δ 0.91 (d, J = 6.1 Hz, 6 H, CH_3 Leu), 1.36 (br s, 3 H, CH_3CH_2O), 1.44 (s, 9 H, CH_3 Boc), 1.58, 1.79 (2 m, 7 H, CH, CH_2 Leu, $2CH_2$ cycl), 3.12, 3.41 (2 m, 4 H, β CH_2 Phe, CH_2 cycl), 3.74 (m, 1 H, α CH Leu), 4.09 (m, 2 H, CH_2N cycl), 4.24 (m, 2 H, CH_2O), 4.81 (m, 1 H, α CH Phe), 5.48 (m, 1 H, NH Boc), 7.28 (m, 5 H, Ar), 8.3 (m, 1 H, NH Phe); IR 2995, 2200, 1720, 1680, 1540, 1285 cm^{-1}; exact mass calcd for $C_{29}H_{42}N_4O_5$ 526.3158, found 256.3206.

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Registry No. **1a**, 10441-57-3; **2a**, 53583-60-1; **2b**, 26978-74-5; **2c**, 125138-99-0; **2d**, 125139-00-6; **2e**, 125139-01-7; **2f**, 125139-02-8; **2g**, 125139-03-9; **2j**, 125139-04-0; **4**, 118525-55-6; **4a**, 125139-05-1; **4b**, 118525-57-8; **5a**, 118525-58-9; **5b**, 125139-06-2; **5c**, 125139-07-3; **6a**, 41792-67-0; **6b**, 6482-39-9; **7**, 100477-67-6; **8**, 13326-10-8; $CH_2(CN)_2$, 109-77-3; $NCCH_2COOMe$, 105-34-0; $NCCH_2COOBu$-t, 1116-98-9; $PhCOCH_2CN$, 614-16-4; $NCCH_2NO_2$, 13218-13-8; $PhSO_2CH_2ICN$, 7605-28-9; O_2NCH_2COOEt, 626-35-7; $NCCH_2COOEt$, 105-56-6; $PhCH_2Br$, 100-39-0; Ag_2CO_3, 534-16-7; 2-pyridineacetonitrile, 2739-97-1.

Halogen Effect on the Ring Opening of Pulegone Hydrohalides

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The ring-opening reaction of pulegone hydrochloride (**2a**) with nucleophiles such as NaOH, $LiNMe_2$, and LAH, reported by Plesek[1] and Overberger,[2] serves as a convenient means for the synthesis of acyclic chiral compounds (see Scheme I). In conjunction with our continuing interest in the stereocontrolled synthesis of steroid side chains,[3] an application of this useful ring-opening reaction of α-(2-halo-2-methylethyl)cyclohexanones was envisioned. However, the yields reported by the above two groups were relatively low for synthetic applications, and it was our intent to improve the yields and expand the scope of this reaction through the understanding of the dynamics that control it. Of particular interest to us were the effect of halogens in these reactions and the possible use of carbon nucleophiles for such a ring-opening reaction.

Results and Discussion

The pulegone hydrohalides, hydrochloride **2a**,[1,2] hydrobromide **2b**,[4] and hydroiodide **2c**,[4] were prepared quantitatively by passing the corresponding dry hydrogen halide gas through neat (+)-(*R*)-pulegone (1) at 0–5 °C. These relatively unstable hydrohalides were obtained as a 4.9–5.6:1 mixture of stereoisomers, of which the trans isomer is predominant in all cases as judged from their ^1H NMR spectra, indicating the presence of the characteristic axial hydrogen at C-2 ($^3J_{2,3eq}$ = 3.8–4.6 Hz, $^3J_{2,3ax}$ = 12.1–12.9 Hz, and $^4J_{2,6ax}$ = 1.0–2.3 Hz). Treatment of pulegone hydrochloride (**2a**) with NaOH, $LiNMe_2$, and LAH resulted in the formation of (+)-(*R*)-citronellic acid (**5**), (−)-(*R*)-*N*,*N*-dimethylcitronellamide (**6**), and (+)-(*R*)-citronellol (**7**), respectively, with yields comparable to those reported by Overberger[2] (see Table I). In an attempt to improve the low yield of (+)-(*R*)-citronellol, hydrobromide **2b**[4] was treated with LAH under the same conditions employed with hydrochloride **2a**, which resulted in the improvement of the yield of **7** from 16% to 45%. In a belief that this may be an indication of a trend, hydroiodide **2c** was next treated with LAH as above, and the yield of **7** was further improved to 60%. Encouraged by these results, we then investigated the ring opening of the pulegone hydrohalides with NaOH and $LiNMe_2$ but found that as the atomic weight of the halogen increases the yield of these reactions decrease (Table I). It should be noted in this regard that the hydrofluoride derivative of pulegone was not successfully prepared when pulegone was exposed to dry HF gas.

In an effort to yet further improve the yield of citronellol (**7**), reduction of pulegone hydrohalides **2a–c** with non-lithium-based hydrides such as $NaB(OMe)_3H$ and DIBAL was examined. The reduction with the former reagent gave mixtures of stereoisomeric pulegols and some unidentifiable olefinic compounds in low yields from each of the three hydrohalides. In contrast, the use of the latter reagent resulted in the formation of **7** in 79, 59, and 0% yields for the hydrochloride, hydrobromide, and hydroiodide, respectively. It is interesting to note that the trend observed for LAH was opposite to that of all of the other nucleophiles studied. We next sought to directly obtain the ester or thioester of citronellic acid (**5**) from the pulegone hydrohalides with an alkoxide or thiolate anion as a nucleophile, respectively. However, treatment of the

Scheme I

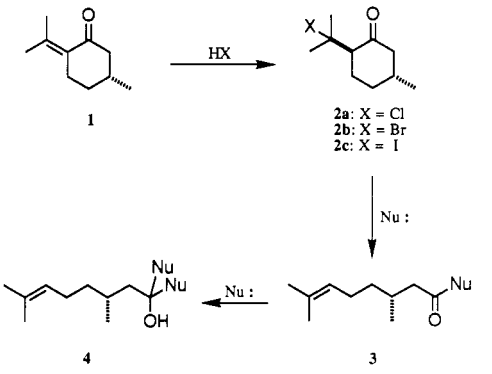

Table I. Nucleophilic Addition of Pulegone Hydrohalides

reagent	product R	yield (%)[a] from 2a (X = Cl)	2b (X = Br)	2c (X = I)
NaOH	COOH (**5**)	52[b,c]	28[c]	0[c]
$LiNMe_2$	$CONMe_2$ (**6**)	47[b]	30	0
LAH	CH_2OH (**7**)	16[b]	45	60
DIBAL	CH_2OH (**7**)	79	59	0
MeLi	$COCH_3$ (**8**)	78	44[d]	0[e]
n-BuLi	CO-*n*-Bu (**9**)	75	0[e]	0[e]
t-BuLi	CO-*t*-Bu (**10**)	63[c]	31[c]	0[c]
PhLi	COPh (**11**)	60	0	0

[a] Isolated yields except where indicated. [b] Yields reported by Oberverger,[2] confirmed in this study. [c] Recovered pulegone makes up the balance. [d] Isolated as a 1.4:1 inseparable mixture of **8** and bis-adduct **4** (Nu = Me). [e] Only bis-adducts and pulegone recovered.

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pulegone hydrohalides with excess lithium ethoxide[5] in either THF or ethanol resulted in the clean generation of the elimination product, pulegone (**1**). The use of the more nucleophilic thiolate such as excess lithium thioethoxide or lithium thiophenoxide in THF led to the highly efficient formation of the β-thiolate adduct of pulegone (X = SR in **2**), and no ring-opening products were detected even after prolonged refluxing. Addition of a Lewis acid such as $TiCl_4$ facilitated the formation of pulegone in addition to these β-thiolate adducts.

The use of carbon nucleophiles met with a much greater success than the oxygen and sulfur nucleophiles. Thus, treatment of pulegone hydrochloride (**2a**) with MeLi, *n*-BuLi, and PhLi at −78 °C in THF resulted in the formation of the ring-opening products methyl ketone **8**, *n*-butyl ketone **9**, and phenyl ketone **11** in 78, 75, and 60% yields, respectively. Even the reaction of **2a** with the bulky *t*-BuLi gave *tert*-butyl ketone **9** in 63% yield. However, in this case the remainder of the reaction product was the elimination product pulegone (ca. 35% yield). Interestingly, when hydrobromide **2b** was treated with MeLi, a 1.4:1 ratio of mono- to bis-adducts, **8** and **4** (Nu = Me), respectively, along with pulegone was obtained, and when hydroiodide **2c** was used, only the bis-adduct (**4**: Nu = Me) (in approximately 50% yield) and pulegone (in 36% yield) were isolated. This problem of formation of the bis-adduct was even more pronounced when *n*-BuLi was used; both hydrobromide **2b** and hydroiodide **2c** gave only the bis-adduct (**4**: Nu = *n*-Bu) and pulegone. The production of the bis-adduct **4** with virtually no formation of the expected ring-opening product may be explainable in terms of both steric and kinetic effects. Ring opening of the initially generated mono-adduct of pulegone hydrochloride **2a** is likely to be slow compared with the nucleophilic attack on the ketone carbon, thus practically all of the organolithium reagent must have reacted with pulegone hydrochloride before any appreciable quantities of the ring-opened product are accumulated. In contrast, with the hydrobromide **2b**, the rate of this ring opening of the initial mono-adduct is probably as fast or faster than that of the addition, and with the hydroiodide **2c**, the rate of the ring opening is likely to be significantly faster. Accordingly, both the product ketone **3** and pulegone hydrobromide/hydroiodide are in solution at the same time. Given that axial attack on the pulegone hydrohalide ring system would take place from the same side as the isopropyl halide unit, the open chain product ketone would have to be considered significantly less hindered toward addition and therefore would explain the formation of appreciable amounts of the bis-adduct **4** when hydrobromide **2b** is treated with MeLi and its exclusive formation in the other three cases mentioned above. When a less reactive nucleophile than the alkyllithium reagents was used, e.g., MeMgBr in THF at −78 °C, the formation of only the bis-adduct (**4**: Nu = Me) was observed for pulegone hydrochloride **2a** and hydrobromide **2b** and only the recovery of pulegone for hydroiodide **2c**. Although the yield decreased with increasing halide atomic weight when *t*-BuLi was used as the nucleophile, the formation of the bis-adduct was not observed, presumably due to the bulkiness of the product ketone **10**.

Attempts to open the pulegone hydrohalide ring with refluxing TMSMgBr in THF surprisingly failed and resulted in recovering the starting hydrohalide. Treatment of pulegone hydrochloride with TMSLi in THF in the presence of 1 equiv of HMPA resulted in the smooth formation of pulegone. Likewise, pulegone was the only product obtained when all three hydrohalides were treated with $(n\text{-Bu})_3\text{SnLi}$[6] in THF.

In summary, the formation of (*R*)-(+)-citronellol (**7**) from a pulegone hydrohalide has been improved from 16% to 60% (from hydroiodide **2c** with LAH) and 79% (from hydrochloride **2a** with DIBAL in THF). It was found that with one exception, the yields of the ring-opening products with non-carbon nucleophiles decreased as the atomic weight of the starting hydrohalide halogen is increased. Most significantly, a variety of carbon nucleophiles are also found to cause a similar ring-opening reaction of the pulegone hydrohalides. In all cases with carbon nucleophiles, pulegone hydrochloride gave the best yield for the formation of the ring-opened product **3** among three hydrohalides. Apparently, the relative propensity of hydrobromide and hydroiodide for ring opening of the initial mono-adduct contributes to the greater formation of bis-adduct **5** with the exception of the reaction with *t*-BuLi.

Experimental Section

General Methods. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$. Only resonances of the major isomers of the pulegone hydrohalides are reported.

Column chromatographic separation was performed with the method of flash column chromatography with Merck 230–400-mesh silica gel.[7] Reactions were monitored by thin-layer chromatography (TLC) with Analtech 250 plates with fluorescent indicator. Spots were detected by ultraviolet light (254 nm), iodine vapor, and ceric ammonium sulfate–sulfuric acid.

Air- and/or moisture-sensitive reactions were performed under a static pressure of dry nitrogen after the reaction vessel was flushed with a stream of dry nitrogen. All glassware was oven-dried. Reagents and solvents were transferred by standard syringe techniques through rubber septa. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl.

(+)-Pulegone was purchased from Aldrich Chemical Co. and purified by vacuum distillation: $[\alpha]^{23}_D$ +24.4° (neat); $[\alpha]^{23}_D$ +24.1° (*c* 2.80, $CHCl_3$). All three pulegone hydrohalides **2a–c** have been reported.[2,4] However, with the exception of **2a**, no experimental details were given, and in no cases were physical or spectroscopic properties listed. In the experimental below, the product pulegone hydrohalides are accompanied by a small amount of the acid. With the exception of *t*-BuLi, which was used in a slight excess, the amount of alkyl/phenyllithium and DIBAL utilized was adjusted so that the acid present in the starting hydrohalide could be neutralized. The amount given in the experimental data is that which was used after the neutralization of the residual acid. Methyl ketone **8**,[8] *n*-butyl ketone **9**,[9] and phenyl ketone **11**[10] have been prepared from (*R*)-citronellal, but incomplete or no physical/spectroscopic data were provided.

(2*R*,5*R*)-2-(1-Chloro-1-methylethyl)-5-methylcyclohexanone (Pulegone Hydrochloride, 2a). HCl gas was generated by the addition of concentrated HCl (30 mL) to ice-cold concentrated H_2SO_4 (70 mL), and the resultant gas was dried by passing through $CaCl_2$. Dry HCl gas bubbled through 14.8 g of pulegone in a 25-mL, round-bottomed flask at 0–5 °C. After the addition was complete (3.854 g of HCl absorbed, 0.308 g excess over the theoretical amount), the red oily product, a 4.9:1 ratio of diastereomers, was kept at 0 °C for 1 day to ensure complete

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reaction: ^{1}H NMR (300 MHz) δ 1.035 (d, 3 H, J = 6.2 Hz, 5-Me), 1.417 (dddd, 1 H, J = 3.3, 11.3, 12.9, 13.0 Hz, 4ax-H), 1.611 (dddd, 1 H, J = 3.1, 12.2, 12.9, 13.0 Hz, 3ax-H), 1.620 and 1.724 (s, 3 H each, $CClMe_2$), 1.880 (m, 1 H, 5ax-H), 1.960 (m, 1 H, 4eq-H), 2.064 (ddd, 1 H, J = 1.1, 12.4, 12.4 Hz, 6ax-H), 2.321 (ddd, 1 H, J = 2.2, 3.9, 12.4 Hz, 6eq-H), 2.563 (dddd, 1 H, J = 3.3, 3.3, 4.6, 12.2 Hz, 3eq-H), 2.731 (ddd, 1 H, J = 1.1, 4.6, 12.9 Hz, 2-H); ^{13}C NMR (75.47 MHz) δ 22.22 (q), 27.91 (q), 29.85 (t), 32.28 (q), 34.37 (t), 36.59 (d), 51.99 (t), 61.46 (d), 72.20 (s), 209.15 (s); IR (neat) 1712 cm^{-1}.

(2*R*,5*R*)-2-(1-Bromo-1-methylethyl)-5-methylcyclohexanone (Pulegone Hydrobromide, 2b). HBr gas was generated by the addition of 40 mL of 48% aqueous HBr to ice-cold P_2O_5 (80 g), and the resultant gas was dried by passing through $CaCl_2$. Dry HBr gas was bubbled through 15.0 g of pulegone at 0–5 °C. After the addition was complete (8.73 g of HBr absorbed, 0.76 g excess over the theoretical amount), the orange solid product, a 5.4:1 ratio of diastereomers, was kept at 0 °C until needed: ^{1}H NMR (300 MHz) δ 1.035 (d, 3 H, J = 6.2 Hz, 5-Me), 1.435 (dddd, 1 H, J = 3.3, 11.4, 13.0, 13.0 Hz, 4ax-H), 1.671 (dddd, 1 H, J = 3.2, 12.9, 13.0, 13.0 Hz, 3ax-H), 1.861 and 1.997 (s, 3 H each, $CBrMe_2$), 1.942 (m, 2 H, 4eq- and 5ax-H), 2.061 (ddd, 1 H, J = 1.0, 12.0, 12.3 Hz, 6ax-H), 2.301 (ddd, 1 H, J = 2.1, 3.9, 12.0 Hz, 6eq-H), 2.626 (dddd, 1 H, J = 3.1, 3.3, 4.6, 13.0 Hz, 3eq-H), 2.818 (ddd, 1 H, J = 1.0, 4.6, 12.9 Hz, 2-H); ^{13}C NMR (75.47 MHz) δ 22.15 (q), 29.81 (q), 31.49 (t), 34.07 (q), 34.48 (t), 36.71 (d), 52.56 (t), 62.38 (d), 69.68 (s), 208.59 (s); IR (neat) 1710 cm^{-1}.

(2*R*,5*R*)-2-(1-Iodo-1-methylethyl)-5-methylcyclohexanone (Pulegone Hydroiodide, 2c). HI gas was generated by the addition of 50 mL of 57% aqueous HI to ice-cold P_2O_5 (100 g), and the resultant gas was dried by passing through $CaCl_2$. Dry HI gas was bubbled through 15.0 g of pulegone at 0 °C. After the addition was complete (12.87 g of HI absorbed, 0.270 g over the theoretical amount) the dark purple solid, a 5.6:1 ratio of diastereomers, was kept at 0 °C until needed: ^{1}H NMR (300 MHz) δ 1.038 (d, 3 H, J = 6.2, 5-Me), 1.461 (dddd, 1 H, J = 3.4, 11.3, 12.8, 12.8 Hz, 4ax-H), 1.728 (dddd, 1 H, J = 3.3, 12.8, 12.9, 12.9 Hz, 3ax-H), 1.945 (m, 2 H, 4eq- and 5ax-H), 2.041 and 2.218 (s, 3 H each, $CIMe_2$), 2.056 (ddd, 1 H, J = 1.0, 12.1, 12.4 Hz, 6ax-H), 2.273 (ddd, 1 H, J = 2.3, 3.8, 12.1 Hz, 6eq-H), 2.554 (m, 2 H, 2ax- and 3eq-H); ^{13}C NMR (90.56 MHz) δ 22.07 (q), 33.81 (t), 34.06 (q), 34.43 (t), 36.69 (d), 37.57 (q), 51.99 (t), 53.13 (s), 63.92 (d), 208.39 (s); IR (neat) 1712 cm^{-1}.

(+)-(*R*)-3,7-Dimethyl-6-octen-1-ol [(+)-Citronellol, 7]. Pulegone hydrochloride (1.50 g) in 25 mL of THF was cooled to −78 °C, after which point 17 mL of 1 M DIBAL (2.1 equiv) in THF was added. The solution was stirred at this temperature for 1 h and then allowed to warm slowly to room temperature. The reaction mixture was quenched with 50 mL of ether and washed with 10% aqueous HCl (2 × 50 mL), saturated aqueous $NaHCO_3$ (25 mL), and brine (25 mL). The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed. The crude product was purified by silica gel chromatography with 20% ethyl acetate/hexanes as the eluent to give 0.978 g of 7 (79%) as a colorless liquid which showed ^{1}H and ^{13}C NMR spectra identical with those of an authentic sample: $[\alpha]^{23}_D$ +5.40° (neat) [lit.[11] $[\alpha]^{25}_D$ +5.45° (neat)], $[\alpha]^{23}_D$ +5.14° (*c* 2.22, $CHCl_3$).

(*R*)-4,8-Dimethylnon-7-en-2-one (8). Pulegone hydrochloride (0.507 g) in 20 mL of THF was cooled to −78 °C, after which point 2.7 mL of 1.25 M methyllithium in ether (1.00 equiv) was added. The solution was stirred at this temperature for 1 h and then warmed slowly up to room temperature. The solution was poured into 50 mL of 5% aqueous NaOH, and the resulting mixture was stirred for 2 h, ether was added (40 mL), and the organic layer washed with brine, dried over $MgSO_4$, and filtered, and the solvent was evaporated off. The crude product was purified by silica gel chromatography with 5% ethyl acetate–hexanes as the eluent to give 0.352 g of 8 (78%) as a colorless liquid: bp 44 °C (1.5 mmHg); $[\alpha]^{23}_D$ +9.44° (*c* 2.50, $CHCl_3$); ^{1}H NMR (360 MHz) δ 0.904 (d, 3 H, J = 6.6 Hz), 1.224 (m, 1 H), 1.306 (m, 1 H), 1.600 (br s, 3 H), 1.679 (d, 3 H, J = 1.1 Hz), 2.004 (m, 3 H), 2.124 (s, 3 H), 2.228 (dd, 1 H, J = 8.2, 15.8 Hz), 2.423 (dd, 1 H, J = 5.6, 15.8 Hz), 5.085 (ddqq, 1 H, J = 1.1, 1.3, 7.1, 7.1 Hz); ^{13}C NMR (90.56 MHz) δ 17.64 (q), 19.75 (q), 25.50 (t), 25.69 (q), 29.02 (d), 30.34 (q), 37.02 (t), 51.22 (t), 124.38 (d), 131.46 (s), 208.79 (s); IR (neat) 1718 cm^{-1}. Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.95. Found: C, 78.58; H, 11.80.

(*R*)-7,11-Dimethyldocec-10-en-5-one (9). Pulegone hydrochloride (1.00 g) in 40 mL of THF was stirred and cooled to −78 °C after which point 3.6 mL of 1.5 M *n*-BuLi in hexanes (1.00 equiv) was added. The reaction mixture was stirred for 1 h at this temperature and then warmed slowly to room temperature. The reaction mixture was poured into 50 mL of aqueous NaOH, and the resulting mixture was stirred overnight. Ether (100 mL) was added, the organic layer was washed with 40 mL of brine, dried over $MgSO_4$, and filtered, and the solvent was evaporated off. Silica gel chromatography with 10% ethyl acetate/hexanes as the eluent gave 0.090 g (6%) of dialkylated product and 0.831 g (75%) of 9 as a colorless liquid: bp 58 °C (1.5 mm); $[\alpha]^{23}_D$ +6.40° (*c* 3.50, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.892 (d, 3 H, J = 6.6 Hz), 0.903 (t, 3 H, J = 6.8 Hz), 1.208 (m, 1 H), 1.308 (m, 3 H), 1.549 (m, 2 H), 1.595 (br s, 3 H), 1.676 (d, 3 H, J = 1.1 Hz), 1.988 (m, 3 H), 2.199 (dd, 1 H, J = 8.0, 15.7 Hz), 2.382 (m, 3 H), 5.084 (ddqq, 1 H, J = 1.1, 1.4, 7.1, 7.1 Hz); ^{13}C NMR (90.56 MHz) δ 13.86 (q), 17.64 (q), 19.86 (q), 22.46 (t), 25.58 (t), 25.69 (q), 26.02 (t), 29.04 (d), 37.13 (t), 43.13 (t), 50.32 (t), 124.50 (d), 131.41 (s), 210.96 (s); IR (neat) 1711 cm^{-1}. Anal. Calcd for $C_{14}H_{26}O$: C, 79.93; H, 12.46. Found: C, 79.95; H, 12.37.

(*R*)-2,2,5,9-Tetramethyldec-8-en-3-one (10). Pulegone hydrochloride (1.00 g) in 35 mL of THF was cooled to −78 °C, after which point 4.5 mL of 1.43 M *t*-BuLi in pentane (1.20 equiv) was added. The reaction mixture was stirred at this temperature for 1 h before slowly warming up to room temperature. Ether (100 mL) was added, the organic layer was washed with 50 mL of brine, dried over $MgSO_4$, and filtered, and the solvent was evaporated off. Silica gel chromatography with 10% ethyl acetate/hexanes as the eluent gave 0.702 g of 10 (63%) as a colorless liquid and 0.291 g of pulegone (36%) recovered. For 10: bp 56 °C (1.5 mmHg); $[\alpha]^{23}_D$ −2.63° (*c* 2.40, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.863 (d, 3 H, J = 6.6 Hz), 1.121 (s, 9 H), 1.161 (m, 1 H), 1.264 (m, 1 H), 1.594 (br s, 3 H), 1.676 (br s, 3 H), 1.972 (m, 2 H), 2.046 (m, 1 H), 2.327 (dd, 1 H, J = 7.6, 17.1 Hz), 2.418 (dd, 1 H, J = 5.8, 17.1 Hz), 5.091 (ddqq, 1 H, J = 1.3, 1.3, 7.0, 7.0 Hz); ^{13}C NMR (75.47 MHz) δ 17.64 (q), 19.83 (q), 25.70 (t,q), 26.37 (q, 3 C), 28.38 (d), 37.09 (t), 43.96 (t), 44.16 (s), 124.68 (d), 131.24 (s), 215.08 (s); IR (neat) 1708 cm^{-1}. Anal. Calcd for $C_{14}H_{26}O$: C, 79.93; H, 12.46. Found: C, 79.66; H, 12.45.

(*R*)-1-Phenyl-3,7-dimethyloct-6-en-1-one (11). Pulegone hydrochloride (3.00 g) in 80 mL of THF was cooled to −100 °C, after which point 7.5 mL of 2 M phenyllithium in 70:30 cyclohexane/ether (1.00 equiv) was added. The solution was stirred at this temperature for 1 h before slowly warming up to room temperature. The reaction mixture was then poured into 50 mL of 5% aqueous NaOH and stirred for 4 h. Ether (200 mL) was added, and the organic layer was washed with brine, dried over $MgSO_4$, and filtered, and the solvent was evaporated off. Silica gel chromatography (10% ethyl acetate/hexanes as the eluent) gave 2.20 g of 11 (60%) as a colorless liquid: bp 72–74 °C (1.5 mmHg); $[\alpha]^{23}_D$ −1.67° (*c* 3.18, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.965 (d, 3 H, J = 6.6 Hz), 1.297 (m, 1 H), 1.416 (m, 1 H), 1.599 (br s, 3 H), 1.676 (d, 3 H, J = 1.1 Hz), 2.028 (m, 2 H), 2.280 (m, 1 H), 2.742 (dd, 1 H, J = 8.1, 15.7 Hz), 2.966 (dd, 1 H, J = 5.5, 15.7 Hz), 5.099 (ddqq, 1 H, J = 1.1, 1.3, 7.1, 7.1 Hz), 7.450 (ddd, 2 H, J = 1.5, 7.1, 7.4 Hz), 7.547 (dddd, 1 H, J = 1.5, 1.5, 7.4, 7.4 Hz), 7.945 (dd, 2 H, J = 1.5, 7.1 Hz); ^{13}C NMR (75.47 Hz) δ 17.65 (q), 19.98 (q), 25.63 (t), 25.68 (q), 29.60 (d), 37.28 (t), 45.64 (t), 124.46 (d), 128.10 (d, 2 C), 128.49 (d, 2 C), 131.36 (s), 132.73 (d), 137.59 (s), 200.14 (s); IR (neat) 1686 cm^{-1}. Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.30; H, 9.73.

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