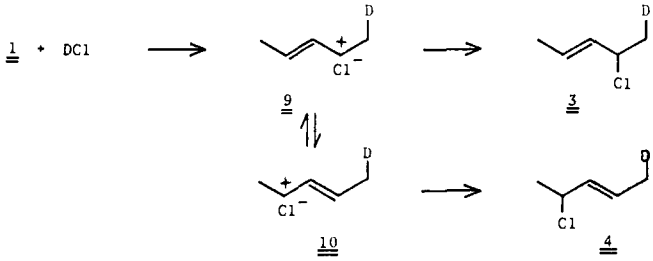
Scheme II

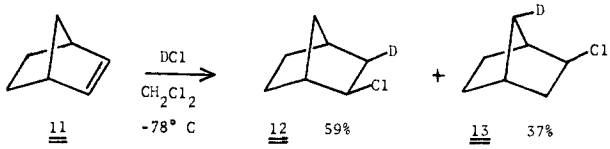


The results of the additions to **1** are presented in Table I. In two reactions, as noted, recovered excess diene was found to have incorporated no deuterium, showing carbenium-ion formation to be irreversible. While the products have been shown to be stable through the analytical procedure, minor incursions of allylic isomerization concurrent with addition cannot be excluded at this point. The significance of the results, however, is clear.

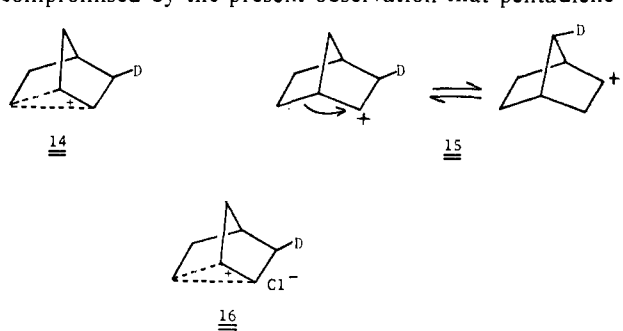
1,2 is seen to predominate over 1,4 addition in all cases, by factors of from 1.6 to 3.5. These reactions thus proceed by a mechanism more complex than that of Scheme I, where a free dimethylallyl cation has equivalent electrophilic centers.

Ion-paired intermediates are indicated.[9] The simplest rationalization of the present findings is that deuteronation of the diene at C-1 occurs from a molecule of undissociated DCl (possibly precomplexed) to give initially a carbenium chloride ion pair, **9**, with the anion (doubtless complexed with another molecule of DCl in nonpolar media[1c]) associated at C-2, as shown in Scheme II. Interconversion with the isomeric ion pair having the chloride opposite C-4, **10**, at a rate not greatly faster than that of covalent collapse would produce **3** in excess of **4**. Partial molecular addition, as suggested for several Brønsted acid additions to olefins,[10,11] could also contribute. A transition state with pronounced carbenium-ion character would be necessary, however, to explain exclusive addition to the less substituted double bond. Studies with *cis*-1,3-pentadiene and 1,3-cyclohexadiene are in progress to provide further information.

The present results furnish a new perspective toward earlier findings on the addition of acids to norbornene (**11**). Stille[11] and Brown[12] and co-workers have found through isotopic labeling that a variety of acids react with norbornene to produce unequal quantities of degenerate Wagner–Meerwein isomers. DCl in CH_2Cl_2 at −78 °C, for example,[12b] gives 59 ± 2% **12** and 37 ± 5% **13** (along with products arising from 6,2-hydride shift). Both authors have taken their data to disqualify a single



symmetrically delocalized carbonium ion, **14**, in these reactions, in favor of a pair of interconverting classical ions, **15**, trapped prior to equilibration. We consider this conclusion compromised by the present observation that pentadiene **1** characteristically favors 1,2 addition by way of a cation which by itself is plainly symmetrically delocalized. Deuteronation (protonation) of norbornene to produce a bridged ion unsymmetrically associated with its gegenion, **16**, is as reasonable a pathway for these additions as the corresponding mechanism for **1** through **9**.



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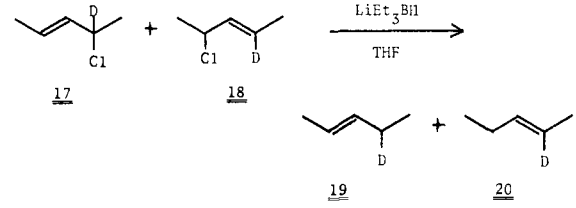
(8) In a further control experiment *trans*-3-penten-2-one was converted via *trans*-3-penten-2-ol-*2-d* to a mixture of 57% *trans*-4-chloro-2-pentene-*4-d* (**17**) and 43% *2-d* isomer (**18**), whose well-separated ^2H NMR signals permitted direct integration. Lithium triethylborohydride reduction gave



a mixture of 56% *trans*-2-pentene-*4-d* (**19**) and 44% *trans*-2-pentene-*2-d* (**20**), again by uncomplicated ^2H NMR analysis, confirming clean S_N2 displacement.
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^{13}C NMR Assignment of the Side-Chain Methyls of C_{27} Steroids

Sir:

The ^{13}C NMR spectrum[1] of cholesterol (**1a**) has been analyzed in detail and all signals were assigned unambiguously with the exception of C-26 and C-27. The recent work of Popják[2] who studied samples of ^{13}C-enriched cholesterol obtained biosynthetically from labeled mevalonate completed the interpretation of the spectrum. Their assignments of the terminal methyls are based on the knowledge of the hydroge-

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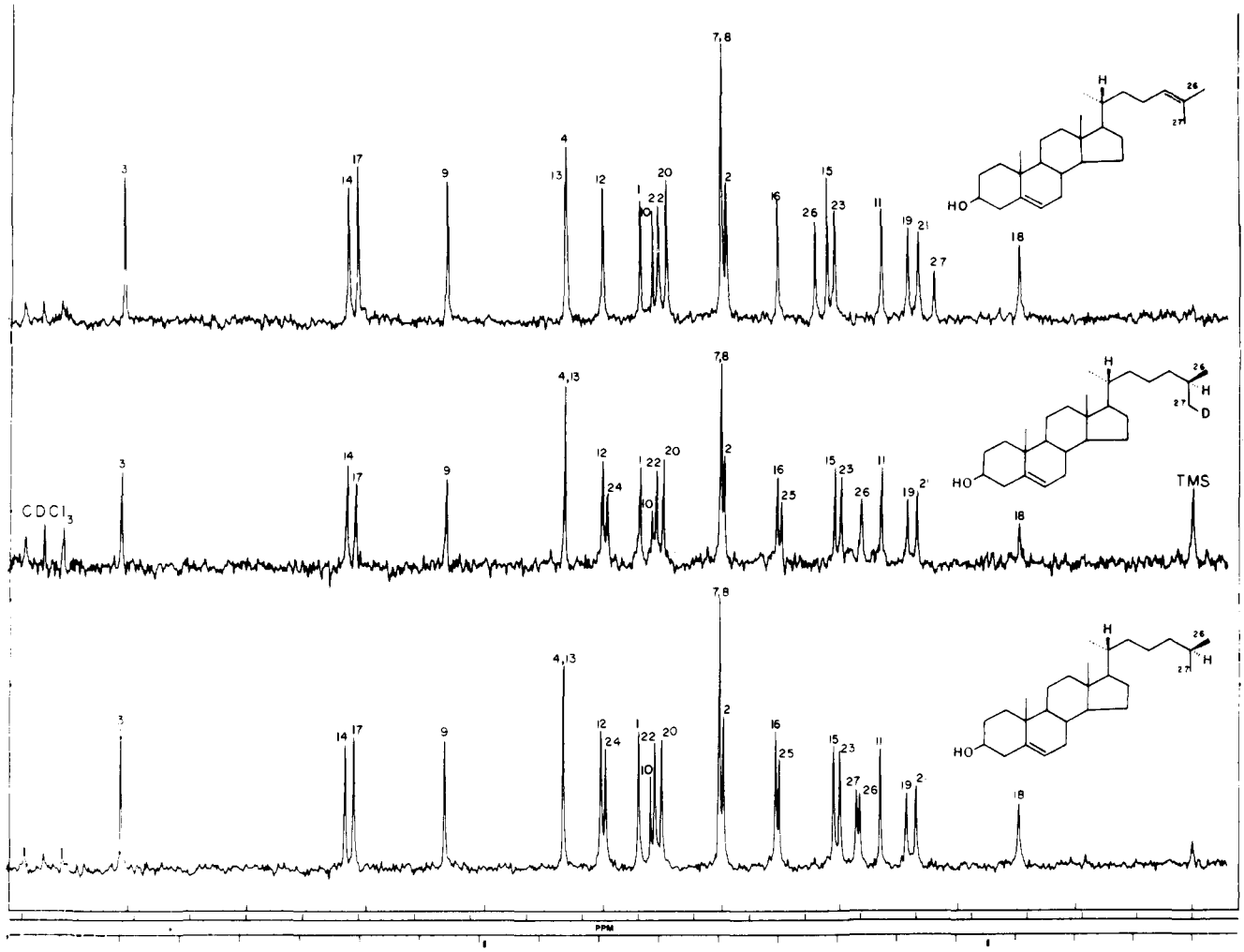

Figure 1. High-field region of the PND ^{13}C NMR spectra of cholesterol (lower), 27-deuteriocholesterol (center), and desmosterol (upper).

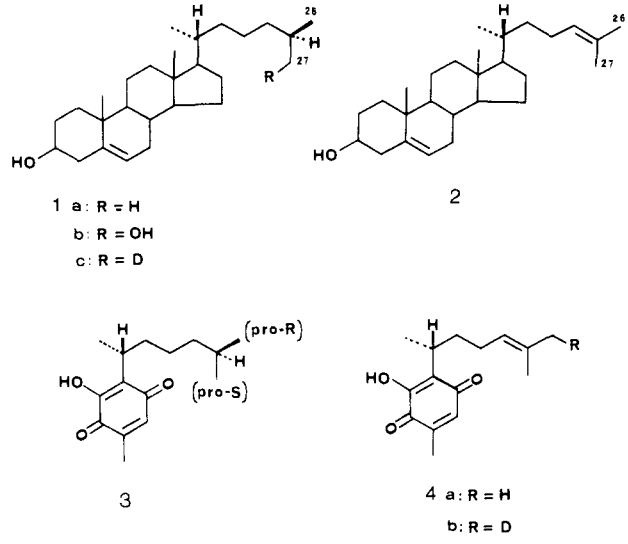

Table I. Chemical Shifts of the Side-Chain Carbon Atoms[a]

	1a	3	2	4a	
CH_3	18.75	18.02	18.62	18.28	CH_3
R-C··H	35.77	29.39	35.52	29.41	R-C··H
CH_2	36.23	34.19	36.06	34.18	CH_2
CH_2	23.88	25.71	24.73	26.76	CH_2
CH_2	39.53	38.76	125.04	124.44	CH
-CH-	27.98	27.65	130.59	131.19	-C-
(*pro-R*)-CH_3	22.54	22.35	17.61	17.63	*cis*-CH_3
(*pro-S*)-CH_3	22.78	22.43	25.59	25.68	*trans*-CH_3

[a] In parts per million from internal Me_4Si determined at 25.2 MHz in $CDCl_3$ on an XL-100A-12-FT.

nation step[3] of the Δ^{24} double bond in lanosterol (or desmosterol (**2**)) to yield cholesterol (**1a**), which was postulated as resulting from an addition of two hydrogens from the back side of the molecule. This was deduced from a radioactive labeling experiment followed by a microbiological oxidation of the resulting cholesterol and further chemical degradation. However the possibility of a rearrangement during the oxigenation step could not be absolutely excluded. Furthermore, in contrast to the cis addition of two hydrogens to the Δ^{24} double bond in lanosterol when performed by rat liver enzymes, it has also been shown that the reduction of the Δ^{24} bond in the precursor[4] of tigogenin in *Digitalis lanata* corresponds to a trans addition. Therefore, an independent test to confirm the ^{13}C NMR assignments seemed desirable and is described herein.

Kryptogenin[5] (cholest-5-ene-3β,26-diol-16,22-dione), which is known to have the 25*R* configuration,[6] was used to prepare a sample of cholesterol with a deuterium atom at one of the terminal methyls. The carbonyl groups of the natural product

were removed by successive Clemmensen and Wolff-Kishner reductions to afford 26-hydroxycholesterol (**1b**), mp 175–177 °C (lit.[7] 177–178 °C), which was transformed into the corresponding ditosylate.[8] Selective hydrolysis[9] of the ester group at C-3 yielded the 26-monotosylate,[10] which after treatment with lithium aluminium deuteride afforded 26-deuteriocholesterol,[11] mp 144–146 °C. Proper application of the sequence rules,[12] in combination with the recently proposed nomenclature[2] for cholesterol (**1a**), shows that kryptogenin is a (25*R*)-27-hydroxy steroid and that the transformation of its derived (25*R*)-27-tosylate affords (25*S*)-27-deuteriocholesterol (**1c**), even though, during all these reactions, the C-25 chiral center is never touched.

We found the C-26 and C-27 peaks of cholesterol (**1a**) at 22.54 and 22.78 ppm in the ^{13}C NMR spectrum. In the deuterated sample (Figure 1) the lower field peak at 22.78 ppm was not observed owing to the quadrupole moment and the spin–spin coupling of the directly attached deuterium atom and corresponds, therefore, to the (*pro-S*)-methyl groups (C-27). The signal at 22.54 ppm remains unchanged and is due to the (*pro-R*)-methyl group (C-26). These assignments are in agreement with those made from the biosynthetic experiments[2] and, therefore, it is now clear that no rearrangements occur when cholesterol is oxidized by *Mycobacterium smegmatis*.[3] The side-chain carbon atoms of cholesterol (**1a**) show chemical shifts similar to those of the dihydroperezone (**3**) side chain[13] with the obvious exception of the carbon directly bonded to the rings (Table I). This allows also the assignment of the isopropyl methyl groups in the sesquiterpene. An analogous situation is found between the side chains of perezone (**4a**) and desmosterol (**2**), thus allowing also the definitive assignment of individual methyl groups.

Although several hundred steroids[14] have been analyzed by ^{13}C NMR, surprisingly no data appear to be available for desmosterol (**2**) and its spectrum was therefore recorded. It shows (Figure 1) the ring carbons and angular methyl groups[15] at essentially the same values found for cholesterol (**1a**), while the side-chain carbons appear (Table I) as in perezone (**4a**). The isopropylidene methyl groups are assigned unambiguously using a sample of deuterioperezone (**4b**) obtained by a regioselective synthesis.[16] The *trans*-methyl groups appears at 25.65 ppm, while the *cis*-methyl is found at 17.61 ppm.

The chiral center of dihydroperezone (**3**) has the same *R* configuration as C-20 in the steroids and this appears to be the main factor controlling the chemical shift difference between the isopropyl methyl groups which is observed[1a] even in 2,6-dimethyloctane where the rings are replaced by a methyl group. Future biosynthetic studies on the hydrogenation of isopropylidene residues might be followed by deuterium labeling and ^{13}C measurements.

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(10) It showed mp 131–133 °C; IR ($CHCl_3$) at 3600 and 3430 (hydroxyl), 1612 (aromatic ring), 1370 and 1180 cm^{-1} (sulfonic ester); ^1H NMR (100 MHz $CDCl_3$, internal Me_4Si) at 7.84 (2 H), 7.38 (2 H), and 2.45 (3 H) from the tosylate, 5.39 (H-6), 3.85 (26-CH_2), 3.56 (H-3), 1.02 (CH_3 at C-13), 0.87 (two CH_3 at C-20 and C-25) and 0.67 ppm (CH_3 at C-10). Anal. Calcd for $C_{34}H_{52}O_4S$: C, 73.38; H, 9.35; O, 11.51; S, 5.76. Found: C, 73.36; H, 9.33; O, 11.42; S, 5.65.

(11) The 100-MHz ^1H NMR spectrum of this sample was identical with that of cholesterol, with the exception of the isopropyl doublet at 0.87 ppm which was smaller.

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The Unlikelihood of an Electron-Transfer (Haber–Weiss) Reaction between Superoxide and Peroxides

Sir:

While an increasing number of investigations have recently been directed toward the reactions of superoxide ion ($O_2^{-}\cdot$) with a range of molecules,[1-3] its fundamental reactivity is yet poorly understood. It has recently been proposed, and shown for at least one case, that ultimate products in mixtures of $O_2^{-}\cdot$ with many molecules are the result of $O_2^{-}\cdot$ *decomposition products* acting as oxidizing species or as very strong bases.[4] We report here on a very simple, but centrally important system, $O_2^{-}\cdot$ in the presence of peroxides. It is found that, while *tert*-butyl hydroperoxide acts solely as a proton source toward $O_2^{-}\cdot$ in toluene and pyridine, attack upon solvent by the peroxide anion occurs in acetonitrile, leading ultimately to products of peroxide decomposition. Additional studies, together with precedents from the literature, show that experimental support is lacking for the assumed electron-transfer process between $O_2^{-}\cdot$ and peroxides.

Both hydrogen peroxide and organic hydroperoxides undergo electron transfer from Fe^{2+} (and other reduced metals) via

$$ROOH + Fe^{2+} \rightarrow RO\cdot + HO^- + Fe^{3+} \qquad (1)$$

R = H or alkyl

The evidence for this reaction is quite strong, and it has been studied in detail.[5,6] By analogy, it has been generally accepted that a similar process occurs with $O_2^{-}\cdot$ as the electron donor:[2,3,7,8]

$$HOOH + O_2^{-}\cdot \rightarrow HO\cdot + HO^- + O_2 \qquad (2)$$

Both eq 1 and 2 have been discussed in terms of biological effects of H_2O_2 (and its destructiveness in systems in which it is produced) by generating the reactive $HO\cdot$ radical.[8,9]

Noting the absence of direct evidence for reaction 2, Peters and Foote recently examined the reaction of *t*-BuOOH with $O_2^{-}\cdot$ in acetonitrile.[10] They observed rapid O_2 evolution and

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