J. Org. Chem. 1992, 57, 2757-2760 2757

A New Synthesis of α- and β-Damascones from the Ionones

Luis A. Sarandeses and Jean-Louis Luche*

LEDSS, Université Joseph Fourier, BP 53X,
38041-Grenoble Cedex, France

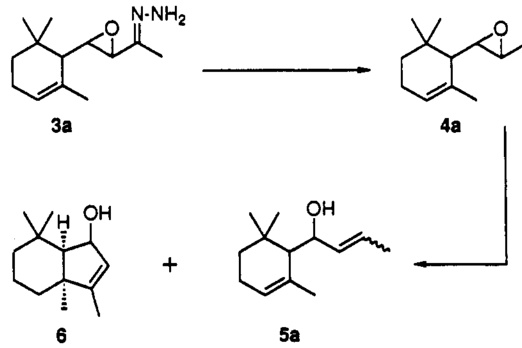
Received September 13, 1991

Scheme I[a]

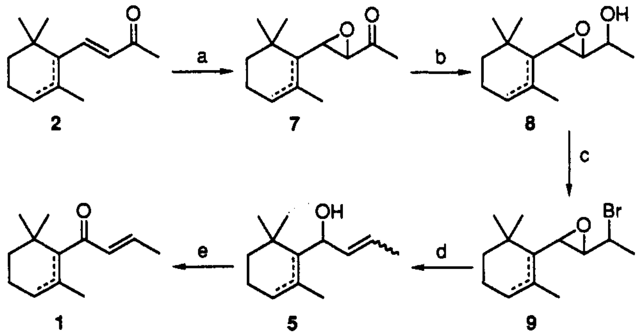
1a $\Delta^{2,3}$: α-Damascone
1b $\Delta^{1,2}$: β-Damascone
2a $\Delta^{2,3}$: α-Ionone
2b $\Delta^{1,2}$: β-Ionone

[a] Key: **a** series, $\Delta^{2,3}$; **b** series, $\Delta^{1,2}$.

Scheme II



Scheme III[a]



[a] Key: (a) H_2O_2, NaOH, MeOH (**a**: 85%, **b**: 52%); (b) $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH (**a**: 94%, **b**: 96%); (c) CBr_4, Ph_3P, py (**a**: 95%, **b**: 89%); (d) Zn, CuI, H_2O, EtOH, ultrasound (**a**: 91%, **b**: 80%); (e) MnO_2, CH_2Cl_2 (**a**), pentane (**b**); p-TsOH, THF, Δ (**a**: 86%, **b**: 71%).

The members of the damascone family (**1**, Scheme I) extracted from Bulgarian roses constitute a popular class of perfumes.[1] Although this structure is relatively simple, their synthesis is not as easy as expected, and they are considered as valuable targets to test new synthetic methods. Several more or less complicated approaches have been explored,[2,3] but the more simple access starts from the inexpensive, naturally occuring ionones **2**, requiring a 1,3-allylic transposition of the carbonyl group.

This transposition is not as straightforward as it seems, and the small number of really useful methods attests to the absence of a reasonably general good one.[4] Early work from the Firmenich group following this route via the Wharton transposition[5] led to unsatisfactory results. As shown in Scheme II, hydrazone **3a** yields 20% of the expected α-damascol (**5a**) and 30% of the bicyclic compound **6**. The intermediacy of radical **4a** has been suggested.[6]

More recently, α- and β-ionones served as the starting materials in a six-step synthesis of **1a** and **1b**, with an overall yield of 22% and 28%, respectively.[2c] We also proposed a modification of the Wharton transposition with fair to good (30–70% overall) yields.[7] In this paper, we wish to describe a new, and improved synthesis, in which the key step is the selective allylic transposition induced by sonication in the presence of a zinc–copper couple.[8]

Commercial α-ionone (**2a**, Scheme III) is converted to epoxy ketone **7a** with alkaline hydrogen peroxide in 85% yield,[5] and then the carbonyl group is reduced by sodium borohydride in the presence of cerium chloride[9] to give the epoxy alcohols **8a** (94%) as a pair of diastereomers. No separation (TLC, column chromatography) was found possible. However, as the desired final product **1a** is a simple racemic mixture, the relative stereoselectivity has no relevance. Thus, no effort was made to modify the selectivity of the reduction, and the mixture was used in the following steps. Conversion of **8a** to **9a** is achieved with carbon tetrabromide and triphenylphosphine in 95% yield. The epoxybromides are then submitted to the ring-opening conditions.

Zinc dust and cuprous iodide are sonicated in water to give a black, heavy suspension to which an ethanol solution of **9a** is added.[8] Sonication is continued for 90 min, and then the mixture is worked up to give the allylic alcohol **5a** in 91% yield as a 2:1 mixture of the E/Z isomers. The same ratio is obtained when the reaction is effected from a single diastereomer of the epoxy bromide, making the difficult separation unnecessary. The synthesis of **1a** is completed by manganese dioxide oxidation (96%) followed by an acid-catalyzed isomerization leading to α-damascone (**1a**) as a 9:1 mixture of the E/Z isomers which is generally the form used in perfumery. The pure E-isomer can be obtained by column chromatography (86% from **5a**). The overall yield for the 5 steps is 60%, which is the best result for the routes using α-ionones as the starting material.

The same sequence is repeated from β-ionone in a effort to obtain β-damascone. However, it is worth mentioning that the compounds involved in this synthetic sequence are significantly less stable than in the α series. The difficult regioselective epoxidation of **2b** is effected by the same procedure as for **2a** and provides epoxy ketone **7b** in 52% yield.[10]

The following steps of reduction to **8b** and preparation of the bromide **9b** can be accomplished with the excellent 96% and 89% yields, respectively. The sonochemical reductive ring opening to **5b** is then achieved easily (80%).

---

(1) Demole, E.; Enggist, P.; Säuberli, U.; Stoll, M.; Kováts, E. S. *Helv. Chim. Acta* **1970**, *53*, 541–551.

(2) (a) Fehr, C.; Galindo, J. *Helv. Chim. Acta* **1986**, *69*, 228–235. (b) Snowden, R. L.; Linder, S. M.; Muller, B. L.; Schulte-Elte, K. H. *Helv. Chim. Acta* **1987**, *70*, 1858–1878. (c) Azzari, E.; Faggi, C.; Gelsomini, N.; Taddei, M. *J. Org. Chem.* **1990**, *55*, 1106–1108.

(3) (a) Zaidlewicz, M. *Tetrahedron Lett.* **1986**, *27*, 5135–5138. (b) Gosselin, P. *Tetrahedron Lett.* **1986**, *27*, 5495–5496.

(4) (a) Barton, D. H. R.; Motherwell, R. H. S.; Motherwell, V. B. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2363–2367. (b) Hirota, H.; Yokoyama, A.; Miyaji, K.; Nakamura, T.; Takahashi, T. *Tetrahedron Lett.* **1987**, *28*, 435–438 and references cited therein.

(5) Ohloff, G.; Uhde, G. *Helv. Chim. Acta* **1970**, *53*, 531–541.

(6) Stork, G.; Williard, P. G. *J. Am. Chem. Soc.* **1977**, *99*, 7067–7068.

(7) Dupuy, C.; Luche, J. L. *Tetrahedron* **1989**, *45*, 3437–3444.

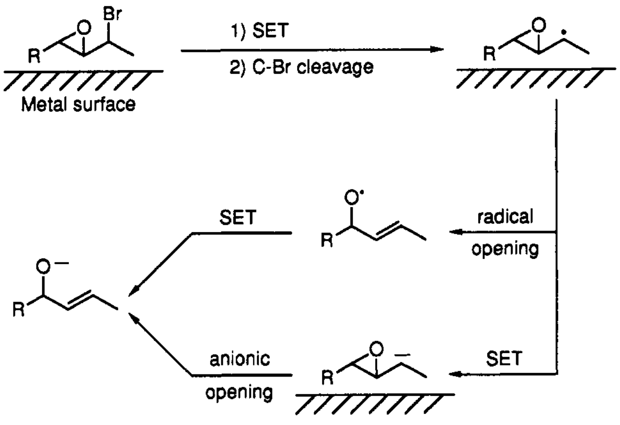
(8) Sarandeses, L. A.; Mouriño, A.; Luche, J. L. *J. Chem. Soc., Chem. Commun.* **1991**, 818–820.

(9) Luche, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 2226–2227.

(10) Davalian, D.; Heathcock, C. H. *J. Org. Chem.* **1979**, *44*, 4458–4461. Several attempts to improve the yields remained unsuccessful. Changing the reagent led to lower yields (anhyd t-BuOOH, KH or n-BuLi, THF) or to undesired regioselectivity ($KHSO_5$, acetone, H_2O).

0022-3263/92/1957-2757$03.00/0 © 1992 American Chemical Society

Scheme IV



It is interesting to note that, in contrast to the α-series, the NMR spectrum of the crude reaction mixture exhibits a set of signals corresponding to the bicyclic alcohol **6** (Scheme II). Even if the amount is low, it provides an indication that the reaction can proceed via the radical **4b**, the fate of which is probably governed by its adsorption at the surface of the strongly reductive zinc metal. This point was not examined in detail but it is worth mentioning as it constitutes a difference with the behavior of radicals such as **4** in homogeneous solution,[5] and also because our first results[8] did not allow us to make a clear choice between the radical and the anionic pathways for this ring cleavage (Scheme IV).

As in the case of α-damascone, the last steps of the synthesis involve a MnO_2 oxidation, and isomerization of the resulting 1:1 *E*/*Z* mixture to give β-damascone (**1b**) as a 9:1 equilibrium mixture. The major *E* isomer can be obtained pure by flash chromatography (71% from **5b**). The overall yield from β-ionone is 25%.

In summary, the synthesis of α- and β-damascones can be effected in a very simple manner from cheap and available materials and reagents. The yields are generally high, and the key step, the reductive ring opening of an α-epoxyalkyl bromide, constitutes a synthetic illustration of the possibilities offered by the new sonochemical methods.

Experimental Section

General. All air-sensitive reactions were conducted in a flame-dried apparatus under Ar. CH_2Cl_2, pyridine, and pentane were dried by distillation from CaH_2, and THF was dried by distillation from the sodium ketyl of benzophenone. Zn dust and CuI were purified by the usual methods.[11,12] MnO_2 was activated at 120 °C for 48 h and cooled under vacuum over P_2O_5. All other reagents were commercial products and used as received. Sonications were carried out in a Pulsatron 250, 38-kHz cleaning bath (Kerry Ultrasonics, Hitchin, England), filled with water, and thermostated (18–20 °C) by running tap water in a stainless steel coil. Bulb-to-bulb distillations were performed in a kugelrohr apparatus, and bp corresponds to the external air temperature. TLC was effected on silica gel 60 F_{254} (layer thickness 0.2 mm, Merck). Column chromatography was performed with use of silica gel 60 (70–230 mesh, Merck). Flash chromatography[13] was performed with use of silica gel 60 (230–400 mesh, Merck). All NMR spectra were performed in $CDCl_3$ solution. GC analyses were done using a 2.5-m × 2-mm column coated with 10% Carbowax 20M, with a flame ionization detector, using N_2 as carrier gas (oven 170 °C; injector 200 °C; detector 170 °C). Diastereomeric ratios were determined by ^1H NMR unless otherwise stated.

1-[3-(2,6,6-Trimethyl-2-cyclohexen-1-yl)oxiranyl]ethanone (7a):[5] 85%; bp (bulb-to-bulb) 115–120 °C (0.3 mmHg); TLC (10% EtOAc/hexane) R_f 0.50; IR (neat) 2950, 2850, 1710, 1440, 1365, 1250, 875, 840 cm^{-1}; ^1H NMR (80 MHz) δ 0.93 (s, 3 H), 1.10 (s, 3 H), 1.70 (m, 3 H), 2.07 (s, 3 H), 2.92 (dd, $J_1 = 8.6$ Hz, $J_2 = 2.0$ Hz, 1 H) 3.30 (d, $J = 2.0$ Hz, 1 H), 5.52 (m, 1 H); ^{13}C NMR (20 MHz) δ 22.9, 23.6, 24.4, 26.9, 27.3, 31.7, 32.6, 52.5, 58.6, 59.2, 124.6, 130.3, 205.9.

α-Methyl-3-(2,6,6-trimethyl-2-cyclohexen-1-yl)oxiranemethanol (8a). To a solution of **7a** (5.00 g, 24.00 mmol) in MeOH (50 mL) was added $CeCl_3{\cdot}7H_2O$ (9.84 g, 26.4 mmol). The resulting mixture was cooled to 0 °C, and then $NaBH_4$ (1.00 g, 26.00 mmol) was added in portions. After the solution was stirred for 5 min, water was slowly added, and the resulting mixture extracted with CH_2Cl_2 (6 × 50 mL). The combined organic phases were washed with saturated aqueous NaCl (100 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure in a rotary evaporator. The residue was purified by column chromatography (10–20% EtOAc/hexane) to afford, after evaporation and high vacuum drying, 4.74 g of **8a** (94%, colorless oil, diastereomeric ratio 2.4:1 by NMR): TLC (15% EtOAc/hexane) R_f 0.30; IR (neat) 3450, 2980, 2920, 1450 cm^{-1}; ^1H NMR (200 MHz) δ 0.91 (s, 3 H), 1.08 (s, 3 H), 1.28 (d, $J = 6.4$ Hz, 3 H), 1.71 (br s, 3 H), 2.86 (m, 2 H), 3.96 (m, 1 H), 5.50 (br s, 1 H); ^{13}C NMR (50 MHz) δ 18.9, 23.1, 23.8, 26.8, 27.8, 31.4, 32.6, 52.2, 55.8, 60.3, 65.3, 123.9, 131.0; MS (EI, 70 eV) *m*/*z* 210 (M^+, 0.2), 147 (4), 136 (8), 134 (7), 122 (65), 107 (95), 97 (100); HRMS (EI) calcd for $C_{13}H_{22}O_2$ (M^+) 210, 1620, found 210, 1625. Minor diastereomer: ^1H NMR (200 MHz) δ 3.64 (br q, $J = 6.4$ Hz, 1 H); ^{13}C NMR (50 MHz) δ 19.9, 26.9, 27.5, 31.6, 57.5, 61.4, 67.7, 124.0.

2-(1-Bromoethyl)-3-(2,6,6-trimethyl-2-cyclohexen-1-yl)oxirane (9a). To a cooled (0 °C) solution of the diastereomeric mixture **8a** (2.11 g, 10.03 mmol) in pyridine (40 mL) was added Ph_3P (3.42 g, 13.04 mmol) and, to the resulting solution, CBr_4 (4.32 g, 13.04 mmol). The red solution was stirred for 2 h under Ar at 0 °C followed by a further 2 h at room temperature. Then MeOH (5 mL) was added, and the solvents were removed under reduced pressure. Saturated aqueous $NaHCO_3$ (20 mL) was added to the residue which then was extracted with hexane (5 × 40 mL). The combined organic phase was dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Purification was performed by column chromatography (10–30% EtOAc/cyclohexane) to afford, after evaporation and high vacuum drying 2.61 g of the diastereomeric mixture **9a** (95%, colorless liquid, diastereomeric ratio 3.0:1 by NMR): TLC (15% EtOAc/hexane) R_f 0.77; IR (neat) 3050, 2950, 2850, 1450, 1380, 1365, 1200, 895, 820, 795 cm^{-1}; ^1H NMR (200 MHz) δ 0.89 (s, 3 H), 1.06 (s, 3 H), 1.72 (br s, 3 H), 1.78 (d, $J = 7.1$ Hz, 3 H), 2.80 (dd, $J_1 = 8.6$ Hz, $J_2 = 2.0$ Hz, 1 H), 3.11 (dd, $J_1 = 7.6$ Hz, $J_2 = 2.0$ Hz, 1 H), 3.82 (m, $J = 7.1$ Hz, 1 H), 5.50 (br s, 1 H); ^{13}C NMR (50 MHz) δ 21.9, 23.0, 23.9, 26.7, 27.8, 31.2, 32.5, 49.7, 52.3, 61.2, 61.3, 124.2, 130.6; MS (EI, 70 eV) *m*/*z* 274 ($M^+ + 2$, 0.1), 272 (M^+, 0.1), 259 (2.5), 257 (2.8), 175 (15), 137 (38), 123 (100), 107 (95); HRMS (EI) calcd for $C_{13}H_{21}BrO$ (M^+) 272.0776, found 272.0776. Minor diastereomer: ^1H NMR (200 MHz) δ 2.74 (dd, $J_1 = 8.5$ Hz, $J_2 = 2.1$ Hz, 1 H), 3.05 (dd, $J_1 = 8.0$ Hz, $J_2 = 2.1$ Hz, 1 H), 3.64 (m, $J_1 = 8.0$ Hz, $J_2 = 7.1$ Hz, 1 H); ^{13}C NMR (50 MHz) δ 22.9, 24.2, 47.9, 52.2, 60.6, 61.0, 123.8, 130.8.

2,6,6-Trimethyl-α-(1-propenyl)-2-cyclohexene-1-methanol (5a). A mixture of Zn dust (120 mg, 1.86 mmol) and CuI (120 mg, 0.62 mmol) in H_2O (7 mL) was sonicated under Ar for 5 min to prepare the Zn(Cu) couple. To this black mixture was added a solution of **9a** (170 mg, 0.62 mmol diastereomeric ratio 3.0:1) in EtOH (3 mL). The reaction was monitored by TLC and after sonication for 90 min was judged complete. Saturated aqueous NH_4Cl (10 mL) was added and the sonication continued for another 10 min. The resulting mixture was filtered through Celite and washed with Et_2O (2 × 10 mL). The aqueous phase was extracted with Et_2O (3 × 40 mL), and the solids were extracted under sonication with Et_2O (2 × 10 mL). The combined organic phase was washed with saturated aqueous NaCl (60 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel–5% Et_3N, 20% EtOAc/hexane) to afford, after evaporation and high vacuum drying, 110 mg of **5a**[2,5] (91%, colorless liquid, *E*:*Z* = 2:1): TLC (20% EtOAc/hexane) R_f 0.60; IR (neat) 3350, 3050, 2950,

---

[11] Tsuda, K.; Ohki, E.; Nozoe, S. *J. Org. Chem.* **1963**, *28*, 783–785.

[12] Kauffman, G. B.; Teter, L. A. *Inorg. Synth.* **1963**, *7*, 9–12.

[13] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

2925, 2850, 1450, 1385, 995, 960, 820 cm^{-1}. **(E)-5a**: ^{1}H NMR (300 MHz) δ 0.86 (s 3 H), 0.97 (s, 3 H), 1.68 (d, J = 4.4 Hz, 3 H), 1.77 (m, 3 H), 4.36 (dd, J_1 = 7.2 Hz, J_2 = 2.9 Hz, 1 H), 5.57 (m, 3 H). **(Z)-5a**: ^{1}H NMR (300 MHz) δ 4.76 (dd, J_1 = 8.1 Hz, J_2 = 2.8 Hz, 1 H); MS (EI, 70 eV) m/z 194 (M$^+$, 0.1), 177 (0.1), 133 (0.2), 124 (58), 109 (100).

(*E*)-1-(2,6,6-Trimethyl-2-cyclohexen-1-yl)-2-buten-1-one (1a). To a solution of **5a** (38 mg, 0.196 mmol, E:Z = 2:1) in CH_2Cl_2 (10 mL), under Ar, was added MnO_2 (170 mg, 1.95 mmol). The mixture was stirred for 17 h before being filtered through Celite and washing the solids with CH_2Cl_2 (3 × 20 mL). The solution was evaporated under reduced pressure and dried under high vacuum to afford 36 mg of **1a** (96%): TLC (10% EtOAc/hexane) R_{f1} 0.74, R_{f2} 0.60; GC t_{R1} 11.2, t_{R2} 14.8, E:Z = 2.2:1. A E/Z mixture of **1a** (52 mg, 0.27 mmol, E:Z = 2.2:1) was equilibrated by refluxing a solution in dry THF (5 mL) with a catalytic amount of *p*-TsOH, for 4 h. The solution was cooled, solvents were removed under reduced pressure, and saturated aqueous $NaHCO_3$ (25 mL) was added. The mixture was extracted with CH_2Cl_2 (2 × 25 mL), and the combined organic phase was dried (Na_2SO_4 anhyd), filtered, and concentrated. The residue was purified by flash chromatography (5% EtOAc/hexane) to afford, after evaporation and high vacuum drying, 5 mg of **(Z)-1a**[2b,5] (10%) and 47 mg of α-damascone[2,5] (**1a**, 90%, colorless liquid, 60% overall yield from α-ionone (**2a**)): bp (bulb-to-bulb) 80–90 °C (0.3 mmHg); TLC (10% EtOAc/hexane) R_f 0.60; IR (neat) 3030, 2960, 2920, 2860, 1690, 1670, 1630, 1440, 1360, 1145, 1080, 970, 820 cm^{-1}; ^{1}H NMR (80 MHz) δ 0.86 (s 3 H), 0.95 (s, 3 H), 1.56 (dd, J_1 = 3.5 Hz, J_2 = 2.0 Hz, 3 H), 1.90 (dd, J_1 = 6.7 Hz, J_2 = 1.4 Hz, 3 H), 2.89 (m, 1 H), 5.62 (m, 1 H), 6.34 (dq, J_1 = 15.5 Hz, J_2 = 1.4 Hz, 1 H), 6.87 (dq, J_1 = 15.5 Hz, J_2 = 6.7 Hz, 1 H); ^{13}C NMR (20 MHz) δ 18.1, 22.7, 23.2, 27.8, 28.0, 31.3, 32.4, 61.3, 123.5, 130.5, 132.2, 142.1, 202.1; MS (EI, 70 eV) m/z 192 (M$^+$, 17), 177 (M$^+$ − 15, 2), 149 (2), 135 (10), 123 (100), 107 (34), 91 (24), 81 (33). **(*Z*)-1a**: TLC (10% EtOAc/hexane) R_f 0.74; ^{1}H NMR (80 MHz) δ 0.89 (s, 6 H), 2.09 (d, J = 5.4 Hz, 3 H), 2.69 (m, 1 H), 5.60 (m, 1 H), 6.27 (m, 1 H).

1-[3-(2,6,6-Trimethyl-1-cyclohexen-1-yl)oxiranyl]ethanone (7b):[10] 52%; bp (bulb-to-bulb) 115–118 °C (0.2 mmHg); TLC (10% EtOAc/hexane) R_f 0.70; IR (neat) 2930, 2860, 1710, 1670, 1455, 1355, 1240, 870 cm^{-1}; ^{1}H NMR (80 MHz) δ 1.04 (s, 3 H), 1.18 (s, 3 H), 1.64 (br s, 3 H), 2.10 (s, 3 H), 3.24 (d, J = 2.1 Hz, 1 H), 3.57 (m, 1 H).

α-Methyl-3-(2,6,6-trimethyl-1-cyclohexen-1-yl)oxiranemethanol (8b). To a solution of **7b** (1.20 g, 5.77 mmol, freshly distilled in a kugelrohr apparatus) and $CeCl_3 \cdot 7H_2O$ (2.20 g, 5.90 mmol) in MeOH (35 mL), at 0 °C, was added $NaBH_4$ (110 mg, 2.88 mmol) in portions. The resulting mixture was stirred for 5 min, and then water (40 mL) was slowly added. The mixture was extracted with Et_2O (4 × 40 mL), and the combined organic phase was washed with saturated aqueous NaCl (50 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure in a rotary evaporator. The residue was purified by flash chromatography (15% EtOAc/hexane) to afford, after evaporation and high vacuum drying, 1.16 g of **8b** as a mixture of diastereomers (96%, colorless oil, diastereomeric ratio 2.2:1 by NMR): bp (bulb-to-bulb) 120–124 °C (0.1 mmHg); TLC (20% EtOAc/hexane) R_f 0.40; IR (neat) 3450, 2930, 2860, 1450, 1370, 1355, 1095, 1060, 940, 900 cm^{-1}; ^{1}H NMR (200 MHz) δ 1.08 (br s, 3 H), 1.16 (s, 3 H), 1.34 (d, J = 6.5 Hz, 3 H), 1.68 (br s, 3 H), 2.89 (br t, J = 3.0 Hz, 1 H), 3.52 (m, 1 H), 4.01 (m, 1 H); ^{13}C NMR (50 MHz) δ 19.0, 19.1, 19.9, 20.1, 28.4, 28.6, 32.8, 40.4, 54.7, 62.2, 65.6, 131.4, 132.7; MS (EI, 70 eV) m/z 211 (M$^+$ + 1, 23), 210 (M$^+$, 28), 195 (18), 193 (17), 175 (10), 165 (64), 151 (40), 147 (15), 137 (33), 121 (64), 109 (63), 93 (78), 79 (52), 41 (100); HRMS (EI) calcd for $C_{13}H_{22}O_2$ (M$^+$) 210, 1620, found 210, 1623. Minor diastereomer: ^{1}H NMR (200 MHz) δ 1.35 (d, J = 6.5 Hz, 3 H), 1.65 (br s, 3 H), 2.82 (dd, J_1 = 4.9 Hz, J_2 = 2.5 Hz, 1 H), 3.46 (m, 1 H), 3.73 (m, 1 H); ^{13}C NMR (50 MHz) δ 32.7, 40.3, 56.4, 63.2, 67.6.

2-(1-Bromoethyl)-3-(2,6,6-trimethyl-1-cyclohexen-1-yl)oxirane (9b). To a cooled (0 °C) solution of **8b** (285 mg, 1.35 mmol, diastereomeric ratio 2.2:1, freshly distilled in a kugelrohr apparatus) and CBr_4 (875 mg, 2.64 mmol) in pyridine (15 mL), under Ar atmosphere, was slowly added a solution of Ph_3P (615 mg, 2.34 mmol) in pyridine (7 mL) over a 2-h period, and the resulting red solution was stirred at the same temperature for 12 h. Then MeOH (5 mL) was added, and the solvents were removed under reduced pressure at room temperature. Saturated aqueous $NaHCO_3$ (20 mL) was added to the residue which was then extracted with hexane (3 × 40 mL). The combined organic phase was dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane) to afford, after evaporation and high vacuum drying, 330 mg of the diastereomeric mixture **9b** (89%, diastereomeric ratio 4.3:1 by NMR): TLC (15% EtOAc/hexane) R_f 0.82; IR (neat) 2930, 2860, 1445, 1375, 1355, 1190, 990, 915, 890, 660 cm^{-1}; ^{1}H NMR (200 MHz) δ 1.08 (br s, 3 H), 1.16 (br s, 3 H), 1.68 (br s, 3 H), 1.82 (d, J = 6.9 Hz, 3 H), 3.08 (dd, J_1 = 7.3 Hz, J_2 = 2.2 Hz, 1 H), 3.51 (m, 1 H), 3.92 (m, J = 6.9 Hz, 1 H); ^{13}C NMR (50 MHz) δ 19.1, 20.1, 22.0, 28.3, 28.4, 32.9, 34.5, 40.4, 50.0, 60.1, 63.0, 131.9, 132.3; MS (EI, 70 eV) m/z 274 (M$^+$ + 2, 4), 272 (M$^+$, 4), 256 (4), 254 (3), 244 (2), 175 (5), 153 (15), 133 (32), 107 (20), 89 (23), 77 (51), 61 (85), 43 (100); HRMS (EI) calcd for $C_{13}H_{21}BrO$ (M$^+$) 272.0776, found 272.0773. Minor diastereomer: TLC (15% EtOAc/hexane) R_f 0.88; ^{1}H NMR (200 MHz) δ 1.75 (br s, 3 H), 1.81 (d, J = 6.7 Hz, 3 H), 3.06 (dd, J_1 = 7.8 Hz, J_2 = 2.2 Hz, 1 H), 3.43 (m, 1 H), 3.72 (m, 1 H); ^{13}C NMR (50 MHz) δ 48.1, 59.9, 62.6.

2,6,6-Trimethyl-α-(1-propenyl)-1-cyclohexene-1-methanol (5b). As previously described for the synthesis of **5a**, a mixture of Zn dust (135 mg, 2.09 mmol) and CuI (132 mg, 0.70 mmol) in H_2O (6 mL) was sonicated under argon for 5 min to prepare the Zn(Cu) couple. To this black mixture was added a solution of **9b** (175 mg, 0.64 mmol diastereomeric ratio 4.3:1) in EtOH (3 mL). The reaction was conducted as for **5a**. Purification was performed by flash chromatography (5% EtOAc/hexane) to afford, after evaporation and high vacuum drying, 100 mg of **5b**[1,2] (80%, colorless liquid, E:Z = 1:1): bp (bulb-to-bulb) 110–115 °C (0.2 mmHg); TLC (10% EtOAc/hexane) R_f 0.37; IR (neat) 3350, 3020, 2900, 2850, 1445, 1375, 1355, 1020, 950, 890, 870, 740 cm^{-1}. **(*E*)-5b**: ^{1}H NMR (200 MHz) δ 0.92 (s, 3 H), 1.08 (s, 3 H), 1.67 (d, J = 5.3 Hz, 3 H), 1.74 (br s, 3 H), 1.82 (br s, 3 H), 4.74 (br d, J = 5.1 Hz, 1 H), 5.68 (m, 2 H); **(*Z*)-5b**: ^{1}H NMR (200 MHz) δ 0.89 (s, 3 H), 1.12 (s, 3 H), 5.08 (br d, J = 8.6 Hz, 1 H); MS (EI, 70 eV) m/z 194 (M$^+$, 13), 179 (46), 161 (22), 151 (27), 137 (12), 123 (55), 109 (46), 81 (43), 69 (48), 42 (100); HRMS (EI) calcd for $C_{13}H_{22}O$ (M$^+$) 194.1671, found 194.1675. A trace of the alcohol **6** can be observed in the spectrum of the crude reaction mixture: ^{1}H NMR (200 MHz) δ 0.99 (s, 6 H), 1.18 (s, 3 H), 4.36 (m, 1 H), 5.30 (s, 1 H).

(*E*)-1-(2,6,6-Trimethyl-1-cyclohexen-1-yl)-2-buten-1-one (1b). To a solution of **5b** (48 mg, 0.247 mmol E:Z = 1:1) in pentane (10 mL), under argon atmosphere, was added MnO_2 (215 mg, 2.47 mmol). The reaction was monitored by TLC analysis and after stirring for 24 h was judged complete. Et_2O (10 mL) was added, and the resulting mixture was filtered through Celite, washing the solids with Et_2O (3 × 20 mL). The solution was concentrated under reduced pressure and dried under high vacuum to afford 42 mg of **1b** as an E/Z mixture (89%, E:Z = 1.2:1): TLC (10% EtOAc/hexane) R_{f1} 0.70, R_{f2} 0.54; GC t_{R1} 11.2, t_{R2} 14.8, E:Z = 1.2:1. To equilibrate the E/Z mixture of **1b** (50 mg, 0.26 mmol, E:Z = 1.2:1), a solution in dry THF (10 mL) was refluxed with a catalytic amount of *p*-TsOH for 4 h. The solution was cooled, solvents removed under reduced pressure, and saturated aqueous $NaHCO_3$ (25 mL) was added. The mixture was extracted with CH_2Cl_2 (2 × 25 mL), and the combined organic phase was dried (Na_2SO_4 anhyd), filtered, and concentrated in a rotary evaporator. The residue was purified by flash chromatography (5% EtOAc/hexane) to afford, after evaporation and high vacuum drying, 4 mg of **(*Z*)-1b**[1,2b] (7%) and 40 mg of β-damascone[1,2] (**1b**, 80%, colorless liquid, 25% overall yield from β-ionone (**2b**)): TLC (10% EtOAc/hexane) R_f 0.54; IR (neat) 3020, 2910, 2840, 1635, 1610, 1430, 1370, 1355, 1280, 1230, 960, 920 cm^{-1}; ^{1}H NMR (200 MHz) δ 1.00 (s, 6 H), 1.49 (s, 3 H), 1.89 (dd, J_1 = 6.8 Hz, J_2 = 1.6 Hz, 3 H), 6.12 (dq, J_1 = 15.6 Hz, J_2 = 1.6 Hz, 1 H), 6.70 (dq, J_1 = 15.6 Hz, J_2 = 6.8 Hz, 1 H); ^{13}C NMR (50 MHz) δ 18.4, 18.9, 21.3, 28.9, 29.7, 31.2, 33.4, 38.8, 130.4, 134.6, 140.2, 145.8, 202.3. **(*Z*)-1b**: TLC (10% EtOAc/hexane) R_f 0.69; ^{1}H NMR (80 MHz) δ 1.07 (s, 6 H), 1.54 (s, 3 H), 2.10 (d, J = 5.7 Hz, 3 H), 6.14 (m, 1 H), 6.30 (m, 1 H).

Acknowledgment. L.A.S. thanks NATO for a postdoctoral fellowship. Valuable comments and suggestions

from Prof. A. Mouriño (Santiago de Compostela, Spain) are gratefully acknowledged.

Registry No. (±)-(*E*)-**1a**, 57549-92-5; (±)-(*Z*)-**1a**, 57549-93-6; (*E*)-**16**, 23726-91-2; (*Z*)-**16**, 23726-92-3; **2a**, 127-41-3; **2b**, 79-77-6; **5a**, 52610-46-5; (*E*)-**5b**, 124099-60-1; (*Z*)-**5b**, 139608-99-4; **6**, 42741-51-5; **7a**, 37079-64-4; (±)-**7b**, 139609-00-0; **8a**, 139609-01-1; (±)-**8b** (isomer 1), 139609-02-2; (±)-**8b** (isomer 2), 139684-74-5; **9a**, 139609-03-3; (±)-**9b** (isomer 1), 139609-04-4; (±)-**9b** (isomer 2), 139686-52-5.

Supplementary Material Available: NMR spectra of **8b** and **9b** (6 pages). Ordering information is given on any current masthead page.

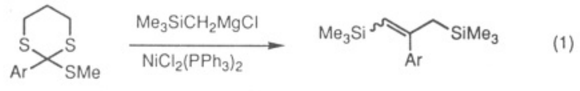
1,3-Bis(trimethylsilyl)propene as 1,3- and 3,3-Propene Dianion Synthons. Reactions of 2-Aryl-1,3-bis(trimethylsilyl)propenes with Electrophiles

Wu-Wang Weng and Tien-Yau Luh*

Department of Chemistry, National Taiwan University, Taipei, Taiwan 10764, Republic of China

Received January 2, 1992

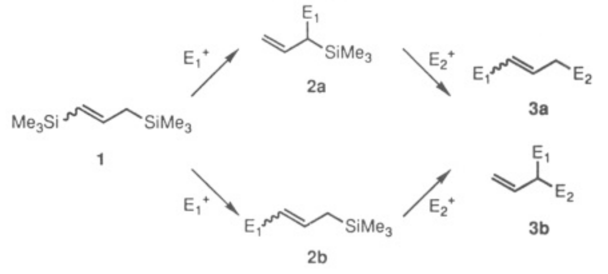
Whereas allylsilanes and vinylsilanes can be considered as allyl anion and vinyl anion synthons,[1] 1,3-bis(trimethylsilyl)propene (**1**) which contains both functionalities could couple with an electrophile E_1 to give either **2a** or **2b**. Further reaction of the latter species with a second electrophile E_2 could afford 1,3-substitution product **3a** or the isomeric 3,3-substitution product **3b** (Scheme I).[2] Given this versatility it is surprising that the chemistry of **1** has not been explored more extensively. The reactions of **1** or its derivatives with carbonyl compounds under different conditions leading to the corresponding dienes,[3] substituted allylsilanes[4,5] and vinylsilanes[6] have been reported. The formation of **4** by treatment of **1** with trimethylsilyl chlorosulfonate appears to be the only known example of using **1** as a 1,3-propene dianion synthon **5a**.[7] Recently, we reported a facile synthesis of 2-aryl-1,3-(bistrimethylsilyl)propenes **7** from the corresponding orthothioesters **6** (eq 1).[8] The availability of these compounds prompted our exploration of using **7** as 1,3- and 3,3-propene dianion synthons **5a** and **5b**.

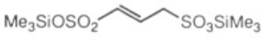


6

7 a Ar = Ph
b Ar = 1-Naphthyl
c Ar = 2-Naphthyl
d Ar = 4-MeC$_6$H$_4$

Scheme I





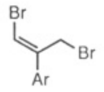
4

5a

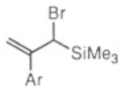
5b

Results and Discussion

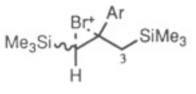
When a mixture of *E*- and *Z*-isomers of 2-aryl-1,3-bis(trimethylsilyl)propenes **7**[8] was treated with 2 equiv of *N*-bromosuccinimide (NBS) in CH_2Cl_2 at −78 °C, (*Z*)-2-aryl-1,3-dibromopropenes **8** were obtained in satisfactory yields (Table I, entries 1–4). The stereochemical assignments of **8** are based on NOE experiments. The formation of **8** is stereoselective regardless of the stereochemistry of the starting materials **7**. Thus, the reaction of (*E*)-**7a** with NBS under the same conditions afforded **8a** in 71% yield.



8



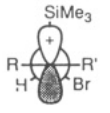
9



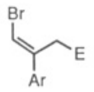
10

Treatment of **7** with 1 equiv of NBS under the same conditions afforded the monobromo products **9** in satisfactory yields (Table I, entries 5–8). These results indicated that the first reaction of **7** proceeds via the typical allylsilane reaction pattern. The bromonium ion intermediate **10** is postulated. Hence, the carbon–silicon bond at C-3 in **10** is apparently more labile giving the α-bromoallylsilane **9** selectively.

The reaction of α-haloallylsilanes with electrophiles has been briefly investigated.[9] Exposure of **9a** to NBS in CH_2Cl_2 at −78 °C yielded **8a** (entry 9). The interaction of the carbon–silicon bond with the empty p-lobe in intermediate **11a** leading to the double-bond formation may account for the stereoselectivity of this reaction. Presumably, the conformer **11a** is more stable than **11b**.[9]



11 a R = Ph, R′ = CH$_2$Br
b R = CH$_2$Br, R′ = Ph



12 a E = MeCH(OEt)-
b E = Me(CH$_2$)$_4$CO-
c E = PhCH(OH)-

The $TiCl_4$-mediated reactions of **9a** with 1,1-diethoxyethane afforded **12a** (entry 10). Similarly, treatment of **9a** with hexanoyl chloride at −60 °C yielded **12b** (entry 11). These observations indicated that 1,3-silylpropenes **7** behave in the manner of two overlapped and transposed allyl silanes. In other words, **7** can be considered as a 1,3-propene dianion synthon **5a**. In fact, it is possible to carry out the two reactions in one pot, by allowing **7a** to react

---

(1) Chan, T. H.; Fleming, I. *Synthesis* **1979**, 761. Sakurai, H. *Pure Appl. Chem.* **1982**, *54*, 1. Hosomi, A. *Acc. Chem. Res.* **1988**, *21*, 200.

(2) The Lewis acid-catalyzed regioselective α-attack of allylsilanes with carbon electrophiles has been extremely rare. An ester group at the γ-position is required to promote such a reaction, and a first silyl group migration from carbon to oxygen has been suggested. Cf. Chan, T.-H.; Kang, G. J. *Tetrahedron Lett.* **1982**, *23*, 3011.

(3) Trost, B. M.; Brandi, A. *J. Org. Chem.* **1984**, *49*, 4811.

(4) House, H. O.; Gaa, P. C.; Lee, J. H. C.; VanDerveer, D. *J. Org. Chem.* **1983**, *48*, 1670.

(5) Fleming, I.; Langley, J. A. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1421.

(6) Corriu, R.; Escudie, N.; Guerin, C. *J. Organomet. Chem.* **1984**, *264*, 207.

(7) Grignon-Dubois, M.; Pillot, J. P.; Dunogues, J.; Duffaut, N.; Calas, R. *J. Organomet. Chem.* **1977**, *124*, 135.

(8) (a) Tzeng, Y.-L.; Luh, T.-Y.; Fang, J.-M. *J. Chem. Soc., Chem. Commun.* **1990**, 399. (b) For a review, see: Luh, T.-Y. *Acc. Chem. Res.* **1991**, *24*, 257.

(9) Hosomi, A.; Ando, M.; Sakurai, H. *Chem. Lett.* **1984**, *25*, 1385.

0022-3263/92/1957-2760$03.00/0 © 1992 American Chemical Society