flect the relative activities of the various transferase and hydrolyase enzymes which are capable of reacting with the glutathione conjugates once they are formed. The differences among the plant species in the subsequent metabolism of the glutathione conjugates may not affect susceptibility since glutathione conjugation is the initial detoxication reaction. It is not certain, however, whether these differences in the subsequent rate of metabolism of the glutathione conjugates would have any lasting effect on the ultimate disposition of these triazines in the plants.

The substrate specificity of excised corn leaves for the various triazine herbicides is compared with the data of Frear and Swanson (1970) for glutathione *S*-transferase isolated from corn (Table II). The general order of reactivity was the same in both studies, with the exception of atrazine, which appeared to be more reactive than GS-13529 in excised corn leaves. Quantitatively, there was much less difference among these compounds in the amount of water-soluble metabolites formed in excised corn leaves than might have been expected on the basis of the *in vitro* studies. In excised leaves the rate of conjugation was so rapid that other factors such as absorption, translocation, and penetration of the substrate into the site of metabolism may have been limiting factors.

It is not certain whether the formation of glutathione and γ-glutamylcysteine conjugates is an enzymatic reaction in excised barley shoots. The metabolism of atrazine to water-soluble metabolites was faster in barley (36.9% in 20 hr) than in the other susceptible species (1.2 to 17% in 20 hr). The rate of formation of water-soluble metabolites in barley seems to be faster than expected on the basis of a nonenzymatic reaction (Table I). However, a glutathione *S*-transferase was not detected in barley leaves (Frear and Swanson, 1970); the substrate specificity of excised barley leaves is quite different than that observed in the tolerant species, and the rate of conversion of the substrates to water-soluble metabolites was much slower in barley than in the tolerant species.

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LITERATURE CITED

Frear, D. S., Swanson, H. R., *Phytochemistry* **9,** 2123 (1970).
Funderburk, H. H., Jr., Davis, D. E., *Weeds* **11,** 101 (1963).
Hamilton, R. H., J. AGR. FOOD CHEM. **12,** 14 (1964).
Lamoureux, G. L., Shimabukuro, R. H., Swanson, H. R., Frear, D. S., J. AGR. FOOD CHEM. **18,** 81 (1970).
Lamoureux, G. L., Stafford, L. E., Tanaka, F. S., J. AGR. FOOD CHEM. **19,** 346 (1971).
Ross, J. A., Tweedy, B. G., *Org. Mass Spectrom.* **3,** 219 (1970).
Schroeder, W. A., Jones, R. T., Cormick, J., McCalla, K., *Anal. Chem.* **34,** 1570 (1962).
Shimabukuro, R. H., J. AGR. FOOD CHEM. **15,** 557 (1967a).
Shimabukuro, R. H., *Plant Physiol.* **42,** 1269 (1967b).
Shimabukuro, R. H., Kadunce, D. D., Frear, D. S., J. AGR. FOOD CHEM. **14,** 392 (1966).
Shimabukuro, R. H., Swanson, H. R., Walsh, W. C., *Plant Physiol.* **46,** 103 (1970).
Shimabukuro, R. H., Frear, D. S., Swanson, H. R., Walsh, W. C., *Plant Physiol.* **47,** 10 (1971).
Shimabukuro, R. H., Lamoureux, G. L., Frear, D. S., Bakke, J. E., *J. Pure Appl. Chem.* 323 (1971).

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The following papers form Part II of a symposium on The Chemistry of Essential Oils and Related Products. For Part I, see J. AGR. FOOD CHEM., pages 1074–1123, November/December 1971.

Oxymercuration of Terpenoid Alcohols

Gottfried Brieger* and Elizabeth P. Burrows

Oxymercuration of geraniol was shown to give two products, a bicyclic ketal and the related alcohol 2-[2-methyl-5-isopropyl tetrahydrofuranyl]ethanol. No normal addition products were found. Oxymercuration of *cis*-linalool oxide gave as single product the related bicyclic ether. Myrcenol also cyclized in high yield on oxymercuration to 1-[2,6,6-trimethyltetrahydropyranyl]ethanol. Oxymercuration with less than one equivalent of mercuric acetate gave the rearranged ether, 2-allyl-6,6-dimethyltetrahydropyran. Ethoxymercuration proceeded normally and selectively at the terminal double bond of both geraniol and farnesol, yielding the corresponding monoethoxy ethers 7-ethoxygeraniol and 11-ethoxyfarnesol.

Intramolecular cyclizations during the addition of mercuric salts to olefins were noted earlier by Sand and Singer (1902, 1903). They observed that 2-allylphenol cyclized during reactions with mercuric salts to give 2-methyl-2,3-dihydrobenzofuran. Similarly, α-terpineol was found to give 1,8-cineole, a report recently confirmed by Coxon *et al.* (1968). Cyclization of β-(7-norbornenyl)ethanol was reported by Bly *et al.* (1967). Cyclization was also observed during the oxymercuration of cyclooctadienes by Bordwell and Douglass (1966) and Moon *et al.* (1969). Moon and Waxman (1969) also noted the formation of bicyclic ethers on oxymercuration of 2-(2-cyclohexenyl)ethanol and 2-(2-cyclopentenyl)ethanol.

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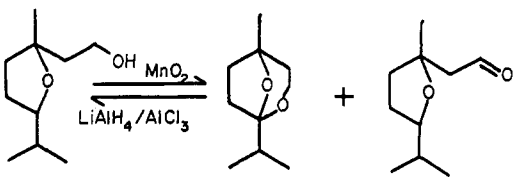
We have examined the reaction of several terpene alcohols: geraniol, linalool, linalool oxide, myrcenol, and farnesol, with mercuric acetate using the Brown hydration procedure (water/tetrahydrofuran) as well as when using alcohol as solvent, and report here the unexpected results.

RESULTS AND DISCUSSION

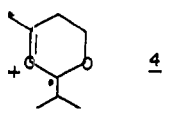
Oxymercuration of geraniol under the Brown conditions for Markonikov hydration of olefins (Brown and Geoghegan, 1970) gave, in addition to unchanged starting material, the ketal **1** and the cyclic alcohol **2** in a relative ratio of 1:2. Structural assignments were made on the basis of elemental analyses and spectroscopic properties, as well as by virtue of their facile interconversion under relatively mild conditions. Thus manganese dioxide oxidation of alcohol **2** gave, in addition to small amounts of aldehyde **3**, a fair yield of **1**. Ether **1** was cleaved quantitatively to alcohol **2** on treatment with $LiAlH_4$–$AlCl_3$.



2 **1** **3**

The nmr spectrum of **1** showed the isopropyl methyls as an unsymmetrical quartet centered at δ 0.92, a methyl singlet at δ 1.30, and 2 protons on carbon next to oxygen as doublets with further splitting, centered at δ 3.77 and 3.92. The spectrum of **2** similarly showed the isopropyl methyls at δ 0.89 and the methyl singlet at δ 1.20, and in addition showed the hydroxyl proton as a broad singlet (ρ 2.65) and the 3 protons on carbon next to oxygen as a multiplet centered at δ 3.57. Aldehyde **3** showed, in addition to the quartet centered at δ 0.89 and the singlet at δ 1.27, a broad 1 *H* multiplet at δ 3.6, a 2 *H* doublet at δ 2.45 for the α hydrogens, and the aldehyde proton as a triplet at δ 9.63. Olefinic protons were absent in all three spectra.

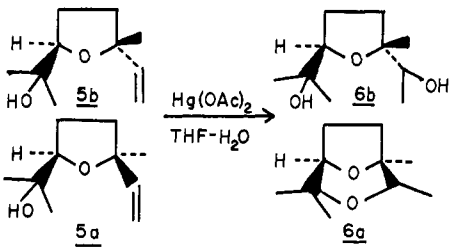
Mass spectra also support the structural assignments. All three compounds displayed prominent peaks corresponding to loss of the isopropyl group. Ketal **1**, in addition, showed a very intense M^+ (40% of base peak), and a significant peak at *m/e* 142 due to cleavage of the tetrahydrofuran ring and loss of ethylene to give an oxonium cation, possibly **4**.



4

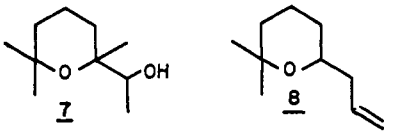
Surprisingly, farnesol was entirely inert to the conditions under which geraniol underwent cyclization; even after 1 week only traces of hydroxylic products were present, but there were no bicyclic ethers. The allylic isomer of geraniol, linalool, also was quite resistant to oxymercuration. After 18 hr, no normal addition products were observed; in addition to the starting material, only trace amounts of at least eight peaks of shorter retention time appeared.

The reported cyclization of α-terpineol to the bicyclic ether 1,8-cineole under oxymercuration conditions (Coxon *et al.*, 1968), prompted us to investigate the possible cyclization of linalool oxide. The linalool oxide sample actually used for oxymercuration (Aldrich Chemical Co.) was a 1:1 mixture of isomers **5a** and **5b**, only partially resolvable under optimum gas chromatographic conditions. Trans isomer **5b**, incapable of forming a bicyclic product, was transformed quantitatively to the known diol **6b**, the product of normal Markonikov addition (see Experimental Section). Oxymercuration of **5a** gave in high yield a single product, bicyclic ether **6a**, whose structural assignment follows from elemental analysis and spectral data. The nmr spectrum displayed four peaks in the CH_3–C–O region: a singlet at δ 0.95 coincident with the down-



field peak of a doublet centered at δ 0.90 (totaling 6 *H*) and two 3 *H* singlets at δ 1.10 and δ 1.27. A broad 4 *H* triplet at δ 1.90 was attributed to the methylene protons, and an unsymmetrical quartet (δ 3.60, 2 *H*) was attributed to the protons on carbon bound to oxygen.

Myrcenol also underwent a similar cyclization yielding a mixture of isomeric hydroxy ethers **7**, only partially resolved by gas chromatography, whose structures follow from elemental analysis and spectral data. The nmr spectrum of **7** displayed six peaks in the CH_3–C–O region totaling 12 *H* (δ 0.92, 1.02, 1.10, 1.13, 1.15, 1.22), as well as a singlet at δ 2.53 for the hydroxyl proton, a 1 *H* quartet at δ 3.40, and a 6 *H* multiplet at δ 1.35–1.85 for the methylene protons. Two equivalents of mercuric acetate were necessary for a high yield of **7**, and when oxymercuration was carried out with an insufficiency (<1 equiv) of mercuric acetate and interrupted after 1 hr, an unsaturated ether **8** was the major product. Its



structure is supported by the nmr spectrum, showing a 2-proton triplet for the allylic hydrogens at δ 2.20, the vinyl protons appearing at δ 4.90, 5.15, and 5.90 (quartet), respectively. The methyl protons appear at δ 1.23 as a singlet. Additional support for the proposed structure comes from the mass spectrum of **8**, which shows an intense peak at $M^+ - 41$, corresponding to the loss of an allyl group.

It appears then that the oxymercuration of terpene alcohols is frequently accompanied by major rearrangements, which may be rationalized mechanistically as products arising from the solvolysis of the presumed intermediate organomercury adducts. Thus a possible mechanism for the formation of the bicyclic ketal **1** is depicted below.

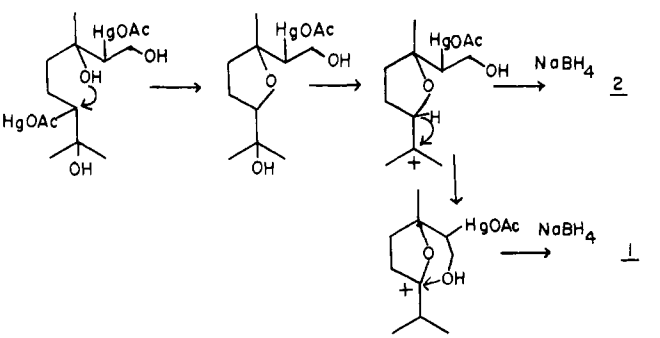
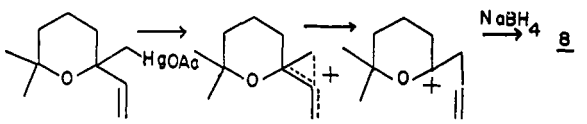


Table I. Oxymercuration of Olefinic Alcohols

Olefinic alcohol	Reaction time	Unchanged starting material	Products
Geraniol	18 hr	45%	20% **1**; 35% **2**
Linalool	18 hr	*ca.* 90%	>8 trace components
Linalool oxide (50% cis, 50% trans)	10 min[c]	<10%	40% **6a** 50% **6b**
Myrcenol[a]	15 hr	13%	75% **7**
Farnesol[b]	7 days	>90%	Trace hydroxy compounds[d]

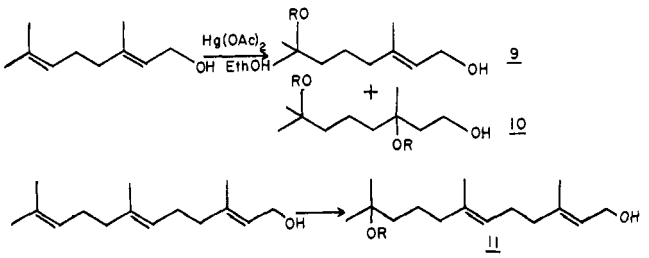
[a] 2 mmol $Hg(OAc)_2$/1 mmol myrcenol. [b] In 2 ml H_2O and 3.5 ml THF. [c] Product distribution essentially unchanged after 2 hr. [d] By column chromatography on silica gel.

The rearrangement of the initial myrcenol adduct to give **8** may be pictured as follows.



The initially formed adduct, which could generate a cyclopropylcarbinyl system, rearranges to the more stable tertiary structure as shown.

Recently Brown and Rei (1969) reported an oxymercuration procedure involving use of low molecular weight alcohols for the preparation of alkoxy ethers from olefins. Our interest in synthesis and physiological activity of some higher acyclic terpenoids led us to investigate possible application of this alkoxymercuration to geraniol and farnesol. Treatment of the polyene alcohol with one equivalent of mercuric acetate in excess ethanol gave in both cases exclusively the product of normal ethoxymercuration at the terminal double bond. No evidence was found for the presence of another monoethoxy ether. However, in the geraniol case, in addition to a preponderance of 7-ethoxygeraniol (**9**) and unchanged starting material, 3,7-diethoxygeraniol (**10**) was found.



The observed ratio of CH_3C- to CH_3-C= protons in the nmr spectrum of 7-ethoxygeraniol (**9**) (3:1) established its structure and eliminated the alternative 3-ethoxy isomer as a possibility (CH_3-C- to CH_3C=, 1:1). Similarly, the spectrum of 11-ethoxyfarnesol (**11**) showed a CH_3-C- to CH_3C= ratio of 3:2, inconsistent with either alternative monoethoxy ether.

We may therefore add mercuric acetate to the list of electrophilic agents which add selectively to terminal bonds of terpenoid polyenes (Van Tamelen and Curphey, 1962; Van Tamelen and Sharpless, 1967).

PROCEDURE

The gas chromatographic column was 5 ft × 0.25-in. packed with 20% Carbowax 20M. Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich. Nmr spectra were determined in CCl_4 on a Varian Associates T-60, and are reported as δ (ppm) relative to TMS as internal standard. Infrared spectra were measured as thin films on a Beckman IR-5. Mass spectra were determined on an Atlas CH-5.

Table II. Ethoxymercuration of Olefinic Alcohols

Olefinic alcohol	Reaction time	Unchanged starting material	Products
Geraniol	30 min	30%	50% **9**, 20% **10**
Farnesol	45 min	70%	30% **11**

Oxymercurations. To a stirred solution of 2 mmol of $Hg(OAc)_2$ in 2 ml of H_2O was added a solution of 2 mmol of olefinic alcohol in 2 ml of tetrahydrofuran. After stirring at room temperature for the duration indicated in Table I, the mixture was ice-cooled while 2 ml of 3 *N* NaOH, followed by 2 ml of 3 *N* NaOH containing 2 mmol of $NaBH_4$, were added. Stirring was continued at room temperature until the mercury had coagulated. The mixture was saturated with NaCl, ether was added, and the organic layer was separated and dried. The solvents were removed and the residues were analyzed and separated by gas chromatography, unless noted otherwise. Results are summarized in Table I.

Ethoxymercurations. To a stirred suspension of 2 mmol of $Hg(OAc)_2$ in 1 ml of absolute EtOH was added 2 mmol of olefinic alcohol in 1 ml of absolute EtOH. The mixture became homogeneous after 10–15 min and was stirred at room temperature 20–30 min longer. It was ice-cooled while 2 ml of 3 *N* NaOH, followed by 2 ml of 3 *N* NaOH containing 2 mmol of $NaBH_4$, were added. Stirring was continued at room temperature until the mercury had coagulated. The mixture was saturated with NaCl and extracted with pentane, and the pentane layer was washed with H_2O and dried. The solvent was removed and the residue was analyzed and separated (by gas chromatography in the geraniol case; by silica gel column chromatography in the farnesol case). Results are summarized in Table II.

Conversion of 1 to 2. Aluminum chloride (270 mg) in ether (3 ml) was ice-cooled and stirred under N_2 while $LiAlH_4$ (80 mg) was added. A solution of ketal **1** (70 mg) in ether (5 ml) was added dropwise, and the mixture was stirred under reflux 4 hr. It was cooled in ice while H_2O was added dropwise, followed by dilute H_2SO_4 until the solids dissolved. The ether layer was separated, washed with Na_2CO_3 and NaCl solutions, dried, and evaporated. Gas chromatography of the residue (64 mg) showed a single peak identified as alcohol **2** by retention time and identity of ir and nmr spectra.

Manganese Dioxide Oxidation of 2. A mixture of MnO_2 (2 g, activated by azeotropic distillation, Goldman 1969) and **2** (220 mg) in benzene (15 ml) was stirred under reflux 18 hr. The mixture was cooled, filtered through Celite, and the filtrate was concentrated to a residue of 92 mg. Gas chromatographic analysis and separation showed that it consisted of (in order of increasing retention times) ketal **1** (30%), aldehyde **3** (10%), and unchanged **2** (60%).

Microanalyses. **1** Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 71.05; H, 10.86. **2** Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.72; H, 11.18. **6a** Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.45; H, 10.68. **7** Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 70.17; H, 11.36. **8** Calcd for $C_{10}H_{18}O$: C, 77.91; H, 11.68. Found: C, 77.09; H, 11.31. **9** Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08. Found: C,

72.25; H, 11.95. **10** Calcd for $C_{14}H_{30}O_3$: C, 68.24; H, 12.27. Found: C, 68.49; H, 12.15. **11** Calcd for $C_{17}H_{32}O_2$: C, 76.06; H, 12.02. Found: C, 75.99; H, 11.86.

Nmr Spectra. Spectra of **1, 2, 3, 6a, 7,** and **8** are described in discussion section. **6b** (Klein *et al.*, 1964) δ 1.10 (s) overlapping with 1.05 (d) [12 *H* total], 1.6–2.3 (m, 4 *H*), 3.33 (s, 2 *H*), 3.6–3.9 (m, 2 *H*). **9** δ 1.12 (s, 3 *H*; t, 3 *H*), 1.40 (4 *H*), 1.72 (s, 3 *H*), 2.08 (m, 2 *H*), 3.32 (q, 2 *H*), 4.00 (d, 2 *H*), 5.40 (t, 1 *H*). **10** δ 1.08, 1.12 (t centered at 1.08, s at 1.08, s at 1.12; total 15 *H*), 1.38 (8 *H*), 3.1–3.75 (complex irregular multiplet > 8 peaks, 6 H). **11** δ 1.10 (s, 6 *H*; t, 3 *H*), 1.38 (4 *H*), 1.60 (s, 3 *H*), 1.68 (s, 3 *H*), 1.85–2.2 (m, 6 *H*), 3.30 (q, 2 *H*), 4.00 (d, 2 *H*), 5.07 (t, 1 *H*), 5.37 (t, 1 *H*).

Mass Spectra. Listed as follows *m/e* (% intensity of base peak): **1** *m/e* 170 (M^+, 40), 142 (13), 127 (20), 109 (11), 99 (100), 82 (100), 71 (100), 67 (100), 43 (100). **2** *m/e* 172 (M^+, 1.5), 157 (5), 129 (46), 127 (37), 111 (35), 109 (45), 81 (69), 43 (100). **3** *m/e* 170 (M^+, 8), 127 (52), 109 (54), 99 (27), 81 (100), 43 (91). **7** *m/e* 172 (M^+, <1), 139 (15), 136 (8), 128 (32), 127 (98), 109 (100), 95 (44), 81 (39), 71 (100), 69 (100), 43 (100), 41 (98). **8** *m/e* 154 (M^+, 4), 121 (9), 113 (98), 96 (23), 95 (100), 81 (72), 69 (98), 68 (100), 67 (87), 59 (94), 56 (94), 55 (51), 43 (100), 41 (100).

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LITERATURE CITED

Bly, R. S., Bly, R. K., Bendenbaugh, A. O., Vail, O. R., *J. Amer. Chem. Soc.* **89,** 880 (1967).
Bordwell, F. G., Douglass, M. S., *J. Amer. Chem. Soc.* **88,** 993 (1966).
Brown, H. C., Rei, M. H., *J. Amer. Chem. Soc.* **91,** 5645 (1969).
Brown, H. C., Geoghegan, P. J., Jr., *J. Org. Chem.* **35,** 1844 (1970).
Coxon, J. M., Hartshorn, M. P., Mitchell, J. W., Richards, K. E., *Chem. Ind.* 652 (1968).
Goldman, I. M., *J. Org. Chem.* **34,** 1979 (1969).
Klein, E., Rojahn, W., Henneberg, D., *Tetrahedron* **20,** 2025 (1964).
Moon, S., Waxman, B. H., *J. Org. Chem.* **34,** 288 (1969).
Moon, S., Takakis, J. M., Waxman, B. H., *J. Org. Chem.* **34,** 2951 (1969).
Sand, J., Singer, F., *Ber.* **35,** 3170 (1902).
Sand, J., Singer, F., *Justus Liebigs Ann. Chem.* **329,** 166 (1903).
Van Tamelen, E. E., Curphey, T. J., *Tetrahedron Lett.* 121 (1962).
Van Tamelen, E. E., Sharpless, K. B., *Tetrahedron Lett.* 2655 (1967).

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Studies on Terpenes Using Carbon-13 Nuclear Magnetic Resonance Spectroscopy

Ajay K. Bose* and Raymond J. Brambilla

Methods of carbon-13 nmr spectroscopy have been reviewed. The spectral assignments for citronellol, citronellal, and related terpenes have been made using techniques of off-resonance decoupling, single frequency decoupling, and lanthanide-induced shift. An appreciable effect of the solvent on chemical shifts has been noted which must be taken into account for accurate measurement of chemical shift. For conformational analysis using cmr spectra, a simple additivity rule has been found to be useful but not entirely adequate. The potential of carbon-13 labeling for biosynthetic studies has been examined.

Carbon-13 nuclear magnetic resonance spectroscopy (cmr) was, until recently, the domain of physical chemists studying small molecules. The advent of spectrometers specially designed to overcome the poor sensitivity of ^{13}C nuclei and capable of averaging spectra over many hours of recording time attracted organic chemists interested in large and complex molecules (Weigert *et al.*, 1968). In the last 2 or 3 yr further advances in instrumentation have occurred; commercial units have become available for broad band proton decoupling (Ernst, 1966) and for rapid averaging of spectra by the Fourier Transform (FT) technique (Ernst and Anderson, 1966). Organic and bioorganic chemists are now flocking to this field. It is obvious that cmr spectroscopy has achieved a permanent place of importance among physical organic methods.

EXPERIMENTAL TECHNIQUES

For the present study, carbon-13 nmr spectra were recorded on a Bruker HX-90 spectrometer operating at 22.628 MHz and equipped with a Fourier Transform accessory consisting of a model BSV-2 pulse generator and power amplifier and a Fabri-Tek 1074 signal averaging device for accumulating the free induction decay signals. The Fourier transform was accomplished with a PDP-8L computer. Time for a 4K transformation required approximately 4.5 min. Broad band proton decoupling at 90 MHz was achieved with a Bruker BSV-2 power amplifier.

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INTERPRETATION OF CMR SPECTRA

The natural abundance of ^{13}C is sufficiently low (1.1%) so that ^{13}C–^{13}C spin–spin coupling can be neglected. Since protons have a spin of $^1/_2$, cmr signals are singlets, doublets, triplets, or quartets, depending on whether there are 0, 1, 2, or 3 hydrogens bonded to the carbon under observation. The coupling constants are usually large (100 to 200 Hz) so that the spectrum of a compound containing several carbon atoms may be quite complex due to overlap of signals. Long-range spin coupling with protons in the vicinity adds to the complexity of the spectrum. "Noise" or "broad-band" proton decoupling removes all the proton couplings and simplifies the cmr spectrum to a series of narrow singlets. Because of the Nuclear Overhauser Effect (NOE), which varies from one