury halides (Scheme 1).

\[
\begin{align*}
R\text{HgX} \xrightarrow{hv} R^- + X\text{Hg}^+ \\
X\text{Hg}^+ + RHgX \rightarrow R^- + HgX_2 + \text{Hg}^0 \\
R^- + \text{PhN}^+=\text{C}^- \rightarrow \text{PhN}^+=\text{C}^+ \text{R} \\
\text{PhN}=\text{C}^+\text{R} \rightarrow \text{PhN}^+=\text{CR} \\
\text{PhN}^+=\text{CR} + \text{X}^- \rightarrow \text{PhN}=\text{C}(\text{X})\text{R} \\
\text{PhN}=\text{C}(\text{X})\text{R} + \text{H}_2\text{O} \rightarrow \text{PhNHCO(O)R} \\
\end{align*}
\]

Scheme 1. (R = t-Bu or i-Pr).

Alkylmercury halides are mild oxidizing agents which are reduced to R−, Hg0 and X− with a reduction potential of ≈ −0.6 V vs. SCE.6–7 The rate of electron transfer to RHgCl from radical anions such as RCMgCl− or PhC(O)−CH3R in Me2SO increases with the stability of the incipient alkyl radical, suggesting that electron transfer to RHgX is dissociative with the stability of R− contributing to the transition state for electron transfer.8

Thus, secondary and tertiary alkylmercury halides are much more reactive than primary alkylmercury halides in ETC processes. Alkylmercury halides can also serve as initiators in free radical processes.9 Convenient rates of initiation are observed at 25–35 °C upon fluorescent sunlamp irradiation in Me2SO or PhH. In the presence of I− in Me2SO the photochemical initiation rate is increased and the formation of t-Bu even becomes appreciable in the dark at 25 °C,9 possibly because of comproportionation to form the thermally labile (t-Bu)2Hg.10 Because of the increased rate of initiation, the reactions of PhNC with t-BuHgCl were examined mainly in the presence of added iodide ion (KI in Me2SO and Et4NCl in PhH).

Results

Photolysis of t-BuHgX or i-PrHgX with PhNC in Me2SO at 35 °C leads to the precipitation of Hg0 in a process inhibited by the presence of 10 mol% of (t-Bu)2NO−. The reaction also occurs in the dark at 80 °C with t-BuHgl and at 25 °C with the redox system KI–K2S2O8. After work-up with aqueous Na2S2O4 (to remove unchanged organomercurials), excellent yields of the amide PhNHCO(O)R with R = t-Bu or i-Pr are found. Table 1. Reactions with primary alkylmercury halides were not investigated because results from other systems suggested they would be much less reactive than secondary or tertiary alkylmercurials.8

Scheme 1 predicts the initial formation of the imidoyl halide but GC–MS analysis of reaction mixtures in Me2SO before aqueous work-up failed to detect this product. Instead this analysis revealed the formation of

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Table 1. Reaction of t-BuHgX with PhNC to yield PhNHC(O)CMes₂ in Me₂SO.

<table>
<thead>
<tr>
<th>t-BuHgX (X, equiv.)</th>
<th>KI (equiv.)</th>
<th>Conditions*</th>
<th>% PhNHC(O)CMes²b</th>
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<tr>
<td>Cl, 5</td>
<td>0</td>
<td>4 h, dark, 25 °C</td>
<td>0</td>
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<tr>
<td>Cl, 4</td>
<td>0</td>
<td>2 h, hv, 35 °C</td>
<td>42</td>
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<tr>
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<td>0</td>
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<td>4 h, hv, 35 °C</td>
<td>59</td>
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<tr>
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<td>4 h, 10 mol% (t-Bu)₂NO', 35 °C</td>
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<tr>
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<td>4</td>
<td>4 h, hv, 35 °C</td>
<td>84</td>
</tr>
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<td>4 h, HMPA, hv, 35 °C</td>
<td>76</td>
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<tr>
<td>Cl, 4</td>
<td>4</td>
<td>4 h, dark, 80 °C</td>
<td>54</td>
</tr>
<tr>
<td>Cl, 4</td>
<td>4</td>
<td>4 h, 2 equiv. K₂S₂O₈, dark, 25 °C</td>
<td>65</td>
</tr>
</tbody>
</table>

*0.5 Mmol of substrate in 10 ml of Me₂SO; hv = irradiation by a 275 W fluorescent sunlamp. *By GC or ¹H NMR with toluene as an internal standard.

t-BuC(=NPh)OCH₃SCH₃ in Me₂SO and the corresponding pentadeutero compound in Me₂SO-d₆. Apparently the nitritium ion, or the imidoyl halide, reacts readily with Me₂SO to form an intermediate that can undergo the Pummerer reaction,¹¹ Scheme 2.

\[
t-BuC=NO\cdot Ph (or t-BuC(=NPh) + Me₂SO) \\
\rightarrow [t-BuC(=NPh)OS⁻Me₂X⁺] \\
\equiv HX + t-BuC(=NPh)OS(=CH₂)CH₃ \\
\rightarrow t-BuC(=NPh)OCH₃SCH₃\stackrel{H₂O}{\rightarrow}PhNHCOCMe₃
\]

Scheme 2.

In the hope of observing the imidoyl halides, the solvent was changed to PhH. Photolysis of t-BuHgCl with PhNC in PhH in the absence of I⁻ afforded the imidoyl chloride which could be detected by GC−MS before hydrolysis or reduction to PhNHCH₂CMe₃ by NaBH₄ work-up.

However, photolysis of PhNC and t-BuHgI or t-BuHgCl−KI for 4 h in PhH led to complex reaction mixtures in which the imidoyl halide could not be detected by GC−MS prior to work-up. With t-BuHgI, photolysis for 5 h produced 1 (30% yield) as the major product. With added primary or secondary amines (2 equiv.) in PhH the amidines 2 were formed in 85–90% yield. With 10 mol% of MeOH or EtOH the amine was again observed in high yield after hydrolysis, presumably formed by hydrolysis of the imino esters [ArN⁺C(OR)CMe₃]. In the absence of a nucleophilic trapping agent apparently the imidoyl iodide undergoes further ionic or homolytic reactions. One possible route to 1 is shown in Scheme 3 where unreacted t-BuHgX may serve as a Lewis acid catalyst.

PhN≡C(OR)CMe₃ + PhNC "\rightarrow" PhN≡C(OR)CMe₃ + PhNC + PhNC + C≡NPh

Scheme 3.

To avoid the cyclization to an indole derivative, the reaction of 2,4,6-trimethylphenyl isocyanide with t-BuHgX was examined. Photolysis in Me₂SO in the iodide promoted reaction gave the amide in 86% yield after hydrolytic work-up while in PhH with t-BuHgCl the imidoyl chloride could be detected by GC−MS before hydrolytic work-up. However, photolysis with t-BuHgI in PhH for 4 h failed to yield the imidoyl iodide by GC−MS. Instead the major products detected in addition to the amide (from traces of H₂O) were the imines 3 and 4. Since this type of product was not observed with PhNC, and in Me₂SO excellent yields of the amide are formed, it appears that the imidoyl iodides are photochemically labile regenerating the imidoyl radical, which at low t-BuHgI concentrations can abstract benzylic hydrogen atoms from the mesityl groups. With PhNC in Me₂SO there was no evidence of this reaction occurring even in the presence of 2 equiv. of Ph₃CH. The formation of 4 is most reasonably formulated by addition of ArN⁺C(OR)CMe₃ to ArNC as in Scheme 3. However with Ar=2,4,6-trimethylphenyl cyclization cannot occur and a photochemically labile imidoyl iodide would be the initial reaction product.
The reactivity of t-Bu' towards PhNC in Me₂SO was measured by examining the competition of Scheme 4 at 35 °C. From product analysis of the competitive photostimulated reaction of t-BuHgCl the reactivity of PhNC was measured to be 6.5-times that of (E)-PhCH=CH₂, i.e., \( k_{\text{add}} = 1.6 \times 10^8 \text{ M}^{-1} \text{s}^{-1} \).

\[
\begin{align*}
(\text{E})\text{-PhCH}=\text{CH}_2 & \xrightarrow{k = 2.5 \times 10^4 \text{M}^{-1} \text{s}^{-1}} (\text{E})\text{-PhCH}=\text{CHCMe}_3 + \text{H}^+ \\
\text{t-Bu'} + \text{PhN}^+ &= \text{C}^- \xrightarrow{k_{\text{add}}} \text{PhN}=\text{C}^-\text{CMe}_3 \\
& \xrightarrow{\text{H}_2\text{O}} \text{PhNHCOCHMe}_3 \end{align*}
\]

Scheme 4.

The initial kinetic chain length in the ETC reaction of t-BuHgCl with PhNC is appreciable with sunlamp initiation at 35 °C. Figure 1 shows the inhibition period created by 15 mol% of (t-Bu)₂NO' in a reaction monitored in Me₂SO-d₆ by ¹H NMR spectroscopy. The initial reaction rate is much greater (40–45) than the rate of radical production measured by the time required to consume the nitroxide, i.e., the initial kinetic chain length is 40–45. Shorter chain lengths are observed with higher rates of initiation, e.g., in the photostimulated reactions in the presence of I'.

![Figure 1](image-url)

Fig. 1. Photostimulated reaction of t-BuHgCl with PhNC in Me₂SO-d₆ at 35 °C. ○, 0.133 M t-BuHgCl, 0.065 M PhNC; •, in the presence of 0.020 M (t-Bu)₂NO'.

Containing Et₂NH the N,N-diethylamide of 7 was formed, reaction (2).

These results seem conclusively to demonstrate that acyl radicals can also undergo electron transfer to t-BuHgCl to form the acyl cation as the precursor to 7 or its amide, reaction (3). The oxidation of acyl radicals by t-BuHgX must occur rapidly since there was no evidence of decarboxylation products.

\[
\text{RCO}' + \text{t-BuHgCl} \rightarrow \text{RCO}^+ + \text{t-Bu}' + \text{Hg}^0 + \text{Cl}^- \quad (3)
\]

In conclusion, oxidative electron transfer to t-BuHgX has been demonstrated to occur for imidoyl and acyl radicals. Other easily oxidized neutral radicals which undergo electron transfer to t-BuHgX include amino-methyl radicals (R₂NCH₂),¹⁴ and pyridinyl radicals, which are easily oxidized to the cations with \( E^+ \) values of \( \approx -1 \text{ V (SCE)} \). The Bu₂Sn' radical, with an oxidation potential no lower than \(-0.43 \text{ V}\), also reacts with alkylmercury halides to generate an alkyl radical, probably by an electron transfer process.²²

**Experimental**

*General.* ¹H and ¹³C NMR spectra were obtained at 300 and 75 MHz for samples in CDCl₃ with Me₄Si as an...
internal standard. Mass spectra were obtained with a Finnegan 4000 spectrometer in El and Cl modes and with high resolution with a Kratos MS-50 spectrometer. Most products were isolated by flash chromatography on silica gel (Kieselgel 60, 230–400 mesh ASTM) while thin layer separations used silica gel with hexane (90%)-ethyl acetate (10%) as the eluent. Photostimulated reactions utilized a Sylvania 275W sunlamp ~20 cm from the reaction vessel which maintained a reaction temperature of 35°C. tert-Butylmercury halides were prepared according to literature procedures.12 Commercial MeSO was stored over molecular sieves and deoxygenated by nitrogen-bubbling before use.

Typical reactions were performed on a 0.5 mmol scale with work-up by aqueous Na2S2O7 followed by CH2Cl2 extraction. For GC-MS analysis prior to work-up the reaction mixtures were passed through a Celite column and concentrated under vacuum.

Conversion of aryl isonitriles into N-aryl-propynilamides. Photolysis of PhNC with 4 equiv. of R'HgCl and 4 equiv. of KI in Me2SO for 4 h under nitrogen followed by work-up with aqueous Na2S2O7, extraction with CH2Cl2 and evaporation of the solvent gave the N-phenyl-propynilamide, which was isolated by column chromatography. 2,2-Dimethyl-N-phenyl-propynilamide had m.p. 128–129°C (lit. 23 127–128°C) and a 1H NMR spectrum in agreement with literature.23 HRMS: m/z 177.1154 (calc. for C14H15NO 177.1154).

2-Methyl-N-phenylpropynilamide was isolated as a white solid, m.p. 102–104°C (lit.21 104–105°C) with a 1H NMR spectrum in agreement with the literature.24 HRMS: m/z 163.0997 (calc. for C14H13NO 163.0997).

2,2-Dimethyl-N-(2,4,6-trimethylphenyl)propynilamide had 1H NMR (CDCl3): 6 1.34 (s, 9 H), 2.15 (s, 6 H), 2.26 (s, 3 H), 6.81 (s, 1 H), 6.87 (s, 2 H). GC–MS: m/z (relative intensity) 219 (M+ 22), 62 (9), 135 (37), 134 (21), 120 (19), 119 (6), 91 (10), 57 (100).

Conversion of isonitriles into amidines. A mixture of the isonitrile, t-BuHgI (4 equiv.) and amine (2 equiv.) was stirred in PhH under N2 for 4 h with sunlamp irradiation. Work-up with aqueous Na2S2O7 and evaporation of the solvent gave the amidines, which were purified by column chromatography.

2,2-Dimethyl-N,N'-diphenyl-propynilamide (2a) was isolated as a liquid from the reaction of PhNC, t-BuHgI and PhNH2 in benzene. 1H NMR: (CDCl3): 6 1.37 (s, 9 H), 6.60–6.60 (m, 5 H), 6.96 (m, 5 H). GC and HRMS: m/z (relative intensity) 525.1620 (7, calc. for C30H20N2 525.1627), 195 (4), 160 (54), 105 (8), 104 (100). FTIR (CDCl3): 3427, 1641, 1498, 754, 692 cm−1.

N,N'-Diethyl-2,2-dimethyl-N'-2'-phenylpropynilamide (2b) was isolated as a liquid. 1H NMR: 6 0.94 (t, J = 6.9 Hz, 6 H), 1.32 (s, 9 H), 2.86 (q, J = 6.9 Hz, 4 H), 6.72 (dd, J = 7.2, 1.2 Hz, 2 H), 6.88 (t, J = 7.5 Hz, 1 H), 7.20 (t, J = 7.5 Hz, 2 H). GC and HRMS: m/z (relative intensity) 232.1935 (15, calc. for C15H22N2 232.1940), 203 (32), 175 (18), 160 (18), 147 (5), 119 (19), 105 (9), 104 (100). FTIR (CDCl3): 1603, 1589, 1481, 763, 696 cm−1.

Benzyl isocyanide with t-BuHgI and PhNH2 yielded 2,2-dimethy-N-phenylpropynilamide as a white solid, m.p. 62–63°C. 1H NMR: 6 1.25 (s, 9 H), 3.98 (s, 2 H), 4.56 (s, 1 H), 6.78 (d, J = 7.2 Hz, 2 H), 6.84 (t, J = 7.5 Hz, 1 H), 7.13–7.32 (m, 7 H). GC and HRMS: m/z (relative intensity) 266.1789 (10, calc. for C18H18N2 266.1783), 182 (8), 167 (5), 104 (11), 91 (100). FTIR (CDCl3): 3449, 1649, 1591, 744, 696 cm−1.

N1-(1,1-Dimethylithyl)-2,2-dimethyl-N'-2'-phenylpropynilamide was isolated as a liquid. 1H NMR: 6 1.09 (s, 9 H), 1.36 (s, 9 H), 4.28 (s, 1 H), 6.65 (dd, J = 8.4, 1.2 Hz, 2 H), 6.77 (tt, J = 7.2, 1.2 Hz, 1 H), 7.14 (td, J = 8.1, 0.6 Hz, 2 H). GC and HRMS: m/z (relative intensity) 232.1995 (26, calc. for C18H18N2 232.1940), 175 (14), 161 (3), 141 (6), 120 (8), 119 (100). FTIR (CDCl3): 3583, 1736, 1647 cm−1.

2-(1,1-Dimethylethy1)-3-phenylimino-JH-indole (1). Photolysis of 3 equiv. of t-BuHgI with PhNC in benzene gave 1 as a yellow solid, m.p. 100–101°C. 1H NMR: 6 1.54 (s, 9 H), 6.45 (d, J = 7.5 Hz, 1 H), 6.83 (td, J = 8.4, 0.9 Hz, 1 H), 6.92 (dd, J = 7.2, 1.5 Hz, 2 H), 7.21–7.32 (m, 2 H), 7.39–7.44 (m, 3 H). 13C NMR: 6 179.81 (s), 163.15 (s), 157.19 (s), 150.19 (s), 132.31 (d), 129.37 (d), 126.39 (d), 125.56 (d), 124.97 (d), 121.93 (s), 121.06 (d), 117.42 (d), 36.56 (s), 28.39 (q). GC and HRMS: m/z (relative intensity) 262.1469 (86, calc. for C18H18N2 262.1470), 263 (14), 247 (20), 221 (26), 205 (8), 118 (23), 102 (9), 77 (100). FTIR (CDCl3): 1643, 1608, 1593 cm−1. Anal. Calc. for C18H18N2: 82.40; H, 6.92; N, 10.60. Found: C, 82.07; H, 7.14; N, 10.44.

Trideuteriomythyl/2,2-dimethyl-N-phenylpropynilamide [(PhNCOCD2SCD2)](CMes3). Photolysis of t-BuHgI in Me2SO-d6 for 3 h gave the imidate ester identified by GC–MS: m/z (relative intensity) 242 (M+ 4), 207 (4), 194 (13), 193 (6), 192 (22), 185 (13), 160 (7), 157 (50), 57 (100). GC–MS (CI, isobutane) 243 (100).

2,2-Dimethyl-N-(2,4,6-trimethylphenyl)propanimidoyl chloride. Photolysis of t-BuHgCl with 2,4,6-trimethylphenyl isocyanide in PhH followed by filtration through Celite gave the imidoyl chloride detected by GC–MS: m/z (relative intensity) 237 (M+ 3), 239 (4), 202 (42), 186 (3), 147 (11), 146 (100).

N-(2,2-Dimethylpropenylene)-2,4,6-trimethylaniline (3). 1H NMR: 6 1.21 (s, 9 H), 2.03 (s, 6 H), 2.24 (s, 3 H), 6.82 (s, 2 H), 7.49 (s, 1 H). GC–MS: m/z (relative intensity) 203 (M+ 27), 188 (10), 146 (100).

3,3-Dimethyl-1,2-bis[2,4,6-trimethylphenyl]butane (4). GC–MS: m/z (relative intensity), 348 (M+ 0.5), 334 (8), 333 (35), 281 (10), 208 (6), 207 (30), 202 (53), 144 (100). GC–MS (Cl: ammonia) 349 (100).
Reaction of ethyl p-(pent-4-enoyl)benzoate (5) with t-BuHgCl. Photolysis of 5 with 3 equiv. of t-BuHgCl and 4 equiv. of DABCO in Me$_2$SO for 18 h produced 6 and 7 isolated by thin layer chromatography after work-up with aqueous Na$_2$S$_2$O$_3$ and CH$_2$Cl$_2$ extraction.

4-(2,2-Dimethylpropyl)-6-(ethoxy carbonyl)-x-tetralone (6). The ketone was isolated as a colorless liquid. $^1$H NMR: δ 1.06 (s, 9 H), 1.41 (t, $J$ = 7.2 Hz, 3 H), 1.53 (dd, $J$ = 14.7, 3.0 Hz, 1 H), 1.75 (dd, $J$ = 14.7, 8.1 Hz, 1 H), 2.10 – 2.19 (m, 1 H), 2.27 (tt, $J$ = 13.5, 4.5 Hz, 1 H), 2.62 (dt, $J$ = 17.7, 4.8 Hz, 1 H), 2.85 (dd, $J$ = 17.7, 12.4, 5.1 Hz, 1 H), 3.13 (m, 1 H), 4.40 (q, $J$ = 7.2 Hz, 2 H), 7.91 (dd, $J$ = 8.1, 1.8 Hz, 1 H), 7.95 (s, 1 H), 8.04 (d, $J$ = 8.1 Hz, 1 H). $^{13}$C NMR: δ 198.03, 165.91, 150.24, 145.06, 134.58, 129.85, 127.19, 127.00, 61.37, 48.05, 34.70, 34.54, 31.45, 29.91, 28.13, 14.13. GC and HRMS: m/z (relative intensity) 288.1721 (35, calc. for C$_{16}$H$_{24}$O$_5$: 288.1725), 243 (14), 232 (14), 218 (74), 217 (100).

4-(4-Ethoxycarbonylphenyl)-6,6-dimethylheptanoic acid (7). The compound was isolated as a colorless liquid. $^1$H NMR: δ 0.76 (s, 9 H), 1.38 (q, $J$ = 7.2 Hz, 3 H), 1.56 (dd, $J$ = 14.1, 3.3 Hz, 1 H), 1.72 – 2.18 (m, 1 H), 2.69 – 2.78 (m, 1 H), 4.36 (q, $J$ = 7.2 Hz, 1 H), 7.22 – 7.25 (m, 2 H), 7.94 – 7.98 (m, 2 H), 10.5 (br s, 1 H). $^{13}$C NMR: δ 178.97, 166.59, 151.75, 129.81, 128.52, 127.87, 60.81, 50.42, 41.95, 33.97, 31.92, 31.34, 30.03, 14.33. GC and HRMS: m/z (relative intensity) 306.1827 (48, calc. for C$_{16}$H$_{24}$O$_4$: 306.1831), 261 (28), 249 (65), 203 (64), 189 (92), 177 (100).

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References

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