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Intramolecular cyclizations via photostimulated tethered free radical reaction towards α-tetralones and their analogues

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Abstract

Photostimulated tethered free radical reactions for the intramolecular cyclizations towards α-tetralones, N-containing α-tetralone analogues, 3,4,4a,10b-tetrahydro-2*H*-pyrano[3,2-*c*]chromen-5-ones and 2,3,4,4a,6,10b-hexahydropyrano[3,2-*c*]quinolin-5-one were investigated. Photolysis of the *t*-BuHgX/Dabco with 1-aryl-4-penten-1-ones produced α-tetralones via *tert*-butyl radical attacks on the terminal, followed by secondary radical attack to the aromatic ring, proton abstraction and electron transfer from the radical anion intermediate to *t*-BuHgX. At similar conditions, formation of N-containing α-tetralone analogues, 3,4,4a,10b-tetrahydro-2*H*-pyrano[3,2-*c*]chromen-5-ones and 2,3,4,4a,6,10b-hexahydropyrano[3,2-*c*]quinolin-5-one also occurs in reasonable yields.

Keywords: Photolysis; α-Tetralones and their analogues; Radical anion; Oxidative alkylation

1. Introduction

The production of radicals by oxidation–reduction reactions offers some advantages over the use of other conventional radical initiators. For the generation of alkyl radicals, the photolysis of alkylmercury halides proved to be a convenient method. The photochemically generated alkyl radicals can undergo either reductive or oxidative homolytic reactions with unsaturated compounds, depending on the reaction condition. In the presence of a base, such as the 1,4-diazabicyclo[2,2,2]octane (Dabco) and alkylmercury halide, the photostimulated oxidative alkylation was most successful. We have earlier reported on various examples of oxidative alkylations with unsaturated compounds such as coumarin, maleimide, acyclic 1,4-enediones, 1,4-naphthoquinone, fumaronitrile, benzothiazole and benzoimidazole [1]. Our oxidative alkylation method worked well for electron-deficient arenes, such as fluoro or trifluoromethyl-substituted acylbenzenes and benzonitriles [2], and highly deactivated difluorinated acylbenzenes and cyanobenzenes as well [3]. In addition to the benzene derivatives, the electron-deficient heteroatomic aromatic compounds, such as the acylpyridines, cyanopyridine and acylthiophenes also worked well with the radical mediated alkylations [4]. To the best of our knowledge, alkylations of heteroatomic aromatics using the radical chain reactions described above does not have much precedence in the literature [5,6]. We also reported that bimolecular aromatic homolytic substitutions proceeded with similar mechanisms, as shown in Scheme 1 where the substituent E could stabilize the radical adduct **1** and the radical anion **2** [7]. Dabco can abstract a proton from **1** and then a chain reaction is initiated by the electron transfer to *t*-BuHgX with the regeneration of *t*-Bu$^{\bullet}$.

Based on our previous work, we have extended the oxidative alkylation reaction for intramolecular cyclization

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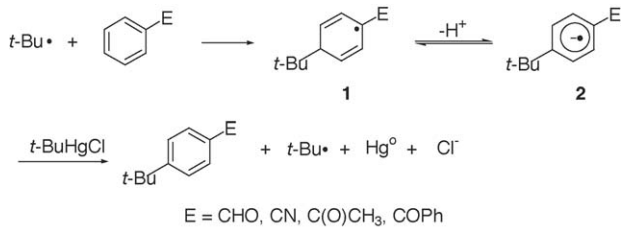


Scheme 1.

reactions to form α-tetralones, N-containing α-tetralone analogues (kairolines and naphthyridines), 3,4,4a,10b-tetrahydro-2*H*-pyrano[3,2-*c*]chromen-5-ones and 2,3,4,4a,6,10b-hexahydro-pyrano[3,2-*c*]quinolin-5-one. If the initially formed radical intermediate that was attacked by the alkyl radical was properly oriented in the molecule containing aromatic ring, the cyclization towards the aromatic ring would be possible. In this paper, we describe an application of the oxidative alkylation processes through the photolysis of the alkylmercury chloride in the presence of Dabco as a proton acceptor, with electron-deficient aromatics, heteroatomic aromatics or coumarin derivatives that have olefinic groups in the same molecule.

2. Experimental

2.1. Materials and instrumentation

Chemical reagents were purchased mostly from Aldrich and the reagents were used without further purification in most cases. Solvents were purchased and dried through the usual Lab. techniques. Analytical gas chromatography (GC) was performed on a Donam 6200 gas chromatograph equipped with a DB-1 capillary column and a Hitachi D-2500 integrator. ^{1}H NMR spectra were recorded on a 300 MHz Bruker or a 400 MHz Jeol instrument and the ^{13}C NMR spectra were recorded on a 75 MHz Bruker or a 100 MHz Jeol instrument. Chemical shifts were reported in ppm from the tetramethylsilane (TMS). High-resolution mass spectra were recorded on a Jeol JMS-DX 303 mass spectrometer and the GC–MS was recorded on a HP6890 mass spectrometer. Infrared spectra (IR) were recorded on a Nicolet 205 FT-IR.

Most products were isolated by flash column chromatography on silica gel (230–400 mesh ASTM, purchased from Merck) with eluents of mixed solvents (ethyl acetate and hexane). The GC yields were determined using an internal standard (octane) and were corrected with predetermined response factors.

2.2. tert-Butyl radical triggered cyclizations

2.2.1. General procedure for tert-butylation initiated radical cyclizations

2.2.1.1. In the presence of DABCO. The substrate (1 mmol), *t*-BuHgCl (4 mmol) and DABCO (4 mmol) were dissolved in 10 mL of DMSO in a flame-dried Pyrex test tube under a nitrogen atmosphere and irradiated with a UV lamp (360 nm) in a Rayonet photoreactor. Workup involved treatment with 50 mL of aqueous $Na_2S_2O_3$ solution, followed by a diethyl ether extraction (three times) and the washing of the organic layer with brine. After drying over $MgSO_4$ and the evaporation of the solvent, the GC yield was determined with an internal standard (octane). If necessary, the products were isolated by flash column chromatography using ethyl acetate–hexane as the eluent.

2.2.1.2. In the presence of PTSA. The substrate (1 mmol), *t*-BuHgCl (4 mmol), KI (4 mmol) and *p*-toluenesulfonic acid (2 mmol) were dissolved in 10 mL of DMSO in a flame-dried Pyrex test tube under a nitrogen atmosphere, and irradiated with a UV lamp (360 nm) in a Rayonet photoreactor. Workup involved treatment with 50 mL of aqueous $Na_2S_2O_3$ solution, neutralization if required and extraction with diethyl ether three times. The ether extracts were washed with brine solution. After drying over $MgSO_4$ and the evaporation of the solvent, the GC yield was determined with an internal standard (octane) and if necessary, the products were isolated by flash column chromatography using ethyl acetate–hexane as the eluent.

*2.2.1.3. 3,4-Dihydro-4-(2,2-dimethylpropyl)-1(2H)-naphthalenone (**3a**) [6].* The compound was an oily liquid, ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (s, 9H), 1.50 (dd, 1H, J = 14.4, 2.1 Hz), 1.75 (dt, 1H, J = 14.4, 7.8 Hz), 2.11 (dq, 1H, J = 18.0, 4.5 Hz), 2.20–2.33 (m, 1H), 2.57 (dt, 1H, J = 17.4, 4.8 Hz), 2.83 (ddd, 1H, J = 17.4, 12.3, 4.8 Hz), 3.02–3.12 (m, 1H), 7.24–7.30 (bdt, 2H), 7.48 (t, 1H, J = 7.2 Hz), 7.99 (d, 1H, J = 7.2 Hz); FT-IR ($CDCl_3$): 3063 (w), 2852 (s), 2865 (m), 1686 (vs) cm^{-1}; GC–MS *m/z* (rel. intensity): 216 (42, M$^+$), 201 (1), 160 (5), 145 (100), 131 (21), 117 (30), 103 (7), 91 (13), 57 (25); HRMS *m/z* calcd. for $C_{15}H_{20}O$ 216.1514, found 216.1517.

*2.2.1.4. 3,4-Dihydro-6-trifluoromethyl-4-(2,2-dimethylpropyl)-1(2H)-naphthalenone (**4**).* Pale yellow liquid, TLC (30% ethyl acetate/hexane) R_f 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (s, 9H), 1.43 (dd, 1H, J = 14.4, 2.4 Hz), 1.69 (dd, 1H, J = 14.4, 7.9 Hz), 2.05–2.11 (m, 1H), 2.18–2.24 (m, 1H), 2.55 (dt, 1H, J = 17.8, 4.5 Hz), 2.79 (ddd, 1H, J = 17.8, 12.4, 5.1 Hz), 3.03–3.06 (m, 1H), 7.44–7.46 (m, 2H), 8.02 (d, 1H, J = 7.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.39, 150.79, 134.76 (q, J_{C-F} = 32.1 Hz), 134.12, 127.85, 125.48, 125.44, 126.61 (q, J_{C-F} = 271.7 Hz), 123.09, 123.05, 48.08, 34.76, 34.43, 31.48, 29.88, 28.13; FT-IR ($CDCl_3$): 3045, 2985, 1679, 1414 cm^{-1}; GC–MS *m/z* (rel. intensity): 284 (30, M$^+$), 265 (9), 228 (36), 214 (100), 185 (21), 165 (20), 145 (13), 115 (21), 71 (25), 57 (34); HRMS *m/z* calcd. for $C_{16}H_{19}F_3O$ 284.1388, found 284.1398.

*2.2.1.5. 3,4-Dihydro-7-trifluoromethyl-4-(2,2-dimethylpropyl)-1(2H)-naphthalenone (**5a**).* Pale yellow

liquid, TLC (30% ethyl acetate/hexane) R_f 0.44; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (s, 9H), 1.48 (dd, 1H, J = 14.5, 2.6 Hz), 1.78 (dd, 1H, J = 14.5, 7.9 Hz), 2.14 (dq, 1H, J = 13.8, 4.8 Hz), 2.23–2.35 (m, 1H), 2.64 (dt, 1H, J = 17.8, 4.6 Hz), 2.86 (ddd, 1H, J = 18.3, 12.5, 5.1 Hz), 3.06–3.16 (m, 1H), 7.40 (d, 1H, J = 8 Hz), 7.72 (d, 1H, J = 8 Hz), 8.27 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.02, 167.60, 163.06, 153.54, 130.35, 130.22, 128.47, 128.43, 114.29 (q, J_{C-F} = 21.4 Hz) 34.86, 34.43, 31.43, 29.84, 28.52; FT-IR ($CDCl_3$): 3045, 2979, 1686, 1414 cm^{-1}; GC–MS *m/z* (rel. intensity): 284 (28, M^+), 265 (13), 228 (24), 214 (100), 199 (20), 185 (17), 165 (17), 115 (18), 71 (17), 57 (26); HRMS *m/z* calcd. for $C_{16}H_{19}F_3O$ 284.1388, found 284.1392.

*2.2.1.6. 3,4-Dihydro-5-trifluoromethyl-4-(2,2-dimethylpropyl)-1(2H)-naphthalenone (**5b**).* Pale yellow liquid, TLC (30% ethyl acetate/hexane) R_f 0.44; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (s, 9H), 1.36–1.61 (m, 2H), 2.11–2.18 (m, 1H), 2.33–2.48 (m, 1H), 2.63 (ddd, 1H, J = 19.4, 5.7, 1.7 Hz), 2.92 (ddd, 1H, J = 19.6, 13.9, 5.8 Hz), 3.58–3.67 (m, 1H), 7.41 (dd, 1H, J = 7.8, 7.8 Hz), 7.83 (d, 1H, J = 7.8 Hz), 8.19 (d, 1H, J = 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.02, 167.60, 163.06, 153.54, 130.35, 130.22, 128.47, 128.43, 114.29 (q, J_{C-F} = 21.4 Hz), 34.86, 34.43, 31.43, 29.84, 28.52; FT-IR ($CDCl_3$): 3045, 2979, 1679, 1420 cm^{-1}; GC–MS *m/z* (rel. intensity): 284 (9, M^+), 228 (22), 214 (100), 200 (26), 185 (17), 165 (19), 115 (19), 71 (25), 57 (29); HRMS *m/z* calcd. for $C_{16}H_{19}F_3O$ 284.1388, found 284.1395.

*2.2.1.7. 2,3-Dihydro-6-fluoro-4-(2,2-dimethylpropyl)-1(2H)-naphthalenone (**6**).* Pale yellow liquid, TLC (10% ethyl acetate/hexane) R_f 0.68; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 (s, 9H), 1.49 (dd, 1H, J = 14.5, 2.1), 1.75 (dd, 1H, J = 14.5, 7.8), 2.05–2.12 (m, 1H), 2.22–2.30 (m, 1H), 2.57 (dt, 1H, J = 17.7, 4.8 Hz), 2.79 (ddd, 1H, J = 19.5, 12,3, 4.8 Hz), 3.01–3.04 (m, 1H), 6.91–6.98 (m, 2H), 8.03 (dd, 1H, J = 8.6, 6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.97, 165.93 (d, J_{C-F} = 255.0 Hz), 153.48 (d, J_{C-F} = 8.3 Hz), 130.31 (d, J_{C-F} = 9.9 Hz), 128.50 (d, J_{C-F} = 2.9 Hz), 114.56 (d, J_{C-F} = 21.9 Hz), 114.03 (d, J_{C-F} = 22.3 Hz), 47.97, 34.90, 34.91, 31.44, 29.85, 28.57; FT-IR ($CDCl_3$): 3045, 2985, 1680, 1421 cm^{-1}; GC–MS *m/z* (rel. intensity): 234 (66, M^+), 219 (4), 178 (15), 164 (100), 149 (33), 135 (27), 115 (10), 109 (12), 71 (15), 57 (23); HRMS *m/z* calcd. for $C_{15}H_{19}FO$ 234.1420, found 234.1430.

*2.2.1.8. 1-{3-Cyano-4-(1,1-dimethylethyl)phenyl}-4-penten-1-one (**7**).* Pale yellow liquid, TLC (20% ethylacetate/hexane) R_f 0.61; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.55 (s, 9H), 2.47–2.54 (m, 2H), 3.06 (m, 2H), 5.00–5.13 (m, 2H), 5.80–6.00 (m, 1H), 7.6 (d, 1H, J = 8.4 Hz), 8.08 (dd, 1H J = 8.4, 1.8 Hz), 8.25 (d, 1H, J = 1.8 Hz); FT-IR ($CDCl_3$): 3052, 2979, 2303, 1693, 1421 cm^{-1}; GC–MS *m/z* (rel. intensity): 241 (4, M^+), 226 (10), 186 (100), 171 (11), 143 (11), 115 (14), 57 (2); HRMS *m/z* calcd. for $C_{16}H_{19}NO$ 241.1467, found 241.1470.

*2.2.1.9. 1-{2-(1,1-Dimethylethyl)-5-pyridyl}-4-penten-1-one (**8**).* Colorless liquid, TLC (30% ethyl acetate/hexane) R_f 0.76; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (s, 9H), 2.48–2.55 (m, 2H), 3.05–3.10 (t, 2H, J = 7.2 Hz), 5.01–5.05 (dd, 1H, J = 10.2, 0.9 Hz), 5.07–5.13 (dd, 1H, J = 17.1, 1.2 Hz), 5.56–5.91 (m, 1H), 7.44–7.47 (d, 1H, J = 8.4 Hz), 8.16–8.19 (dd, 1H, J = 8.4, 2.4 Hz) 9.13–9.14 (d, 1H, J = 2.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.91, 173.82, 148.56, 136.82, 135.55, 129.30, 119.04, 115.43, 38.01, 37.92, 30.01, 27.97; FT-IR ($CDCl_3$): 3057, 2975, 1691, 1601, 1425, 1277 cm^{-1}; HRMS(EI) calcd. for $C_{14}H_{19}NO$ 217.1467, found 217.1472.

*2.2.1.10. 1-{2-(1,1-Dimethylethyl)-8-(2,2-dimethylpropyl)-7,8-dihydro-6H-quinolin-5-one (**9**).* Colorless liquid, TLC (30% ethyl acetate/hexane) R_f 0.82; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.36–1.46 (m, 10H, including 9H of *t*-Bu singlet at 1.38), 1.95–2.05 (m, 1H), 2.15–2.20 (dd, 1H, J = 13.8, 3.3 Hz), 2.29–2.36 (m, 1H), 2.54–2.64 (m, 1H), 2.74–2.84 (m, 1H), 3.06–3.08 (m, 1H), 7.25–7.29 (d, 1H, J = 8.4 Hz), 8.14–8.17 (d, 1H, J = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.28, 178.53, 166.28, 134.83, 124.71, 116.94, 46.71, 38.34, 37.78, 36.33, 31.51, 29.99, 29.91, 29.87; FT-IR ($CDCl_3$): 3057, 2959, 1691, 1589, 1482, 1265 cm^{-1}; HRMS(EI) calcd. for $C_{18}H_{27}NO$ 273.2093, found 273.2095.

*2.2.1.11. 1-Methyl-4-(2,2-dimethylpropyl)-1,2,3,4-tetrahydro-[1,8]naphthyridine (**11**).* Pale yellow liquid, TLC (10% MeOH/CH_2Cl_2) R_f 0.55; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (s, 9H), 1.43–1.46 (m, 2H), 1.73–1.82 (m, 1H), 1.88–2.00 (m, 1H), 2.80–2.87 (m, 1H), 3.11 (s, 3H), 3.24–3.46 (m, 2H), 6.45 (dd, 1H, J = 7.2, 5.0 Hz), 7.15 (m, 1H), 7.96 (dd, 1H, J = 7.2, 1.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.69, 145.39, 134.87, 123.43, 111.54, 50.97, 46.31, 36.56, 32.72, 31.47, 30.01, 27.87; FT-IR ($CDCl_3$): 3056, 2995, 2959, 1596, 1425, 1268, 745 cm^{-1}; GC–MS *m/z* (rel. intensity): 218 (41, M^+), 161 (5), 147 (100), 131 (10), 118 (2), 104 (2), 92 (1), 77 (2); HRMS(EI) calcd. for $C_{14}H_{22}N_2$ 218.1783, found 218.1811.

*2.2.1.12. 1-Methyl-4-(2,2-dimethylpropyl)-1,2,3,4-tetrahydroquinoline (**12**).* Colorless liquid, TLC (20% ethyl acetate/hexane) R_f 0.60; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (s, 9H), 1.43 (d, 2H, J = 5.3 Hz), 1.70–1.77 (m, 1H), 1.89–1.97 (m, 1H), 2.77–2.82 (m, 4H, including 3H of N–CH_3 singlet at 2.81), 3.01–3.23 (m, 2H), 6.51–6.58 (m, 2H), 6.93–7.01 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.97, 129.10, 128.77, 126.71, 116.29, 110.97, 52.29, 47.28, 39.06, 32.51, 31.52, 30.07, 28.85; FT-IR ($CDCl_3$): 3052, 2955, 1604, 1503, 1262, 742 cm^{-1}; GC–MS *m/z* (rel. intensity): 217 (48, M^+), 160 (4), 146 (100), 131 (16), 118

(7), 103 (2), 91 (3), 77 (3), 57 (1); HRMS(EI) calcd. for $C_{15}H_{23}N$ 217.1830, found 217.1838.

*2.2.1.13. 6-Fluoro-1-methyl-4-(2,2-dimethylpropyl)-1,2,3,4-tetrahydroquinoline (**13**).* Brownish liquid, TLC (10% ethyl acetate/hexane) R_f 0.64; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (s, 9H), 1.50 (d, 2H, J = 5.2 Hz), 1.73–1.83 (m, 1H), 1.93–2.06 (m, 1H), 2.77–2.85 (m, 4H, including 3H of N–CH_3 singlet at 2.84), 3.03–3.23 (m, 2H), 6.46–6.52 (m, 1H), 6.71–6.72 (m, 1H), 6.75–6.79 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.20 (d, J_{C-F} = 232.6 Hz), 142.68, 130.78, 115.11 (d, J_{C-F} = 21.7 Hz), 112.92, 112.78 (d, J_{C-F} = 21.7 Hz), 52.34, 47.58, 39.61, 32.81, 31.53, 30.36, 30.03, 29.15; FT-IR ($CDCl_3$): 3056, 2989, 1505, 1420, 1262, 733 cm^{-1}; GC–MS *m/z* (rel. intensity): 235 (56, M^+), 178 (4), 164 (100), 148 (17), 136 (8), 109 (3), 57 (1); HRMS(EI) calcd. for $C_{15}H_{22}FN$ 235.1736, found 235.1739.

*2.2.1.14. 6-Bromo-1-methyl-4-(2,2-dimethylpropyl)-1,2,3,4-tetrahydroquinoline (**14**).* Pale yellow liquid, TLC (30% ethyl acetate/hexane) R_f 0.81; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (s, 9H), 1.39–1.49 (m, 2H), 1.69–1.75 (m, 1H), 1.84–2.78 (m, 5H), 3.02–3.06 (m, 1H), 3.13–3.21 (m, 1H), 6.37 (d, 1H, J = 8.8 Hz), 6.99–7.06 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.88, 131.12, 131.03, 129.28, 112.41, 107.81, 51.81, 47.01, 38.95, 32.63, 31.51, 30.04, 28.42; FT-IR ($CDCl_3$): 3052, 2959, 1596, 1503, 1258, 750 cm^{-1}; GC–MS *m/z* (rel. intensity): 295 (56, M^+), 238 (3), 224 (100), 210 (6), 158 (3), 144 (50), 130 (11), 115 (5), 102 (3), 89 (2), 77 (2), 57 (2); HRMS(EI) calcd. for $C_{15}H_{22}BrN$ 259.0936, found 295.0939.

*2.2.1.15. 4-(2,2-Dimethylpropyl)-3,4,4a,10b-tetrahydro-2H-pyrano[3,2-c]chromen-5-one (**15**).* Grayish liquid, TLC (30% ethylacetate/hexane) R_f 0.69; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (s, 9H), 1.21 (dd, 1H, J = 14.1, 9.0 Hz), 1.54 (d, 1H, J = 14.1 Hz), 1.90–1.98 (m, 2H), 2.85–2.88 (m, 1H), 4.16–4.25 (m, 1H), 4.27–4.46 (m, 1H), 7.13–7.21 (m, 2H), 7.37–7.43 (m, 1H), 7.66 (dd, 1H, J = 7.9, 1.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.33, 159.07, 152.22, 131.09, 123.51, 122.40, 116.36, 115.80, 106.45, 63.55, 47.57, 31.68, 30.18, 26.92, 25.16; FT-IR ($CDCl_3$): 3056, 2959, 1712, 1629, 1493, 1258 cm^{-1}; GC–MS *m/z* (rel. intensity): 218 (41, M^+), 161 (5), 147 (100), 131 (10), 118 (2), 104 (2), 92 (1), 77 (2); HRMS(EI) calcd. for $C_{17}H_{20}O_3$ 272.1412, found 272.1415.

*2.2.1.16. 9-Methyl-4-(2,2-dimethylpropyl)-3,4,4a,10b-tetrahydro-2H-pyrano[3,2-c]chromen-5-one (**16**).* Grayish solid, TLC (30% ethyl acetate/hexane) R_f 0.72; mp 109.5–110 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (s, 9H), 1.17–1.25 (m, 1H), 1.53 (d, 1H, J = 11.0 Hz), 1.89–1.98 (m, 2H), 2.32 (s, 3H), 2.85–2.88 (m, 1H), 4.13–4.25 (m, 1H), 4.41–4.47 (m, 1H), 7.11 (d, 1H, J = 8.4 Hz), 7.21 (dd, 1H, J = 8.4, 2.0 Hz), 7.49 (d, 1H, J = 2.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.59, 159.09, 150.40, 133.19, 132.11, 122.13, 116.17, 115.47, 106.40, 63.53, 47.60, 31.71, 30.23, 26.97, 25.21, 20.92; FT-IR ($CDCl_3$): 3056, 2989, 1615, 1420, 1268, 897, 739 cm^{-1}; GC–MS *m/z* (rel. intensity): 286 (7, M^+), 269 (20), 229 (4), 215 (100), 201 (3), 128 (6), 81 (2); HRMS(EI) calcd. for $C_{18}H_{22}O_3$ 286.1569, found 286.1574.

*2.2.1.17. 6-Methyl-4-(2,2-dimethylpropyl)-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]quinolin-5-one (**17**).* Pale yellow liquid, TLC (30% ethylacetate/hexane) R_f 0.52; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.01 (s, 9H), 1.16–1.17 (m, 1H), 1.57 (d, 1H, J = 14.1 Hz), 1.89–1.95 (m, 2H), 2.98–3.01 (m, 1H), 3.61 (s, 3H), 4.14–4.23 (m, 1H), 4.38–4.41 (m, 1H), 7.10–7.24 (m, 2H), 7.41–7.46 (m, 1H), 7.85 (dd, 1H, J = 8.1, 1.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.76, 155.77, 138.44, 129.18, 122.76, 121.33, 116.18, 113.60, 111.92, 62.84, 47.44, 31.82, 30.41, 29.22, 27.07, 25.62; FT-IR ($CDCl_3$): 3052, 2983, 1631, 1266, 1111 cm^{-1}; GC–MS *m/z* (rel. intensity): 285 (12, M^+), 268 (22), 228 (27), 214 (100), 200 (12), 186 (4), 172 (2), 158 (2), 144 (3), 128 (2), 115 (2), 77 (2); HRMS(EI) calcd. for $C_{18}H_{23}NO_2$ 285.1729, found 285.1734.

3. Results and discussion

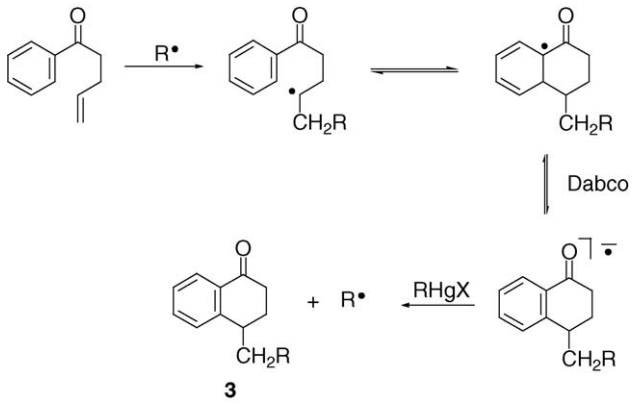
3.1. Alkyl radical tethered cyclization towards α-tetralones

To examine the alkyl radical tethered intramolecular cyclization reaction, the photolysis of *t*-BuHgCl and $PhCOCH_2$–CH=CH_2 was tried. If the *tert*-butyl radical attacks the terminal olefin, a secondary alkyl radical will be generated and it may attack the phenyl ring consequently for the oxidative alkylation. However, the photolysis of the *t*-BuHgCl and the $PhCOCH_2$–CH=CH_2 led to isomerization only to give α,β-unsaturated ketone. None of the cyclized products were observed. In the presence of I^-, good yields of the adduct PhCOCH(HgI)CH(Me)CMe_3 were formed as evidenced by the isolation of $PhCOCH_2$CH(Me)CMe_3 after an aqueous workup [8]. The addition of Dabco to the reaction mixture was not helpful for the cyclization reaction either. The five-membered ring formation via radical attack towards aromatic ring, therefore, did not occur. However, for the six-membered ring formation with the 1-phenyl-4-penten-1-one, modest yields of the α-tetralone **3** were observed with a significant increase in yield in the presence of Dabco (Table 1).

Table 1
Photolysis of RHgX with 1-phenyl-4-penten-1-one to from **3**[a]

Entry	R	X	Additive	Time (h)	Yield (%)[b]
1	*t*-Bu	I	None	24	8 (**3a**)
2	*t*-Bu	Cl	DABCO (4 equiv.)	24	42 (**3a**)
3	*i*-Pr	Cl	DABCO (4 equiv.)	24	37 (**3b**)

[a] Sunlamp irradiation of 0.02 M substrate with 0.08 M *t*-BuHgX.
[b] GC yield with an internal standard after workup with aqueous $Na_2S_2O_3$.



Scheme 2.

The reaction seems to fit Scheme 2, where the loss of a proton from the cyclized cyclohexadienyl radical, yields a radical anion, which readily transfers an electron to the *t*-BuHgX. Table 1 summarizes the observed yields of **3**.

As we prove previously [3], the relative reactivity of acylbenzenes towards the *t*-Bu• was enhanced when an additional electron withdrawing group, such as fluoro or trifluoromethyl group, was introduced on the aromatic ring. It might have a chance to improve the reaction for the intramolecular radical cyclization step if we enhance the relative reactivity of the aromatic site for the radical attack. We, therefore, examined the tethered radical cyclization reaction with the trifluoromethyl, fluoro or cyano-substituted 1-aryl-4-penten-1-one derivatives. The results are summarized in Table 2. In the case of the trifluoromethyl group-substituted substrate, the yields were improved with a longer irradiation time as the reactivity of the aromatic ring site towards the *t*-Bu• was enhanced (Table 2, entries 1 and 2).

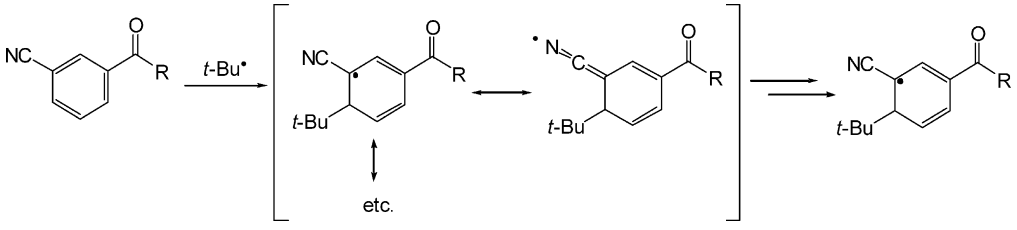
In the case of the 1-(3-cyanophenyl)-4-penten-1-one, the photolysis with *t*-BuHgCl/DABCO produced 1-(3-cyano-4-*tert*-butylphenyl)-4-penten-1-one as a major product without any of the cyclized products (Table 2, entry 5). The cyano appeared to be the better activating group compared to the trifluoromethyl group, since the linear resonance structure of the cyanobenzenes (Eq. (1)) avoided the steric hindrance requirement. Consequently, the resonance effect of the cyano group seemed more effective than the inductive effect of the trifluoromethyl group for the nucleophilic radical attack, which resulted in *tert*-butylation on the aromatic ring rather than on the terminal olefin.

3.2. Alkyl radical tethered cyclization towards N-containing α-tetralone analogues

Since acylpyridine derivatives are 2–10 times more reactive than acylbenzene in photostimulated oxidative alkylations [3], the pyridyl analogue of the 1-phenyl-4-penten-1-one could be another candidate for the tethered free radical cyclization reaction towards α-tetralone analogues. To prove this assumption, 1-(3-pyridyl)-4-penten-1-one was prepared and examined for intramolecular cyclization. The photolysis of 1-(3-pyridyl)-4-penten-1-one with *t*-BuHgCl (6 mmol)/Dabco (4 mmol) was examined and 3 h irradiation produced a mixture of *tert*-butylated product **8** and cyclized product **9** (Table 3, entry 1). Unlike in the 1-phenyl-4-penten-1-one case, *tert*-butylation seems to occur on pyridine ring first rather than in the terminal olefin. Since the acylpyridines were more reactive towards the *tert*-butyl radical than were the acylbenzenes [3], the *tert*-butyl radical attacked the pyridine ring prior to attacking the terminal olefin. However, at a longer irradiation at the same reaction condition, the *tert*-butylated product was further cyclized to the six-membered ring in good yield (Table 3, entry 2). The longer irradiation improved the yield of cyclized products **9** and **10** with decrements of the amount of **8** (Table 3, entry 3). It is clear that the *tert*-butyl radical attacks the terminal olefinic site of **8** to form the secondary radical, and it attacks to the pyridyl ring to accomplish the cyclization.

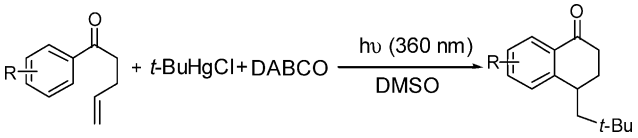
Meanwhile, the photoylsis of the *t*-BuHgCl/PTSA with 1-(3-pyridyl)-4-penten-1-one, gave rise to the **8** as an exclusive product (Table 3, entry 4) despite its short reaction time. In terms of the frontier orbital theory, the pyridinium salt, protonated heteroatomic base had considerably lower HOMO and LUMO energies than the normal benzene derivatives. In addition, the protonation of the basic heteroaromatics, such as pyridine, was known to activate them towards radical additions [9]. We observed the promoting effect of the protonation in pyridines, quinolines and isoquinolines previously [7]. The reaction was, therefore, accomplished quite cleanly, affording the mono alkylated product on the pyridyl ring. This was probably because of the enhanced reactivity of the pyridyl ring towards the *tert*-butyl radical, compared to the olefin functional group. Even with the longer irradiation, the cyclization was not observed (Table 3, entry 5).

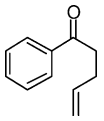
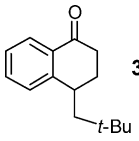
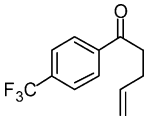
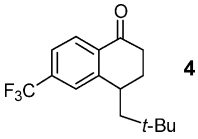
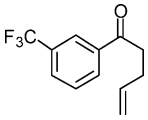
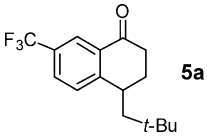
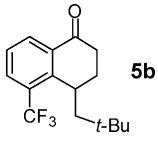
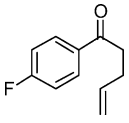
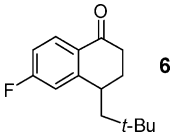
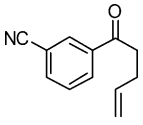
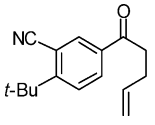
The relative reactivity of the terminal olefin versus the aromatic ring is critically dependent on the orientation of substituent. Thus we examined the cyclization of the 2-(3-butenylmethylamino)pyridine, which has amino electron



(1)

Table 2
Photolysis of *t*-BuHgCl with 1-phenyl-4-penten-1-one derivatives[a]



Entry	Substrate	Time (h)	Product	Yield (%)[b]
1[c]		24	 **3a**	42
2		48	 **4**	52
3		48	 **5a**	27
			+  **5b**	26
4		48	 **6**	50
5		3	 **7**	65

[a] 0.05 mmol of substrate, 3 mmol of *t*-BuHgCl and 2 mmol of Dabco in 10 mL of DMSO, irradiated with 360 nm at 35–40 °C.
[b] GC yield with an internal standard.
[c] Irradiated with sunlamp at 35–40 °C, ref. [5].

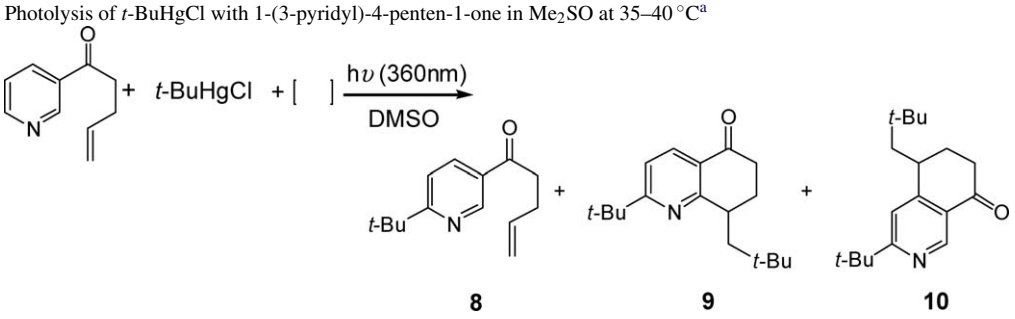
donating group at 1-position of the pyridine and homoallyl group as well. As expected, the photolysis of the 2-(3-butenylmethylamino)pyridine in the presence of *t*-BuHgCl (6 equiv.) and Dabco (6 equiv.) in DMSO, produced the desired cyclized product (Table 4, entry 1). A similar type of compound, *N*-homoallyl-*N*-methyl aniline, having a terminal olefin group and phenyl ring (less reactive than pyridyl ring), was examined for radical cyclization. Surprisingly, the photolysis of *N*-homoallyl-*N*-methylaniline/*t*-BuHgCl (6 equiv.)/Dabco (6 equiv.) in DMSO successfully yielded cyclized product in 43% (Table 4, entry 2). Since the benzene ring, which that has an electron donating group, such as the aniline, is hard to be attacked by alkyl radical intermolecularly, the successful intramolecular cyclization of *N*-homoallyl-*N*-methylaniline via a tethered free radical reaction was somehow unexpected.

If the electron withdrawing group was introduced to the phenyl ring, the reactivity of the phenyl ring for the incoming radical would be enhanced, which may improve the intramolecular radical cyclization. Thus, fluoro and bromo-substituted *N*-homoallyl-*N*-methylanilines were examined for intramolecular cyclization. As expected, the photolysis of 4-fluoro and 4-bromo-substituted *N*-homoallyl-*N*-methylaniline with the same reaction conditions, showed improved yields of the desired product (Table 4, entries 3 and 4).

3.3. Alkyl radical tethered cyclization towards 3,4,4a,10b-tetrahydro-2H-pyrano[3,2-c]chromen-5-ones and its analogue

As we have studied earlier, the photostimulated chain reaction of the alkylmercury chlorides with α,β-unsaturated

Table 3
Photolysis of *t*-BuHgCl with 1-(3-pyridyl)-4-penten-1-one in Me_2SO at 35–40 °C[a]



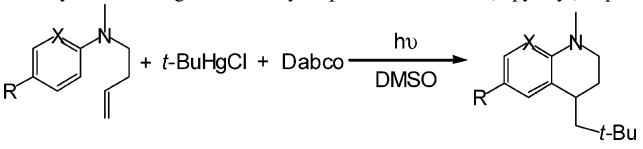
Entry	[·] (equiv.)	Time (h)	Yield (%)[b]		
			8	**9**	**10**
1	Dabco (4)	3	39	9	0
2	Dabco (4)	22	33	47	~15[c]
3	Dabco (4)	48	4	62	~20[c]
4	PTSA (2)	3	85[d]	0	0
5	PTSA (2)	48	73	0	0

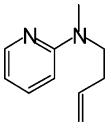
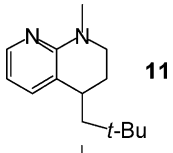
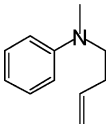
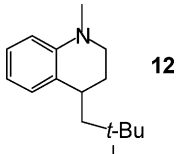
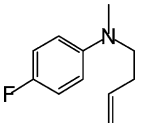
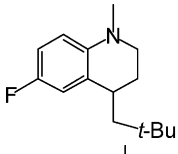
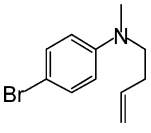
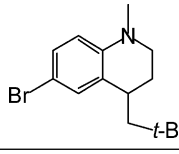
[a] 0.5 mmol of substrate and 3 mmol of *t*-BuHgCl were used.
[b] GC yield with an internal standard (octane).
[c] Identified by GC–MS only.
[d] 3 mmol of Kl was used.

compounds, such as coumarin in the presence of Dabco, give rise to the oxidative alkylation to form the 3-alkylcoumarin [10]. If an olefinic functional group was properly substituted on the 4-position of coumarin, such as 4-but-3-enyloxycoumarin, alkyl radical tethered intramolecular cyclization would be possible under the *t*-BuHgCl/Dabco/*hυ* condition, as shown in Scheme 3.

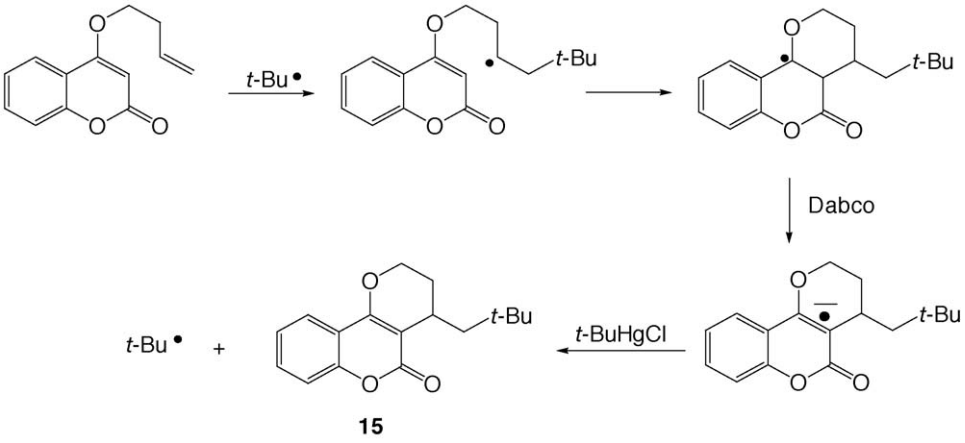
The photolysis of *t*-BuHgCl with 4-but-3-enyloxycoumarin in the presence of Dabco was examined. It produced the desired product **15** somehow in low yield (Table 5, entry

Table 4
Photolysis of *t*-BuHgCl with 1-aryl-4-penten-1-one or 1-(3-pyridyl)-4-penten-1-one in Me_2SO at 35–40 °C[a]



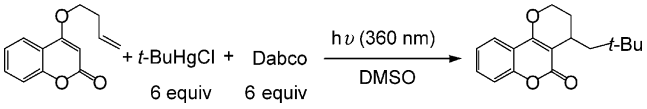
Entry	Substrate	*t*-BuHgCl:Dabco	Time (h)	Product	Yield (%)[b]
1		6:6	48	 **11**	31
2		6:6	48	 **12**	43
3		6:6	48	 **13**	48
4		6:6	48	 **14**	52

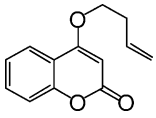
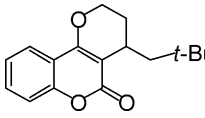
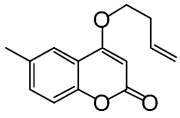
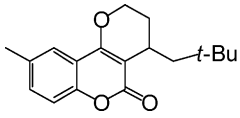
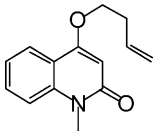
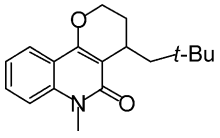
[a] 0.05 M of substrate in 10 mL of DMSO was irradiated with a 360 nm UV lamp at −40 °C.
[b] GC yield with an internal standard (octane).



Scheme 3.

Table 5
Photolysis of *t*-BuHgCl with coumarin derivatives in Me_2SO at 35–40 °C[a]



Entry	Substrate	Time (h)	Product		Yield (%)[b]
1		48		**15**	23
2		24		**16**	53
3		24		**17**	38

[a] 0.05 M of substrate in 10 mL of DMSO was irradiated with a 360 nm UV lamp at −40 °C.
[b] GC yield with an internal standard (octane).

1). However, the same reaction with the 4-but-3-enyloxy-6-methylcoumarin or the 4-but-3-enyloxy-1-methyl-2(1*H*)-quinolone revealed a quite improved yield up to 53% with a relatively short reaction time (Table 5, entries 2 and 3). This proves that the tethered free radical reaction can be used for the construction of the multi-ring compound.

4. Conclusion

We demonstrated free radical involved intramolecular cyclizations via tethered free radical reaction towards α-tetralone, N-containing α-tetralone analogues, 3,4,4a,10b-tetrahydro-2*H*-pyrano[3,2-*c*]chromen-5-ones, and 2,3,4,4a,6,10b-hexahydropyrano[3,2-*c*]quinolin-5-one, which are not easy to make using other ionic methodologies.

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