HETEROCYCLES, Vol. 63, No. 5, 2004, pp. 1185 - 1192
Received, 28th January, 2004, Accepted, 4th March, 2004, Published online, 12th March, 2004

SYNTHESIS OF NEW MEDIUM RING AROMATIC LACTONES *VIA* HALOCYCLIZATION OF 2-HYDROXYPHENYLALKANOIC ACID ALLYLIC ESTERS

David P. Brown* and Lalitha Krishnamurthy

Department of Chemistry, Saint John's University, 8000 Utopia Parkway, Jamaica, New York 11439

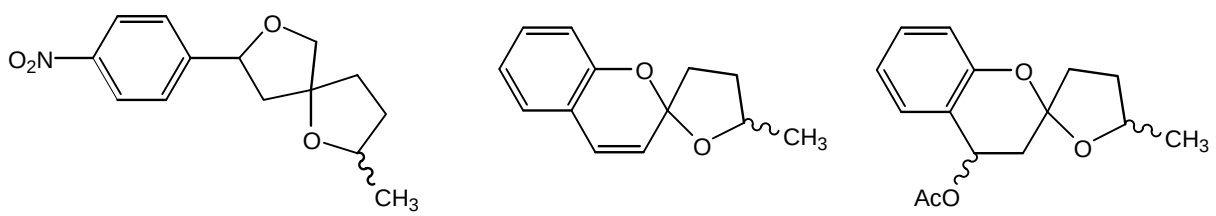
Abstract - Stable medium size ring aromatic lactones have been synthesized through electrophilic heteroatom cyclization reactions in moderate yields.

INTRODUCTION

The synthesis of seven and larger membered heterocyclic compounds from linear substrates, albeit a difficult process,[1] has been well established,[2] with the methodology of electrophilic heteroatom cyclization being among the most widely used approaches.[3] Generally, for eight and larger membered compounds, these cyclizations are of greater practical merit when steric constraints are introduced into the chain.[4] Lactones of varied ring sizes were routinely prepared from β,γ- and γ,δ-unsaturated carboxylic acids, employing a variety of electrophilic reagents, wherein products of *exo*- and *endo*-cyclizations were observed.[5] Among the structural modifications that would promote cyclization is the *oxygen effect*[6] that results when an oxygen atom is introduced in the carbon chain. For ring sizes 8 to 13, a positive oxygen effect was observed since these lactones were obtained in modest yields. Also, for these ring sizes, a competition between the *exo*- and *endo*-cyclization modes was often observed.[7]

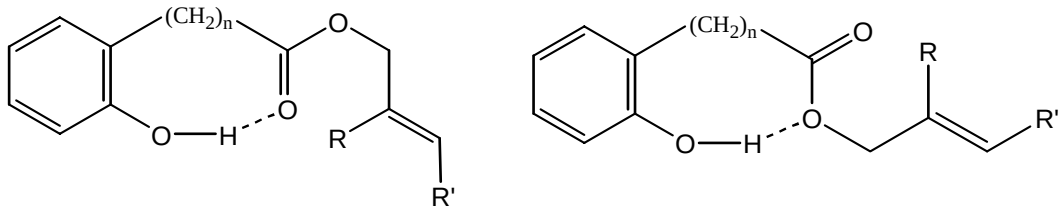
The iodocyclization protocol has also been employed in other cyclofunctionalization reactions. For instance, in a previously published paper, the preparation of some novel spiro-heterocyclic compounds, Figure 1, was reported.[8]

Figure 1



All of the hydroxy-ester systems, which were the substrates for the present iodoetherification reaction gave spectroscopic data consistent with geometries that enabled intramolecular hydrogen bonding, Figure 2. Specifically stretching absorption bands in the IR spectrum for the hydroxyl and carbonyl groups were broadened with a consistent shifting of values to lower frequencies. Typically, average values of 3412 and 1712 cm^{-1} were respectively observed.

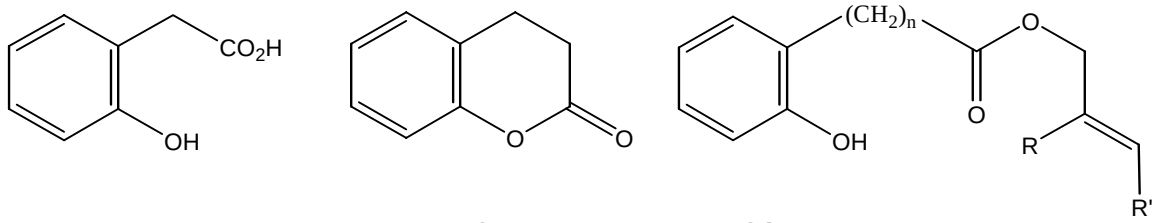
Figure 2



RESULTS AND DISCUSSION

2-Hydroxyphenylacetic acid **(1)** was quantitatively converted into the allylic esters (**3A** and **3B**), by allylation of the potassium carboxylate in DMF. Dihydrocoumarin **(2)** was similarly converted into the allylic esters (**4A**, **4B** and **4C**) by saponification with aqueous potassium hydroxide, and subsequent allylation of the potassium carboxylate in DMF.[9] The esters (**4A-C**) were each obtained in about 90 % yield for both steps.

Figure 3



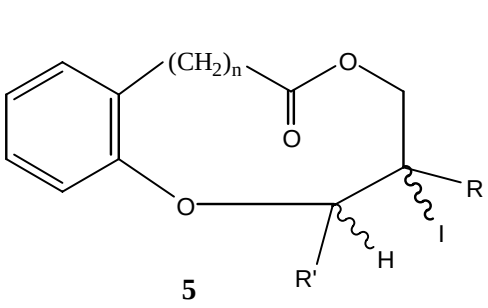
1 **2**

3A n=1, R=R'=H
3B n=1, R=CH_3, R'=H
4A n=2, R=R'=H
4B n=2, R=CH_3, R'=H
4C n=2, R=H, R'=Ph

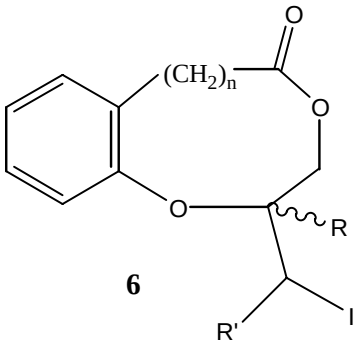
The allylic esters were each subjected to iodocyclization under different conditions as reported in the literature.[3] Best results were obtained from reactions performed with iodine in acetonitrile containing suspended sodium bicarbonate at room temperature. Product compositions were determined by GC

analyses of the lactone mixtures. The stereoisomers of the cyclic adducts were not separated, hence the respective stereochemical assignments were not ascertained. The results indicate that there was a slight preference for the *endo* cyclization processes which are summarized in Figure 4 below.

Figure 4



5

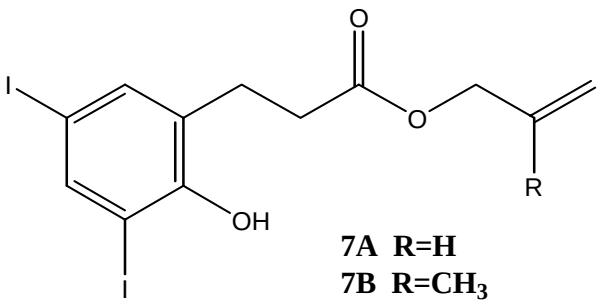


6

5A n = 1, R = R' = H	**25%**	**6A n = 1, R = R' = H**	**30%**
5B n = 1, R = CH_3, R' = H	**25%**	**6B n = 1, R = CH_3, R' = H**	**20%**
5C n = 2, R = R' = H	**45%**	**6C n = 2, R = R' = H**	**30%**
5D n = 2, R = CH_3, R' = H	**48%**	**6D n = 2, R = CH_3, R' = H**	**32%**
5E n = 2, R = H, R' = Ph	**60%**	**6E n = 2, R = H, R' = Ph**	**5%**

Treatment of compounds (**4A** and **4B**) with the more reactive electrophilic reagent bis(*sym*-collidine)iodine perchlorate,[10] BCIP, resulted in electrophilic aromatic substitution yielding the compounds (**7A** and **7B**) respectively, each in about 80% yield, Figure 5. Small quantities of the starting materials were also recovered from these reactions.

Figure 5



7A R=H
7B R=CH_3

Consistent with the reports of other investigators, we found that an average reaction time of about 20 hours was optimum for the cyclization reactions. Lower yields of the cyclization products were obtained at shorter reaction times, and reaction periods in excess of 36 hours tended to have a deleterious effect on the product purity as well as yields.

EXPERIMENTAL

IR spectra were recorded on a Perkin Elmer Spectrum 1000 FT-IR spectrophotometer. NMR spectra were recorded on a Bruker 400 MHz spectrometer with chemical shifts being reported in parts per million (δ) downfield from tetramethylsilane as the internal reference. GC/MS spectral analyses were performed on a Hewlett Packard G1800A GCD system. Elemental analyses were performed by Atlantic Microlab, Inc. (Norcross, GA).

Allyl (2-hydroxyphenyl)ethanoate (3A): A mixture of **1** (5.00 g, 33.0 mmol) and KOH (2.39 g, 36.0 mmol) in 50 mL of water was heated with stirring at 40 ^{o}C for 10 min. The water was removed *in vacuo* and the residue dissolved in 60 mL of DMF. Allyl bromide (4.39 g, 36.0 mmol) was added followed by stirring at rt for 20 h. The reaction mixture was mixed with brine (50 mL) and extracted with ethyl acetate (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, concentrated *in vacuo*, and the residue purified by column chromatography on silica gel with hexanes-ethyl acetate (5:1, v:v, R_f = 0.54) to give **3A** (6.1 g, 97%). IR (neat, cm^{-1}): 3416, 3077, 2846, 1713, 1648, 1597**.** ^{1}H NMR ($CDCl_3$, δ): 3.71 (s, 2H), 4.63 (d, *J* = 5.8 Hz, 2H), 5.30 (m, 2H), 5.90 (m, 1H), 6.89 (t, *J* = 7.4 Hz, 1H), 6.92 (d, *J* = 8.1 Hz, 1H), 7.10 (d, *J* = 7.5 Hz, 1H), 7.20 (dt, *J* = 1.4, 7.8 Hz, 1H), 7.32 (s, 1H). ^{13}C NMR ($CDCl_3$, δ): 38.2, 66.8, 118.0, 119.5, 121.0, 121.3, 129.6, 131.4, 131.8, 155.5, 173.9. MS (EI, *m/z*): 192 (M^+). *Anal.* Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.28; O, 24.97. Found: C, 68.45; H, 6.33; O, 25.20.

2-Methylpropenyl (2-hydroxyphenyl)ethanoate (3B): Compound (**3B**) was prepared in quantitative yield according the method outlined for **3A** above. IR (nujol, cm^{-1}): 3417, 3080, 2917, 2848, 1714, 1660, 1598, 1504, 1455, 1099, 754. mp 42-43 ^{0}C (EtOH-H_2O)**.** ^{1}H NMR ($CDCl_3$, δ): 1.58 (s, 3H), 3.73 (s, 2H), 4.57 (s, 2H), 4.89 (d, *J* = 1.4 Hz, 1H), 4.90 (d, *J* = 1.4 Hz, 1H), 6.89 (dt, *J* = 1.0, 7.4 Hz, 1H), 6.95 (dd, *J* = 1.5, 8.0 Hz, 1H), 7.12 (dd, *J* = 1.0, 7.5 Hz, 1H), 7.21 (dt, *J* = 1.5, 8.0 Hz, 1H), 7.27 (m, 1H). ^{13}C NMR ($CDCl_3$, δ): 19.8, 38.2, 69.3, 114.1, 118.0, 121.0, 121.3, 129.6, 131.4, 139.6, 155.5, and 173.9. MS (EI, *m/z*): 206 (M^+). *Anal.* Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84; O, 23.27. Found: C, 69.73; H, 6.88; O, 23.05.

Allyl 3-(2-hydroxyphenyl)propanoate (4A): A mixture of **2** (5.00 g, 33.7 mmol) and KOH (2.10 g, 37.1 mmol) dissolved in 50.0 mL of water was refluxed for 2 h. The water was removed *in vacuo*, and the resulting brown crystals dissolved in 50.0 mL of DMF. Allyl bromide (4.59 g, 38.0 mmol) was then added in one portion followed by vigorous stirring for 2 h at rt. The reaction mixture was combined with chilled brine (50.0 mL) and extracted with ether. The combined organic extracts was dried over $MgSO_4$ and concentrated *in vacuo* to a pale-yellow oil, which was purified by column chromatography on silica

gel with hexanes-ethyl acetate (5:1, v:v, R_f = 0.4) to give **4A** (6.6 g, 95%, for both steps). IR (neat, cm^{-1}): 3409, 3073, 3036, 2940, 2918, 1711, 1609, 1594. ^{1}H NMR ($CDCl_3$, δ): 2.15 (s, 1H), 2.73 (t, *J* = 6.8 Hz, 2H), 2.92 (t, *J* = 6.8 Hz, 2H), 4.57 (ddd, *J* = 1.3, 1.3, 5.8 Hz, 2H), 5.20 (ddt, *J* = 1.2, 1.2, 11.6 Hz, 1H), 5.27 (ddt, *J* = 1.5, 1.5, 17.2 Hz, 1H), 5.85 (ddt, *J* = 5.8, 10.4, 17.2 Hz, 1H), 6.83 (m, 2H), 7.07 (m, 2H). ^{13}C NMR ($CDCl_3$, δ): 25.5, 35.5, 65.5, 116.5, 118.5, 120.5, 127.0, 127.8, 130.5, 131.5, 154.0, 175.0. MS (EI, *m/z*): 206 (M^+). *Anal.* Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.21; H, 6.69.

2-Methylpropenyl 3-(2-hydroxyphenyl)propanoate (4B): Compound (**4B**) was prepared in 90% yield (both steps) according to the method outlined above for **4A.** IR (neat, cm^{-1}): 3415, 3079, 3037, 2975, 2938, 2918, 2871, 1713, 1659, 1609, 1595, 1505, 905, 754. ^{1}H NMR ($CDCl_3$, δ ppm): 1.71 (s, 3H), 2.76 (t, *J* = 6.7 Hz, 2H), 2.93 (t, *J* = 6.7 Hz, 2H), 4.50 (s, 2H), 4.91 (dt, *J* = 0.7, 8.7 Hz, 1H); 4.93 (dt, *J* = 1.1, 8.7 Hz, 1H), 6.85 (m, 2H), 7.09 (m, 2H). ^{13}C NMR ($CDCl_3$, δ): 19.6, 25.0, 35.2, 68.6, 113.5, 117.0, 121.0, 127.3, 128.1, 130.6, 139.7, 154.4, 175.3. MS (EI, *m/z*): 220 (M^+). *Anal.* Calcd for $C_{13}H_{16}O_3$: C, 70.87; H, 7.33. Found: C, 70.53; H, 7.32.

(*E*)-1-Phenylpropenyl 3-(2-hydroxyphenyl)propanoate (4C): Compound (**4C**) was also prepared in 95% yield (both steps) according to the method outlined for **4A.** IR (neat, cm^{-1}): 3334, 3040, 2960, 2847, 1731, 1599, 1494, 1449, 967, 692. ^{1}H NMR ($CDCl_3$, δ ppm): 2.77 (t, *J* = 6.8 Hz, 2H), 2.93 (t, *J* = 6.2 Hz, 2H), 4.74 (dd, *J* = 1.0, 6.6 Hz, 2H), 6.23 (dt, *J* = 6.5, 15.9 Hz, 1H), 6.62 (d, *J* = 15.9 Hz, 1H), 6.87 (t, *J* = 8.0 Hz, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 7.00 (s, 1H), 7.10 (m, 2H), 7.30 (m, 5H). ^{13}C NMR ($CDCl_3$, δ): 25.0, 35.6, 66.3, 117.6, 121.3, 123.0, 127.1, 127.6, 128.4, 128.6, 129.0, 131.0, 135.1, 136.4, 137.6, 152.1, 154.7, 175.7. MS (EI, *m/z*): 282 (M^+). *Anal*. Calcd for $C_{18}H_{18}O_3$: C, 76.56; H, 6.43; O, 17.01. Found: C, 76.04; H, 6.48; O, 17.41.

Lactones (5A and 6A): A solution of compound (**3A**) (2.69 g, 14.0 mmol) and iodine (5.33 g, 21.0 mmol) in 50.0 mL of CH_3CN containing sodium bicarbonate (1.76 g, 21.0 mmol), was stirred at rt under a positive nitrogen atmosphere for 20 h. The reaction mixture was shielded from light for the duration of the reaction. After mixing with $Na_2S_2O_3$ (10%, 75.0 mL), the mixture was extracted with CH_2Cl_2. The organic layer was dried ($MgSO_4$) and then concentrated *in vacuo* to a yellow syrup. The product was purified by chromatography on silica gel with hexanes-ethyl acetate (5:1, v:v, R_f = 0.57) to give the lactones as an inseparable mixture with a composition of 25% **5A** and 30% **6A,** determined by GC analysis**.** IR (neat, cm^{-1}): 3026, 2965, 2948, 1737, 1586, 1522, 1468, 1208, 1140, 918, 748. ^{1}H NMR ($CDCl_3$, δ ppm): 3.17 (dd, *J* = 7.6, 10.1 Hz, 1H), 3.23 (dd, *J* = 4.6, 10.1 Hz, 1H), 3.29 (dd, *J* = 9.3, 9.7 Hz, 1H), 3.39 (s, 2H), 3.40 (s, 2H), 3.42 (dd, *J* = 4.5, 9.6 Hz, 1H), 3.93 (dd, *J* = 4.6, 8.3 Hz, 1H), 3.97

(dd, *J* = 7.3, 7.3 Hz, 1H), 4.34 (d, *J* = 8.2 Hz, 1H), 4.35 (d, *J* = 8.2 Hz, 1H), 4.56 (m, 2H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.76 (d, *J* = 8.3 Hz, 1H), 6.86 (t, *J* = 7.4 Hz, 1H), 7.13 (m, 4H). ^{13}C NMR ($CDCl_3$, δ): 37.5, 37.7, 70.3, 71.1, 76.2, 78.0, 109.7, 109.8, 121.4, 121.5, 124.4, 124.5, 124.6, 124.7, 124.8, 124.9, 128.6, 128.7, 131.9, 132.0, 156.8, 157.0. MS (EI, *m/z*): 318 (M^+). *Anal.* Calcd for $C_{11}H_{11}O_3I$: C, 41.53; H, 3.49; O, 15.09; I, 39.89. Found: C, 41.30; H, 3.46; O, 15.12; I, 39.87.

Lactones (5B and 6B): Compounds (**5B** and **6B**) were prepared according to the method outlined for **5A,** and obtained in a combined yield of about 45%. Flash chromatographic purification on silica gel using hexanes-ethyl acetate (5:1, v:v, R_f = 0.55) afforded a pure sample of **5B.** Analytical data for **5B** are as follows: IR (neat, cm^{-1}): 3050, 2918, 2849, 1737, 1598, 1462, 1033, 970, 740. ^{1}H NMR ($CDCl_3$, δ ppm): 1.70 (s, 3H), 3.28 (d, *J* = 10.4 Hz, 1H), 3.34 (d, *J* = 10.3 Hz, 1H), 3.38 (d, *J* = 16.7 Hz, 1H), 3.45 (d, *J* = 17.2 Hz, 1H), 4.07 (d, *J* = 8.5 Hz, 1H), 4.22 (d, *J* = 8.5 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.87 (t, *J* = 7.7 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.14 (d, *J* = 7.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, δ): 13.3, 24.9, 38.2, 74.0, 81.8, 109.6, 121.2, 124.4, 124.7, 128.5, 131.8, 157.9. MS (EI, *m/z*): 332 (M^+). *Anal.* Calcd for $C_{12}H_{13}O_3I$: C, 43.40; H, 3.95; O, 14.45; I, 38.21. Found: C, 42.92; H, 3.86; O, 14.29; I, 38.72.

Lactones (5C and 6C): Compounds (**5C** and **6C**) were similarly prepared by the general method for iodolactonization as exemplified in the preparation of **5A. 5C** IR (neat, cm^{-1}): 3038, 2947, 2915, 2837, 1731, 1583, 1487, 1456, 1213, 1112, 1056, 983, 925, 877, 755. ^{1}H NMR ($CDCl_3$, δ ppm): 2.21 (ddd, *J* = 2.1, 7.2, 7.2 Hz, 2H), 3.00 (t, *J* = 7.0 Hz, 2H), 3.23 (dd, *J* = 8.0, 10.1, Hz, 1H), 3.31 (dd, *J* = 4.3, 10.1 Hz, 1H), 3.97 (dd, *J* = 4.6, 8.3, Hz, 1H), 4.45 (ddd, *J* = 0.4, 6.9, 8.2, Hz, 1H), 4.66 (dddd, *J* = 4.5, 4.5, 6.9, 8.8 Hz, 1H), 6.81 (dd, *J* = 1.0, 8.2, Hz, 1H), 6.90 (ddd, *J* = 1.2, 7.4, 7.4, Hz, 1H), 7.10 (dd, *J* = 1.0, 7.2, Hz, 1H), 7.12 (ddd, *J* = 1.6, 7.2, 7.2, Hz, 1H). ^{13}C NMR ($CDCl_3$, δ): 6.6, 24.4, 29.4, 70.0, 76.0, 117.2, 120.7, 121.6, 121.7, 127.9, 129.3, 153.2. MS (EI, *m/z*): 332 (M^+). *Anal.* Calcd for $C_{12}H_{13}O_3I$: C, 43.40; H, 3.95. Found: C, 43.58; H, 3.96. **6C** IR (neat, cm^{-1}): 3024, 2949, 2917, 2848, 1737, 1583, 1487, 1456, 1215, 1112, 1057, 983, 921, 877, 755. ^{1}H NMR ($CDCl_3$, δ ppm): 2.13 (t, *J* = 7.1 Hz, 2H), 2.95 (t, *J* = 7.0 Hz, 2H), 3.31 (dd, *J* = 9.6, 10.1 Hz, 1H), 3.42 (dd, *J* = 4.7, 9.4 Hz, 1H), 4.05 (dd, *J* = 7.2, 8.4 Hz, 1H), 4.35 (dd, *J* = 6.8, 8.4 Hz, 1H), 4.57 (dddd, *J* = 4.7, 6.9, 6.9, 10.3 Hz, 1H), 6.78 (dd, *J* = 0.9, 8.1 Hz, 1H), 6.88 (ddd, *J* = 1.2, 7.4, 7.4 Hz, 1H), 7.07 (dd, *J* = 0.8, 7.5 Hz, 1H), 7.10 (ddd, *J* = 1.4, 7.2, 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, δ): 6.8, 24.3, 29.2, 70.9, 77.5, 117.2, 120.9, 121.6, 121.7, 127.9, 129.3, 153.2. MS (EI, *m/z*): 332 (M^+). *Anal.* Calcd for $C_{12}H_{13}O_3I$: C, 43.40; H, 3.95. Found: C, 43.72; H, 3.98.

Lactones (5D and 6D): These were similarly prepared by the general iodolactonization method**. 5D** IR

(neat, cm^{-1}): 3024, 2976, 2917, 2846, 1731, 1612, 1583, 1487, 1455, 1211, 1056, 875, 753, 695. ^1H NMR ($CDCl_3$, δ ppm): 1.57 (s, 3H), 2.13 (ddd, *J* = 3.4, 6.7, 7.5 Hz, 2H), 2.95 (ddd, *J* = 9.3, 14.0, 14.0 Hz, 2H), 3.41 (d, *J* = 9.8 Hz, 1H), 3.56 (d, *J* = 9.9 Hz, 1H), 3.93 (d, *J* = 8.3 Hz, 1H), 4.27 (d, *J* = 8.3 Hz, 1H), 6.79 (dd, *J* = 1.1, 8.2 Hz, 1H), 6.88 (ddd, *J* = 1.2, 7.4, 7.4 Hz, 1H), 7.08 (dd, *J* = 1.0, 7.9 Hz, 1H), 7.10 (ddd, *J* = 0.8, 7.3, 7.3 Hz, 1H). ^{13}C NMR ($CDCl_3$, δ): 13.2, 24.0, 25.0, 29.7, 74.7, 81.7, 117.0, 120.5, 121.3, 121.4, 127.6, 129.0, 153.1. MS (EI, *m/z*): 346 (M^+). *Anal*. Calcd for $C_{13}H_{15}O_3I$: C, 45.09; H, 4.37; O, 13.87; I, 36.68. Found: C, 45.16; H, 4.41; O, 13.79; I, 36.64. **6D** IR (neat, cm^{-1}): 3028, 2977, 2918, 1732, 1612, 1584, 1488, 1455, 1238, 1116, 1056, 947, 877, 754. ^1H NMR ($CDCl_3$, δ ppm): 1.66 (s, 3H), 2.16 (ddd, *J* = 6.6, 6.7, 7.8 Hz, 2H), 2.94 (ddd, *J* = 9.2, 14.0, 14.0 Hz, 2H), 3.23 (d, *J* = 10.4 Hz, 1H), 3.30 (d, *J* = 10.3 Hz, 1H), 4.09 (d, *J* = 8.5 Hz, 1H), 4.16 (d, *J* = 8.4 Hz, 1H), 6.78 (dd, *J* = 1.0, 8.1 Hz, 1H), 6.86 (ddd, *J* = 1.1, 7.4, 7.4 Hz, 1H), 7.08 (m, 2H). ^{13}C NMR ($CDCl_3$, δ ppm): 13.8, 24.0, 25.0, 29.4, 74.6, 81.6, 116.9, 120.4, 121.2, 121.3, 127.4, 128.9, 153.0. MS (EI, *m/z*): 346 (M^+). *Anal*. Calcd for $C_{13}H_{15}O_3I$: C, 45.09; H, 4.37; O, 13.87; I, 36.68. Found: C, 45.12; H, 4.43; O, 13.82; I, 36.67.

Lactones (5E and 6E): These were similarly prepared by the general iodolactonization method**.** A pure sample of **5E** was obtained as a grey solid by recrystallization of the crude product from 95% aqueous ethanol; mp 86 ^oC (decomp). **5E** IR (nujol, cm^{-1}): 3019**,** 2972, 1732, 1583, 1452, 1207, 1120, 1050, 759. ^1H NMR ($CDCl_3$, δ ppm): 2.11 (ddd, *J* = 6.7, 13.3, 13.3 Hz, 1H), 2.86 (ddd, *J* = 8.7, 15.8, 15.8 Hz, 1H), 4.10 (dd, *J* = 5.0, 11.2 Hz, 1H), 4.33 (ddd, *J* = 5.0, 10.9, 10.9 Hz, 1H), 4.64 (dd, *J* = 11.4, 11.4 Hz, 1H), 5.41 (d, *J* = 10.8 Hz, 1H), 6.92 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.99 (d, *J* = 8.1 Hz, 1H), 7.06 (d, *J* = 7.5 Hz, 1H), 7.17 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.37 (m, 5H). ^{13}C NMR ($CDCl_3$, δ): 23.2, 27.9, 30.2, 31.0, 67.2, 104.0, 111.0, 117.1, 121.4, 121.9, 122.5, 127.7, 128.3, 128.7, 129.4, 129.5, 138.5, 152.3. MS (EI, *m/z*): 408 (M^+). *Anal*. Calcd for $C_{18}H_{17}O_3I$: C, 52.94; H, 4.20; O, 11.76; I, 31.10. Found: C, 53.71; H, 4.26; O, 11.18; I, 30.42.

Aryl iodide (7A): A 100 mL RB flask, equipped for magnetic stirring, was flame-dried under a stream of dry nitrogen, and charged with a solution of bis(*sym*-collidine)silver(I) perchlorate (2.96 g, 6.60 mmol) dissolved in 50.0 mL of dry CH_2Cl_2. Iodine (1.68 g, 6.60 mmol) was next added and the mixture was stirred at rt for 30 min under nitrogen. A solution of compound (**4A**) (1.32 g, 6.00 mmol) dissolved in 15 mL of CH_2Cl_2 was then added via syringe with continued stirring for 20 h at rt. The reaction mixture was suction-filtered, rinsing the silver iodide residue with about 60.0 mL of CH_2Cl_2. The filtrate was successively washed with sodium thiosulfate solution (75.0 mL, 10.0%, hydrochloric acid (75.0 mL, 1.00 M) and finally saturated aqueous sodium bicarbonate solution (75.0 mL). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to afford the crude product as a light yellow syrup.

Chromatographic purification using hexanes-ethyl acetate (2:1, v:v, R_f = 0.55) afforded a pure sample of **7A** as a pale-yellow syrup which solidified on standing overnight at rt (2.21 g, 80% , mp 42 – 44 ^oC). IR (nujol, cm^{-1}): 3472, 3272, 3079, 2971, 2947, 2843, 1737, 1659, 1546, 1216, 1126, 905. ^1H NMR ($CDCl_3$, δ ppm): 2.72 (t, *J* = 6.9 Hz, 2H), 2.93 (t, *J* = 6.9 Hz, 2H), 4.62 (ddd, *J* = 1.3, 1.3, 5.8 Hz, 2H), 5.26 (ddt, *J* = 1.2, 1.2, 11.6 Hz, 1H), 5.32 (ddt, *J* = 1.5, 1.5, 17.2 Hz, 1H), 5.91 (ddt, *J* = 5.8, 10.4, 17.2 Hz, 1H), 7.40 (d, *J* = 2.0 Hz, 1H); 6.74 (s, 1H), 7.85 (d, *J* = 2.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, δ ppm): 26.3, 34.6, 66.3, 83.4, 88.4, 119.3, 130.2, 132.1, 139.9, 144.5, 153.7, 174.3. MS (EI, *m/z*): 458 (M^+). *Anal.* Calcd for $C_{12}H_{12}O_3I_2$: C, 31.47; H, 2.64. Found: C, 32.47; H, 2.70.

Iodide (7B): Compound (**7B**) was prepared according to the method outlined for compound (**7A**), and was also obtained as a yellow solid after chromatography with hexanes-ethyl acetate (2:1, v:v, R_f = 0.49) in 78% yield, (mp 32 – 34 ^oC). IR (nujol, cm^{-1}): 3474, 3273, 3079, 2973, 2939, 2909, 2871, 1731, 1658, 1577, 1546, 1233, 1043, 906, 861, 652. ^1H NMR ($CDCl_3$, δ ppm): 1.73 (s, 3H), 2.71 (t, *J* = 6.9 Hz, 2H), 2.91 (t, *J* = 6.9 Hz, 2H), 4.51 (s, 2H), 4.92 (dt, *J* = 0.7, 8.7 Hz, 1H), 4.94 (dt, *J* = 1.1, 8.7 Hz, 1H), 6.75 (s, 1H), 7.37 (d, *J* = 2.0 Hz, 1H), 7.82 (d, *J* = 2.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, δ ppm): 19.7, 26.6, 68.6, 83.2, 88.2, 113.7, 122.6, 130.0, 139.9, 145.5, 153.5, 174.1. MS (EI, *m/z*): 472 (M^+). *Anal.* Calcd for $C_{13}H_{14}O_3I_2$: C, 33.06; H, 2.99. Found: C, 34.52; H, 3.13.

ACKNOWLEDGEMENTS

We acknowledge the support of St. John's University through the seed grant venture capital fund.

REFERENCES

1. J. Liebnan and A. Greenberg, *Chem. Rev*., 1976, **76**, 311.
2. M. Nagarajan, V. Kumar, and B. Rao, *Tetrahedron*, 1999, **55**, 12349.
3. G. Rousseau and F. Homsi, *Chem. Soc. Rev*., 1997, **26**, 435.
4. J. Bottaro and G. Berchtold, *J. Org. Chem*., 1980, **45**, 1176.
5. J. Baldwin, *J. Chem. Soc., Chem. Commun*., 1976, 734.
6. B. Simonot and G. Rousseau, *J. Org. Chem*., 1994, **59**, 5912.
7. G. Illuminati and L. Mandolini, *Acc. Chem. Res*., 1981, **14**, 95.
8. V. Box and D. Brown, *Heterocycles*, 1991**, 32**, 1273.
9. D. Brown, E. Griffith, and L. Krishnamurthy, *J. Undergrad. Chem. Res*., 2003, **3**, 121.
10. C. Nichols and J. Parks, *J. Undergrad. Chem. Res*., 2002, **1**, 27; R. Evans, J. Magee, and J. Schauble, *Synthesis*, 1988, 862.