°C (10 mm)]; IR ν_{max} (film) 3360 (OH), 1645 (C=C), 1055, 995, 920 cm^{-1}; NMR δ_{Me_4Si} (CCl_4) 6.1–5.55 (complex pattern, C**H**=CH_2), 5.3–4.87 (complex pattern, CH=C**H**$_2$), 3.98 (br q, J = 6 Hz, C**H**OH), 2.32 (s, OH), 1.28 (br, 16 H), 0.88 (br t, J = 5 Hz, CH_3). VPC analysis (oven temperature 180 °C, flow 15 mL/min) indicated the product (retention time 5.9 min) to be >98% pure.

1-Dodecen-3-one (3). A solution of 1.042 g (5.66 mmol) of 1-dodecen-3-ol (**2**) in 10 mL of dichloromethane was added dropwise rapidly to 4.69 g (21.7 mmol) of pyridinium chlorochromate[4] in 20 mL of dichloromethane. After this mixture was stirred vigorously at room temperature for 90 min, it was transferred with 120 mL of ether and 150 mL of 1 M aqueous NaOH to a separatory funnel. After separation of the layers, the organic layer was washed thoroughly with 1 M aqueous sodium hydroxide solution, 2 M aqueous hydrochloric acid, saturated aqueous sodium bicarbonate, and saturated brine in successive order. Isolation of the product from the organic extract in the usual manner, followed by evaporative distillation, afforded 837 mg (81%) of enone **3**:[5] bp 55–70 °C (bath temperature, 0.07 mm); IR ν_{max} (film) 1695 (C=O), 1620 (C=C), 1465, 1405, 1378, 1203, 1130, 1088, 990, 963, 725 cm^{-1}; NMR δ_{Me_4Si} (CCl_4) 6.19 (d, J = 8 Hz, 1 vinyl H), 6.15 (d, J = 4 Hz, 1 vinyl H), 5.66 (dd, J_1 = 8 Hz, J_2 = 4 Hz, C**H**=CH_2), 2.48 (t, J = 6 Hz, CH_2C=O), 0.88 (br t, J = 5 Hz, CH_3). VPC analysis (oven temperature 190 °C, flow 15 mL/min) indicated the product (retention time 3.9 min) to be >96% pure.

Diethyl Methyl-(3-oxododecyl)propanedioate (4). To a dilute solution of sodium ethoxide (prepared in situ by using 10 mg of sodium metal) in 4.0 mL of absolute ethanol were added 1.0 mL (5.8 mmol) of diethyl methylmalonate[4] and 799 mg (4.38 mmol) of 1-dodecen-3-one (**3**). After being stirred at room temperature for 22 h, the mixture was diluted with 40 mL of 0.05 M aqueous hydrochloric acid and the product was isolated in the usual manner by extraction with dichloromethane. Fractional[14] evaporative distillation afforded 1.29 g (83%) of diester **4**: bp 115–135 °C (bath temperature, 0.08 mm); IR ν_{max} (film) 1730 (br, C=O), 1460, 1375, 1295, 1255, 1170, 1110, 1020 cm^{-1}; NMR δ_{Me_4Si} (CCl_4) 4.10 (q, 4 H, J = 7 Hz, OC**H**$_2$CH$_3$), 1.32 (s, CH_3), 1.25 (t, 6 H, J = 7 Hz, OCH$_2$C**H**$_3$), 0.88 (br t, J = 5 Hz, $CH_2CH_2CH_3$). VPC analysis (oven temperature 215 °C, flow 20 mL/min) indicated the product (retention time 27.5 min) to be >98% pure.

Anal. Calcd for $C_{20}H_{38}O_5$: C, 67.38; H, 10.18. Found: C, 67.60; H, 10.13.

2-Methyl-5-oxotetradecanoic Acid (5). A mixture of 1.02 g (2.86 mmol) of diester **4**, 4.0 mL of glacial acetic acid, and 4.5 mL of 2 M aqueous hydrochloric acid was heated at reflux for 68 h. The crude product was isolated by dilution of this mixture at room temperature with 100 mL of 1:1 (v/v) water–saturated brine and extraction with dichloromethane. Further purification of the reaction product was accomplished by thoroughly washing an ether solution of the crude material (765 mg) with 0.5 M aqueous sodium hydroxide solution. The combined base washes were extracted with dichloromethane to remove traces of any nonacidic components and then subsequently were acidified by using 2 M aqueous hydrochloric acid. Extraction of the acidified aqueous layer with ether afforded 651 mg (89%) of keto acid **5**:[9] mp (after recrystallization from 1:1 (v/v) hexane–cyclohexane) 58–60 °C (lit.[9] mp 59–60 °C); NMR δ_{Me_4Si} ($CDCl_3$) 10.43 (br s, COOH), 2.08–2.75 (m, 5 H, CHCOOH, C**H**$_2$C(O)C**H**$_2$), 1.20 (d, J = 7 Hz, CHC**H**$_3$), 0.88 (br t, J = 5 Hz, CH_2CH_3).

2-Methyl-5-nonyl-5-hexenoic Acid (6). A mixture of 281 mg (7.13 mmol) of 61% sodium hydride (washed with hexane to remove the mineral oil) and 9 mL of anhydrous dimethyl sulfoxide was heated at 70 °C (bath temperature) for 30 min or until hydrogen evolution had ceased. The mixture was then cooled to room temperature and 2.60 g (7.28 mmol) of methyltriphenylphosphonium bromide[4] was added. After this mixture was stirred at room temperature for 20 min to ensure formation of the ylide a solution of 350 mg (1.36 mmol) of ketone **5** in 4.0 mL of anhydrous dimethyl sulfoxide was added dropwise and the ensuing reaction mixture was stirred vigorously at room temperature for an additional 4 h. The product was isolated by dilution of this mixture with 125 mL of 0.1 M aqueous hydrochloric acid followed by thorough extraction with 1:1 (v/v) hexane–ether. The combined extracts were washed thoroughly with water and saturated brine, after which the aqueous washes were discarded. The organic layer was then washed thoroughly with 0.5 M aqueous sodium hydroxide solution, after which the combined base washes were extracted with dichloromethane to remove traces of any nonacidic components. Subsequent acidification of the aqueous layer using 2 M hydrochloric acid, followed by extraction with ether in the usual manner, afforded 265 mg (77%) of unsaturated acid **6**: bp 115–130 °C (bath temperature, 0.10 mm); IR ν_{max} (film) 1705 (C=O), 1642 (C=C), 1460, 1413, 1378, 1290, 1240, 1185, 935, 885 cm^{-1}; NMR δ_{Me_4Si} (CCl_4) 10.9 (br s, COOH), 4.66 (br s, C=C**H**$_2$), 2.38 (m, C**H**COOH), 1.19 (d, J = 7 Hz, CHC**H**$_3$), 0.87 (br t, J = 5 Hz, CH_2CH_3).

Anal. Calcd for $C_{16}H_{30}O_2$: C, 75.53; H, 11.89. Found: C, 75.79; H, 12.00.

Preparation of (±)-Malyngolide (8). A mixture of 126 mg (0.50 mmol) of unsaturated acid **6** and 137 mg of 85% *m*-chloroperbenzoic acid[4] in 1.5 mL of cyclohexane and 0.5 mL of toluene was stirred at room temperature for 6 h. The mixture was then filtered through a micro Büchner funnel in order to remove *m*-chlorobenzoic acid, which had been produced during the epoxidation. The solid acid was washed[15] with five 1.0-mL portions of cyclohexane, and the filtrate and combined washes were subsequently heated at reflux for 24 h. After this solution was cooled to room temperature, it was diluted with 20 mL of ether. The organic layer was then washed thoroughly with 2:1 (v/v) 1 M aqueous sodium hydroxide solution–saturated brine, followed by the operations described in the general experimental isolation procedure. Removal of the solvent, followed by chromatography on silica gel (10 mL, elution with hexane–60% ether) afforded 67 mg (50%) of (±)-malyngolide (**8**), >99% pure by VPC analysis (oven temperature 215 °C, flow 20 mL/min, retention time 21.3 min). The IR and NMR spectral properties of this hydroxy lactone (**8**) were virtually identical[12] with those previously reported[1] for the naturally occurring (–)-malyngolide (**8**).

Acknowledgment. We thank Professor Richard E. Moore of the University of Hawaii for comparing the IR and NMR spectra of our synthetic (±)-malyngolide with those of the natural product. The assistance of Dr. David S. Crumrine of Loyola University of Chicago in determining the ^{13}C NMR spectrum of our synthetic malyngolide is also gratefully acknowledged.

Registry No. 1, 112-31-2; 2, 4048-42-4; 3, 58879-39-3; 4, 74684-33-6; 5, 74742-18-0; 6, 74709-66-3; 8, 74742-19-1; diethyl methylmalonate, 609-08-5; vinyl bromide, 593-60-2.

(14) The unreacted diethyl methylmalonate was collected at 50–75 °C (bath temperature, 2.5 mm).

(15) On a larger scale, considerably smaller amounts of cyclohexane should be used during this step to minimize dissolution of the *m*-chlorobenzoic acid, which is sparingly soluble in cyclohexane. The presence of this latter acid in the reaction mixture during the lactonization can lead to a competing intermolecular reaction between the epoxide **7** and *m*-chlorobenzoic acid. This was demonstrated by a similar experiment in which the initial epoxidation mixture was diluted, without filtering off the aromatic acid, with 5 mL of cyclohexane prior to refluxing the reaction mixture to induce the cyclization. Under such conditions, the yield of malyngolide was only 34%.

Constraints on Long-Range Aryl Migration.[1] Solvolysis of *exo*-3,3-Fluorenylidenetricyclo[3.2.1.0^{2,4}]oct-*anti*-8-yl Tosylate and 6,6-Diphenylbicyclo[3.1.0]hex-*exo*-3-yl Tosylate

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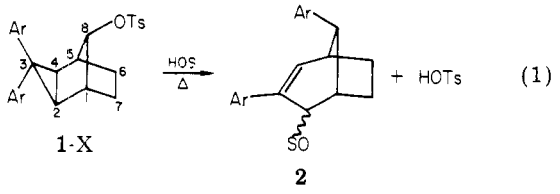
The solvolytic rearrangement shown in eq 1 involves both aryl migration and cyclopropyl ring opening.[3] The

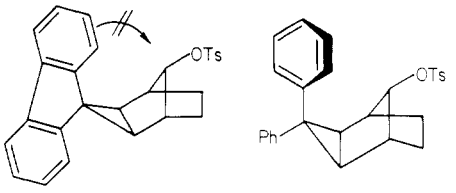


rearrangement is quantitative and exhibits anchimeric acceleration by the migrating aryl group, 1-Ph being 7000-fold faster than the parent 1 (Ar = H) at 110.5 °C. This migration is Ar_1-5 in nature and is characterized by rather low ρ^+ values (−1.68 in 80% dioxane at 112 °C and −1.30 in acetic acid at 110.5 °C). This latter fact led to the suggestion that the long-range aryl migration (LRAM) was concerted with the electrocyclic ring opening (ERO) of the cyclopropyl portion of the molecule. We describe here some probes to test the strictures on this rearrangement.

As the first probe, the fluorenylidene analogue was prepared as shown in Scheme I. The reaction of diazofluorene with *anti*-7-norbornenol in benzene was slow. Little reaction occurred at 25 °C over 45 h or at 56 °C for the same time period. After 20 h at reflux, however, alcohol **3** and bifluorenylidene (**4**) were isolated in 29% and 23% yields, respectively, based upon the diazofluorene. Considerable tar was also formed. Tosylate **5** was prepared in routine fashion from alcohol **3** in 70% yield. As a piece of structural evidence, both tosylate **5** and alcohol **3** showed in the ^{1}H NMR spectrum a downfield shift for the *syn* H-8 proton relative to 1-Ph and its alcohol ($\Delta\delta$ = 1.73 ppm for the tosylates and 1.85 ppm for the alcohols). This paramagnetic shift is expected for H-8 in **3** and **5** because it lies directly in the plane of the fluorenylidene ring system and is close enough to be affected by the ring current of the aromatic moiety. The same effect was noted by Filipescu and DeMember in related compounds.[4]

Solvolysis of tosylate **5** was performed in dioxane–water (80:20 v/v), as described earlier for **1**.[3] Because **5** was obviously slow in solvolysis at those temperatures used earlier for 1-Ar, a temperature of 160 °C was eventually employed. The rate constant was $\sim 5 \times 10^{-6}$ s^{-1}, indicating that tosylate **5** *is ca. 160-fold slower than 1-Ph at this temperature* ($k^{1\text{-Ph}}$ extrapolated from earlier data[3] is 8×10^{-4} s^{-1} at 160 °C). No product determination was accomplished for **5** because NMR analysis indicated a very complex mixture. From literature data[5] the rate constant for the parent tosylate **1** (Ar = H) may be calculated to be $\sim 0.6 \times 10^{-6}$ s^{-1} at 160 °C. It is clear, therefore, that at 160 °C tosylate **5** is but modestly faster (~8-fold) than the parent, whereas 1-Ph is considerably more rapid (~1300-fold).

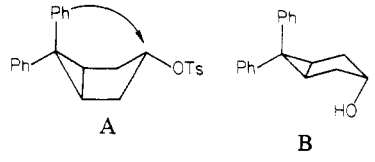
The explanation for these rate differences seems clear. As shown below, tosylate **5** has its aryl π system rigidly orthogonal to the proper direction for anchimeric π participation at C-8, whereas 1-Ph can achieve face-on π attack upon C-8 by proper rotation of the aromatic ring.



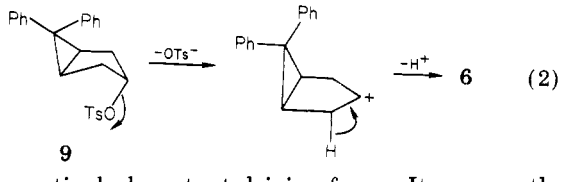
Hence LRAM can occur in the latter but not in the former. The slightly faster rate for **5** relative to that for the parent system **1** (Ar = H) illustrates a possible steric effect. The crowded syn proton at C-8 would have its condition relieved by departure of the tosylate group, allowing C-8 to approach sp^2 hybridization. The effect is not large, however, and its small magnitude even in the rigid case of **5** emphasizes that the high reactivity of 1-Ar, where rotation would further minimize the effect, is not due to such steric crowding to any significant extent.

As a second probe, tosylate **8** was prepared as shown in Scheme II. Hydroboration–oxidation of 6,6-diphenylbicyclo[3.1.0]hex-2-ene (**6**)[6] led to the isomeric exo alcohols **7** and **8** in an ~3:2 ratio, in fair agreement with reported findings.[6,7] Their chromatographic separation was just partly successful, however, and only an enriched sample of **7** (83%) was obtained. This was then converted to tosylate **9** in purity sufficient for solvolysis purposes.

Solvolysis of tosylate **9** was carried out in dioxane–water (80:20 v/v) as described.[3] The rate constants found were as follows (in s^{-1}): 1.4×10^{-4} (100 °C), 1.5×10^{-6} (60 °C), 1.0×10^{-7} (40 °C). *The sole product observed was olefin 6, indicating the absence of LRAM and ERO.* From earlier data[3] one can compute and compare the rate data for 1-Ph with the above results. Such calculations indicate that *tosylate 9 is 25 to 30-fold faster than 1-Ph at these temperatures.* Because **9** is a secondary, relatively unhindered tosylate, it is likely that a solvent-mediated E1 or E2 process intervened, swamping out any potential k_Δ process leading to LRAM and ERO. Furthermore, LRAM would require conformer A for reaction, and Crumrine and



Yen[7] have presented evidence that the preferred conformer for alcohol **7** (and presumably, therfore, also tosylate **9**) is B. This axial orientation for the leaving group would favor a rapid dissociation and elimination as shown in eq 2. The result with tosylate **9** indicates that LRAM–ERO



is not a particularly potent driving force. It apparently requires prescribed preexisting geometry in the substrate and is not able to overcome alternative pathways in less rigid molecules.

Experimental Section

Melting points were taken on a calibrated Fisher-Johns block. Infrared spectra were determined on a Perkin-Elmer Model 700A spectrophotometer. Only portions of the IR spectra are reported. NMR spectra were taken in deuteriochloroform containing 1%

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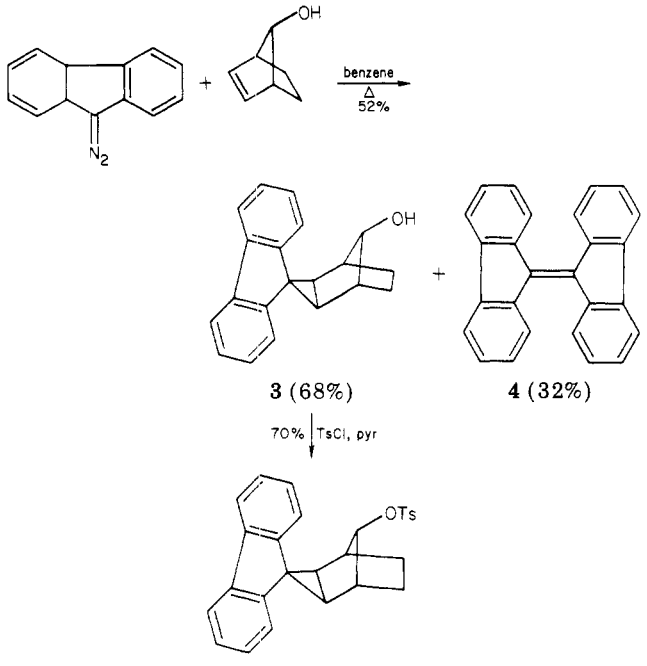
Scheme I



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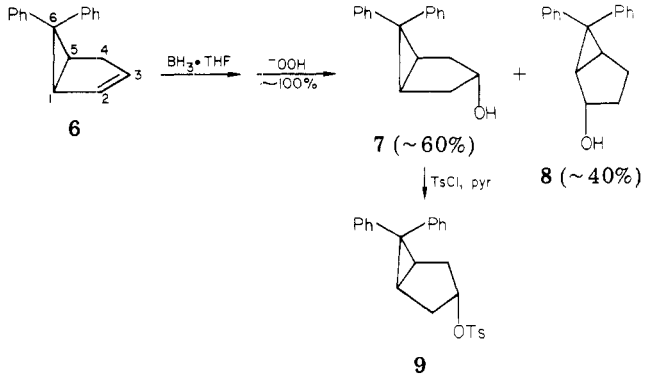
Scheme II



9

Me_4Si on a Varian A-60A spectrometer. The usual splitting abbreviations are used. Sharp multiplets are given as their centers. Microanalyses were performed by Micro-Tech Laboratories.

***exo*-3,3-Fluorenylidenetricyclo[3.2.1.0^{2,4}]octan-*anti*-8-ol (3).** 9-Diazofluorene[8] (5.005 g, 24.5 mmol) was added to a solution of *anti*-7-norborneol[9] (3.371 g, 30.6 mmol) in dry benzene (30 mL). Infrared analysis of small aliquots showed little reaction at temperatures under reflux even for extended time periods (45 h). Refluxing the orange solution for 20 h did lead to reaction, however, with the IR-determined disappearance of the diazofluorene. Removal of the benzene left an orange-red solid (6.188 g). Chromatography of this dark solid on alumina (150 g) with 1:1 hexane–ether gave first an orange-red, beautifully crystalline solid identified as **bifluorenylidene** (4): 0.989 g (25%); mp 192–194 °C (from ethanol) (lit.[10] mp 194–195 °C); NMR δ 8.4 (m, H-1, -1′, -8, -8′), 7.67 (m, 4 H), 7.23 (m, 8 H). Later fractions afforded alcohol 3: 1.936 g (29%); white micrycrystalline solid; mp 189–190 °C (from benzene–petroleum ether); NMR δ 7.73, 7.27, 6.97 (3 m, ratio 3:4:1, Ar H's), 5.22 (m, H-8), 2.58 (m, H-1, -5), 1.93 (s, H-2, -4), 2.2–1.2 (br m, exo and endo H-6, -7), 1.47 (br s, OH, exchangeable); IR (KBr) ν 3600–3400, 1720, 1450, 1080 cm^{-1}. Anal. Calcd for $C_{20}H_{18}O$: C, 87.56; H, 6.61. Found: C, 87.18; H, 6.54. Tarry material remained on the column.

***exo*-3,3-Fluorenylidenetricyclo[3.2.1.0^{2,4}]oct-*anti*-8-yl Tosylate (5).** Reaction of alcohol 3 with *p*-toluenesulfonyl chloride in dry pyridine in the usual fashion[11] produced tosylate 5: 70%; white crystals; mp 182–185 °C (from benzene–hexane, 1:2); NMR δ 7.77, 7.27, 6.87 (3 m, ratio 5:6:1, Ar H's), 5.68 (sharp m, H-8), 2.67 (sharp m, H-1, 5), 2.47 (s, Ar CH_3), 1.93 (s, H-2, -4), 2.3–1.3 (br m, exo and endo H-6, -7)]. Anal. Calcd for $C_{27}H_{24}O_3S$: C, 75.67; H, 5.64. Found: C, 75.63; H, 5.62.

Solvolysis of Tosylate 5. The study was carried out on 0.0304 M tosylate 5 at 160 ± 1 °C in 80:20 (v/v) purified dioxane–water containing 2,6-lutidine as described earlier.[3] Removal of solvent from the solvolysate afforded dark, oily material with a very complex NMR spectrum. The characteristic singlet at δ 1.93 for the H-2, H-4 pair in 3 was absent, so clearly rearranged materials were formed with eventual disruption of the cyclopropyl ring. No further investigation of the products was undertaken.

6,6-Diphenylbicyclo[3.1.0]hexan-*exo*-3-ol (7). Hydroboration–oxidation of 6,6-diphenylbicyclo[3.1.0]hex-2-ene (6) was performed as reported.[6] The mixture so produced of 7 together with the isomeric *exo*-2-hydroxy alcohol 8 (ca. 3:2) was chromatographed on deactivated silica gel (60–200 mesh) as described.[6,7] Elution with ether–hexane (1:1) afforded at length a fraction rich in alcohol 7. NMR analysis using the CHOH multiplets at δ 2.87 and 4.3 for alcohols 7 and 8, respectively, indicated a ratio of 7/8 of 83.3:16.7.

6,6-Diphenylbicyclo[3.1.0]hex-*exo*-3-yl Tosylate (9). Reaction of the enriched mixture of alcohols 7 and 8 with *p*-toluenesulfonyl chloride in dry pyridine in the standard fashion[11] produced tosylate 9: 50%; white crystalline solid; mp 129.5–130 °C (upon several recrystallizations from benzene and hexane); NMR δ 7.5–7.0 (m, Ar H), 3.2 (m, H-3), 2.4 (s, Ar CH_3), 2.3–1.9 (m, H-1, -2, -4, -5)]. Anal. Calcd for $C_{25}H_{24}O_3S$: C, 74.23; H, 5.98. Found: C, 74.28; H, 5.88.

Solvolysis of Tosylate 9. Samples (0.030 M) of tosylate 9 that contained small amounts of the tosylate from alcohol 8 (~5%) were solvolyzed in dioxane–water (80:20 v/v) containing 2,6-lutidine (0.044 M) at 100, 60, and 40 °C (±0.5 °C) by using the procedure previously described.[3] The rate constants observed are given in the text. The first 5–10% of reaction was considerably faster due to the presence of the *exo*-2-tosylate. Rates for tosylate 9 were determined subsequent to the time required to consume this contaminant. The solvolysate was reduced in volume by evaporation and extracted with several portions of ether. The ether extracts were washed, dried, and stripped of solvent. Aside from minor contaminants due to the products from the *exo*-2-tosylate, the single product observed in essentially quantitative yield was olefin 6, as established by NMR comparison.

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Registry No. 3, 74808-91-6; 4, 746-47-4; 5, 74808-92-7; 6, 22524-13-6; 7, 57774-40-0; 8, 74808-93-8; 9, 74808-94-9; 9-diazofluorene, 832-80-4; *anti*-7-norbornenol, 694-70-2; *p*-toluenesulfonyl chloride, 98-59-9.

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An Unusually Selective Photochemical Reaction of a Flavin

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Photoreductive alkylation of 3-methyllumiflavin (1, 3-MLF) by β,γ-acetylenic amines has been a convenient route to model flavin compounds[1] whose structures are

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