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-

† Dedicated to Professor André Dreiding, University of Zürich, on the occasion of his 60th birthday.

(1) Seaman, F. C.; Fischer, N. H. *Phytochemistry* **1978**, *17*, 2131.
(2) (a) Fischer, N. H.; Wiley, R. A.; Wander, J. D. *J. Chem. Soc., Chem. Commun.* **1972**, 137. (b) Neidle, S.; Rogers, D. *Ibid.* **1972**, 140.

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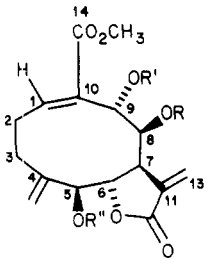
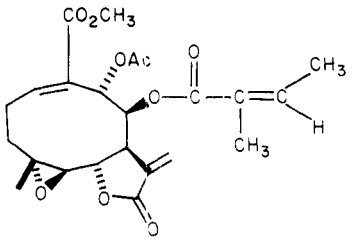


1a, R = A; R′ = C; R″ = H
1b, R = A acetate; R′ = C; R″ = Ac
2a, R = A; R′ = D; R″ = H
2b, R = A acetate; R′ = D; R″ = Ac
3, R = B; R′ = C; R″ = H
4a, R = B; R′ = D; R″ = H
4b, R = B; R′ = D; R″ = Ac



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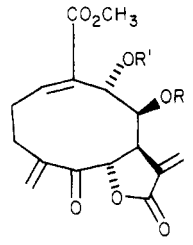
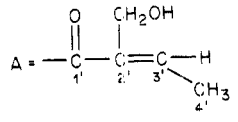
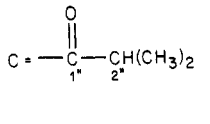
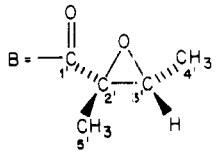
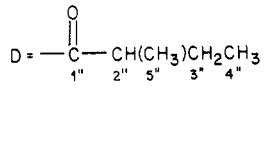


6, R = B; R′ = D









tributed to the lactone function and the carbomethoxy group [evident from the three-proton singlet at 3.83 ppm and a low-resolution mass spectral peak at m/e 461 (M – OCH_3)], one more oxygen function must be present in the medium-ring skeleton.

The assignments of the remaining NMR signals were as follows. Irradiation (in $CDCl_3$ and in CD_3CN) of the multiplet at 3.07 ppm (H-7) collapsed both doublets at 5.88 (H-13a) and 6.40 ppm (H-13b), the doublet of doublets at 4.91 ppm (H-6) to a doublet ($J_{5,6}$ = 9.5 Hz), and the doublet of doublets at 6.28 ppm (H-8) to a doublet ($J_{8,9}$ = 9.5 Hz). Irradiation of the doublet at 3.95 ppm (H-5) collapsed the large coupling ($J_{5,6}$ = 9.5 Hz) of H-6 at 4.91 ppm. The chemical shift attributed to the H-5 doublet at 3.95 ppm suggested that C-5 possesses an allylic hydroxyl. Acetylation of **1a** gave the diacetate **1b** with a H-5 absorption at 4.92 ppm which confirmed the presence of a C-5 OH in **1a**. Irradiation of the H-5 signal of **1a** in CD_3CN also sharpened the broadened two-proton singlet at 4.91 ppm assigned to two vinylic C-15 methylene protons. The position of H-9 was located by irradiation (100-MHz NMR in CD_3CN) at a low audiofrequency level of a doublet at 6.04 ppm which produced a spin-tickling effect causing two lines of the doublet of doublets at 6.17 ppm (H-8) to split into four lines. The chemical shifts of H-8 and H-9 indicated the presence of ester functions at C-8 and C-9. The location of ester side chains at these sites was supported by Eu(fod)$_3$ shift reagent studies in which large lanthanide-induced shifts were observed for H-8 and H-9, in addition to the expected shifts for C-2′ CH_2OH, H-13a, and H-13b. Irradiation at either 2.45 ppm (H-2a) or 2.81 ppm (H-2b) collapsed the most downfield signal at 6.74 ppm (H-1) to a doublet ($J_{1,2a}$ = 5.0 Hz, $J_{1,2b}$ = 13.5 Hz). The low-field chemical shift of H-1 indicated its cis relationship with the C-14 carbomethoxy group, typical for most melampolides.[2,3]

Repandin B (2a), $C_{26}H_{34}O_{10}$ (high-resolution mass spectrum), mp 127–128 °C, contains an α-methylbutyrate side chain (D) at C-9 instead of the isobutyrate group (C) in **1a**. Besides the typical NMR absorptions, mass spectral peaks at 506 (M^+, $C_{26}H_{34}O_{10}$), 390 (M – $C_5H_8O_3$), 288 (M – $C_5H_8O_3$ – $C_5H_{10}O_2$), 99 ($C_5H_7O_2$), 85 (C_5H_9O), and 57 (C_4H_9) also support the presence of an α-methylbutyrate (D) in addition to the sarracinate side chain (A) in **2a**. The attachments of the two side chains at C-8 and C-9 in repandin A and B were tentatively derived from NMR chemical shift data of the two compounds. All chemical shifts for the medium-ring protons of **1a** and **2a** are practically identical except the ones due to H-9; this is exemplified in the presence of shift reagent. It is therefore reasonable to argue that the two compounds most likely differ in the C-9 attachment, that is, repandins A and B having attached to C-9 the isobutyrate (C) and α-methyl-*n*-butyrate (D), respectively, and both carrying the sarracinic acid moiety at C-8.

Repandin C (3), $C_{25}H_{32}O_{10}$ (high-resolution mass spectrum), was a noncrystalline gum, which on the basis of NMR and MS data showed the same medium-ring skeleton as **1a** except for the presence of a 2,3-epoxy-2-methylbutanoyl moiety (B) instead of the sarracinoyl group A. The 100-MHz NMR spectrum of **3** showed signals characteristic of the 2,3-epoxy-2-methylbutanoate group,[2] and the low-resolution mass spectrum provided significant peaks at 492 (M^+), 376 (M – $C_5H_8O_3$), and 288 (M – $C_4H_8O_2$ – $C_5H_8O_3$) which are in accord with the NMR parameters.

Repandin D (4a), $C_{26}H_{34}O_{10}$ (high-resolution mass spectrum), a noncrystalline gum, contained an 2,3-epoxy-2-methylbutanoyl moiety (B) at C-8 and an α-methylbutyrate group at C-9. This was based on chemical shift arguments for H-8 and H-9 in **3** and **4a** as outlined for **1a** and **2a**. NMR parameters obtained at 100 MHz (Table I) and the low-resolution mass spectral data [506 (M^+), 390 (M – $C_5H_8O_3$), 288 (M – $C_5H_8O_3$ – $C_5H_{10}O_2$), 85 (C_5H_9O), and 57 (C_4H_9)] confirmed the presence of B in **4a**.

Stereochemical Considerations

Except for the presence of a 4(15)-exocyclic methylene function and a C-5 hydroxyl group instead of a 4,5 double bond, the repandins A–D have typical features of the melampolide skeleton.[2,3] The co-occurrence of the repandin-type compounds and the normal skeletal type melampolide longipilin (**5**) in *T. repanda* strongly suggests that the repandins are biogenetically derived from those, possibly by an allylic rearrangement of a C-15 hydroxymelampolide. Alternatively, a singlet-oxygen process via the C-5 hydroperoxide, followed by bioreduction of the hydroperoxide group to give the C-5 alcohol function, could be formulated. The latter process would be analogous to the in vivo as well as in vitro formation of 2-hydroxygermacra-1(14),4(5)-dienolides which were recently described by Doskotch, El-Feraly, and co-workers.[4] The stereochemistry of the C-5 hydroxyl function was assigned on biogenetic and NMR spectral grounds with the as-

(3) Fischer, N. H.; Wiley, R. A.; Perry, D. L. *Rev. Latinoam. Quim.* **1976**, 7, 87, and references therein.
(4) (a) Doskotch, R. W.; El-Feraly, F. S.; Hufford, C. D. *J. Chem. Soc., Chem. Commun.* **1976**, 402. (b) El-Feraly, F. S.; Chan, Y. M.; Fairchild, E. H.; Doskotch, R. W. *Tetrahedron Lett.* **1977**, 1973.

Table I. ^{1}H NMR Parameters[a] of Repandin A (1a)[b] and Its Acetate (1b), Repandin B (2a)[b] and Its Acetate (2b), Repandin C (3), Repandin D (4a) and Its Acetate (4b), and Oxidation Product 6

	1a	1b	2a	2b	3	4a	4b	6
H-1	6.74 dd (13.5, 5.0)	6.76 dd (12.5, 5.0)	6.74 dd (13.0, 5.0)	6.74 dd (13.0, 5.0)	6.75 dd (12.5, 5.0)	6.74 dd (12.5, 5.0)	6.72 dd (12.0, 5.0)	7.00 dd (12.0, 5.0)
H-2a	2.32 m		2.32 m					
H-2b	2.81 m		2.81 m					
H-3a	2.47 m		2.47 m					
H-3b	3.05 m		3.05 m					
H-5	3.95 d (9.5)	4.92 d (9.5)	3.95 d (9.5)	4.92 d (9.5)	3.95 d (9.5)	3.93 d (9.5)	4.97 d (10.0)	
H-6	4.91 br d (9.5)	5.12 br d (9.5)	4.91 br d (9.5)	5.12 br d (9.5)	4.85 br d (9.5)	4.84 br d (9.5)	5.13 d (10.0)	5.51 d (9.5)
H-7	3.07 br s	3.11 br s	3.07 br s	3.11 br s	3.07 br s	3.07 br s	3.13 br s	3.10 m
H-8	6.28 dd (2.5, 9.5)	6.28 dd (2.0, 9.5)	6.29 dd (2.5, 9.5)	6.28 dd (2.0, 9.5)	6.18 dd (2.5, 9.5)	6.18 dd (2.5, 9.5)	6.21 dd (2.5, 10.0)	6.79 dd (1.0, 8.5)
H-9	6.09 d (9.5)	5.97 d (9.5)	6.06 d (9.5)	5.97 d (9.5)	5.98 d (9.5)	6.02 d (9.5)	5.98 d (10.0)	5.70 d (8.5)
H-13a	5.88 d (1.7)	5.87 d (1.7)	5.89 d (1.7)	5.87 d (1.7)	5.85 d (1.7)	5.85 d (1.7)	5.87 d (1.7)	5.93 d (3.0)
H-13b	6.40 d (2.0)	6.38 d (2.0)	6.40 d (2.0)	6.38 d (2.0)	6.31 d (2.0)	6.33 d (2.0)	6.34 d (2.0)	6.40 d (3.5)
H-15a	4.99 br s	5.11 br s	4.99 br s	5.11 br s	4.99 br s	4.99 br s	5.12 br s	6.18
H-15b	5.01 br s	5.11 br s	5.01 br s	5.11 br s	4.99 br s	4.99 br s	5.12 br s	6.21
H-3′	6.41 q (7.0)	6.51 q (7.0)	6.41 q (7.0)	6.51 q (7.0)	3.02 q (5.5)	3.02 q (5.5)	2.98 q (5.5)	3.05 q (5.5)
H-4′ [3]	2.01 d (7.0)	2.07 d (7.0)	2.03 d (7.0)	2.07 d (7.0)	1.21 d (5.5)	1.21 d (5.5)	1.21 d (5.5)	1.21 d (5.5)
H-5′	(a) 4.12 d (13.0), (b) 4.22 d (13.0)	(a) 4.57 d (12.0), (b) 4.71 d (12.0)	(a) 4.12 d (13.0), (b) 4.22 d (13.0)	(a) 4.57 d (12.0), (b) 4.71 d (12.0)	1.45 [3]	1.45 [3]	1.45 [3]	1.49
H-2″	2.45 sext (7.0)	2.45 sext (7.0)	2.31 sext (7.0)	2.31 sext (7.0)	2.45 m	2.31 m	2.31 m	2.31 m
H-3″			(a) 1.33 m, (b) 1.55 m					
H-4″			0.77 [3] t (7.5)	0.77 [3] t (7.5)		0.83 [3] t (7.5)	0.82 [3] t (7.5)	0.82 [3] t (7.5)
H-5″			1.01 [3] d (7.0)	1.01 [3] d (7.0)		1.06 [3] d (7.0)	1.06 [3] d (7.0)	1.06 [3] d (7.0)
C-2″-CH_3	1.03 [3] d (7.0), 1.05 [3] d (7.0)	1.03 [3] d (7.0), 1.05 [3] d (7.0)			1.06 [3] d (7.0) 1.06 [3] d (7.0)			
C-5-OC(O)CH_3		2.14 [3] s		2.14 [3] s			2.14 [3]	
C-5′-OC(O)CH_3		2.07 [3] s		2.07 [3] s				

[a] Except for 1a and 2a, all spectra were run in $CDCl_3$ at 100 MHz, and Me_4Si was used as internal standard. Values are recorded in ppm relative to Me_4Si. Singlets are unmarked; multiplets are designated as follows: d, doublet; t, triplet; q, quartet, m, multiplet whose center is given; br, broad. Figures in parentheses are coupling constants or line separations in hertz; figures in brackets indicate the number of protons. [b] Spectra were run in $CDCl_3$ at 270 MHz.

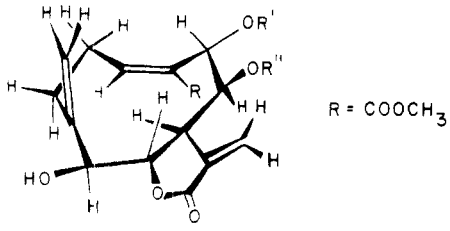


Figure 1. Probable conformation of the repandins.

sumption that melampolides represent the biogenetic precursor for the repandins. It has been demonstrated by X-ray and NMR studies[2] that melampolides adopt a fixed conformation, with the trans-4,5 double bond being perpendicular to the plane of the medium ring, with a β orientation of the C-4 methyl dictating an α orientation of H-5. Oxidative or nucleophilic attack at the C-5 olefinic carbon from the sterically accessible outer face of the 4,5 double bond would automatically lead to a C-5 β-hydroxyl function. A C-5 β-hydroxyl in the repandins was supported by comparison of chemical shift data of **1a**, **2a**, and **4a** with those of their acetates, **1b**, **2b**, and **4b**. In each case, the introducton of acetate functions at C-5 caused a downfield shift of H-6 by about 0.2 ppm, an effect which was interpreted as a deshielding of the β-oriented H-6 by the acetate carbonyl. From model considerations, this is only possible if the oxygen function at C-5 is also β oriented. Since this effect is also observed in **4b**, a possible influence of the newly introduced acetate at the sarracinoate side chain upon H-6 in **1b** and **2b** was excluded. The inspection of stereo models of a trans-lactonized repandin-type medium ring, with H-5α, H-6β, H-7α, H-8α, and H-9β the dihedral angles, shows good correlation with the NMR coupling constants of the four repandins. The large coupling ($J_{5,6}$ = 9.5 Hz) suggests an antiperiplanar orientation of the two protons. The small coupling between H-7 and H-8 ($J_{7,3} \approx 2.0$ Hz) requires an α orientation of both protons, and $J_{8,9}$ = 10 Hz necessitates that H-8 and H-9 be antiperiplanar, that is, H-9 being β oriented.

The NMR couplings of H-6, H-7, and the two H-13's require comments. The very small coupling between H-6 and H-7 ($J_{6,7} < 1$ Hz) together with the allylic couplings of the exocyclic methylene lactone protons ($J_{7,13} \leq 2.0$ Hz) are typical for heliangolides,[5,6] compounds with a 1(10)-*trans*,4,5-*cis*-cyclodecadiene ring. The conversion of the C-5 sp^2 carbon in a melampolide to an sp^3 carbon in the repandins causes considerable relief of ring strain, allowing conformational relaxation of the lactone ring, which causes the dihedral angle between H-6 and H-7 to change to about 90° which results in a small $J_{6,7}$ value. Furthermore, the angle between the plane of the lactonic exocyclic methylene group and H-7 is changing from near 90° in melampolides (maximum allylic coupling, $J_{7,13} \geq 3$ Hz) to about 60° in the repandins; this results in lower $J_{7,13}$ values near 2.00 Hz.[6] Similar $J_{6,7}$ and $J_{7,13}$ values are observed for melnerin A and B, 4,5-dihydromelampolides with established X-ray structures.[7]

A β orientation of the C-4 methylene function is required in the repandins to adopt dihedral angles at C-5 to C-9 which satisfy the NMR coupling constants of the involved protons. On the basis of the above arguments, we suggest the conformation shown in Figure 1 for the medium-ring portion of the repandins A–D.

Finally, it is of interest to note that the conversion of the C-5 hydroxyl in repandin D (**4a**) to a carbonyl group by chromate oxidation strongly changes the coupling in the oxidation product (**6**). The $J_{6,7}$ in **6** shows a value of 9.5 Hz ($J_{6,7} < 1$ in **4a**), indicating an antiperiplanar orientation of H-6 and H-7. Furthermore, the allylic couplings between H-7 and the lactonic exocyclic methylenes show $J_{7,13a}$ and $J_{7,13b}$ values of 3.0 and 3.5 Hz, respectively, that are typical of melampolides with a 4,5-trans double bond.[2] This suggests that the introduction of a carbonyl function at C-5 in repandin D causes an increase in ring strain which seems to be equivalent to the contribution of a 4,5-double bond in the melampolide skeleton. This is most likely due to the planarity of the C-6 carbonyl and the C-4,15 methylene function, which assures maximum conjugation of this chromophore. The chemical shift values for the two C-15 methylene protons (6.18 and 6.21 ppm) indeed indicate an s-trans conformation of the α,-β-unsaturated ketone moiety.

Experimental Section[8]

Stems and leaves of *Tetragonotheca repanda* (collected 14 mi south of Falfurrias, Brooks Co., TX, along highway 281 on April 30, 1976; Urbatch and Fischer 2460, voucher at LSU) were extracted and worked up as previously described,[9] providing 8.5 g of crude syrup. This syrup was chromatographed over 250 g of silica gel with $CHCl_3$/acetone (9:1) as eluant; 20-mL fractions were taken, and all fractions were monitored by TLC. Fractions 36–46 yielded 55 mg of longipilin (**5**) which was identical with authentic material by NMR and MS. Fractions 47–70 contained a mixture of **5** and repandins C (**3**) and D (**4a**). These fractions were combined and chromatographed over 75 g of silica gel with the same solvent system and yielded 20 mg of **3** and 15 mg of **4a**. From the combined fractions 141–156, a mixture of **1a** and **2a** (1.3 g) crystallized upon trituration with Et_2O. A 250-mg sample of the crystalline mixture of **1a** and **2a** was chromatographed by high-pressure LC on a 1 ft × $^3/_8$ in. μ-Bondapak, C-18 column using CH_3CN–5 M phosphate buffer (pH 3) over 12 min and yielded 100 mg of **1a** and 120 mg of **2a**.

Repandin A (1a): mp 132–133 °C; UV λ_{max} (MeOH) 210 nm (ϵ 2.3 × 10^4); CD $[\theta]_{215}$ −1.72 × 10^5, $[\theta]_{251}$ 1.23 × 10^4; IR$_{max}$ (Nujol) 3510 (OH), 1760 (γ-lactone), 1730, 1720 (esters), 1680, 1660 (double bonds), 1240, 1130 cm^{-1} (strong C–O stretching absorptions: lactone or conjugated ester); significant low-resolution mass spectral peaks (20 eV, 100 °C), *m/e* (rel intensity) 492 (0.01, $C_{25}H_{32}O_{10}$), 474 (0.02, $C_{25}H_{30}O_9$), 461 (0.01, $C_{24}H_{29}O_9$), 421 (0.01, $C_{21}H_{25}O_9$), 404 (0.01, $C_{21}H_{24}O_8$), 395 (0.02, $C_{20}H_{27}O_8$), 394 (0.02, $C_{20}H_{26}O_8$), 377 (0.10, $C_{20}H_{25}O_7$), 376 (0.03, $C_{20}H_{24}O_7$), 323 (0.02), 307 (0.02, M − $C_5H_5O_2$ − $C_4H_8O_2$), 306 (0.02, M − $C_5H_6O_2$ − $C_4H_8O_2$), 289 (0.03, $C_{16}H_{17}O_5$), 288 (0.04, M − $C_5H_8O_2$ − $C_9H_8O_2$), 256 (0.07), 229 (0.04), 99 (0.19, $C_5H_7O_2$), 71 (0.26, C_4H_7O). 43 (100, C_3H_7).

Anal. Calcd for $C_{25}H_{32}O_{10}$: mol wt 492.1995. Found (MS): mol wt 492.1989.

Acetylation of 60 mg of **1a** gave 55 mg of the diacetate **1b**: mp 130–131 °C; IR$_{max}$ (CCl_4) 1770, 1740, 1730, 1720, 1655 cm^{-1}; significant low-resolution mass spectral peaks (70 eV, 130 °C), *m/e* (rel intensity) 576 (not observed, $C_{29}H_{36}O_{12}$), 421 (0.11, $C_{21}H_{16}O_5$), 331 (0.02, $C_{18}H_{19}O_6$), 330 (0.02, $C_{18}H_{18}O_6$), 288 (0.21, $C_{16}H_{16}O_5$), 270 (0.12, $C_{16}H_{14}O_4$), 141 (0.84, $C_7H_9O_3$), 99 (0.26, $C_5H_7O_2$), 81 (0.67, C_5H_5O), 71 (0.44, C_4H_7O), 43 (100, C_3H_7 and

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C_2H_3O).

Repandin B (2a): mp 127–128 °C; UV λ_{max} (MeOH) 210 nm (ϵ 2.3 × 10^4); CD $[\theta]_{207}$ −1.77 × 10^5, $[\theta]_{249}$ 1.01 × 10^4; IR_{max} ($CHCl_3$) 3450 (OH), 1760 (γ-lactone), 1725, 1710, 1700 (carbonyls), 1680, 1640 cm^{-1} (double bonds); significant low-resolution mass spectral peaks (20 eV, 125 °C), *m/e* (rel intensity) 506 (0.01, $C_{26}H_{34}O_{10}$), 488 (0.01, $C_{26}H_{32}O_9$), 475 (0.01, $C_{25}H_{31}O_9$), 409 (0.04), 404 (0.03, $C_{21}H_{24}O_8$), 391 (0.20, $C_{21}H_{27}O_7$), 390 (0.05, $C_{21}H_{26}O_7$), 323 (0.08), 307 (0.11), 306 (0.05, M − $C_5H_{10}O_2$ − $C_5H_6O_2$), 289 (0.06, $C_{16}H_{17}O_5$), 288 (0.07, $C_{16}H_{16}O_5$), 256 (0.19), 229 (0.41), 228 (0.13), 99 (0.76, $C_5H_7O_2$), 85 (0.53, C_5H_9O), 57 (100, C_4H_9).

Anal. Calcd for $C_{26}H_{34}O_{10}$: mol wt 506.2152. Found (MS): mol wt 506.2170. CI: M + 1, *m/e* 507.

Acetylation of 40 mg of **2a** gave 35 mg of the diacetate **2b** as a gum: IR_{max} (CCl_4) 1770, 1740, 1730, 1720, 1655 cm^{-1}; significant low-resolution mass spectral peaks (70 eV, 130 °C), *m/e* (rel intensity) 590 (not observed, $C_{30}H_{38}O_{12}$), 435 (0.07, $C_{22}H_{27}O_9$), 331 (0.02, $C_{18}H_{19}O_6$), 330 (0.02, $C_{18}H_{18}O_6$), 288 (0.21, $C_{16}H_{16}O_5$), 270 (0.12, $C_{16}H_{14}O_4$), 141 (0.84, $C_7H_9O_3$), 99 (0.26, $C_5H_7O_2$), 85 (0.28, C_5H_9O), 57 (0.56, C_4H_9), 43 (100, C_2H_3O).

Repandin C (3): gum; CD $[\theta]_{213}$ −1.34 × 10^5, $[\theta]_{249}$ 1.34 × 10^4; IR_{max} ($CHCl_3$) 3500 (OH), 1765 (γ-lactone), 1735, 1720 (carbonyls), 1660, 1640 cm^{-1}; significant low-resolution mass spectral peaks (70 eV, 150 °C), *m/e* (rel intensity) 492 (0.01, $C_{25}H_{32}O_{10}$), 461 (0.01, $C_{24}H_{29}O_9$), 404 (2.8, $C_{21}H_{24}O_8$), 377 (0.11, $C_{20}H_{25}O_7$), 376 (0.09, $C_{20}H_{24}O_7$), 289 (0.29), 288 (0.36, M − $C_5H_8O_3$ − $C_4H_8O_2$), 256 (0.26, $C_{15}H_{12}O_4$), 99 (0.06, $C_5H_7O_2$), 71 (100, C_4H_7O), 43 (0.70, C_3H_7).

Anal. Calcd for $C_{25}H_{32}O_{10}$: mol wt 492.1986. Found (MS): mol wt 492.1979.

Repandin D (4a): gum; CD $[\theta]_{212}$ −2.85 × 10^5, $[\theta]_{247}$ 2.53 × 10^4; IR_{max} ($CHCl_3$) 3480, 1760, 1730, 1720 cm^{-1}; significant low-resolution mass spectral peaks (70 eV, 150 °C), *m/e* (rel intensity) 506 (0.01, $C_{26}H_{34}O_{10}$), 475 (0.02, $C_{25}H_{31}O_9$), 405 (0.02, $C_{21}H_{25}O_8$), 404 (0.05, $C_{21}H_{24}O_8$), 391 (0.29), 390 (0.14, $C_{21}H_{26}O_7$), 289 (0.20), 288 (0.22, $C_{16}H_{16}O_5$), 256 (0.37, $C_{15}H_{12}O_4$), 85 (0.86, C_5H_9O), 57 (100, C_4H_9).

Anal. Calcd for $C_{26}H_{34}O_{10}$: mol wt 506.2152. Found (MS): mol wt 506.2148.

Acetylation of 55 mg of **4a** gave 50 mg of acetate **4b** as a gum: IR_{max} (CCl_4) 1770, 1745, 1735, 1720, 1650 cm^{-1}; significant low-resolution mass spectral peaks (70 eV, 120 °C), *m/e* (rel intensity) 548 (0.01, $C_{28}H_{36}O_{11}$), 517 (0.01, $C_{27}H_{33}O_{10}$), 488 (0.02, $C_{26}H_{32}O_9$), 447 (0.04, $C_{23}H_{27}O_9$), 433 (0.17, $C_{23}H_{29}O_8$), 404 (0.02, $C_{21}H_{24}O_8$), 390 (0.11, $C_{21}H_{26}O_7$), 372 (0.03, $C_{21}H_{24}O_6$), 288 (0.36, $C_{16}H_{16}O_5$), 270 (0.22, $C_{16}H_{14}O_4$), 257 (0.20, $C_{15}H_{13}O_4$), 256 (0.36, $C_{15}H_{14}O_4$), 85 (0.95, C_5H_9O), 71 (0.24, C_4H_7O), 57 (100, C_4H_9), 43 (0.48, C_2H_3O).

Oxidation of 4a. To a solution of 0.13 g of **4a** in 15 mL of acetone at 0 °C was added, dropwise with stirring, Jones reagent until the solution remained orange. After an additional 45 min, the reaction was quenched by addition of 30 mL of H_2O. The solution was extracted (3 × 40 mL) with ethyl ether; the ether phase was washed with an equal volume of 5% $NaHCO_3$ solution followed by repeated washes with H_2O. Preparative TLC of the ether residue yielded 20 mg of **6** as a gum: IR_{max} (CCl_4) 1775, 1735, 1715 cm^{-1}; significant low-resolution mass spectral peaks (70 eV, 140 °C), *m/e* (rel intensity) 504 (0.02, $C_{26}H_{34}O_{10}$), 473 (0.01, $C_{25}H_{31}O_9$), 403 (0.04, $C_{21}H_{25}O_8$), 389 (0.16, $C_{21}H_{27}O_7$), 388 (0.03, $C_{21}H_{26}O_7$), 286 (0.22, $C_{16}H_{16}O_5$), 271 (0.21, $C_{15}H_{13}O_5$), 85 (0.87, C_5H_9O), 71 (0.47, C_4H_7O), 57 (100, C_4H_9).

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Registry No. 1a, 71155-66-3; **1b**, 71138-42-6; **2a**, 71170-76-8; **2b**, 71138-43-7; **3**, 71138-44-8; **4a**, 71138-45-9; **4b**, 71138-46-0; **5**, 71135-27-8; **6**, 71138-47-1.

Notes

A Method for Simple Titration of Organolithium Reagents in Ethers or Hydrocarbons Using Metalation of *N*-Benzylidenebenzylamine as Colored Reaction

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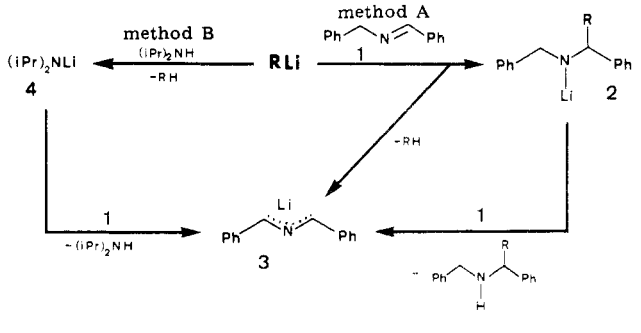
Organolithium compounds are useful reagents in organic synthesis. Generally, it is necessary to know their accurate concentration before their use in metalation and addition reactions; the most widely used methods for their analysis are the double titration procedure of Gilman and Cartledge[1] and the complexometric method of Watson and Eastham, in alkanes or benzene at room temperature[2] or in ethers at −78 °C.[3] Recently, a method was described which used the organolithium in a colored reaction of carbon lithiation: the colored indicator was diphenylacetic acid, whose dianion is yellow while the monoanion is colorless.[4] The organolithium was run from a syringe in the tetrahydrofuran solution of indicator until the end point was reached.

Scheme I



We have observed in the metalation of Schiff base of amino esters that the reaction mixture containing enolate was red or orange, and became pale yellow after protonation of the anion by a carboxylic acid.[5] However, the end point of the protonation was impossible to observe in this case. Reaction mixtures of organolithium and *N*-

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