Regioselective Lithiation of Resorcinol Derivatives: Synthesis of Mono *O*-MOM- and *O*-Benzylresorcinols Prenylated at C-2 or C-4 Positions

Alessandro B. C. Simas,[a,b] Antonio L. Coelho,[a] Paulo R. R. Costa[a]

[a]Laboratório de Síntese Assimétrica (LASA), Núcleo de Pesquisas de Produtos Naturais, Universidade Federal do Rio de Janeiro, CCS, Bl. H, Ilha da Cidade Universitária, 21941-590, Rio de Janeiro, RJ, Brazil

[b]Departamento de Química, ICE, Universidade Federal Rural do Rio de Janeiro, Seropédica, RJ, Brazil

Fax +55(21)2702683; E-mail abcsimas@nppn.ufrj.br; alcoelho@nppn.ufrj.br or prrcosta@nppn.ufrj.br

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Abstract: Resorcinol derivatives 3-benzyloxy-1-methoxymethoxybenzene (**3b)** and 4-benzyloxy-1-bromo-2-methoxymethoxybenzene (**3c)** were regioselectively lithiated. The resulting aryllithium intermediates or their cuprate derivatives were reacted with allyl bromide (**4a**), prenyl bromide (**4b**) and (*E*)-4-benzyl-1-bromo-3-methylbut-2-ene (**4c**), leading to C-2 and C-4 substituted resorcinols **6** and **7**, respectively. The use of 2-methyl-2-vinyloxirane (**5**) as electrophile was also studied as another means of introduction of an oxygenated prenyl side chain on **3b** or **3c**. Prenylated compounds **6** and **7** could be transformed into the corresponding mono *O*-protected resorcinols **8**, **9** and **10** by selective removal of either the benzyl or MOM group.

Key words: resorcinol derivatives, prenylation, lithiation

The presence of prenylated resorcinol moieties such as **1** and **2** (Figure 1) in the structure of natural products isolated from plants and fungi is widespread. The prenyl unity may also appear hydroxylated at the pro-*E* methyl group or as part of an additional furan or pyran ring.[1]

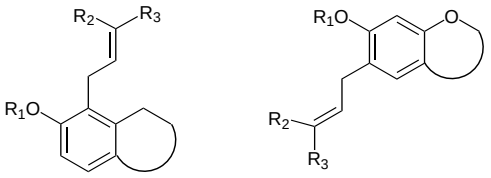
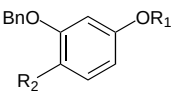


Figure 1. Prenylated resorcinol moieties

While the introduction of the prenyl group in resorcinol or its derivatives under Friedel–Crafts conditions has been reported as suffering from lack of regioselectivity,[2] scattered examples may be found on the regioselective introduction of allylic electrophiles via resorcinol-derived organometallics, leading to substitution at the C-2 position.[3,4] Selective substitution at the C-4 position has been achieved through preliminary protection of the C-2 position with a TMS group.[5]

Due to the potential of prenylated resorcinols as synthetic precursors of natural products,[3] we set out to investigate the possibility of regioselective preparation of such intermediates, prenylated at the C-2 or C-4 position and differentially protected at the phenol groups, as in compounds **1** and **2**, respectively (Figure 1), by using new resorcinol derivatives **3b** and **3c** (Figure 2), easily prepared from 3-benzyloxyphenol (**3a**).



3a, $R_1 = R_2 = H$
3b, R_1= MOM, $R_2 = H$
3c, R_1= MOM, R_2= Br

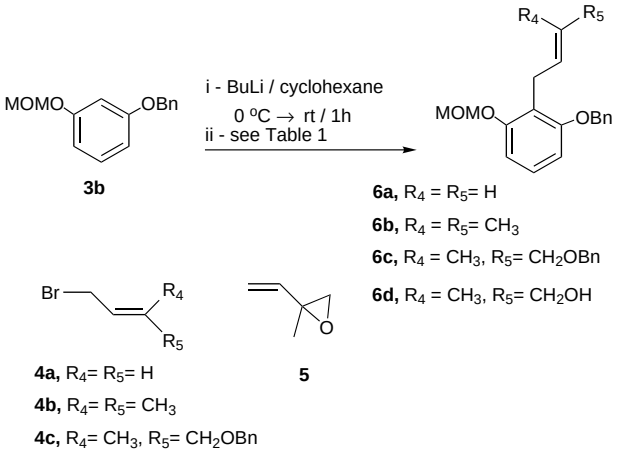
Figure 2. Benzylated resorcinol derivatives

The benzyl and MOM protecting groups were chosen because they can be selectively removed under different conditions.[6] In addition, the MOM group, a strong directing ortho-metallation group,[7] would ensure the regioselectivity of deprotonation at C-2 position of compound **3b**. The regioselectivity for the lithiation of **3c** at C-4 position would be secured by the presence of bromine atom (metal-halogen exchange).

The use of the benzyl protecting group in Directed ortho Metallation (DoM) appears not to have been systematically studied.[8] Therefore, we sought the optimal conditions for the regioselective lithiation of **3b**. We found that the use of BuLi in a mixture of hexanes/cyclohexane at room temperature gives complete and clean deprotonation at C-2 position, proven by quench with D_2O. The lithiation did not require the employment of stronger bases (*s*-BuLi or *t*-BuLi) or deaggregating agents such as TMEDA.[4] The possible deprotonation at the benzylic carbon or self-reprotonation by the benzylic hydrogens was not observed. However, when the deprotonation of **3b** (BuLi) was run in THF and the reaction was quenched with aqueous NH_4Cl, a more polar substance (TLC, silica gel) was obtained along with **3b**. This result points out the requirement of hydrocarbon solvents in the deprotonation step for the achievement of good yields.

The organolithium intermediate generated from **3b** was allowed to react with **4a** (Scheme 1, Table 1, Entry 1) and the best result was obtained when the ether and **4a** were added at 0°C and the resulting mixture was heated to reflux for 2 hours, leading to **6a**. Under the same conditions, the use of **4b** and (*E*)-4-benzyloxy-1-bromo-3-methylbut-2-ene (**4c**) as alkylating agents (Table 1, Entries 2 and 3,

Condition 1) led to prenylated products **6b** and **6c**. We did not observe the presence of regioisomers or products originated by a S_N2' type reaction. The prenylation of **3b** could be accomplished under softer conditions if the organolithium intermediate was first transformed into the corresponding cuprate (Table 1, Entry 2, Conditions 2 or 3) followed by trapping with **4b** (–78ºC to r.t.). Condition 3 (use of CuCN•2 LiCl)[9] is particularly convenient due to the higher solubility of the generated cuprate, which makes it more suitable to large-scale preparations. We also attempted to incorporate an oxygenated prenyl chain through the use of vinyl epoxide **5** as electrophile via the aryllithium intermediate derived from **3b** itself (Table 1, Entry 4, Condition 1).[10] Unfortunately, the starting material was recovered. The cuprate obtained through use of CuCN•2 LiCl as a copper source (Table 1, Entry 4, Condition 3) reacted with epoxide **5** affording allylic alcohol **6d** in moderate yield as an unseparable *E*/*Z* (3.6:1, respectively) mixture of stereoisomers.[11] We expected a stereoselectivity as high as the ones described in the literature for reactions of **5** and cuprates prepared both from organolithium and Grignard reagents (*E*/*Z* ratio ranging from 11:1 to 32:1).[12] The double bond geometry in the major product was confirmed by *O*-benzylation of **6d** and comparison with the ^{1}H NMR spectrum of substance **6c** (*E*-stereoisomer). The low stereoselectivity shown by the reaction of **5** makes the use of electrophile **4c** (Table 1, Entry 3) important as it allows the introduction of an oxygenated prenyl moiety presenting an *E*-controlled geometry.



Scheme 1

In order to obtain compounds **7** (Scheme 2, Table 2), the regioisomers of prenylated resorcinols **6**, bromine-lithium exchange on **3c** was effected. The resulting aryllithium intermediate was reacted with MeI, leading to incorporation of methyl group at the C-4 position in almost quantitative yield. Afterwards, we turned to the alkylation with electrophile **4a** (Scheme 2, Table 2, Entry 1). Since the lithiated species here is less sterically crowded than the one originated from substrate **3b**, we expected milder conditions for the alkylation step. However, we found that the reaction still required use of reflux to give **7a** in good yield. The prenylated resorcinol **7b** was obtained through the use of electrophile **4b** (Table 2, Entry 2). As an attempt to improve the yield of **7b,** a cuprate derivative of **3c** was prepared and reacted with **4b** (Table 2, Entry 2, Condition 3), but the result was disappointing. Besides low yield, the reaction gave substantial amounts of the reduction product **3b** and a small amount of the S_N2' product. Furthermore, the incorporation of an oxygenated prenyl chain on resorcinol **3c** by employment of allylic epoxide **5** was studied. Interestingly, the aryllithium species derived from **3c** reacted quite cleanly with **5** (Table 2, Entry 3, Condition 2), affording the S_N2' product **7c** with high *E*-stereoselectivity (15:1). The double bond geometry was determined by NOE-diff experiments. This stereoselectivity is in contrast with previous reports on the reaction of **5** with aryllithium species, where a *Z*-selectivity was reported.[10] Again, improvement of the yield of the last reaction was attempted by employment of cuprates. The organocopper species produced by using CuCN•2 LiCl as copper source, did not react with epoxide **5**, while the cuprate obtained by using CuI (Table 2, Entry 3, Condition 3) led to product **7c** (2:1 *E*/*Z* mixture of stereoisomers, respectively) in low yield, though. As it had occurred in the

Table 1 Reaction of **3b** with Electrophiles

Entry	Electrophile	Condition	Product	Yield (%)
1	**4a**	1[a]	**6a**	70
2	**4b**	1[a]	**6b**	69
		2[b]	**6b**	62
		3[c]	**6b**	60
3	**4c**	1[a]	**6c**	62
4	**5**	1[d]	**6d**	0
		3[c]	**6d**	46[e]

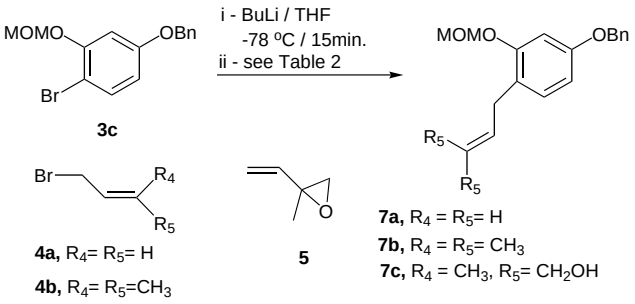
[a] **4** or **5** in Et_2O, reflux, 2h.
[b] CuCN/THF, –78→30 °C; then **4**, –78 °C→r.t.
[c] CuCN · 2 LiCl/THF, –78→30°C; then **4** or **5**, –78 °C→r.t.
[d] THF, –78 °C → r.t. (overnight) (instead of Et_2O, reflux).
[e] 56% based on recovered starting material; *E*/*Z* = 3.6:1.0.

Table 2 Reaction of **3c** with Electrophiles

Entry	Electrophile	Condition	Product	Yield (%)
1	**4a**	1[a]	**7a**	60
2	**4b**	1[a]	**7b**	58
		2[b]	**7b**	<36[d]
3	**5**	2[b]	**7c**	29[e]
		3[c]	**7c**	59[f]

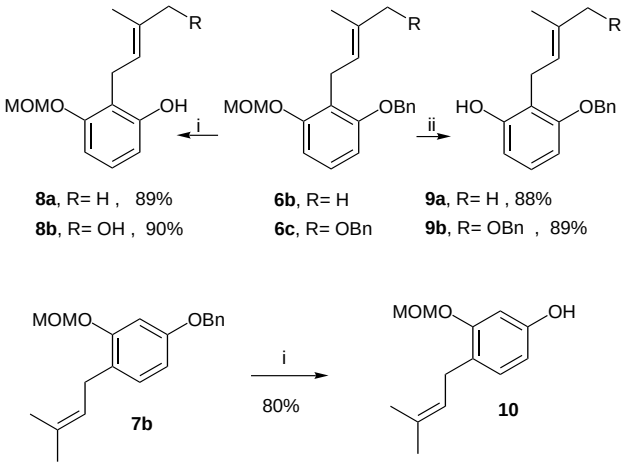
[a] **4**/cyclohexane, reflux 2h.
[b] CuI/THF, –78→ –30 °C; then **4** or **5**, –78 °C→r.t.
[c] **5**/–78 °C→r.t.
[d] An inseparable side product was observed. Yield estimated by ^{1}H NMR spectroscopy.
[e] *E*/*Z* = 2:1.
[f] E/*Z* = 15:1.

formation of **7b** via a cuprate, the reduction product **3b** was an important fraction of the crude product. These disappointing results in reactions involving cuprates prepared from **3c** are somewhat surprising if one takes into account literature reports of similar procedures.[9]



Scheme 2

Once the desired resorcinol derivatives **6** and **7** were obtained, our next goal was the selective removal of the benzyl or MOM (methoxymethyl) protecting group, in order to obtain the corresponding mono protected compounds (Scheme 3). Reaction of **6b** with hydrogen using Pd/C led not only to hydrogenolysis of the *O*-benzyl group but to a simultaneous reduction of the prenyl moiety double bond**.** Nevertheless, the selective cleavage of the benzyl group of **6b** was achieved through reduction with Na/NH_3, leading to **8a**.[13] When **6c** was submitted to the same reaction conditions, both benzyl protecting groups were removed and **8b** was obtained. The MOM group of **6b** and **6c** was selectively removed by reaction with PPTS (pyridinium *p*-toluenesulfonate) in *i*-PrOH under reflux to give compounds **9a** and **9b**.[14] The selective removal of the benzyl group of substance **7b** was achieved by the same conditions used on **6b** affording phenol **10**.



Reagents and conditions: i) $Na/NH_3/Et_2O$, –78°C, 10 min; ii) PPTS/*i*-PrOH, 3 h, reflux, 3 h

Scheme 3

In summary, we have studied the lithiation of *O*-benzyl protected resorcinol derivatives and their reactions with electrophiles **4b**, **4c** and **5**, leading to resorcinols allylated and prenylated at C-2 or C-4 positions.[15] A comparative study of the reactivity of aryllithium intermediates and their corresponding cuprates towards those electrophiles was carried out. It was demonstrated that, in general, the prenylation reactions do not require the intervention of cuprates, although the use of such intermediates allowed that the prenyl side chain be introduced on resorcinol derivative **3b** under softer conditions. Nevertheless, the employment of a cuprate derived from **3b** was required for successful reaction with allylic epoxide **5**. The benzyl protecting group has been shown to be compatible with MOM-directed lithiation of resorcinols under certain conditions. The possibility of selective removal of both protecting groups in resorcinol derivatives **6** and **7** makes these compounds interesting intermediates for the synthesis of natural products.

The use of the described prenylation method in total synthesis is currently under investigation in our laboratory. We are also studying the compatibility of the benzyl protecting group with other strong DMGs.

The electrophile (*E*)-**4c** was prepared by essentially the same procedure which Hiroi and Hirasawa employed in the synthesis of (*E*)-4-acetoxy-1-bromo-3-methylbut-2-ene.[16] Epoxide **5** (purchased from Aldrich) was dried over CaH_2 and distilled. LiCl was heated at 120ºC under a 0.5 Torr vacuum for 1.5 h before use. For general methods, see Ref. 3c.

3-Benzyloxy-1-methoxymethoxybenzene (3b)

To a stirred suspension of NaH (0.576 g, 12 mmol) in THF (10 mL) under N_2 at 0ºC was added dropwise a solution of **3a**[17] (1.93 g, 9.7 mmol) in THF (10 mL). The ice-bath was removed and the mixture was stirred at r.t. for 10 min. Then, it was cooled to 0ºC and DMF (4.0 mL) followed by MOMCl (0.95 mL 12.5 mmol) was added. After 10 min, the ice-bath was removed. After stirring at r.t. for 1 h, H_2O (30 mL) was added and the product was extracted with EtOAc (100 mL). The organic layer was dried (Na_2SO_4) and concentrated. Flash chromatography[18] (EtOAc/hexanes, 3:97, 5:95) of the residue afforded **3b** as a colorless oil (2.15g, 91%).

^{1}H NMR ($CDCl_3$/TMS): δ = 3.46 (s, 3 H), 5.02 (s, 2 H), 5.14 (s, 2 H), 6.59–6.71 (m, 3 H), 7.17 (dd, 1 H, *J* = 8.4, 8.4 Hz), 7.25–7.45 (m, 5 H).

^{13}C NMR: δ = 55.7, 69.7, 94.2, 103.4, 108.0, 108.5, 127.3, 127.7, 128.3, 129.7, 136.7, 158.2, 159.7.

HRMS: *m*/*z* calcd for $C_{15}H_{16}O_3$ (M^+): 244.1099 found: 244.1097.

4-Benzyloxy-1-bromo-2-methoxymethoxybenzene (3c)

To a stirred solution of **3a** (2 g, 10 mmol) in CH_2Cl_2 (30 mL) at –30°C was added solid NBS (1.78 g, 10 mmol) under N_2 atmosphere via a solid addition funnel. The mixture was stirred at the same temperature for 30 min. After removal of the cooling bath, the mixture was kept at r.t. for 10 min. Then, more CH_2Cl_2 was added and the mixture was successively washed with H_2O (20mL), brine (20mL) and H_2O (20mL). The organic layer was dried (Na_2SO_4) and concentrated to give a light-green oil. This material was purified by flash chromatography (hexanes/CH_2Cl_2, 30:70) affording 2-bromo-5-benzyloxyphenol (1.37 g, 49% yield) as low melting solid. This compound had the phenol group protected by MOMCl through the

same procedure described for preparation of resorcinol **3b**. Thus, **3c** was obtained as a colorless thick oil (95% yield).

^{1}H NMR ($CDCl_3$/TMS): δ = 3.51 (s, 3 H), 5.03 (s, 2 H), 5.19 (s, 2 H), 6.53 (dd, 1 H, *J* = 2.75, 8.3 Hz), 6.84 (d, 1 H, *J* = 2.75 Hz), 7.30–7.45 (m, 6 H).

^{13}C NMR: δ = 56.23, 70.21, 95.05, 103.63, 104.16, 108.97, 127.40, 127.98, 128.48, 133.04, 136.36, 154.34, 159.01.

MS (EI): *m*/*z* (%) = 322 (M^+, 2), 91 (100).

3-Benzyloxy-1-methoxymethoxy-2-(3-methylbut-2-enyl)benzene (6b); Typical Procedure for Alkylation of 3b via Aryllithium Species

A solution of BuLi in hexanes (1.13 mL, 1.5 mmol, 1.36 M) was added dropwise to a stirred solution of **3b** (0.25 g, 1.02 mmol) in cyclohexane (2.0 mL) under N_2 at 0°C. After 5 min, the ice bath was removed and the mixture was allowed to warm to r.t. After stirring for 1 h, the resulting brown suspension was cooled to 0°C and Et_2O (2.0 mL) was added followed by prenyl bromide (**4b**; 0.26 mL, 2.25 mmol). The mixture was heated at 60–70°C for 2 h. After cooling to r.t., H_2O (10 mL) was added and the product extracted with EtOAc (50 mL). The organic layer was washed with H_2O (30 mL), dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (EtOAc/hexanes, 1:99, 3:97) which afforded **6b** (0.221 g, 69%) as a yellow oil.

^{1}H NMR ($CDCl_3$/TMS) : δ = 1.65 (s, 3 H), 1.70 (s, 3 H), 3.40–3.47 (d, 2 H), 3.47 (s, 3 H), 5.06 (s, 2 H), 5.19 (s, 2 H), 5.29–5.19 (m, 1 H), 6.61 (d, 1 H, *J* = 8.4 Hz), 6.73 (d, 1 H, *J* = 8.4 Hz), 7.07 (dd, 1 H, *J* = 8.4, 8.4 Hz), 7.45–7.29 (m, 5 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 17.6, 22.5, 25.6, 55.8, 70.1, 94.3, 105.8, 107.2, 119.6, 122.8, 126.6, 127.5, 128.3, 130.8, 137.3, 155.6, 157.2.

HRMS: *m*/*z* calcd for: $C_{20}H_{24}O_3$ (M^+) 312.1725, found: 312.1720.

3-Benzyloxy-2-[(*E*)-4-hydroxy-3-methylbut-2-enyl]-1-methoxymethoxybenzene (6d) (Major Stereoisomer); Typical Procedure for Alkylation of 3b via Cuprates

A solution of BuLi in hexanes (1.57 mL, 2.13 mmol, 1.35 M) was added dropwise to a stirred solution of **3b** (0.40 g, 1.64 mmol) in cyclohexane (1.6 mL) under N_2 at 0°C. After 5 min, the ice-bath was removed and the reaction was allowed to proceed at r.t. for 1 h. Then, THF (2.5 mL) was added to the resulting brown suspension in order to homogenize it. This solution was transferred dropwise to a stirred slurry of CuCN (0.19 g, 2.12 mmol) and LiCl (0.18 g, 4.25 mmol) (CuCN•2 LiCl) in THF (1.5 mL) under N_2 at –78°C. At this temperature, the obtained mixture was kept for 10 min and, then, the –78°C bath was quickly replaced by a –30°C one. After 30 min, the reaction was cooled to –78°C. The epoxide **5** (0.32 mL, 3.28 mmol) was added and the temperature was allowed to rise till r.t. over 1.5 h. After stirring overnight at r.t., a sat. aq solution of NH_4Cl (10 mL) was added. The obtained heterogeneous mixture was subjected to filtration under vacuum and the filtrate was washed thoroughly with EtOAc (100 mL). The organic layer was washed with H_2O (30 mL), dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (EtOAc/hexanes, 4:96, 30:70) to give recovered **3b** (71 mg) and **6d** (249 mg, 46, 56% based on recovery of **3b**) as a yellow oil.

^{1}H NMR: δ= 1.74 (s, 3 H), 3.46 (s, 3 H), 3.44–3.54 (d, 2 H), 3.93 (s, 2 H), 5.05 (s, 2 H), 5.18 (s, 2 H), 5.49 (tq, 1 H, *J* = 7.2, 1.4 Hz), 6.61 (d, 1 H, *J* = 8.2 Hz), 6.73 (d, 1 H, *J* = 8.2 Hz), 7.08 (dd, 1 H, *J* = 8.2, 8.2 Hz), 7.24–7.46 (m, 5 H).

^{13}C NMR ($CDCl_3$/TMS): δ= 13.6, 22.1, 55.9, 69.0, 105.7, 118.7, 126.9, 127.1, 127.7, 128.3, 134.2, 137.2, 155.6, 157.2.

IR (film): ν = 3403 cm^{-1} (br).

MS (EI): *m*/*z* (%) = 328 (M^+, 1).

3-Benzyloxy-1-methoxymethoxy-4-(3-methylbut-2-enyl)benzene (7b); General Procedure for Alkylation of 3c via Aryllithium Species

To a solution of **3c** (0.323 g, 1 mmol) in THF (5 mL) and cyclohexane (5 mL) at –78°C was added BuLi in hexanes (1.13 mL, 1.5 mmol, 1.36 M). The reaction was kept at this temperature for 15 min. Afterwards, prenyl bromide (**4b**; 0.25 mL, 2.15 mmol) was added, the mixture allowed to warm to r.t. and heated to reflux for 2 h. After cooling to r.t., H_2O was added and the product was extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4) and concentrated. The crude product was purified by preparative TLC (EtOAc/hexanes, 5:95) furnishing **2b** (0.181 g, 58%).

^{1}H NMR ($CDCl_3$/TMS): δ = 1.73 (br, 6 H), 3.26 (d, 2 H, *J* = 7.24), 3.48 (s, 3 H), 5.04 (s, 2 H), 5.17 (s, 2 H), 5.28 (m, 1 H), 5.56 (dd, 1 H, *J* = 8.3, 2.5 Hz), 6.76 (d, 1 H, *J* = 2.5 Hz), 7.03 (d, 1 H, *J* = 8.3 Hz), 7.28–7.46 (m, 5 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 17.61, 25.67, 27.92, 55.84, 70.04, 94.35, 102.21, 106.86, 122.86, 123.25, 127.42, 127.76, 128.41, 129.58, 131.88, 137.04, 155.50, 157.94.

MS (EI): *m*/*z* (%)= 312 (M^+, 18).

3-Benzyloxy-6-[(*E*)-4-hydroxy-3-methylbut-2-enyl]-1-methoxymethoxybenzene (7c)

A stirred solution of **3c** (0.323 g, 1.0 mmol) in THF (3.0 mL) under argon at –78°C was treated with BuLi in hexanes (0.96 mL, 1.3 mmol, 1.35 M). After 15 min, epoxide **5** (0.15 mL, 1.5 mmol) was added and the mixture was allowed to warm to r.t. over 1.5 h. After stirring overnight at r.t., an aq sat. solution of NH_4Cl (15 mL) was added and the product was extracted with EtOAc (50 mL). The organic layer was washed with H_2O (20 mL), dried (Na_2SO_4) and concentrated. The crude product was purified by flash chromatography (EtOAc/hexanes, 4:96, 20:80, and 30:70) affording **7c** (0.193 g, 59%) as a yellow oil.

^{1}H NMR ($CDCl_3$/TMS): δ = 1.78 (s, 3 H), 3.33 (d, 2 H, *J* = 7.2 Hz), 3.48 (s, 3 H), 4.03 (s, 2 H), 5.03 (s, 2 H), 5.18 (s, 2 H), 5.57 (tq, 1 H, *J* = 7.2, 1.4 Hz), 6.56 (dd, 1 H, *J* = 8.3, 2.5 Hz), 6.78 (d, 1H , *J* = 2.5 Hz), 7.30–7.48 (m, 5 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 13.5, 27.6, 55.8, 68.6, 69.9, 94.3, 102.2, 106.9, 122.3, 124.4, 127.3, 127.7, 128.3, 129.6, 134.9, 136.9, 155.5, 158.0.

MS (EI): *m*/*z* (%) = 328 (M^+, 6).

IR (film): ν = 3409 cm^{-1} (br).

3-Methoxymethoxy-2-(3-methylbut-2-enyl)phenol (8a); General Procedure for the Cleavage of the Benzyl Group on 6 or 7

A solution of **6b** (0.156 g, 0.5 mmol) in Et_2O (3 mL) was added to liquid ammonia (10 mL) in a dry ice-acetone bath. To the obtained solution pieces of sodium (~ 0.043 g) were added until a characteristic deep blue color persisted. After stirring for 10 min, the reaction was quenched by addition of an aq sat. solution of NH_4Cl. The dry ice bath was removed to allow the ammonia to evaporate. Afterwards, CH_2Cl_2 was added to the residue and the mixture was washed with brine. The organic layer was dried (Na_2SO_4) and evaporated to give the crude product, further purified by preparative TLC to give pure **8a** (0.099 g, 89%) as a yellow solid.

^{1}H NMR ($CDCl_3$/TMS): δ = 1.77 (d, 3 H, *J* = 1.28 Hz), 1.82 (3 H, *J* = 0.82 Hz), 3.44 (d, 2 H, *J* = 5.87 Hz), 3.48 (s, 3 H), 5.18 (s, 2 H), 5.24 (m, 1 H), 5.32 (br, 1 H), 6.50 (dd, 1 H, *J* = 1, 8.24 Hz), 6.66 (dd, 1 H, *J* = 1, 8.24 Hz), 7.02 (t, 1 H, *J* = 8.24 Hz).

^{13}C NMR ($CDCl_3$/TMS): δ = 17.68, 22.40, 25.62, 55.89, 94.55, 109.58, 116.48, 106.59, 121.91, 126.98, 133.68, 155.18, 155.47.

HRMS: *m/z* calcd for: $C_{13}H_{18}O_3$ (M^+) 222.1256, found: 222.1257.

3-Benzyloxy-2-(3-methylbut-2-enyl)phenol (9a); General Procedure for the Cleavage of the MOM Group in 6 or 7

To a solution of **6b** (0.156 g, 0.5 mmol) in *i*-PrOH (2 mL) under N_2 was added PPTS (~ 25 mg) and the mixture was heated to reflux for 3 h. Then, it was cooled to r.t. and CH_2Cl_2 was added. The resulting mixture was successively washed with brine (10 mL) and H_2O (10 mL), dried (Na_2SO_4) and concentrated. The residue was purified by preparative TLC to give **9a** (0.118 g, 88%) as a yellow oil.

^{1}H NMR ($CDCl_3$/TMS): δ = 1.72 (d, 3 H, *J* = 1.19 Hz), 1.78 (s, 3 H), 7.25–7.46 (m, 5 H), 3.47 (d, 2 H, *J* = 7.15 Hz), 5.06 (s, 2 H), 5.25 (t, 1 H, *J* = 7.15 Hz), 5.32 (s, 1 H), 6.48 (dd, 1 H, *J* = 1, 8.24 Hz), 6.54 (dd, 1 H, *J* = 0.92, 8.24 Hz), 7.03 (t, 1 H, *J* = 8.24 Hz).

^{13}C NMR ($CDCl_3$/TMS): δ= 17.73, 22.39, 25.67, 70.36, 104.55, 109.03, 115.65, 121.95, 127.02, 127.13, 127.64, 128.35, 134.04, 137.25, 155.37, 157.03.

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