Allylic Terpenyl Silanes, Versatile Synthons in the Terpene Series. Synthesis of 2-Acyl-Δ(1,7)-*p*-menthenes[1] and 3-Acyl-β-pinenes[2]

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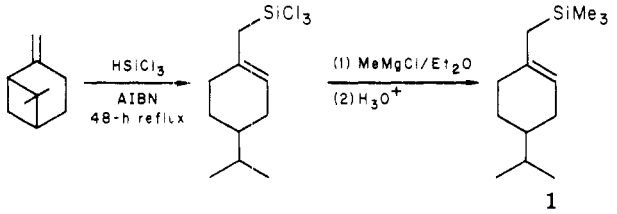
When reacted with acyl chlorides in the presence of aluminium trichloride, 7-(trimethylsilyl)-Δ(1,2)-*p*-menthene underwent substitution of the trimethylsilyl group and allylic rearrangement. Thus, acetyl, isovaleroyl, and senecioyl chlorides yielded their corresponding 2-acyl-Δ(1,7)-*p*-menthenes. Similarly, 7-(trimethylsilyl)-α-pinene (resulting from an ene reaction of α- or β-pinene with $PhSO_2NSO$ followed by reductive silylation) reacted with acetyl and senecioyl chlorides to give the corresponding 2-acyl-β-pinenes. This route proves to be a highly convenient procedure for the synthesis of this series of allyl ketones having the carbon–carbon double bond in the exocyclic position.

Since our previous investigations[3,4] of the substitution of the Me_3Si group by an acyl group in allylsilanes, several successful applications of this reaction have been reported.[5,6] Recognizing the great regioselectivity induced by allylic silicon groups during the course of acylation, we postulated the use of an organosilicon route in the preparation of several new ketones normally inaccessible by Friedel–Crafts reactions on corresponding terpenic hydrocarbons. We used 7-(trimethylsilyl)-Δ(1,2)-*p*-menthene[7] and 7-(trimethylsilyl)-α-pinene[8] as our starting allylsilanes, and we report here our results in this area.[9]

Results and Discussion

Acylation of 7-(Trimethylsilyl)-Δ(1,2)-*p*-menthene (1). This compound was previously prepared by the hydrosilylation of β-pinene with $HSiCl_3$,[7,10] followed by further methylation.[11]

We found an improved consistency of the hydrosilylation yields when using azobis(isobutyronitrile) (AIBN) as initiator. Thus, 1 was obtained in 70% yield from β-pinene:



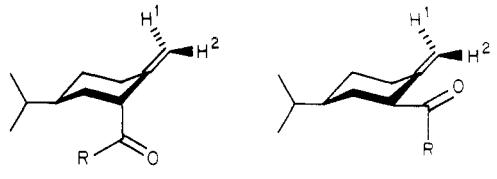
1

Acetylation of stable and readily available 1 in the presence of aluminium trichloride resulted in a substitution of silicon with allylic rearrangement and gave novel β,γ-unsaturated ketones with a carbon–carbon double bond in the exocyclic position (Table I).

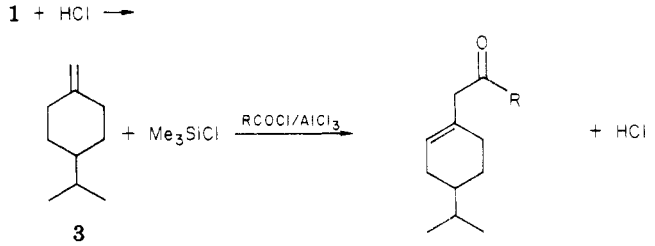
Table I. Preparation of 2-Acyl-Δ(1,7)-*p*-menthenes

R	products	% yield	cis/trans
Me	2a	67	54/46
Me_2CHCH_2	2b	58	1/1
$Me_2C{=}CH$	2c	65	1/1

Scheme I

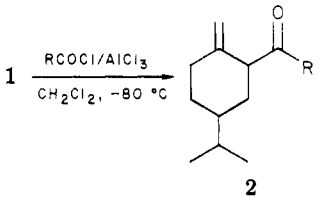


Scheme II



3

4a, R = Me
b, R = Me_2CHCH_2
c, R = $Me_2C{=}CH$



2

The stereochemistry of 2 was resolved on the basis of NMR spectra. The ethylenic protons of one isomer showed very similar shifts, whereas in the other isomer, the ethylenic protons are quite different. As shown in Scheme I, the carbonyl group exerts an influence on H^2 in the cis isomer; in the trans isomer, this shielding is lacking, resulting in similar shifts for H^1 and H^2 (see Experimental Section).

Since Friedel–Crafts acylation of cyclohexene derivatives does not lead to methylenecyclohexanes,[12] few derivatives

(1) Common name for 2-acyl-4-isopropyl-1-methylenecyclohexanes.
(2) Common name for 3-acyl-6,6-dimethyl-2-methylenebicyclo-[3.1.1]heptanes.
(3) R. Calas and J. Dunoguès, *J. Organomet. Chem.*, **27**, C21 (1971).
(4) R. Calas, J. Dunoguès, J.-P. Pillot, C. Biran, F. Pisciotti, and B. Arréguy, *J. Organomet. Chem.*, **85**, 149 (1975).
(5) J.-P. Pillot, J. Dunoguès, and R. Calas, *Tetrahedron Lett.*, 1871 (1976).
(6) I. Fleming and I. Paterson, *Synthesis*, 446 (1979).
(7) (a) R Calas and E. Frainnet, *Bull. Soc. Chim. Fr.*, 241 (1952); (b) E. Frainnet and R. Calas, *C. R. Hebd. Seances Acad. Sci., Ser. C*, **240**, 203 (1955); (c) R. Calas and E. Frainnet, *ibid.*, **243**, 595 (1956); (d) E. Frainnet, Thesis, Bordeaux, France, 1960, p 149.
(8) G. Dêlêris, J. Kowalski, J. Dunoguès, and R. Calas, *Tetrahedron Lett.*, 4211 (1977).
(9) Preliminary results were reported in a communication in the 5th International Symposium on Organosilicon Chemistry, Karlsruhe, West Germany, August 14–18, 1978; cf. Abstracts of Papers, p 220.
(10) L. O. Goldblatt and D. M. Oldroyd, U.S. Patent 2 533 240 (1950); cf. *Chem. Abstr.*, **45**, 2262 (1951).
(11) MeMgCl was used because MeMgI tended to induce desilylation.[7d]
(12) (a) J. K. Groves and N. Jones, *Tetrahedron Lett.*, 1161 (1970); (b) J. K. Groves, *Chem. Soc. Rev.*, 1, 73 (1972).

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Scheme III

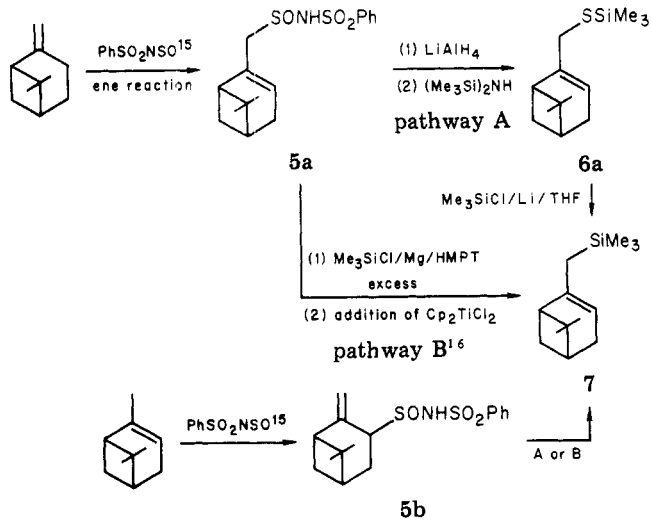


Table II. Preparation of 3-Acyl-β-pinenes

R	product	% yield[a]
Me	**8a** trans only	50
$Me_2C=CH$	**8b** trans only	45

[a] Determined from the ^1H NMR spectra of the crude products.

in this series had been previously prepared, and generally by more sophisticated schemes.[13]

When any HCl was present, the major byproduct of the acylation of 7-(trimethylsilyl)-Δ(1,2)-*p*-menthene (**1**) was compound **4**, in 10–20% yields (Scheme II).

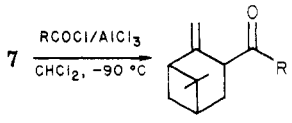
Because $AlCl_3$ enhances the acidity of HCl and favors the splitting of the Si–C allylic bond, it would appear that catalytic amounts of HCl induce the formation of the *p*-menthene-Δ(1,7), **3**. This compound was previously prepared in a convenient way by Calas and Frainnet (protodesilylation of **1** with acetic acid[7]).

This interpretation is supported by several observations. First, best yields of **2** were obtained when the complex was added to **1**. If inverse addition (i.e., **1** added to the $RCOCl/AlCl_3$ complex) was utilized, the formation of the side product **4** was greatly increased. Thus, acylation conditions play a major role on the outcome of the reaction. Second, when we obtained compound **2** by inverse addition, **3** was detected in the product mixture. We also verified that the acylation of **3** resulted in **4a**:

$$3 \xrightarrow[CH_2Cl_2,\ -70°C]{CH_3COCl/AlCl_3} \mathbf{4a} + \text{polymers}$$

And third, racemic **4a** was obtained from optically active **1**, $[\alpha_D]^{15} = -83°$, instead of the expected $[\alpha]^{20}_D = \pm 86.2°$ for optically pure **4a**.[14]

Acylation of 7-(Trimethylsilyl)-α-pinene (7). The first synthesis of this compound was realized according to Scheme III,[8,9,15,16] starting from α- or β-pinene. The ready availability of $PhSO_2NSO$ and the resulting high yields from the subsequent steps made this preparation very convenient. Acylation of **7** gave the ketones via the expected substitution of $SiMe_3$ by an acyl group and allylic rearrangement[17] (Table II):



8

Only the trans isomer was obtained for each of **8a** and **8b**, as interpreted from their NMR spectra. For these derivatives, this result is in accordance with the proposed trans structure resulting from an endo attack generally observed because of steric reasons.[18] Thus by this acylation, we have obtained novel unsaturated ketones possessing the β-pinene skeleton.

Experimental Section

Infrared spectra were obtained on a Perkin–Elmer 457 spectrometer. ^1H NMR spectra were recorded on Varian A-60 and Hitachi Perkin–Elmer R24B spectrometers, in CCl_4, and chemical shifts are reported in δ (ppm), downfield from a Me_4Si internal standard. Gas chromatography was carried out on an Intersmat IGC 120 DFB chromatograph equipped with 3-m columns packed with Carbowax 20 M (5%) or OV-225 (5%) on Chromosorb P.

Elemental microanalyses were performed by Service Central de Microanalyse du CNRS, 94320 Thiais, France, and gave satisfactory results where stability allowed. Optical activities were obtained in chloroform solutions, using a Perkin–Elmer 141 polarimeter.

The synthesized ketones were not distilled because of their instability but were purified on a silica gel column (70–230 mesh) with benzene–pentane (0.25/1 to 1/1), benzene, or ether–benzene (0.25/1) as eluant.

All glassware for reactions involving splitting of the silicon atom bond was dried at 100 °C, assembled hot, and cooled under a stream of argon before use. All these reactions were stirred with magnetic bars and carried out in argon atmosphere in a vacuum line.

Methylene chloride was distilled over potassium hydroxide and stored under argon. All the acyl chlorides were freshly distilled. Aluminium trichloride was kept under high vacuum for 0.5 h before use.

Preparation of 7-(Trimethylsilyl)-Δ(1,2)-*p*-menthene (1). A mixture of β-pinene (125 g, 0.920 mol), trichlorosilane (250 g, excess), and AIBN (1 g) was kept under reflux for 3 days. After distillation of the unreacted chlorosilane and β-pinene, the crude 7-(trichlorosilyl)-Δ(1,2)-*p*-menthene was obtained. This product was then treated with methylmagnesium chloride (6 mol) in ether (at room temperature for 24 h and then for 24 h at reflux) and then hydrolyzed at −20 °C.

After the ethereal solution was neutralized, washed with water, and dried ($MgSO_4$), it was concentrated and gave after distillation 135 g of 7-(trimethylsilyl)-Δ-(1,2)-*p*-menthene (70% yield): bp 127 °C (30 torr); $[\alpha]^{15}_D$ −83°; IR 1660 (very weak), 1250, 845, 750 cm^{-1}; NMR (CCl_4) δ 0.00 (s, 9 H, Me_3Si), 0.84, 0.92 (br d, 6 H,

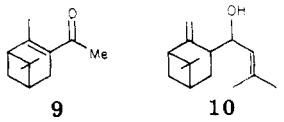
(13) (a) J. C. Dalton, H.-F. Chan, *Tetrahedron Lett.*, 3235 (1977); (b) J. L. C. Kachinski and R. G. Salomon, *Tetrahedron Lett.*, 3235 (1977).

(14) (a) A. Lalande, B. Paskoff, and M. Cazaux, *C. R. Hebd. Seances Acad. Sci., Ser. C*, **264**, 1083 (1967); (b) B. Paskoff, Dr. Ing. Thesis, Bordeaux, France, 1967.

(15) G. Kresze and W. Wucherpfennig, *Newer Methods Prep. Org. Chem.*, **5**, 109 (1968).

(16) Unpublished results. Compound **7** was obtained in one step from the adduct **5a** by direct silylation, but as yields were lower than the one obtained through pathway A, this method is not described in the Experimental Section.

(17) The instability (polymerization) of these products made difficult their complete purification. They were converted instead to more stable species: **8a** was isomerized to **9**, and **8b** was $LiAlH_4$ reduced to **10** at −70 °C (giving two diastereoisomers).



9 **10**

(18) (a) J. M. Quinn, *J. Chem. Eng. Data*, **9**, 389 (1964); (b) R. K. Hill, J. W. Morgan, R. V. Shetty, and M. E. Synerholm, *J. Am. Chem. Soc.*, **96**, 4201 (1974); (c) V. Garsky, D. F. Koster, and R. T. Arnold, *ibid.*, **96**, 4207 (1974); (d) G. B. Gill and B. Wallace, *J. Chem. Soc., Chem. Commun.*, 382 (1977); (e) C. S. Foote, *Acc. Chem. Res.*, **1**, 104 (1968), and references cited therein; (f) A. T. Blomquist, J. Verdol, C. L. Adami, J. Volinsky, and D. D. Philips, *J. Am. Chem. Soc.*, **79**, 4976 (1957).

2 Me of the *i*-Pr group), 1.38 (narrow m, 2 H, CH_2Si), 1.05–1.50 (br m, 2 H, CH_2), 1.50–2.05 (m, 6 H, two allylic CH_2 and two CH), 5.15 (br m, 1 H, =CH). Anal. Calcd for $C_{13}H_{26}Si$: C, 74.28; H, 12.38; Si, 13.33. Found: C, 74.24; H, 12.46; Si, 13.43.

General Procedure for the Preparation of the β,γ-Unsaturated Ketones. Acyl halide (55 mmol) in CH_2Cl_2 (10 mL) was added dropwise at low temperature (0 °C for acetyl chloride or −20 to −40 °C for senecioyl or isovaleroyl chloride) to a mixture of $AlCl_3$ (6.67 g, 50 mmol) and CH_2Cl_2 (50 mL) and stirred for 0.5–1 h until a clear solution was obtained. The complex solution was then poured into an isobaric and isothermal dropping funnel (previously cooled at −80 °C and filled with argon), by means of an appropriate vessel, and added dropwise (0.5–1 h) under stirring to a solution of the allylsilane (50 mmol in 100 mL of CH_2Cl_2) at a temperature of −80 to −90 °C. The solution was then stirred at −80 °C 0.25 h after the end of the addition and poured into a mixture of ice, $NaHCO_3$, and NH_4Cl previously cooled to −35 °C. The layers were separated, and the aqueous layer was extracted twice with ether. The organic layer and ethereal extracts were washed twice with a $NaHCO_3$ solution and twice with water, dried ($MgSO_4$) and concentrated under vacuum to give the crude ketones. In the case of the 7-(trimethylsilyl)-Δ(1,2)-*p*-menthene, as the starting material, the products were separated by using a silica gel column: the trans isomer was first eluted, then the cis isomer, and finally small amounts of the 7-acyl isomer. In the case of the 7-(trimethylsilyl)-α-pinene, the products could be treated with only small quantities of silica gel. Otherwise they isomerized or were lost.

***trans*-2a**: IR 3060 (=CH_2), 1710 (C=O), 1640 (C=C) cm^{-1}; NMR δ 0.80, 0.90 (br d, 6 H, 2 Me of the *i*-Pr group), 1.00–1.80 (m, 6 H, 2 CH_2 and 2 >CH), 2.05 (s, 3 H, CH_3CO), 1.80–2.30 (m, 2 H, allylic CH_2), 3.20 (narrow m, 1 H, >CHCO), 4.80 (br s, 2 H, =CH_2). Anal. Calcd for $C_{12}H_{20}O$: C, 80.00; H, 11.11; O, 8.89. Found: C, 80.75; H, 11.57; O, 8.72.

***cis*-2a**: IR 3060 (=CH_2), 1710 (C=O), 1640 (C=C) cm^{-1}; NMR δ 0.82, 0.92 (br d, 6 H, 2 Me of the *i*-Pr group), 1.05–1.95 (m, 6 H, 2 CH_2 and 2 >CH), 2.08 (s, 3 H, CH_3CO), 2.25 (m, 2 H, allylic CH_2), 2.75–3.15 (br m, 1 H, >CHCO), 4.28 (br s, 1 H), 4.65 (br s, 1 H) (=CH_2).

***trans*-2b**: IR 3075 (=CH_2), 1710 (C=O), 1640 (C=C) cm^{-1}; NMR δ 0.85, 0.95 (br d, 12 H, 4 Me of the *i*-Pr groups), 1.15–2.10 (m, 7 H, 2 CH_2 and 3 >CH), 2.20 (m, 4 H, CH_2CO and allylic CH_2), 3.20 (m, 1 H, CHCO), 4.85 (narrow m, 2 H, =CH_2).

***cis*-2b**: IR 3075 (=CH_2), 1710 (C=O), 1645 (C=C) cm^{-1}; NMR δ 0.85, 0.87, 0.95, 0.97 (br d of d, 12 H, Me of the *i*-Pr groups), 1.10–2.10 (m, 7 H, 2 CH_2, 3 >CH), 2.25 (narrow m, 4 H, CH_2CO and allylic CH_2), 2.75–3.10 (m, 1 H, >CHCO), 4.30 (br s, 1 H), 4.65 (br s, 1 H) (=CH_2).

***trans*-2c**: IR 3055 (=CH_2), 1680 (C=O), 1635 and 1620 (C=C) cm^{-1}; NMR δ 0.87, 0.97 (br d, 6 H, 2 Me of the *i*-Pr group), 1.20–2.30 (m, 6 H, 2 CH_2 and 2 >CH), 1.88 (br s, 3 H), 2.14 (br s, 3 H) (Me_2C=), 3.20 (m, 1 H, >CHCO), 4.86 (narrow m, 2 H, =CH_2), 6.26 (m, 1 H, >C=CH). Anal. Calcd for $C_{15}H_{24}O$: C, 81.82; H, 10.91; O, 7.27. Found: C, 81.95; H, 10.68; O, 7.15.

***cis*-2c**: mp 28 °C; IR (CCl_4) 3060 (=CH_2), 1680 (C=O), 1640 and 1620 (C=C) cm^{-1}; NMR δ 0.85, 0.94 (br d, 6 H, 2 Me of the *i*-Pr group), 1.10–2.10 (m, 6 H, 2 CH_2 and 2 >CH), 1.83 (br, s, 3 H), 2.10 (br s, 3 H) (Me_2C=), 2.20 (m, 2 H, allylic CH_2), 2.70–3.00 (br, m, 1 H, CHCO), 4.25 (br, s, 1 H), 4.70 (br s, 1 H) (=CH_2), 5.90 (m, 1 H, C=CH).

4a: IR 1710 (C=O) cm^{-1}; NMR δ 0.83, 0.92 (br d, 6 H, 2 Me of the *i*-Pr group), 1.10–2.20 (m, 11 H, including CH_2, 2 >CH, and 2 allylic CH_2 at δ 1.95 and CH_3CO at δ 2.08 (s)), 2.98 (br s, 2 H, CH_2CO), 5.60 (m, 1 H, =CH).

4b: IR 1710 (C=O) cm^{-1}; NMR δ 0.85, 0.95 [br d, 12 H, 4 Me (2 *i*-Pr groups)], 1.10–2.40 (m, 11 H, including CH_2, 3 CH, 2 allylic CH_2 at δ 1.90, and CH_2CO at δ 2.25), 2.90 (br s, allylic CH_2CO), 5.50 (m, 1 H, =CH).

4c: IR 1685 (C=O), 1665 (C=C), 1615 (C=C) cm^{-1}; NMR δ 0.85, 0.94 (br d, 6 H, 2 Me of the *i*-Pr group), 1.20–2.20 [m, 14 H, including CH_2, 2 >CH, Me_2C= (2 br s at δ 1.85 and 2.05), and 2 allylic CH_2 at δ 1.95], 2.85 (br s, 2 H, CH_2CO), 5.40 (m, 1 H, ethylenic H in the ring), 5.95 (narrow m, 1 H, =CH).

Preparation of 7-(Trimethylsilyl)-α-pinene (7). (a) From β-Pinene. β-Pinene (20.6 g, 150 mmol) was added (0 °C) to an ethereal solution of $PhSO_2NSO$ (28 g, 138 mmol). A white precipitate of **5a** appeared immediately and quantitatively. The precipate was filtered, washed twice with ether to remove any unreacted pinene, and then left for 2 h under vacuum.

Product **5a** (41.7 g, yield 89%) obtained by this way is spectroscopically pure: mp 140 °C; IR ($CDCl_3$) 3100 (NH), 1380 and 1175 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 1.08 (s, 3 H, Me), 1.07 (d, 1 H, *J* = 8 Hz, >CH), 1.27 (s, 3 H, Me), 2.22 (m, 5 H, ring protons), 3.62 (narrow m, 2 H, CH_2SO), 5.62 (m, 1 H, C=CH), 7.58 and 7.85 (two m, 5 H, $PhSO_2$) (m, 1 H, NH).

(b) From α-Pinene. α-Pinene (4.75 g, 35 mmol) was added (0 °C) to an ethereal solution of $PhSO_2NSO$ (6.1 g, 30 mmol). The reaction mixture was then allowed to stand at room temperature for 40 h. The white solid which had precipitated was filtered, washed twice with ether, and then kept under vacuum.

Product **5b** (4.4 g, 43% yield) was a mixture of two diastereoisomers (probably because the product contains an asymmetric sulfur atom) and is very sensitive to air moisture: mp 115 °C; IR ($CHCl_3$) 3100 (NH), 1550 (C=C), 1380 and 1175 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 0.67 (s, 3 H, Me), 1.18 (s, 3 H, Me), 1.5–2.5 (very br m, ring proton), 3.3–3.8 (very br m, 1 H), 4.8–5.1 (m, 2 H, C=CH_2), 7.50 and 7.80 (two m, 5 H, $PhSO_2$) (m, 1 H, NH).

Reduction with Lithium Aluminium Hydride (Same Technique for Either 5a or 5b). A total of 32.5 g (96 mmol) of the ene adduct in the solid state was added to a suspension of 1.82 g (48 mmol) of $LiAlH_4$ in 150 cm^3 of ether. The reaction was carried out at 0 °C and the reaction mixture was allowed to return to room temperature and then refluxed for 3 h. The medium was cooled to 0 °C, and acetone (ca. 10 mL) was added dropwise to destroy the excess $LiAlH_4$ (methyl acetate induces pinenyl thioacetate formation).

The reaction mixture was then poured onto chlorhydric ice, and the organic layer was separated. The aqueous layer was extracted twice with ether, and the organic layers were collected, washed with water to neutrality, dried ($MgSO_4$), and concentrated under vacuum at room temperature. The pasty product obtained was triturated with pentane and $PhSO_2NH_2$, filtered, and washed with pentane. The clear solution was concentrated under vacuum to give the corresponding thiols.

Because of their instability these thiols had to be blocked with hexamethyldisilazane (reflux for 24 h: quantitative silylation).

6a: 29.3 g, 84% yield; IR (neat) 1650 (very w, C=C), 1250–845 ($SiMe_3$) cm^{-1}; NMR (CCl_4) δ 0.23, (s, 9 H, $SiMe_3$), 0.80 (s, 3 H, Me), 1.1 (d, *J* = 8 Hz, 1 H, =CH), 1.27 (s, 3 H, Me), 2.2 (m, 5 H), 2.97 (very sharp m, 2 H, CH_2S), 5.27 (m, 1 H, C=CH); MS *m/e* (M^+) 240, principal peaks *m/e* 73, 91 (parent peak), 119, 134.

Silylation Reaction. A 1.12 g (160 mmol) amount of granulated lithium was placed with 17.5 g (160 mmol) of Me_3SiCl into 150 mL of anhydrous THF. The medium was cooled to −10 to 0 °C (internal temperature), and 9.6 g (40 mmol) of **6a** was added dropwise, slowly enough to avoid temperature change.

The temperature of the reaction was kept at or under 0 °C overnight.

Then 100 mL of anhydrous pentane was added. The lithium chloride which precipitated was filtered and washed with pentane, and the clear solution was concentrated under vacuum. The remaining product was diluted with 50 mL of ether and then poured onto a $NaHCO_3$–ice mixture to destroy $Me_3SiSSiMe_3$ which was formed during the reaction (a rather long stirring time is required). The organic layer was then washed twice with water, dried over $MgSO_4$, and concentrated under vacuum. Crude **7** was thus obtained spectroscopically pure.

A 7.1-g yield of **7** was obtained as a pure product after distillation: bp 73–75 °C (0.7 mmHg); 85% yield; IR (neat) 1645 (C=C), 1250–850 ($SiMe_3$) cm^{-1}; NMR (CCl_4) δ 0 (s, 9 H, $SiMe_3$, internal reference), 0.9 (s, 3 H, Me), 1.22 (d, *J* = 8 Hz, 1 H, =CH), 1.3 (s, 3 H, Me), 1.5 (m, 2 H, CH_2Si), 1.63–2.57 (m, 5 H), 5.0 (m, 1 H, C=CH). Anal. Calcd for $C_{13}H_{24}Si$: C, 75.00; H, 11.54; Si, 13.46. Found: C, 75.45; H, 11.72; Si, 13.28.

8a: IR 3080 (=CH_2), 1715 (C=O), 1640 (C=C) cm^{-1}; NMR δ 0.75 (s, 3 H, Me), 1.25 (s, 3 H, Me), 2.25 (s, 3 H, CH_3CO), 1.20–2.40 (m, 6 H), 3.35, 3.45 (two-part m), (1 H, >CHCO), 4.90 (narrow m, 1 H, =CH_2).

8b: IR (crude product) 3050 (=CH_2), 1680 (C=O), 1635, 1620 (C=C) cm^{-1}; NMR δ 0.73 (s, 3 H, CH_3), 1.23 (s, 3 H, CH_3), 1.86, 2.09 (2 d, 6 H, Me_2C= with allylic coupling), 3.45 (4 m, 1 H, >CHCO), 4.76 (narrow m, 2 H, =CH_2), 6.20 (m, 1 H, =CH).

Isomerization of the Ketone 8a. Two passages of the ketone **8a** on a silica gel column with benzene–ether as eluant (4/1) gave the isomerized ketones **9** in 45% yield.

9: IR 1670 (C=O), 1600 (C=C) cm^{-1}; NMR δ 0.80 (s, 3 H, Me), 1.25 (s, 3 H, Me), 1.10 (m, 1 H, >CH), 2.00–2.30 (m, 6 H, CH_2, allylic CH_3, and allylic >CH), 2.15 (s, 3 H, CH_3CO), 2.48 (narrow m, 2 H, allylic CH_2).

Reduction of 8b by $LiAlH_4$. Crude ketone (3 g) in 10 mL of ether was added dropwise under magnetic stirring to a suspension of $LiAlH_4$ (0.5 g) in 50 mL of ether, at the temperature of −70 °C. The reaction mixture was then allowed to return to 0 °C. CH_3CO_2Me (5 mL) was then added and the mixture poured into 100 mL of ice-cold chlorhydric water. The ethereal layer was separated, washed three times, dried ($MgSO_4$), and concentrated. The alcohol was purified through a Florisil column with ether/pentane as eluant (1/4).

10: IR 3360 (OH), 3050 (=CH_2), 1670, 1640 (C=C) cm^{-1}; NMR δ 0.73 (s, 3H, Me), 1.26 (s, 3 H, Me), 2.06 (narrow m, 6 H, Me_2C=), 1.15–2.65 (m, H of the ring including allylic H (2 H) showing a multiplet centered at δ 2.70, and OH).

The ethylenic protons and the proton α to oxygen show a multiplet (δ 3.90–5.26) broken down as follows: δ 4.03 (t, >CHO, J = 9 Hz), 4.73 (m, =CH_2), 4.95, 5.14 (d with allylic coupling, >C=CH) for the first diastereoisomer; 4.46 (d of d, J_1 = 9 Hz, J_2 = 2 Hz, >CHO), 4.70 (m, =CH_2), 5.14, 5.23 (d with allylic coupling, >C=CH for the second diastereoisomer, J = 9 Hz).

Registry No. 1, 18406-91-2; *cis*-**2a**, 70982-95-5; *trans*-**2a**, 70982-96-6; *cis*-**2b**, 70982-97-7; *trans*-**2b**, 70982-98-8; *cis*-**2c**, 70982-99-9; *trans*-**2c**, 70983-00-5; (±)-**4a**, 70983-01-6; **4b**, 70983-02-7; **5a**, 66275-54-5; **5b**, 66275-55-6; **6a**, 70983-03-8; **7**, 66275-58-9; *trans*-**8a**, 70983-04-9; *trans*-**8b**, 70983-05-0; **9**, 70983-06-1; **10**, 70983-07-2; β-pinene, 127-91-3; trichlorosilane, 10025-78-2; 7-(trichlorosilyl)-Δ(1,2)-*p*-menthene, 17873-21-1; methyl chloride, 74-87-3; acetyl chloride, 75-36-5; senecioyl chloride, 108-12-3; isovaleroyl chloride, 3350-78-5; α-pinene, 80-56-8; **4c**, 70983-08-3.

Repandins A, B, C, and D, Four New Germacranolides from *Tetragonotheca repanda* (Compositae)

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The isolation and structure elucidation of four germacranolides from *Tetragonotheca repanda* (Compositae, Heliantheae) are reported. The four new compounds, repandins A–D, possess a novel type of melampolide skeleton with an exocyclic 4(15) double bond. Longipilin, a melampolide previously reported from *Melampodium longipilum*, is a further constituent in *T. repanda*. All four repandins have the same medium ring skeleton but differ in the ester side chains at C-8 and C-9.

In continuation of our biochemical systematic study within the tribe Heliantheae (Compositae) we report the first sesquiterpene lactones isolated from the genus *Tetragonotheca*. *T. repanda* yielded four new compounds which have the same ring skeleton but differ in the attachments of four- and five-carbon ester side chains at C-8 and C-9. Longipilin (**5**),[1] a melampolide[2] previously found in *Melampodium longipilum*, was also isolated from *T. repanda*.

Results and Discussion

Structural data for the repandins were obtained by chemical transformations and the use of physical methods, mainly NMR and MS of the compounds and their derivatives.

Repandin A (1a), $C_{25}H_{32}O_{10}$ (high-resolution mass spectrum), mp 132–33 °C, was the major constituent in a single *T. repanda* collection from Texas. The structure of **1a** was deduced on the basis of correlation of physical parameters of **1a** and its acetate **1b**. The 270-MHz NMR spectrum of **1a** exhibited two one-proton doublets at 5.88 (J = 1.7 Hz) and 6.40 ppm (J = 2.0 Hz) and a broad one-proton multiplet at 3.07 ppm that characterize α,β-unsaturated γ-lactones. Repandin A displayed gross NMR spectral similarities with melampolides isolated from *Melampodium* and related genera; however, two one-proton singlets at 4.99 and 5.01 ppm which were assigned to 4 (15)-exocyclic methylene protons contrasted with all known constituents of these taxa.

Signals characteristic of two common ester side chains, sarracinate (A) and isobutyrate (C), were apparent in the 270-MHz NMR spectrum of **1a** (Table I). The presence of a sarracinoyl moiety (A) was established by irradiation of the C-3′ methyl at 2.00 ppm which decoupled the H-3′ quartet at 6.41 ppm and sharpened the AB pattern centered at 4.17 ppm. Irradiation (in $CDCl_3$) of the signal at 6.41 ppm (H-3′) sharpened the C-2′ CH_2OH signals at 4.12 and 4.22 ppm. Further irradiation at 4.15 ppm produced a 15% NOE at 6.41 ppm (H-3′), and irradiation at 6.30 ppm caused a small NOE at 4.17 (C-2′ CH_2OH), indicating a cis relationship between H-3′ and C-2′ CH_2OH of the sarracinic acid moiety. In addition, low-resolution mass spectroscopy gave major peaks at 376 (M − $C_5H_8O_3$) and 99 ($C_5H_7O_2$), also in agreement with a sarracinoyl side chain. Further prominent MS peaks at 404 (M − $C_4H_8O_2$), 71 (C_4H_7O), and 43 (C_3H_7) together with two three-proton doublets at 1.03 and 1.05 ppm and a heptet (1 H) at 2.45 ppm supported the presence of an isobutyrate side chain. Loss of both acid side chains in the MS, m/e 288 (M − $C_5H_8O_3$ − $C_4H_8O_2$), indicated that the remainder of the molecule must have a mass corresponding to $C_{16}H_{16}O_5$. This suggested that in addition to the four oxygens at-

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