

Calcd. for $C_{11}H_{13}ClOS$: C, 57.76; H, 5.73. Found: C, 57.55; H, 5.76.) Material identical (m.p., m.m.p. and infrared spectrum) with IV was obtained by chromatography of the residue from the mother liquors from the recrystallization of II. In agreement with the structural assignments, II was eluted from alumina prior to IV.

Reaction of IV with triethyloxonium fluoroborate gave in 83% yield *trans*-4-(*p*-chlorophenyl)-1-ethoxythionia-cyclohexane fluoroborate (V), m.p. 166–167°. (*Anal.* Calcd. for $C_{13}H_{18}BClF_4OS$: C, 45.32; H, 5.26; neut. equiv., 344.5. Found: C, 45.33; H, 5.06; neut. equiv., 343.) Hydrolysis of V with dilute alkali provided in 92% crude yield the *cis* sulfoxide II identical (m.p., m.m.p. and infrared spectrum) after a single recrystallization with that obtained above by the oxidation of the sulfide with periodate.

Infrared spectra indicated that the crude sulfoxides IV and II isolated from solvolysis of III and V, respectively, contained less than 5% of contaminating isomeric sulfoxide. In these examples a hydrolytic pathway involving inversion at the sulfur atom significantly predominates over alternates, *e.g.*, carbon-oxygen cleavage.

Oxidation of the sulfide I with potassium permanganate in glacial acetic acid gave 4-(*p*-chlorophenyl)thian-1,1-dioxide (VI), m.p. 208–209°, $\nu_{\max}^{CH_2Cl_2}$ 1300, 1120 cm^{-1} , (SO_2). (*Anal.* Calcd. for $C_{11}H_{13}ClO_2S$: C, 54.07; H, 5.35. Found: C, 53.90; H, 5.58.) The same sulfone was obtained by oxidation of II and IV with permanganate.

Work now in progress in this Laboratory will provide additional examples of sulfoxide inversion, including the interconversion of optical isomers.

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RECEIVED JANUARY 31, 1963

ISOTOPE EFFECTS IN RECOIL TRITIUM REACTIONS WITH HYDROCARBONS¹

Sir:

The two highest yield reactions of recoil tritium atoms in scavenged alkane systems are almost invariably those involving abstraction of a hydrogen atom or substitution for it by the tritium atom. Several recent publications have concerned themselves with the mechanistic significance of the relative yields of these two reactions, both from individual molecules alone^{2–5} and from two parent alkane molecules in competition with one another in the same system.⁶ One suggested interpretation of these measured yields^{4,5} is consistent with most of the data, but appears to be in direct conflict with previously reported isotope effects observed in hydrogen abstraction from methane by recoil tritium.⁷

In the context of the simple model for the reactions of a very energetic atom slowing down into an energy range for which chemical bond formation is possible,^{2,8–10} several effects could possibly exist that might

(1) This research was supported by A.E.C. Contract No. AT-(11-1)-407, and by a National Science Foundation Pre-doctoral Fellowship (J.W.R.).

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(3) R. Wolfgang, *et al.*, "Chemical Effects of Nuclear Transformations," Vol. 2, I.A.E.A., Vienna, 1961, p. 83.

(4) R. Wolfgang, *J. Am. Chem. Soc.*, **84**, 4586 (1962).

(5) H. C. Jurgeleit and R. Wolfgang, *ibid.*, in press.

(6) J. W. Root and F. S. Rowland, *ibid.*, **84**, 3027 (1962).

(7) J. K. Lee, B. Musgrave and F. S. Rowland, *J. Phys. Chem.*, **64**, 1950, (1960).

(8) P. J. Estrup and R. Wolfgang, *J. Am. Chem. Soc.*, **82**, 2661, 2665 (1960).

(9) R. J. Cross and R. Wolfgang, *J. Chem. Phys.*, **35**, 2002 (1961).

(10) A. Sokolowska, L. Haskin, and F. S. Rowland, *J. Am. Chem. Soc.*, **84**, 2469 (1962).

lead to differences in results measured for isotopically-substituted molecules. If the average energy loss per non-reacting collision is affected by isotopic substitution, different numbers of "hot" collisions would be expected in traversing a given energy range, and thereby could lead to different fractions reacting in that energy range for isotopic molecules. Isotope effects arising from differences in average energy loss are designated here as moderator isotope effects, and have been invoked in explanation of experiments involving CH_4 vs. CD_4 , and CH_3F vs. CD_3F .^{5,9}

If either the energy range over which the substitution reaction occurs or the probability of the reaction per collision varies with isotopic substitution, then isotopic differences could appear. The over-all effect of these two possible differences will be defined here as probability integral isotope effects. In any particular real system, any or all of these sources of isotopic variation could be present.

In general, moderator and probability integral isotope effects can be distinguished through experiments involving measurements of reactions occurring simultaneously in the same system.^{6,10} In such direct competitions possible variations from moderator differences are essentially eliminated since all the molecules are exposed to the same spectrum of tritium energies.

The abstraction reaction has been reinvestigated with higher precision measurements on CH_2D_2 as shown in Table I. The substitution of T for H has been tested for isotope effects through competitions between protonated and deuterated methanes and *n*-butanes, as summarized in Table II. The samples were analyzed by radio-gas chromatography; the nuclear reaction He^3 (n,p) H^3 served as the tritium source.

TABLE I

RELATIVE YIELD OF TRITIATED MOLECULES FROM TYPICAL RECOIL TRITIUM EXPERIMENTS WITH CH_2D_2

Sample number	Scavenger ^a (cm.)	HT + Yields (relative units) ^a		HT	DT	Methane- <i>t</i>
		HT/DT	DT/RT			
438	None	2.34	1.11	94	39	119
440	0.02 I ₂	1.51	0.86	41	27	79
392	1.02 O ₂	1.34	0.79	34	26	75
443	3.27 O ₂	1.34	0.79	36	27	79
445	4.90 O ₂	1.32	0.79	35	27	78

^a Total pressure 100 cm., including 1.0–1.6 cm. of He³; irradiated for 60 min. in a neutron flux of 5×10^{10} neutrons/cm.²/sec. A yield of 75 represents 25% of the total tritium activity stopped in the gas phase.

TABLE II

DISTRIBUTION OF RADIOACTIVITY BETWEEN PARENT COMPOUNDS FOR COMPETITIVE RECOIL TRITIUM REACTIONS IN THE GAS PHASE

Experiment number	<i>n</i> -Butane	Methane	Pressure ratio		Specific activity ratio
			butane/methane	Obsd. Cor. ^a	
418	C ₄ H ₁₀	CD ₄	0.109	2.91	2.98
419	C ₄ H ₁₀	CD ₄	.109	2.89	2.96
422	C ₄ H ₁₀	CH ₄	.113	2.19	2.23 ^b
423	C ₄ H ₁₀	CH ₄	.113	2.26	2.30
412	C ₄ D ₁₀	CH ₄	.112	1.81	1.88

^a Corrected for production of methane-*t* by reaction of T with *n*-butane. ^b The original measurements of substitution into fully-protonated methane and butane⁶ gave values for the specific activity ratio ranging from 2.29 to 2.60. This scatter has now been eliminated, and the lower limit is approximately correct.

We conclude from Table I that the isotope effect in hydrogen abstraction is essentially constant at 1.32 for HT/DT¹¹ between 1 and 5% O₂. Similarly, an isotopic preference for the recoil tritium substitution of T for H vs. T for D can be estimated from Table II: for CH₄ and CD₄ vs. *n*-C₄H₁₀, 2.97/2.27 = 1.31, and for C₄H₁₀

(11) Corrected for CH₃D impurity in the CH₂D₂.

and C_4D_{10} vs. CH_4 as $2.27/1.88 = 1.21$. We assume 1.26 ± 0.05 as an average value.

The more extended measurements on the isotope effect in abstraction confirm the earlier results,⁷ and indicate that the preference for abstraction of H over D by tritium is qualitatively in the proper direction for the suggested dependence of hot abstraction on bond energy,⁶ and of sufficient magnitude to account for the observed changes in HT/RT for various alkane molecules. If the observed isotope effect on the substitution reaction arises primarily from some origin other than carbon-hydrogen bond energy, measurements of the ratio of deuterium abstraction to deuterium replacement can give a misleading estimate of the possible magnitude of bond energy effects on the abstraction reaction itself.^{4,5}

The observation of probability integral isotope effects favoring H over D by 20–30% for both hydrogen abstraction and substitution in alkane systems suggests that similar effects are probably also in operation with other target molecules. Such isotope effects with the molecules CH_3F and CD_3F , taken separately, would account quite satisfactorily for the lower hot tritium yields observed for both abstraction and hydrogen substitution in the deuterated species, without the necessity for postulating appreciable differences in moderator effects for the two molecules.^{4,5} With this change in explanation for the isotopic variations observed for the methyl fluorides, no significant discrepancies would remain in such isotopic experiments.

Since the observed yield of CD_3T from CD_3F is also less than that of CH_3T from CH_3F , a probability integral isotope effect (in this case, a secondary isotope effect) presumably also exists in the energetic substitution of T for F.

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RECEIVED FEBRUARY 23, 1963

THE STRUCTURE OF ARGEMONINE; IDENTIFICATION AS (-)-N-METHYLPAPAVINE

Sir:

Argemonine, $C_{21}H_{29}NO_4$, $[\alpha]^{24D} -187.93^\circ$ ($CHCl_3$), is one of three related alkaloids found in the perennial plants *Argemone hispida* G. and *Argemone munita* Dur. and Hilg. subsp. *rotundata* (Rydb.) G. B. Ownb.¹ Kier and Soine^{1d,e} and Shamma² provisionally proposed tetramethoxylated aporphine structures (I)³ for argemonine based on its oxidation to N-methyl-m-hemipinimide and upon its exhaustive Hofmann elimination to a non-nitrogenous product, which was subsequently oxidized to what was believed to be a tetramethoxy biphenyltricarboxylic acid.^{1d}

Our examination of argemonine by mass spectrometry confirmed the molecular formula and molecular weight and, in addition, showed a large fragmentation peak at m/e 204, which probably corresponds to a N-methyl-6,7-dimethoxyisoquinolinium cation. Two aporphine alkaloids, bulbocapnine and glaucine, gave much different results, however, undergoing dehydrogenation in the metal inlet at 200° extremely rapidly, presumably to give fully aromatic structures.

The ultraviolet spectrum of argemonine (λ_{max} 287 $m\mu$ ($\log \epsilon$ 4.01)) is substantially different from known aporphines⁴ which have several intense peaks at

(1) (a) T. O. Soine and O. Gisvold, *J. Am. Pharm. Assoc. (Sci. Ed.)*, **33**, 185 (1941); (b) J. W. Schermerhorn and T. O. Soine, *ibid.*, **40**, 19 (1951); (c) L. B. Kier and T. O. Soine, *ibid.*, **49**, 187 (1960); (d) L. B. Kier and T. O. Soine, *J. Pharm. Sci.*, **50**, 321 (1961); (e) T. O. Soine and L. B. Kier, *ibid.*, **51**, 1196 (1962).

(2) M. Shamma, *Experientia*, **18**, 64 (1962).

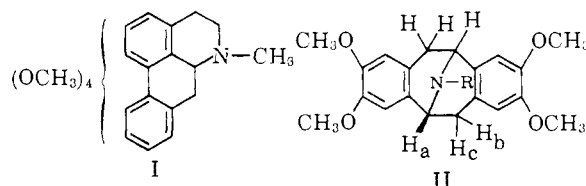
(3) R. H. F. Manske and H. L. Holmes, "The Alkaloids," Vol. 4, Academic Press, Inc., New York, N. Y., 1954 p. 119; Vol. 7, 1960, p. 427.

(4) M. Shamma, *Experientia*, **16**, 484 (1960).

300–310 $m\mu$, 268–282 $m\mu$ and 220 $m\mu$. The intensities are usually higher also, being in the range of $\log \epsilon$ 4.2 or more.⁴ This difference prompted Shamma² to propose alternate methoxyl arrangements to explain this phenomenon.

The n.m.r. spectrum of argemonine exhibited striking symmetry; the four aromatic protons and four methoxyls being arranged in two groups of two each. Published spectra of aporphine alkaloids,⁵ as well as those re-examined by us, readily revealed the lack of similarity to the spectrum of argemonine. This high degree of symmetry of the n.m.r. spectrum, the optical activity and the other spectral evidence mentioned, point uniquely to structure II (R = CH_3) as argemonine.

The n.m.r. spectrum (in $CDCl_3$) is, in part, an ABX system⁶ in which protons H_a couple only with H_b ⁷ and appear as a doublet centering at 5.92 τ ($J_{ab} = 6$ c.p.s.). Protons H_c couple only with protons H_b and are a doublet centering at 7.38 τ ($J_{bc} = 17$ c.p.s.). Protons H_b are split by H_a and H_c and are a pair of doublets centering at 6.47 and 6.58 τ . The aromatic protons are singlets of intensity two each at 3.24 and 3.41 τ and the methoxyl groups are singlets at 6.08 and 6.16 τ . The N-methyl group is a singlet at 7.43 τ .



Structure II has been known in the literature for many years, as N-methylpapavine, a conversion product of papaverine, although its structure was only recently established by Battersby and Binks.⁸ Synthesis of a sample of N-methylpapavine⁸ and comparison of the infrared, ultraviolet, n.m.r. and mass spectra with those of argemonine confirmed their identity.

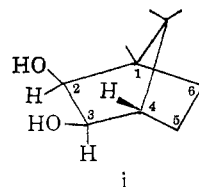
This structure represents a new ring system in nature and furthermore exemplifies a novel type of a benzylisoquinoline alkaloid.

Based on this evidence the structure assigned to the biphenyltricarboxylic acid^{1d} must be in error and its structure is now under investigation.

(5) (a) S. Goodwin, J. N. Shoolery and L. F. Johnson, *Proc. Chem. Soc.*, 306 (1958); (b) I. R. C. Bick, J. Harley-Mason, N. Sheppard and M. J. Vernengo, *J. Chem. Soc.*, 1896 (1961); (c) O. E. Edwards and K. L. Handa, *Can. J. Chem.*, **39**, 1801 (1961); (d) Varian High Resolution N.M.R. Spectra Catalog, Varian Associates, Instrument Division, 1962, spectra 333 and 342.

(6) (a) J. A. Pople, W. G. Schneider and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 132; (b) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p. 90.

(7) This phenomenon has recently been investigated by F. A. L. Anst (*Can. J. Chem.*, **39**, 789 (1961)), and references contained therein) as applied to the bicyclo[2.2.1]heptane system. Thus, 2-exo,3-endo-camphane-2,3-diol (i) exhibits a bridgehead coupling constant of zero ($J_{31} = 0$) with the adjacent proton, as predicted by the Karplus equation (M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959)) where the dihedral angle is 79° .



(8) A. R. Battersby and R. Binks, *J. Chem. Soc.*, 2888 (1955), and references contained therein. Papavine itself (II, R = H) is produced by tin and acid reduction of papaverine. The n.m.r. spectrum of papavine is much like that of N-methylpapavine except that the bridgehead protons are shifted downfield to a doublet centering at 5.55 τ and protons H_c occur as a doublet shifted downfield to 7.25 τ . The NH appears as a singlet at 7.87 τ .