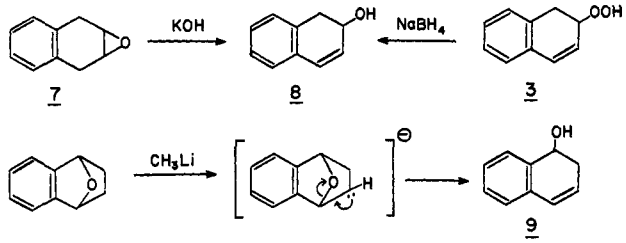
The origin of hydroperoxide **3** during the radical-chain autoxidation of **1** cannot as yet be stated with certainty; either **3** forms directly from the rearranged allylic radical (Scheme I), or the hydroperoxide **2** is first formed and rearranged to **3**. Although the rearrangement of allylic hydroperoxides in dilute solutions is quite facile, such isomerization is strongly inhibited by 2,6-di-*tert*-butyl-4-methylphenol.[9] The presence of **2** in the crude autoxidation mixture could not be established from the nmr spectrum of the mixture determined in deuterioacetone containing this inhibitor. Thus, we favor the arguments of Howard and Ingold[10] for the direct formation of **3**.

Hydroperoxide **3** was reduced with $NaBH_4$ in ethanol (0°, 2 hr) to 2-hydroxy-1,2-dihydronaphthalene (**8**) (78%, mp 20–25°).[11] The assigned structure of **8** (Scheme II) is consistent with its nmr and mass spectra.[12] This "naphthalene hydrate" **8** was also prepared by the base-catalyzed rearrangement (ethanolic KOH at room temperature for 1 week) of 1,4-dihydronaphthalene 2,3-oxide. First reported in 1895,[13] this reaction seems to be the most facile example of such epoxide rearrangements studied to date.[14] The isomeric "hydrate," 1-hydroxy-1,2-dihydronaphthalene **9**, was prepared (Scheme II) by the action of methyllithium on 1,2,3,4-tetrahydronaphthalene 1,4-oxide (28°, 10 days, 10%) and was readily distinguished from **8** by its nmr spectrum.[15] Both **8** and **9** were stable at neutral and basic pH, but readily dehydrated (k_{obsd} = 1.92×10^{-3} sec^{-1} and 3.57×10^{-4} sec^{-1}, respectively) to naphthalene in *n*-butyl alcohol which was 10 m*M* acid with concentrated HCl at 25°.

Scheme II



Perhaps the most interesting reaction of hydroperoxide **3** is thermal decomposition. While **1** is autoxidized at 40°, the resulting **3** spontaneously rearranges to oxepin **6** (Scheme I). Pyrolysis of pure, neat **3** (40°, 12 hr) converted half the material to polymeric peroxides along with a mixture of 60% **4**, 13% **5**, and 27% **6** as volatile components. The proportion of **6** is not increased when solutions of **3** are heated. Sublimation of crude **3** (5 g, 100° (5 mm), 1 hr) gave a mixture of compounds (1 g) from which 0.36 g of pure **6** was isolated by column chromatography on silica gel.[16] Although we do not exclude the possibility of a heterolytic process, formation of **6** seems likely to occur *via* the homolytic mechanism shown in Scheme I. Heterolytic decomposition of hydroperoxides most often occurs under acidic conditions and is typified by alkyl migration to oxygen.[17] In contrast, treatment of **3** with acid (0.5 *M* $HClO_4$ in 50% dioxane) gave naphthalene.

(9) W. F. Brill, *J. Amer. Chem. Soc.*, 87, 3286 (1965).
(10) J. A. Howard and K. U. Ingold, *Can. J. Chem.*, **45**, 785 (1967).
(11) Separated by tlc on silica gel developed with $CHCl_3$; R_f 0.5.
(12) The mass spectrum of **8** showed a weak molecular ion at *m/e* 146 (16%) with the base peak resulting from loss of 18 (100%) while the nmr spectrum was assigned as 2 H_1 2.98, 1 H_2 4.42, 1 H_3 6.06, 1 H_4 6.49, and four aromatic protons 6.9–7.3; $^3J_{1,2}$ = 6.0, $^3J_{2,3}$ = 4.4, and $^3J_{3,4}$ = 9.5 Hz.
(13) E. Bamberger and W. Lodter, *Justus Liebigs Ann. Chem.*, **288**, 100 (1895). Formation of a benzylic carbanion facilitates the reaction.
(14) More current examples can be found in the rearrangement of acyclic epoxides (J. K. Crandall and L. C. Lin, *J. Org. Chem.*, **33**, 2375 (1968)) and of cyclohexene epoxides (J. Starosick and B. Rickborn, *J. Amer. Chem. Soc.*, **93**, 3046 (1971)) to form the "hydrate of benzene" analogous to the "naphthalene hydrates" reported here.
(15) The mass spectrum of **9** showed a molecular ion at *m/e* 146 (39%) with the base peak resulting from loss of 18 (100%): the nmr spectrum was assigned as 1 H_1 4.80, 2 H_2 2.58, 1 H_3 6.00, 1 H_4 6.56, and four aromatic protons 7.0–7.5; $^3J_{1,2}$ = 5.6, $^3J_{2,3}$ = 4.3, $^4J_{2,4}$ = 1.8, and $^3J_{3,4}$ = 9.5 Hz.
(16) The 3-benzoxepin eluted from the column with isopentane and had nmr and mass spectra and melting point identical with authentic material.[2]
(17) See, for example, A. G. Davies, "Organic Peroxides," Butterworths, London, 1961, pp 147–150, and P. A. S. Smith in "Molecular Rearrangements," Part I, P. de Mayo, Ed., Wiley, New York, N.Y., 1963, pp 573–577. The acid-catalyzed rearrangement of 3-hydroperoxycyclohexene to adipaldehyde is the closest analogy to the system studied here.
(18) NATO Postdoctoral Fellow, 1970–1971.

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Cyclopentenyl Cation. A New Degenerate Rearrangement of an Allyl Cation

Sir:

Cyclopentenyl cation has not previously been reported as a stable species even though several alkylated cyclopentenyl cations have been prepared and studied in 96% H_2SO_4 by Deno and his coworkers.[1,2] We wish to report the preparation and properties of solutions of the cyclopentenyl cation and the observation of a new degenerate rearrangement process. 3-Chlorocyclopentene (prepared from cyclopentadiene and HCl gas at Dry Ice temperatures[3]) was treated with an excess of SbF_5 using a new apparatus in which molecular beams of the reagents are formed and impinge on a liquid nitrogen cooled surface in a highly evacuated chamber.[4] With this molecular beam apparatus, the polymerization which ordinarily occurs, using the standard procedure for preparing cations,[5] with unsaturated precursors due to attack of the cation on the unreacted allyl chloride, is almost completely eliminated.

The nmr spectrum of the ion with SO_2ClF added as a solvent, taken at room temperature, is shown in Figure 1. Proton 1 at τ 1.53 is coupled to proton 2 at −0.99 (J = 4 Hz). Proton 2 is coupled to proton 3 at τ 5.87 with a much smaller coupling constant as expected.[6] When peak 3 is spin decoupled, peak 2 becomes a clear doublet (J = 4 Hz). We believe that the sharp peak at τ 0.20 is due to a trace of HF or HCl.

(1) N. C. Deno, J. Bollinger, N. Friedman, K. Hafer, J. Hodge, and J. Houser, *J. Amer. Chem. Soc.*, **85**, 2998 (1963).
(2) N. C. Deno, N. Friedman, J. Hodge, J. Houser, C. Pittman, and H. Richey, *ibid.*, **85**, 2991 (1963).
(3) R. B. Moffet, "Organic Syntheses," Collect. Vol. 1, Wiley, New York, N. Y., 1963, p 238.
(4) M. Saunders and D. Cox, manuscript in preparation.
(5) M. Saunders and E. L. Hagen, *J. Amer. Chem. Soc.*, **90**, 2436 (1968).
(6) Assuming a planar allyl cation form, the dihedral angle between H-2 and -3 would be 60°, which would be predicted to produce a small coupling constant.

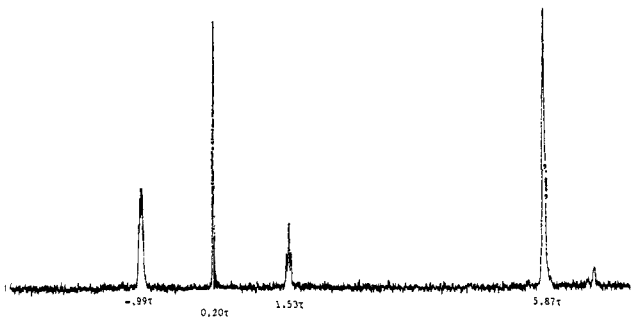


Figure 1.

The ion was found to be stable up to at least 150°. Nmr line broadening was observed over the temperature range 85–112°. (At 42°, the line widths for protons 1, 2, and 3, respectively, were 8.5, 8, and 4 Hz. At 112° the line widths were 19.5, 20, and 8 Hz.) We believe that this broadening is due to a reversible 1,2-hydride shift to B. This mechanism leads to matrix I

Matrix I

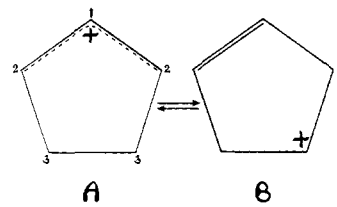
$$\begin{vmatrix} & 1/2 & 0 \\ 1/4 & & 3/8 \\ 0 & 3/16 & \end{vmatrix}$$

of transition probabilities between the spectral lines for a single step of the mechanism. The possibility of a direct 1,4-hydride shift which if suprafacial would be forbidden as a thermal process was considered, and this mechanism would lead to matrix II. Both of these

Matrix II

$$\begin{vmatrix} & 1 & 0 \\ 1/2 & & 1/2 \\ 0 & 1/4 & \end{vmatrix}$$

matrices indicate that there is direct proton exchange between sites 1 and 2 and between sites 3, but no exchange takes place, in a single mechanistic step, between sites 1 and 3. Double resonance experiments at 42° were in agreement with both mechanisms; irradiating



line 1 decreased the integral of line 2 but not line 3. Irradiating line 3 decreased the integral of line 2 but not line 1. These results demonstrate direct exchange between sites 1 and 2 and also 2 and 3, but no direct exchange between 1 and 3. Theoretically calculated curves, computed using matrix I (1,2-hydride shift), agreed satisfactorily with the experimental spectra but using matrix II (that for the 1,4-hydride shift) agreement could not be obtained.

Fitting the rates obtained at different temperatures for the 1,2-hydride shift to the Arrhenius equation gave $E_a = 18.0 \pm 0.9$ kcal/mol and $\log A = 12.2 \pm 0.6$ where errors reported are standard deviations.

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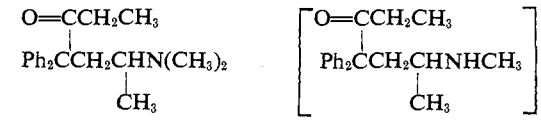
The Identification of Three New Metabolites of Methadone in Man and in the Rat

Sir:

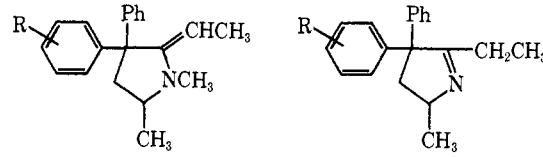
The increasingly wide use of methadone (**1**) in the maintenance therapy of heroin addicts has led to a renewed interest in the metabolic fate of methadone in man and in laboratory animals. In addition to its inherent scientific interest such information is required for a full understanding of the pharmacodynamics of methadone in maintenance subjects.

The initial step in the biotransformation of methadone, in both the rat and in man, is known to occur *via* N-demethylation.[1,2] The de-*N*-methylmethadone (**2**)



methadone (**1**) de-*N*-methylmethadone (**2**) (hypothetical)

resulting from the N-demethylation of methadone has, however, never been directly isolated. Chemical studies[2] have shown that, once formed, **2** spontaneously cyclizes to 1,5-dimethyl-3,3-diphenyl-2-ethylidenepyrrolidine (**3a**). Indeed compound **3a** and its N-de-



3a, R = H
3b, R = OH
3c, R = OCH_3
3d, R = OAc

4a, R = H
4b, R = OH
4c, R = OCH_3
4d, R = OAc

methyl analog, 2-ethyl-5-methyl-3,3-diphenyl-1-pyrroline (**4a**), have been identified as metabolites of methadone in both man and rat.[2,3]

In the course of our studies on the fate of methadone in subjects receiving a daily 80-mg maintenance dose it became clear that urine samples contained metabolites in addition to those already reported (see above). These new metabolites were relatively polar and remained in urine following the removal of **1**, **3a**, and **4a** by extraction with butyl chloride.[4] They were recovered and identified as follows.

Aliquots (100 ml) of extracted urine were adjusted to pH 7 and placed on an Amberlite XAD-2 (Rohm and Haas) column (2 cm × 36 cm) and washed with 200 ml of water. The metabolites were eluted from the column

(1) J. Axelrod, *J. Pharmacol. Exp. Ther.*, 117, 322 (1956).
(2) A. Pohland, H. R. Sullivan, and H. M. Lee, Abstracts, 136th National Meeting of the American Chemical Society, Sept 1959, Atlantic City, N. J., p 15-O.
(3) A. Pohland, H. E. Boaz, and H. R. Sullivan, *J. Med. Chem.*, **14**, 194 (1971).
(4) H. R. Sullivan and D. A. Blake, *Res. Commun. Chem. Pathol. Pharmacol.*, in press.