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PII: S0040-4020(16)31252-2

DOI: 10.1016/j.tet.2016.11.072

Reference: TET 28286

To appear in: *Tetrahedron*

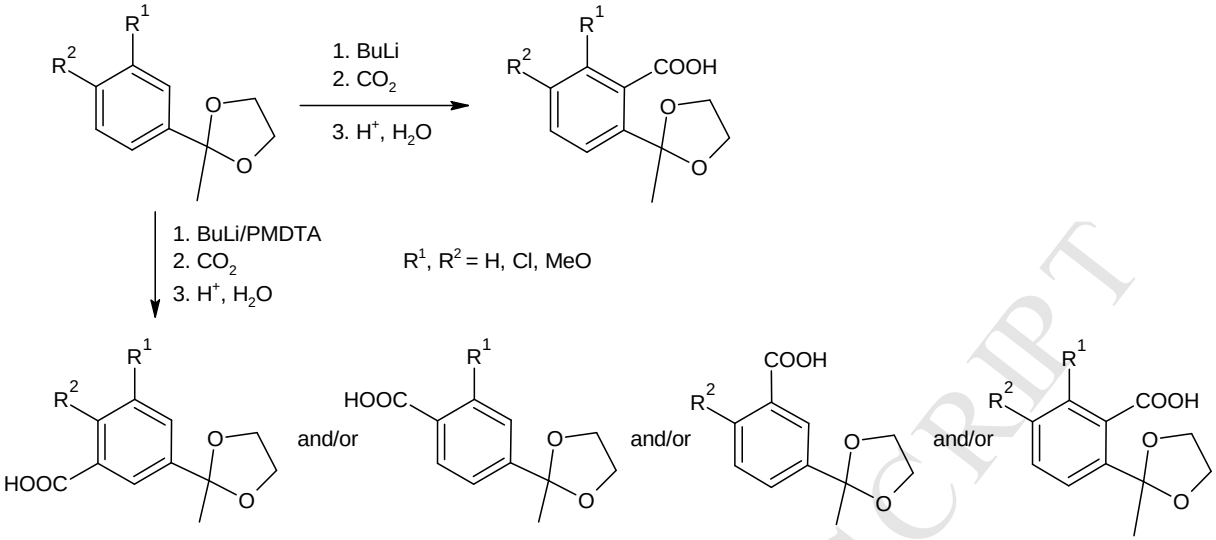
Received Date: 29 August 2016

Revised Date: 14 November 2016

Accepted Date: 28 November 2016

Please cite this article as: Nyulasi B, Németh A, Porcs-Makkay M, Kupai J, Lukács G, Simig G, Volk B, Lithiation of 2-aryl-2-methyl-1,3-dioxolanes with PMDTA-complexed butyllithium, *Tetrahedron* (2016), doi: 10.1016/j.tet.2016.11.072.

Graphical abstract



Lithiation of 2-aryl-2-methyl-1,3-dioxolanes with PMDTA-complexed butyllithium

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Abstract

The metalation of chloro- and methoxy-substituted acetophenone ketals with butyllithium (BuLi) and with *N,N,N',N",N"*-pentamethyldiethylenetriamine-complexed butyllithium (BuLi/PMDTA) has been investigated. The lithio species thus generated were carboxylated to benzoic acids. Lithiations with BuLi occurred regioselectively *ortho* to the ketal substituent. When using BuLi/PMDTA, a regiodivergent behavior has generally been found in the lithiations. However, in some cases a significant selectivity was observed, enabling the

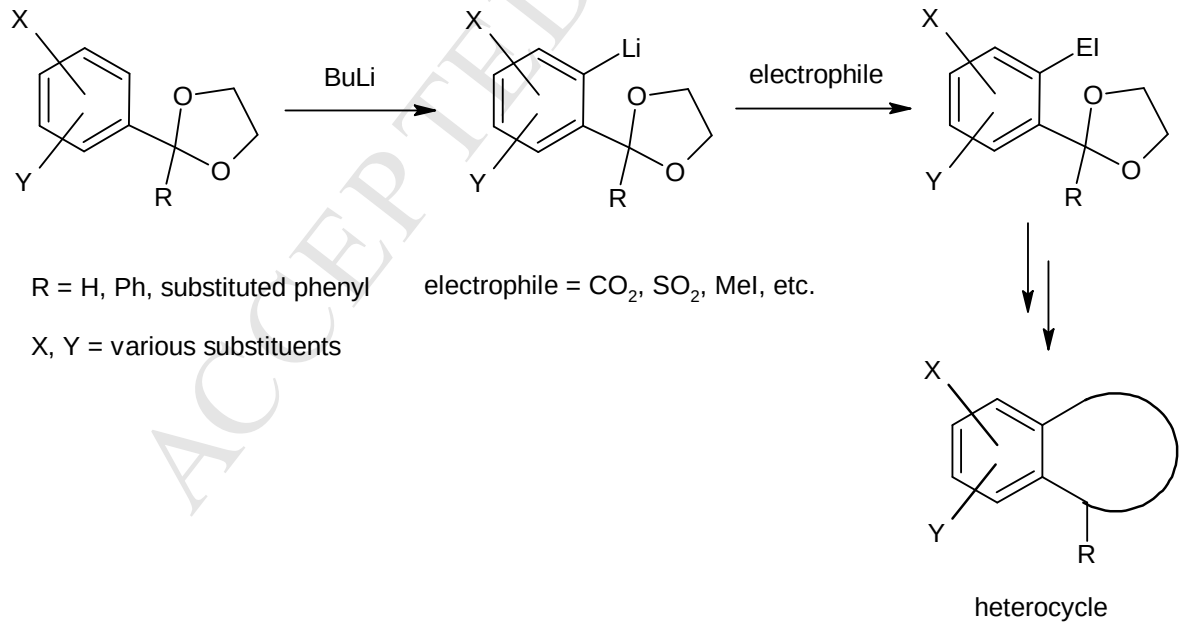
preparation of the main regioisomer, exhibiting a new substitution pattern, with reasonable yield.

Keywords

Metalation; Lithiation; Regioselectivity; Acetophenone Ketals; Carboxylation

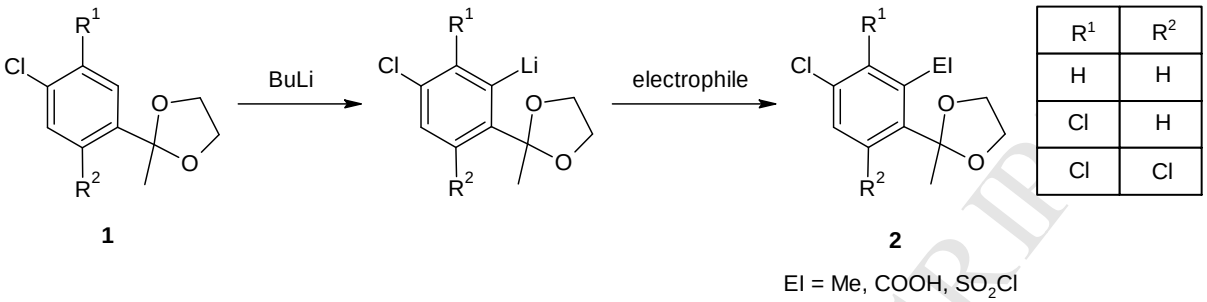
Introduction

In the course of our work in the field of medicinal chemistry we became interested in the preparation of various heterocycles accessible from *ortho*-functionalized benzaldehyde, benzophenone and acetophenone precursors. Our approach for the synthesis of these key intermediates is based on the well-known *ortho*-directing ability of aromatic acetals and ketals in lithiation reactions.[1–4] We have reported in detail on the synthesis of *ortho*-functionalized benzaldehyde[5] and benzophenone[6] derivatives by *ortho*-lithiation of the corresponding ethylene ketals with butyllithium (BuLi) and subsequent treatment with electrophiles (Scheme 1). Regioselectivities of the lithiation reaction of benzophenone ethylene ketals exhibiting variously substituted phenyl rings with BuLi complexed with *N*,*N*,*N'*,*N"*,*N"*-pentamethyldiethylenetriamine (BuLi/PMDTA) were also investigated.[7]



Scheme 1. *Ortho*-lithiation of acetophenone or benzophenone ethylene ketals and subsequent transformation into various heterocycles

Regarding the *ortho*-functionalization of acetophenone ketals, some preliminary results were previously disclosed: lithiation of 2-(4-chloroaryl)-2-methyl-1,3-dioxolanes (**1**) with BuLi followed by treatment with various electrophiles gave the expected products **2** (Scheme 2).[8]



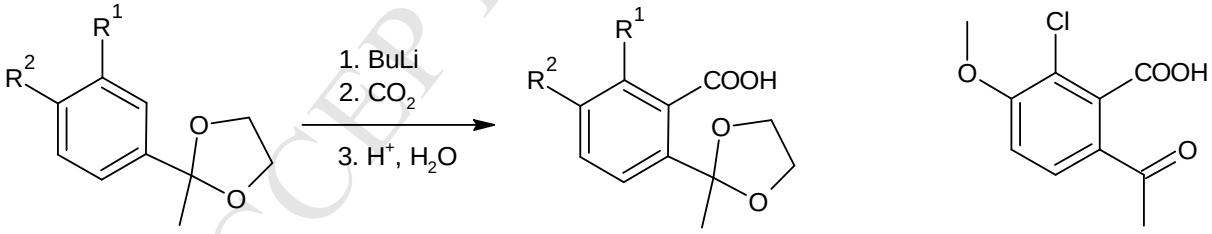
R^1	R^2
H	H
Cl	H
Cl	Cl

Scheme 2. Lithiation of 2-(4-chloroaryl)-2-methyl-1,3-dioxolanes (**1**) reported previously

We now report the extension of this work to new substrates and to the lithiation of acetophenone ketals with BuLi complexed with PMDTA.

Results and discussion

Ethylene ketals **3a−d** and **3h** are known from the literature (Scheme 3).[9–12] Ketals **3f** and **3g** were prepared starting from known acetophenones by conventional methods. Compound **3e** was prepared by *O*-methylation of the corresponding phenol, which was obtained as discussed later.



3,4	R^1	R^2	Reaction conditions	Yield (%)
a	MeO	H	diethyl ether, 1.6 eq BuLi, 0 °C, 4 h	77
b	Cl	H	THF, 1.6 eq BuLi, −78 °C, 2 h	74
c	H	MeO	diethyl ether, 1.3 eq BuLi, 0 °C, 2 h	no reaction
d	H	Cl	THF, 1.6 eq BuLi, 0 °C, 2 h	91[a]
e	MeO	Cl	diethyl ether, 1.6 eq BuLi, 0 °C, 2 h	85
f	Cl	MeO	THF, 1.6 eq BuLi, −78 °C, 2 h	59[b]

g	MeO	MeO	diethyl ether, 1.5 eq BuLi, 0 °C, 1 h	53[c]
h	Cl	Cl	THF, 1.6 eq BuLi, −78 °C, 2 h	91[a]

[a] Described in ref. 8.

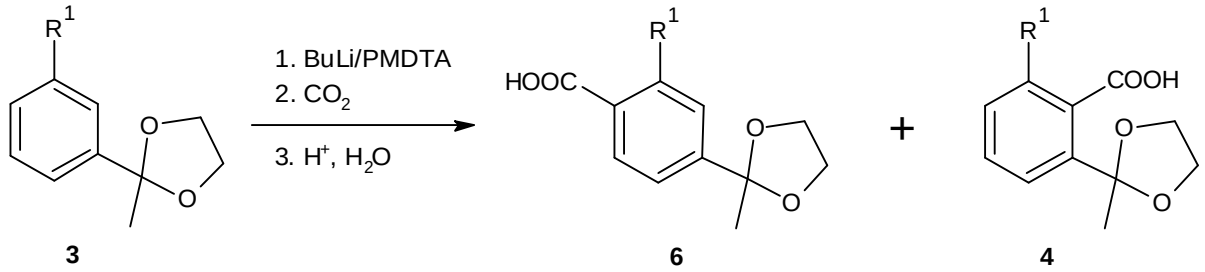
[b] Isolated as the corresponding ketone **5** .

[c] Acidification with citric acid instead of HCl.

Scheme 3. Lithiation of acetophenone ethylene ketals with BuLi into the *ortho* position of the ketal moiety

Lithiation of compounds **3a**, **3e** and **3g** (exhibiting a methoxy group in the *meta* position to the 1,3-dioxolan-2-yl group) with BuLi in diethyl ether at 0 °C occurred at the common *ortho* position of the methoxy and ketal groups, as demonstrated by the formation of the corresponding carboxylic acids **4** after treatment with dry ice (Scheme 3). *para*-Methoxyketal **3c** did not react with BuLi under the applied conditions. Lithiation of the *meta*-chloroketals **3b** and **3f** with BuLi was carried out at −78 °C in order to avoid the generation of benzynes and subsequent treatment with dry ice gave benzoic acids **4b** and **4f**. In certain cases the ketal moiety (especially those exhibiting a methoxy group in the *para* position of the 1,3-dioxolan-2-yl group, e.g. **4f**) partially hydrolyzed, when using aqueous hydrochloric acid in the course of the work-up process. In such cases the hydrolysis was completed and the corresponding acetyl derivative (**5**) was prepared. In order to avoid hydrolysis of the ketal moiety of product **4g**, aqueous citric acid solution was used for acidification of the reaction mixture.

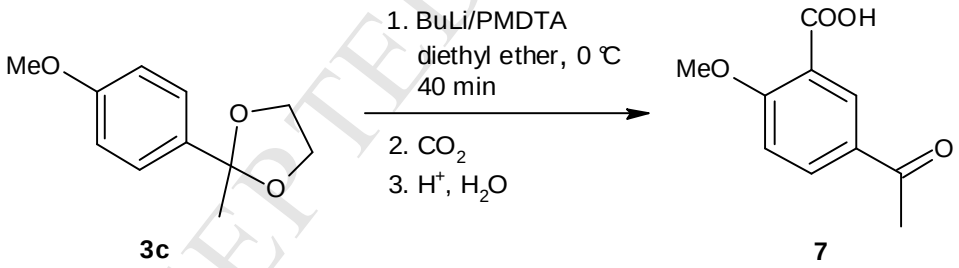
Next, lithiation of acetophenone ketals **3** with PMDTA-complexed BuLi (a reagent frequently used by Schlosser et al. for the lithiation of halogen-adjacent sites)[13] was studied in order to find routes to acetophenone derivatives with new substitution patterns by achieving alternative regiochemistry of the lithiation, compared to BuLi. Lithiation of ketals **3a** and **3b** with BuLi complexed to PMDTA, followed by carboxylation afforded a mixture of acids **6a**,**b** and **4a**,**b** with low yield in a ratio of 68 : 32 in both cases (an accidental coincidence), as indicated by the ^{1}H NMR spectroscopic analysis of the product mixture (Scheme 4). The regioselectivity is likely to be influenced by relative acidities and steric accessibilities of the two positions. In both reactions, the starting material could be isolated indicating an incomplete lithiation. When longer reaction times were applied, the total yield could not be improved and the ratio of products **6** and **4** did not change significantly, while more and more unidentified decomposition products appear.



3,4,6	R^1	Reaction conditions	Yield (%)	6 : 4
a	MeO	diethyl ether, 1.6 eq BuLi/PMDTA, 0 °C, 25 min	22	68 : 32
b	Cl	THF, 1.6 eq BuLi/PMDTA, −78 °C, 30 min	47	68 : 32

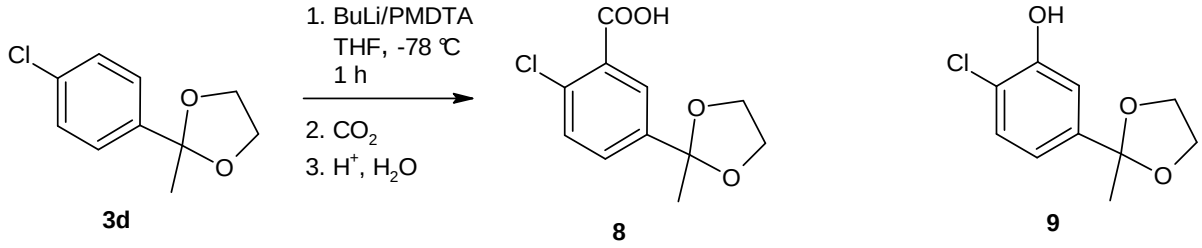
Scheme 4. Lithiation of *meta*-substituted acetophenone ethylene ketals with BuLi/PMDTA leading to mixtures of regioisomers

Lithiation of *para*-methoxy substituted ketal **3c** with PMDTA-complexed BuLi followed by carboxylation afforded benzoic acid **7** with poor yield (20%) after acidic work-up (Scheme 5). Formation of the other regioisomer, indicating the occurrence of lithiation *ortho* to the ketal group, could not be detected in the crude product mixture. The yield of product **7** could not be improved by applying longer reaction times.



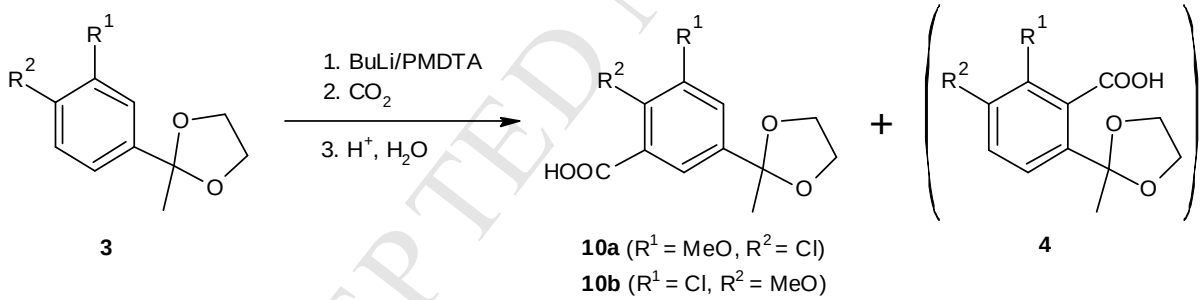
Scheme 5. Regioselective lithiation of *para*-methoxy substituted ketal **3c** with BuLi/PMDTA

Lithiation of *para*-chloro substituted ketal **3d** with BuLi complexed to PMDTA occurred exclusively *ortho* to the chloro substituent as demonstrated by the formation of benzoic acid **8** in good yield (70%, Scheme 6). Similar lithiation of ketal **3d** followed by reaction with triisopropyl borate and hydrogen peroxide gave phenol **9** with 41% yield, which served as the precursor for the synthesis of ketal **3e**. In this case, BuLi/PMDTA promotes hydrogen-lithium exchange at the most acidic site, i.e. adjacent to the halogen atom.[14]



Scheme 6. Regioselective lithiation of *para*-chloro substituted ketal **3d** with BuLi/PMDTA

A high regioselectivity was also observed in the lithiation reaction of chloro-methoxy substituted ketals **3e** and **3f** with BuLi/PMDTA. The metalation occurred mainly at the uncongested site *meta* to the ketal group. ^{1}H NMR spectroscopic analysis of the crude product obtained after carboxylation indicated that only small amounts of acids **4e** and **4f** (4 and 8%, respectively) were formed beside the main products **10a** and **10b** (Scheme 7). The result obtained with compound **3e** is in accord with that observed with derivative **3d**. The influence of the methoxy substituent on the chlorine adjacent site is negligible. The significantly more effective lithiation at the methoxy adjacent site of compound **3f**, when compared with derivative **3c**, can be explained by the meta-acidifying effect of the chloro substituent.[6,15]

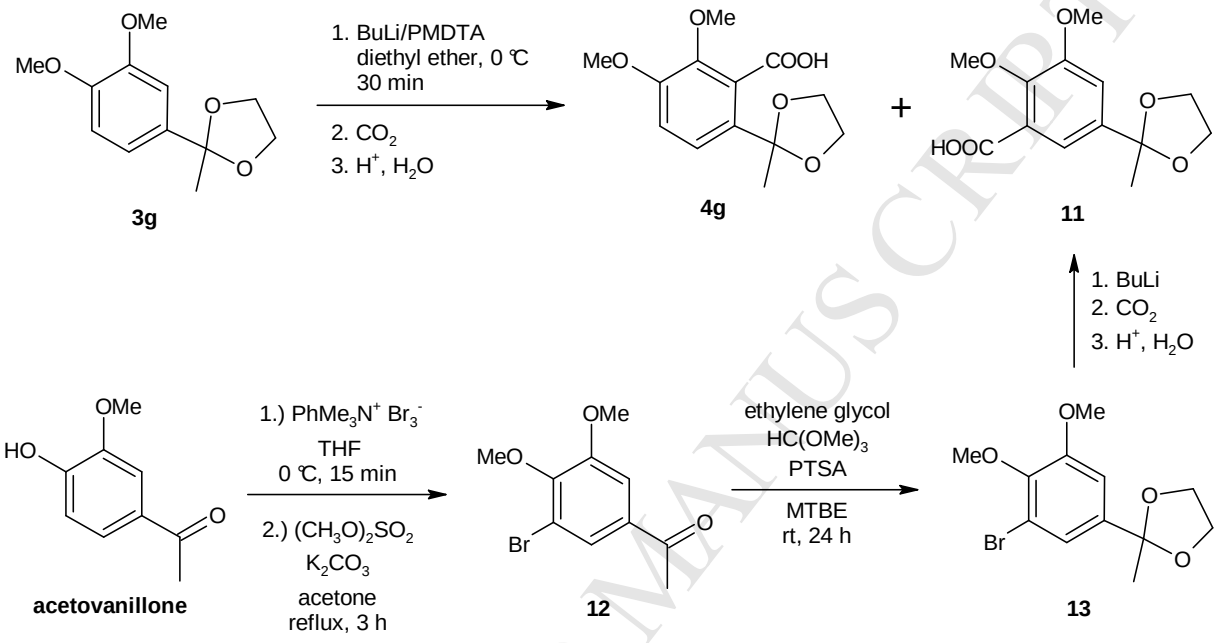


3,4	R^1	R^2	Reaction conditions	Product	Yield (%)
e	MeO	Cl	THF, 1.6 eq BuLi/PMDTA, −78 °C, 20 min	**10a**	60
f	Cl	MeO	THF, 1.6 eq BuLi/PMDTA, −78 °C, 1 h	**10b**	53

Scheme 7. Regioselective lithiation of chloro-methoxy substituted ketals **3e,f** with BuLi/PMDTA

3,4-Dimethoxy substituted ketal **3g** dissolved in diethyl ether was lithiated with PMDTA-complexed BuLi at 0 °C for 30 min. ^{1}H NMR spectroscopic analysis of the product mixture (yield 34%) obtained after carboxylation and work-up proved the presence of products **11** and

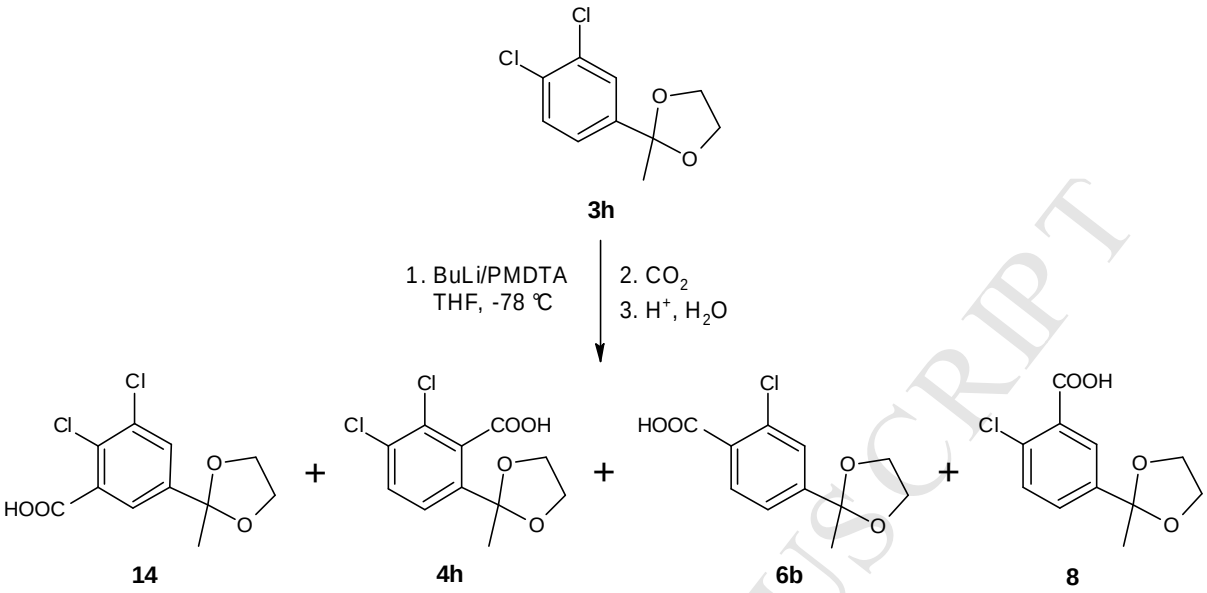
4g in a 39 : 61 ratio (Scheme 8). An authentic sample of compound **11** was prepared by transformation of acetophenone **12** to ketal **13** using ethylene glycol in the presence of trimethyl orthoformate and *para*-toluenesulfonic acid (PTSA), and subsequent carboxylation via bromine-lithium exchange. Acetophenone **12** was prepared from the natural compound acetovanillone via a bromination-methylation sequence.[16]



Scheme 8. Lithiation of 3,4-dimethoxy substituted ketal **3g** with BuLi/PMDTA and alternative synthesis of minor product **11**

Treatment of 3,4-dichloro substituted ketal **3h** with BuLi/PMDTA at 0 °C for 30 min followed by carboxylation resulted in a complex mixture of benzoic acids, isolated in an overall yield of 66% (Scheme 9). The results obtained in our hands in the lithiation reactions of ketal **3h** with BuLi and BuLi/PMDTA are in agreement with the expectations based on the analogous studies with 1,2- and 1,3-dichlorobenzene:[17] lithiation of 3,4-dichloroketal **3h** with BuLi occurred at the common *ortho* position of the chloro and ketal groups (yield of the carboxylated product 91%, see Scheme 3),[8] while the main product **14** obtained with BuLi/PMDTA indicated lithiation at the most acidic uncongested site. In addition to the major and minor dichloro derivatives **14** and **4h**, chlorine-lithium exchange products **6b** and **8** were also formed. Comparison of the ^{1}H NMR spectra of the authentic samples of the products with that of the product mixture, the ratio of the products formed proved to be **14** : **4h** : **6b** : **8** = 61 : 18 : 11 : 10. A similar chlorine-lithium exchange reaction was observed in the

BuLi/PMDTA lithiation reaction of benzophenone ketals containing a 3,4-dichlorophenyl ring.[7]



Scheme 9. Formation of regioisomers and chlorine-lithium exchange reactions observed during the lithiation of 3,4-dichloro substituted ketal **3h** with BuLi/PMDTA

Conclusions

Ortho-functionalized acetophenones can serve as potential precursors of various heterocycles. In the present study, chloro- and/or methoxy-substituted acetophenone ketals were synthesized and the regiochemistry of their lithiation with BuLi and BuLi/PMDTA was investigated. The lithiated intermediates were converted into the corresponding benzoic acids by trapping with carbon dioxide. Lithiations with BuLi occurred regioselectively *ortho* to the ketal substituent. Lithiations with BuLi/PMDTA afforded product mixtures indicating that metalation occurred at the *meta* or *para* position to the ketal group, in chlorine- or methoxy-adjacent positions as well. The occurrence of chlorine-lithium exchange reactions was also observed. Nevertheless, in some cases, the main regioisomer exhibiting a new substitution pattern could be isolated in reasonable yield.

Experimental section

Melting points were determined on a Büchi 535 capillary melting point apparatus. IR spectra were obtained on a Bruker IFS-113v FT spectrometer in KBr pellets or in neat. ^{1}H NMR and

^{13}C NMR spectra were recorded on a Varian Gemini 200 (200 and 50 MHz for ^{1}H and ^{13}C NMR spectra, respectively), a Bruker Avance III (400 and 100 MHz for ^{1}H and ^{13}C NMR spectra, respectively) or a Varian Unity Inova 500 spectrometer (500 and 125 MHz for ^{1}H and ^{13}C NMR spectra, respectively). $CDCl_3$ was used as solvent and tetramethylsilane (TMS) as internal standard. Chemical shifts (δ) and coupling constants (J) are given in ppm and in Hz, respectively. Elemental analyses were performed on a Perkin-Elmer 2400 analyzer. All unspecified reagents were purchased from commercial sources. Analytical samples were obtained by recrystallization from the solvents or solvent mixtures given in parentheses after the melting point ranges.

2-(4-Chloro-3-methoxyphenyl)-2-methyl-1,3-dioxolane (3e). To a mixture of potassium *tert*-butoxide (11.5 g, 0.103 mol) and DMF (60 mL) 2-chloro-5-(2-methyl-1,3-dioxolan-2-yl)phenol (**9**, 3.50 g, 16.3 mmol) was added at 0−5 °C under argon. After stirring for 10 min, methyl iodide (6.4 mL, 14.6 g, 0.103 mol) was added at the same temperature. The mixture was stirred for 2 h at ambient temperature. Ethyl acetate (250 mL) and water (60 mL) were added and the layers were separated. The organic layer was washed with aqueous sodium hydrogencarbonate solution (5 w/w%, 80 mL) and water (2×200 mL), dried ($MgSO_4$) and evaporated to give product **3e** (12.9 g, 88%) as a pale yellow solid, mp 61–62 °C (heptane). IR (KBr, cm^{-1}): 3441, 2987, 2897, 1584, 1486, 1395, 1201, 1054. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (1H, d, J=8.1 Hz), 7.06 (1H, d, J=1.8 Hz), 7.01 (1H, dd, J=8.1 Hz, J=1.8 Hz), 4.05–4.03 (2H, m), 3.92 (3H, s), 3.80–3.78 (2H, m), 1.64 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.8, 143.6, 129.9, 121.8, 118.1, 109.2, 108.4, 64.5, 56.1, 27.5. Anal. Calcd for $C_{11}H_{13}ClO_3$ (228.68): C 57.78, H 5.73, Cl 15.50%. Found: C 57.91, H 5.78, Cl 15.52%.

2-(3-Chloro-4-methoxyphenyl)-2-methyl-1,3-dioxolane (3f). A solution of 1-(3-chloro-4-methoxyphenyl)ethanone[12] (54.3 g, 0.294 mol), ethylene glycol (41.0 mL, 45.6 g, 0.735 mol) and *p*-toluenesulfonic acid monohydrate (1.00 g, 5.0 mmol) in toluene (440 mL) was refluxed in a Dean-Stark apparatus for 35 h. The reaction mixture was extracted with aqueous sodium hydrogen carbonate solution (5 w/w%, 300 mL) and water (300 mL), dried ($MgSO_4$) and evaporated resulting in a colorless oil, which crystallized by treating with petroleum ether to give **3f** (64.2 g, 96%) as a colorless solid, mp 42−43 °C (hexane). IR (KBr, cm^{-1}) 3049, 2992, 2894, 1499, 1380, 1260. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.48 (1H, d, J=2.2 Hz), 7.33 (1H, dd, J=8.5 Hz, J=2.2 Hz), 6.88 (1H, d, J=8.5 Hz), 4.06–3.99 (2H, m), 3.88 (3H, s), 3.81–3.74 (2H, m), 1.62 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.5, 136.7, 127.3, 124.6, 122.1, 111.6, 108.1, 64.4, 56.1, 27.5. Anal. Calcd for $C_{11}H_{13}ClO_3$ (228.68): C 57.77, H 5.73, Cl 15.50%. Found: C 57.58, H 5.69, Cl 15.20%.

2-(3,4-Dimethoxyphenyl)-2-methyl-1,3-dioxolane (3g). A solution of commercially available 1-(3,4-dimethoxyphenyl)ethanone (57.0 g, 0.316 mol), ethylene glycol (80.0 mL, 89.1 g, 1.44 mol) and *p*-toluenesulfonic acid monohydrate (1.50 g, 7.5 mmol) in toluene (400 mL) was refluxed in a Dean-Stark apparatus for 35 h. The reaction mixture was washed with aqueous sodium hydrogen carbonate solution (5 w/w%, 300 mL) and water (300 mL), dried over $MgSO_4$ and the solvent was evaporated resulting a brown oil, which was distilled in vacuo (120–140 °C/0.2 Hgmm). Treatment of the resulting colorless oil with hexane (150 mL) gave **3g** (44.7 g, 62%) as a colorless solid, mp 48−50 °C (hexane). IR (KBr, cm^{-1}): 2988, 2892, 1606, 1512, 1265, 1031. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.04 (1H, dd, *J*=8.3 Hz, *J*=2.0 Hz), 7.01 (1H, d, *J*=1.8 Hz), 6.84 (1H, d, *J*=8.2 Hz), 4.06–3.98 (2H, m), 3.90 (3H, s), 3.87 (3H, s), 3.83–3.76 (2H, m), 1.66 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.9, 148.6, 148.4, 135.8, 117.3, 110.58, 108.6, 108.4, 64.2, 55.7, 27.5. Anal. Calcd for $C_{12}H_{16}O_4$ (224.26): C 64.27, H 7.19%. Found: C 64.01, H 7.03%.

2-Methoxy-6-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (4a). To a solution of 2-(3-methoxyphenyl)-2-methyl-1,3-dioxolane[9] (**3a**, 21.5 g, 0.111 mol) in diethyl ether (180 mL), BuLi (71 mL of a 2.5 M solution in hexane, 0.18 mol) was added at 0 °C under argon and the mixture was stirred for 4 h at 0 °C. It was poured onto a large excess of dry ice. After 1 h, water (360 mL) was added, and the layers were separated. The aqueous layer was extracted with diethyl ether (2×180 mL) and acidified with concentrated hydrochloric acid (15 mL). The crystalline product was filtered to give **4a** (20.3 g, 77%) as a colorless solid, mp 145–146 °C (hexane/ethyl acetate 1:1). IR (KBr, cm^{-1}): 3175, 1735, 1695, 1470, 1301, 1276, 1217, 1027. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.36 (1H, t, *J*=8.1 Hz), 7.14 (1H, d, *J*=8.1 Hz), 6.90 (1H, d, *J*=8.1 Hz), 4.07–4.00 (2H, m), 3.88 (3H, s), 3.82–3.75 (2H, m), 1.77 (3H, s). ^{13}C NMR: (125 MHz, $CDCl_3$): δ 173.3, 156.0, 142.2, 130.4, 121.3, 118.6, 110.5, 108.4, 64.3, 56.0, 27.5. Anal. Calcd for $C_{12}H_{14}O_5$ (238.24): C 60.50, H 5.92%. Found: C 60.31, H 5.94%.

2-Chloro-6-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (4b). To a solution of 2-(3-chlorophenyl)-2-methyl-1,3-dioxolane[11] (**3b**, 19.9 g, 0.100 mol) in THF (100 mL), BuLi (100 mL of a 1.6 M solution in hexane, 0.16 mol) was added at –78 °C, under argon and the mixture was stirred for 2 h at –78 °C. It was poured onto a large excess of dry ice. Water (100 mL) was added, and the layers were separated. The aqueous layer was extracted with diethyl ether (2×50 mL), acidified with an aqueous solution of hydrochloric acid (10 w/w%, 100 mL) and extracted with diethyl ether (3×50 mL). The organic phase was dried ($MgSO_4$) and concentrated. Trituration of the residue with hexane (50 mL) gave **4b** (18.0 g, 74%) as a colorless solid, mp 124–126 °C (hexane/ethyl acetate 3:1). IR (KBr, cm^{-1}): 3175, 1743, 1438,

1251, 1187. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48 (1H, dd, *J*=6.7 Hz, *J*=2.4 Hz), 7.39 (1H, dd, *J*=7.9 Hz, *J*=2.4 Hz), 7.34 (1H, t, *J*=7.3 Hz), 4.09–3.94 (2H, m), 3.87–3.72 (2H, m), 1.76 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.6, 143.1, 130.9, 130.8, 130.4, 129.2, 125.0, 108.2, 64.4, 27.6. Anal. Calcd for $C_{11}H_{11}ClO_4$ (242.66): C 54.45, H 4.57, Cl 14.61%. Found: C 54.67, H 4.62, Cl 14.38%.

3-Chloro-2-methoxy-6-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (4e). To a solution of 2-(4-chloro-3-methyoxyphenyl)-2-methyl-1,3-dioxolane (**3e**, 3.57 g, 15.6 mmol) in diethyl ether (20 mL), BuLi (10 mL of a 2.5 M solution in hexane, 25 mmol) was added at 0 °C under argon and the mixture was stirred for 2 hs at 0 °C. It was poured onto a large excess of dry ice. Water (80 mL) and *tert*-butyl methyl ether (60 mL) were added and the layers were separated. The aqueous layer was extracted with *tert*-butyl methyl ether (60 mL) and acidified with concentrated hydrochloric acid to pH = 2 to give **4e** (3.62 g, 85%) as a colorless solid, mp 133–134 °C (hexane/ethyl acetate 5:3). IR (KBr, cm^{-1}): 3220, 1740, 1490, 1374, 1253. ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.23 (1H, br s), 7.41 (1H, d, *J*=8.4 Hz), 7.26 (1H, d, *J*=8.4 Hz), 4.08–4.00 (2H, m), 3.97 (3H, s), 3.82–3.75 (2H, m), 1.75 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.7, 152.7, 141.0, 131.4, 128.1, 127.5, 123.0, 108.0, 64.4, 62.2, 27.4. Anal. Calcd for $C_{12}H_{13}ClO_5$ (272.69): C 52.86, H 4.81, Cl 13.00%. Found: C 52.91, H 4.89, Cl 13.18%.

6-Acetyl-2-chloro-3-methoxybenzoic acid (5) *via* **2-chloro-3-methoxy-6-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (4f).** To a solution of 2-(3-chloro-4-methyoxyphenyl)-2-methyl-1,3-dioxolane (**3f**, 3.57 g, 15.6 mmol) in THF (25 mL), BuLi (10 mL of a 2.5 M solution in hexane, 25 mmol) was added at –78 °C, under argon atmosphere, stirred for 2 h at –78 °C. It was poured onto a large excess of dry ice. Water (100 mL) and *tert*-butyl methyl ether (60 mL) were added, stirred for 10 min, and the layers were separated. The aqueous layer was extracted with *tert*-butyl methyl ether (40 mL) and acidified with aqueous solution of hydrochloric acid (10 w/w%) to pH = 2. The aqueous layer was extracted with ethyl acetate (2×40 mL), the organic phase was dried ($MgSO_4$) and evaporated to afford partially deketalized **4f**. In order to complete the hydrolysis of the ketal, aqueous solution of hydrochloric acid (10 w/w%, 75 mL) was added and suspension was boiled for 2 h. After cooling to room temperature, the product was filtered and dried to give **5** (2.10 g, 59%) as a colorless solid, mp 202–203 °C (diethyl ether/THF 3:1). IR (KBr, cm^{-1}): 3045, 2951, 1744, 1650, 1562, 1279, 1240, 1041. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.48 (1H, br s), 7.23 (1H, br s), 3.98 (3H, s), 1.91 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.0, 157.2, 142.8, 120.8, 117.9, 103.7, 57.0, 26.7. Anal. Calcd for $C_{10}H_9ClO_4$ (228.63): C 52.53, H 3.97, Cl 15.51%. Found: C 52.82, H 9.96, Cl 15.29%.

2,3-Dimethoxy-6-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (4g). To a solution of 2-(3,4-dimethoxyphenyl)-2-methyl-1,3-dioxolane (**3g**, 2.80 g, 12.5 mmol) in diethyl ether (15 mL), BuLi (7.5 mL of a 2.5 M solution in hexane, 18.8 mmol) was added at 0 °C under argon and stirred for 1 h at 0 °C. It was poured onto a large excess of dry ice. Water (60 mL) was added, and the layers were separated. The aqueous layer was extracted with diethyl ether (2×40 mL), acidified with an aqueous solution of citric acid (20 w/w%). The precipitate was collected by filtration and recrystallized from 2-propanol (16 mL) to give **4g** (1.78 g, 53%) as a colorless solid, mp 142–144 °C (2-propanol). IR (KBr, cm^{-1}) 3198, 2980, 1735, 1490, 1274, 1193. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.23 (1H, d, *J*=8.5 Hz), 6.94 (1H, d, *J*=8.5 Hz), 4.03–3.99 (2H, m), 3.91 (3H, s), 3.88 (3H, s), 3.81–3.77 (2H, m), 1.74 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.5, 152.2, 145.5, 133.2, 127.1, 122.3, 113.2, 108.3, 64.3, 61.7, 56.0, 27.7. Anal. Calcd for $C_{13}H_{16}O_5$ (257.27): C 58.20, H 6.01%. Found: C 58.09, H 5.97%.

Lithiation of 2-(3-methyoxyphenyl)-2-methyl-1,3-dioxolane (3a) with BuLi/PMDTA leading to a mixture of 2-methoxy-6-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (4a) and 2-methoxy-4-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (6a). To a solution of PMDTA (4.33 g, 25.0 mmol) in diethyl ether (15 mL), BuLi (10 mL of a 2.5 M solution in hexane, 25 mmol) was added at 0 °C, under argon. After stirring for 10 min, 2-(3-methyoxyphenyl)-2-methyl-1,3-dioxolane (**3a**, 3.03 g, 15.6 mmol) in diethyl ether (10 mL) was added at 0 °C. The resulting solution was stirred for 25 min and it was poured onto a large excess of dry ice. Water (100 mL) and *tert*-butyl methyl ether (50 mL) were added, and the layers were separated. The aqueous layer was extracted with *tert*-butyl methyl ether (50 mL) and acidified with aqueous solution of hydrochloric acid (10 w/w%) to pH = 3. The resulting solution was extracted with ethyl acetate (2×50 mL), dried ($MgSO_4$) and evaporated. The residue was triturated with hexane to give a 32 : 68 mixture (determined by ^{1}H NMR) of **4a** and **6a** (0.83 g, 22%) as a yellow solid. An analytical sample of 2-methoxy-4-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (**6a**) was obtained by fractional crystallization of the product mixture from diethyl ether to give **6a** as a colorless solid, mp 101–102 °C (diethyl ether). IR (KBr, cm^{-1}): 3281, 2993, 1724, 1612, 1410, 1334, 1202, 1029. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14 (1H, d, *J*=8.1 Hz), 7.26 (1H, dd, *J*=8.1 Hz, *J*=1.5 Hz), 7.20 (1H, d, *J*=1.3 Hz), 4.10 (3H, s), 4.10–4.06 (2H, m), 3.80–3.77 (2H, m), 1.66 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.3, 158.1, 151.3, 133.8, 119.0, 117.0, 108.7, 108.2, 64.6, 56.7, 27.3. Anal. Calcd for $C_{12}H_{14}O_5$ (238.24): C 60.50, H 5.92%. Found: C 60.72, H 6.03%.

Lithiation of 2-(3-chlorophenyl)-2-methyl-1,3-dioxolane (3b) with BuLi/PMDTA leading to a mixture of 2-chloro-6-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (4b) and 2-chloro-4-

(2-methyl-1,3-dioxolane-2-yl)benzoic acid (6b). To a solution of PMDTA (4.61 g, 26.6 mmol) in THF (15 mL), BuLi (10 mL of a 2.5 M solution in hexane, 25 mmol) was added at –78 °C, under argon. After stirring for 10 min, 2-(3-chlorophenyl)-2-methyl-1,3-dioxolane (**3b**, 3.10 g, 15.6 mmol) in THF (15 mL) was added at –78 °C. The resulting solution was stirred for 30 min and it was poured onto a large excess of dry ice. Water (100 mL) and *tert*-butyl methyl ether (60 mL) were added and the layers were separated. The aqueous layer was extracted with *tert*-butyl methyl ether (40 mL) and acidified with aqueous solution of hydrochloric acid (10 w/w%) to pH = 3. The resulting solution was extracted with ethyl acetate (2×40 mL) and dried ($MgSO_4$) and evaporated. The residue was triturated with hexane to give a 32:68 mixture (determined by ^{1}H NMR) of **4b** and **6b** (1.78 g, 47%). An analytical sample of 2-chloro-4-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (**6b**) was obtained by fractional crystallization from heptane to give **6b** as a colorless solid, mp 112–113 °C (heptane). IR (neat, cm^{-1}): 2900, 1690, 1600, 1265, 1204, 1035. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.66 (1H, br s), 8.00 (1H, d, *J*=8.1 Hz), 7.63 (1H, d, *J*=1.4 Hz), 7.47 (1H, dd, *J*=8.1 Hz, *J*=1.5 Hz), 4.09–4.06 (2H, m), 3.80–3.77 (2H, m), 1.67 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.2, 149.7, 134.8, 132.6, 128.5, 127.8, 123.8, 107.9, 64.7, 27.3. Anal. Calcd for $C_{11}H_{11}ClO_4$ (242.66): C 54.45, H 4.57, Cl 14.61%. Found: C 54.07, H 4.56, Cl 14.45%.

5-Acetyl-2-methoxybenzoic acid (7). To a solution of PMDTA (4.33 g, 25.0 mmol) in diethyl ether (20 mL), BuLi (10 mL of a 2.5 M solution in hexane, 25 mmol) was added at 0 °C under argon. After 10 min, 2-(4-methyoxyphenyl)-2-methyl-1,3-dioxolane (**3c**, 3.03 g, 15.6 mmol) in diethyl ether (10 mL) was added to the solution at 0 °C, was stirred for 40 min and was poured onto a large excess of dry ice. Water (80 mL) and *tert*-butyl methyl ether (60 mL) were added and the layers were separated. The aqueous layer was extracted with *tert*-butyl methyl ether (40 mL), acidified with concentrated hydrochloric acid to pH = 2 and stirred at 40 °C for 120 min. After cooling it was extracted with ethyl acetate (2×80 mL), dried ($MgSO_4$) and evaporated. The solid residue was recrystallized to give **7** (0.60 g, 20%) as a yellow solid, mp 156–157 °C (hexane/ethyl acetate 2:1), lit. mp 137 °C,[18] 152 °C.[19] IR (KBr, cm^{-1}): 3238, 1736, 1677, 1605, 1365, 1264. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.53 (1H, br s), 8.73 (1H, d, *J*=2.0 Hz), 8.24 (1H, dd, *J*=8.8 Hz, *J*=2.1 Hz), 7.16 (1H, d, *J*=8.8 Hz), 4.16 (3H, s), 2.63 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.0, 165.7, 161.7, 134.8, 134.5, 131.0, 117.6, 112.0, 57.0, 26.4. Anal. Calcd for $C_{10}H_{10}O_4$ (194.19): C 61.85, H 5.19%. Found: C 61.75, H 5.10%.

2-Chloro-5-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (8). To a solution of PMDTA (4.61 g, 26.6 mmol) in THF (15 mL), BuLi (10 mL of a 2.5 M solution in hexane, 25 mmol) was

added at –78 °C under argon. After stirring for 10 min, 2-(4-chlorophenyl)-2-methyl-1,3-dioxolane (**3d**, 3.10 g, 15.6 mmol) in THF (5 mL) was added at –78 °C. The resulting solution was stirred for 60 min and it was poured onto a large excess of dry ice. Water (110 mL) and *tert*-butyl methyl ether (60 mL) were added and the layers were separated. The aqueous layer was extracted with *tert*-butyl methyl ether (40 mL) and acidified with aqueous solution of hydrochloric acid (10 w/w%) to pH = 3. The resulting solution was extracted with ethyl acetate (3×40 mL), dried ($MgSO_4$) and evaporated. The solid residue was triturated with hexane to give **8** (2.63 g, 70%) as a yellow solid, mp 123–124 °C (heptane/ethyl acetate 2:1). IR (KBr, cm^{-1}): 2987, 2893, 1693, 1308, 1266, 1204, 1033. ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.76 (1H, br s), 8.14 (1H, d, *J*=2.2 Hz), 7.61 (1H, dd, *J*=8.3 Hz, *J*=2.2 Hz), 7.47 (1H, d, *J*=8.3 Hz), 4.09–4.07 (2H, m), 3.81–3.78 (2H, m), 1.67 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6, 142.5, 134.1, 131.4, 130.5, 129.3, 128.4, 108.0, 64.6, 27.4. Anal. Calcd for $C_{11}H_{11}ClO_4$ (242.66): C 54.45, H 4.57, C, 14.61%. Found: C 54.67, H 4.53, Cl 14.32%.

2-Chloro-5-(2-methyl-1,3-dioxolan-2-yl)phenol (9). To a solution of PMDTA (43.3 g, 0.250 mol) in THF (120 mL), BuLi (100 mL of a 2.5 M solution in hexane, 0.25 mol) was added at –78 °C, under argon. After stirring for 10 min, 2-(4-chlorophenyl)-2-methyl-1,3-dioxolane (**3d**, 31.0 g, 0.156 mol) in THF (30 mL) was added at –78 °C in 30 min. The resulting solution was stirred for 30 min and triisopropyl borate (47.2 g, 0.251 mol) in THF (30 mL) was added dropwise to the solution at –78 °C over a period of 1 h. The solution was allowed to warm up to room temperature, stirred for 30 min and then cooled to 0 °C. At this temperature aqueous solution of hydrogen peroxide (35 w/w%, 37.9 g, 0.390 mol) was added dropwise to the solution. Then the solution was warmed to room temperature, stirred for 1 h, water (350 mL) was added and stirred for further 30 min. The solution was neutralized with concentrated hydrochloric acid. Ethyl acetate (250 mL) was added and the layers were separated. The aqueous layer was extracted with ethyl acetate (160 mL), the organic layers were combined and washed with water (2×300 mL), dried ($MgSO_4$) and evaporated. Water (115 mL) and aqueous solution of sodium hydroxide (40 w/w%, 22.5 g) was added to the oily residue. It was stirred for 15 min and *tert*-butyl methyl ether (115 mL) was added. After a 10-min stirring, the layers were separated. The aqueous phase was extracted once more with *tert*-butyl methyl ether (60 mL) and the pH was adjusted to 6–7 with concentrated hydrochloric acid. The resulting solid precipitation was filtered, washed with water and recrystallized from heptane with activated charcoal treatment to give **9** (13.8 g, 41%) as a pale yellow solid, mp 77–79 °C (heptane). IR (KBr, cm^{-1}): 3335, 2896, 1596, 1413, 1300, 1212, 1029. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (1H, d, *J*=8.4 Hz), 7.16 (1H, d, *J*=1.4 Hz), 7.00 (1H, dd, *J*=8.2 Hz,

J=1.4 Hz), 5.79 (1H, s), 4.06–4.02 (2H, m), 3.80–3.76 (2H, m), 1.64 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.2, 144.3, 128.8, 119.3, 118.4, 113.4, 108.3, 64.5, 27.3. Anal. Calcd for $C_{10}H_{11}ClO_3$ (214.65): C 55.96, H 5.17, Cl 16.52%. Found: C 56.17, H 5.20, Cl 16.59%.

2-Chloro-3-methoxy-5-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (10a). To a solution of PMDTA (4.33 g, 25.0 mmol) in THF (20 mL), BuLi (10 mL of a 2.5 M solution in hexane, 25 mmol) was added at 0 °C under argon. After stirring for 10 min, 2-(4-chloro-3-methoxyphenyl)-2-methyl-1,3-dioxolane (**3e**, 3.57 g, 15.6 mmol) in THF (20 mL) was added dropwise to the solution at –78 °C. The resulting solution was stirred for 20 min and it was poured onto a large excess of dry ice. Water (80 mL) and *tert*-butyl methyl ether (60 mL) were added, and the layers were separated. The aqueous layer was extracted with *tert*-butyl methyl ether (2×60 mL) and acidified with concentrated hydrochloric acid to pH = 2. The resulting solution was extracted with ethyl acetate (2×40 mL), dried ($MgSO_4$) and evaporated. ^{1}H NMR analysis of the residue indicated the presence of compounds **10a** and **4e** in a 96 : 4 ratio. The solid residue was triturated with hexane to give **10a** (2.53 g, 60%) as a colorless solid, mp 150–151 °C (hexane/ethyl acetate 1:1). IR (KBr, cm^{-1}): 3161, 1723, 1458, 1321, 1281, 1236, 1030. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.93 (1H, br s), 7.25 (1H, d, *J*=2.0 Hz), 7.26 (1H, d, *J*=1.9 Hz), 4.10–4.06 (2H, m), 3.96 (3H, s), 3.82–3.78 (2H, m), 1.67 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6, 155.9, 143.3, 130.3, 122.3, 120.2, 112.6, 108.1, 64.6, 56.7, 27.5. Anal. Calcd for $C_{12}H_{13}ClO_5$ (272.69): C 52.86, H 4.81, Cl 13.00%. Found: C 52.97, H 4.87, Cl 12.75%.

3-Chloro-2-methoxy-5-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (10b). To a solution of PMDTA (4.61 g, 26.6 mmol) in THF (15 mL), BuLi (10 mL of a 2.5 M solution in hexane, 25 mmol) was added at 0 °C under argon. After stirring for 10 min, 2-(3-chloro-4-methoxyphenyl)-2-methyl-1,3-dioxolane (**3f**, 3.57 g, 15.6 mmol) in THF (15 mL) was added dropwise to the solution at –78 °C. The resulting solution was stirred for 1 h and it was poured onto a large excess of dry ice. Water (100 mL) and *tert*-butyl methyl ether (60 mL) were added, and the layers were separated. The aqueous layer was extracted with *tert*-butyl methyl ether (40 mL) and acidified with aqueous solution of hydrochloric acid (10 w/w%) to pH = 3. Ethyl acetate (50 mL) was added and the phases were separated. The aqueous layer was extracted with ethyl acetate (2×40 mL), dried ($MgSO_4$) and evaporated. ^{1}H NMR analysis of the residue indicated the presence of compounds **10b** and **4f** in a 92 : 8 ratio. The residue was crystallized from a mixture of diethyl ether and hexane to give **10b** (2.47 g, 58%) as an off-white solid, mp 128–130 °C (heptane/ethyl acetate 10:1). IR (neat, cm^{-1}): 2890, 1675, 1475, 1255, 1201, 1037. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.35 (1H, br s), 8.06 (1H, d, *J*=1.6

Hz), 7.75 (1H, d, *J*=1.6 Hz), 4.08–4.05 (2H, m), 4.03 (3H, s), 3.82–3.79 (2H, m), 1.64 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.5, 155.3, 141.2, 132.5, 128.8, 128.0, 124.5, 107.7, 64.7, 62.3, 27.3. Anal. Calcd for $C_{12}H_{13}ClO_5$ (272.69): C 52.86, H 4.81, Cl 13.00%. Found: C 52.98, H 4.85, Cl 12.88%.

Lithiation of 2-(3,4-dimethoxyhenyl)-2-methyl-1,3-dioxolane (3g) with BuLi/PMDTA leading to a mixture of 2,3-dimethoxy-6-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (4g) and 2,3-dimethoxy-5-(2-(methyl-1,3-dioxolane-2-yl)benzoic acid (11). To a solution of PMDTA (4.61 g, 26.6 mmol) in diethyl ether (10 mL), BuLi (10 mL of a 2.5 M solution in hexane, 25 mmol) was added at 0 °C, under argon. After stirring for 10 min, 2-(3,4-dimethoxyhenyl)-2-methyl-1,3-dioxolane (**3g**, 3.50 g, 15.6 mmol) in THF (15 mL) was added at 0 °C. The resulting solution was stirred for 30 min and it was poured onto a large excess of dry ice. Water (100 mL) and *tert*-butyl methyl ether (50 mL) were added, and the layers were separated. The aqueous layer was extracted with *tert*-butyl methyl ether (40 mL) and acidified with concentrated hydrochloric acid to pH = 3 and extracted with ethyl acetate (3×50 mL). Combined organic phases were dried ($MgSO_4$) and evaporated. Trituration with hexane gave a pale yellow solid (1.43 g, 34%). ^{1}H NMR analysis of the residue indicated the presence of compounds **11** and **4g** in a 39 : 61 ratio.

2,3-Dimethoxy-5-(2-(methyl-1,3-dioxolane-2-yl)benzoic acid (11), synthesis of an authentic sample. ***Step A:*** **2-(3-Bromo-4,5-dimethoxyphenyl)-2-methyl-1,3-dioxolane (13).** A solution of 1-(3-bromo-4,5-dimethoxyphenyl)ethanone[16] (**12**, 8.00 g, 30.9 mmol), ethylene glycol (9.62 g, 0.155 mol), trimethyl orthoformate (9.84 g, 92.7 mmol) and *para*-toluenesulfonic acid monohydrate (0.24 g, 1.24 mmol) in *tert*-butyl methyl ether (40 mL) was stirred at room temperature for 24 h. To the reaction mixture ethyl acetate (50 mL) was added. The organic phase was washed with aqueous sodium hydrogen carbonate solution (5 w/w%, 25 mL), water (60 mL) and brine (25 mL). The organic phase was dried over $MgSO_4$ and the solvent was evaporated to give **13** (9.09 g, 97%) as red-brown solid. An analytical sample (1.00 g) was recrystallized from hexane to give **13** (0.64 g) as an off-white solid, mp 98–99 °C (hexane). IR (KBr, cm^{-1}): 2966, 2879, 1566, 1486, 1397, 1300, 1160, 1033. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (1H, d, *J*=1.9 Hz), 6.97 (1H, d, *J*=1.9 Hz), 4.07–4.01 (2H, m), 3.85 (3H, s), 3.88 (3H, s), 3.82–3.77 (2H, m), 1.63 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.4, 145.8, 140.6, 121.5, 117.3, 108.8, 108.0, 64.5, 60.4, 56.1, 27.5. Anal. Calcd for $C_{12}H_{15}BrO_4$ (303.15): C 47.54, H 4.99, Br 26.36%. Found: C 47.60, H 4.96, Br 25.93%. ***Step B:*** **2,3-Dimethoxy-5-(2-(methyl-1,3-dioxolane-2-yl)benzoic acid (11).** To a solution of 2-(3-bromo-4,5-dimethoxyphenyl)-2-methyl-1,3-dioxolane (**13**, 1.78 g, 5.9 mmol) in THF (10 mL), BuLi

(4.0 mL of a 2.5 M solution in hexane, 9.4 mmol) was added at –78 °C, under argon atmosphere, stirred for 30 min at –78 °C, treated with dry ice and left overnight at room temperature. Water (50 ml) and *tert*-butyl methyl ether (30 ml) were added, and the layers were separated. The aqueous layer was extracted with *tert*-butyl methyl ether (30 mL), and then treated with an aqueous solution of hydrochloric acid (10 w/w%) to pH = 3. The resulting solution was extracted with ethyl acetate (2×20 ml), dried ($MgSO_4$) and evaporated to give **11** (1.02 g, 65%) as an orange solid. The crude product was triturated with hexane to give **11** (0.86 g, 55%) as a yellow solid. An analytical sample (0.83 g) was recrystallized from hexane and ethyl acetate to give **11** (0.61 g) as an off-white solid, mp 149–150 °C (hexane/ethyl acetate 1:1). IR (KBr, cm^{-1}): 2983, 1679, 1488, 1400, 1330, 1275. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (1H, d, *J*=2.1 Hz), 7.29 (1H, d, *J*=1.9 Hz), 4.09–4.03 (2H, m), 4.08 (3H, s), 3.95 (3H, s), 3.82–3.76 (2H, m), 1.65 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 152.0, 147.7, 140.6, 121.9, 120.4, 114.5, 108.1, 64.6, 62.1, 56.2, 27.4. Anal. Calcd for $C_{13}H_{16}O_6$ (268.27): C 58.20, H 6.01%. Found: C 58.12, H 5.97%.

Preparation of 2,3-dichloro-5-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (14) from the product mixture obtained by the lithiation of 2-(3,4-dichlorophenyl)-2-methyl-1,3-dioxolane (3h) with BuLi/PMDTA. To a solution of PMDTA (4.61 g, 26.6 mmol) in THF (15 mL), BuLi (10 mL of a 2.5 M solution in hexane, 25 mmol) was added at –78 °C, under argon. After stirring for 10 min, 2-(3,4-dichlorophenyl)-2-methyl-1,3-dioxolane (**3h**, 3.67 g, 15.6 mmol) in THF (15 mL) was added dropwise to the solution at –78 °C. The resulting solution was stirred for 30 min and it was poured onto a large excess of dry ice. Water (100 mL) and *ter*t-butyl methyl ether (60 mL) were added, and the layers were separated. The aqueous layer was extracted with *tert*-butyl methyl ether (40 mL) and acidified with an aqueous solution of hydrochloric acid (10 w/w%) to pH = 3. The resulting solution was extracted with ethyl acetate (3×50 mL), dried ($MgSO_4$) and evaporated to give a pale yellow solid (2.86 g), which proved to be a mixture of compounds **14**, **4h**, **6b**, and **8** in a 61 : 18 : 11 : 10 ratio as determined by ^{1}H NMR. Compounds **4h**, **6b**, and **8** have been isolated and characterized in the experiments described above. An analytical sample of 2,3-dichloro-5-(2-methyl-1,3-dioxolane-2-yl)benzoic acid (**14**) was obtained by fractional crystallization of the product mixture to give **14** as an off-white solid, mp 140–141 °C (heptane/ethyl acetate 10:1). IR (KBr, cm^{-1}): 2994, 2886, 1709, 1435, 1232, 1037. ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.94 (1H, d, *J*=2.0 Hz), 7.77 (1H, d, *J*=2.1 Hz), 4.09–4.06 (2H, m), 3.83–3.77 (2H, m), 1.64 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 170.2, 143.5, 134.9, 131.8,

131.1, 127.1, 107.6, 64.8, 27.4. Anal. Calcd for $C_{11}H_{10}Cl_2O_4$ (277.11): C 47.68, H 3.64, Cl 25.59%. Found: C 47.74, H 3.63, Cl 25.23%.

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