

area was undoubtedly relatively small and hence easily affected by small amounts of material. However, it does suggest that even with the very large area of ordinary nickel catalysts, hydrogenations of a difficult character may well be made more efficient by rigorous drying of all materials in contact with the catalyst during the course of the reaction.

The poisoning was found to be reversible since the catalysts could be reactivated completely by reheating in hydrogen at 375° after having been poisoned to 30% of their original activity. Thus

the effect of the water vapor appears to be due to a preferential adsorption which can be removed by treatment with excess hydrogen.

Summary

Water vapor has been shown to be a poison for nickel hydrogenation catalysts, the effect being noticeable as low as 3×10^{-4} mm. pressure of water vapor in the present experiments.

The poisoning is reversible, the catalyst being reactivated by heating in hydrogen.

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[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 988]

The Structure of Spiropentane

BY JERRY DONOHUE, GEORGE L. HUMPHREY AND VERNER SCHOMAKER

Murray and Stevenson¹ have prepared a C_5H_8 hydrocarbon by the debromination of pentaerythryl bromide with zinc dust. They assigned to this substance the spiro-pentane structure (I) on the basis of its Raman spectrum, chemical properties, and method of preparation. We have confirmed this assignment of structure by an electron diffraction investigation carried out on a sample of the new hydrocarbon supplied us by Dr. Murray.

Experimental.—The electron diffraction apparatus used in this investigation has been described by Brockway.² The camera distance was 10.86 cm., and the wave length of the electrons, determined against zinc oxide smoke,³ was 0.0609 Å. Photographs taken with the sample at 0° showed features extending to q values of about ninety-five ($q = 40/\lambda \sin \theta/2$).

Interpretation.—Both the radial distribution method⁴ and the correlation method⁵ were used in interpreting the photographs. The radial distribution curve was calculated with the equation

$$rD(r) = \sum_{q=1}^{q_{\max}} I(q)e^{-aq^2} \sin\left(\frac{\pi}{10} riq\right)$$

where a was so determined that e^{-aq^2} equals 1/10 at $q = 100$. The values of $I(q)$ were taken from curve V (Fig. 1), which was drawn to represent the appearance of the photographs. The unobservable first feature (dotted) was drawn to agree approximately with the theoretical curves.

Theoretical intensity curves for the correlation treatment were calculated using the simplified theoretical scattering formula

$$I(q) = \sum_{i,j} \frac{Z_i Z_j}{r_{ij}} e^{-b_{ij}q^2} \sin\left(\frac{\pi}{10} r_{ij}q\right)$$

(1) M. J. Murray and E. H. Stevenson, *THIS JOURNAL*, **66**, 812 (1944).

(2) L. O. Brockway, *Rev. Mod. Phys.*, **8**, 231 (1936).

(3) C. S. Lu and E. W. Maimberg, *Rev. Sci. Instr.*, **14**, 271 (1943).

(4) L. Pauling and L. O. Brockway, *THIS JOURNAL*, **59**, 2131 (1937); R. Spurr and V. Schomaker, *ibid.*, **64**, 2693 (1942).

(5) L. Pauling and L. O. Brockway, *J. Chem. Phys.*, **2**, 867 (1934).

The temperature factor b was given the value 0.00016 for bonded C-H terms, 0.0003 for non-bonded C-H terms, and zero for C-C terms. These calculations were made with punched cards on International Business Machines.

The radial distribution curve, R of Fig. 1, shows maxima at 1.09, 1.49, 2.19 and 2.77 Å., and a shelf at 3.0 Å. This curve is in complete agreement with the spiro-pentane structure, as shown by the heavy vertical lines representing the various distances and their amplitudes in the finally accepted model. Direct estimates of the angle parameters of the spiro-pentane structure (I) can easily be made with the information provided by the radial distribution function. The average C-C bond distance 1.49 Å. and the non-bonded C...C distance 2.77 Å. correspond to a $C_2C_3C_1$ bond angle of 61°. Taken with these data, the C-H distance 1.09 Å. and the shortest non-bonded C...H distance 2.19 Å. then imply an HCH bond angle of 121°.

Theoretical intensity curves were drawn (Fig. 1) for various models of the spiro-pentane structure (I) with a molecular symmetry of $D_{2d} - 42m$, with the reasonable assumption that the plane of \angle HCH bisects \angle CCC. There are then three parameters which determine the configuration of the molecule. These were taken as $\angle C_2C_3C_1$, \angle HCH, and the ratio C-H/C₂-C₃. These parameters were varied in a systematic fashion. Since the curves are relatively insensitive to changes involving the hydrogen atoms only, the second and third parameters cannot be determined with great accuracy. Thus if $\angle C_2C_3C_1 = 61.5^\circ$ and C-H/C₂-C₃ = 1.08/1.48, then comparison with the appearance of the photographs show that \angle HCH = $120 \pm 8^\circ$, whereas if C-H/C₂-C₃ = 1.08/1.48 and \angle HCH = 120° , $\angle C_2C_3C_1 = 61.5^\circ$ with an uncertainty of only about one degree. With a longer or shorter C-H distance and/or an HCH angle differing considerably from 120° , however, the range of

$\angle C_2C_3C_1$ in which agreement can be obtained is increased; for example, a C-H distance of 1.12 Å., a larger $\angle HCH$, and a larger $\angle C_2C_3C_1$ would give a curve in fairly satisfactory agreement with the photographs, as can be seen by referring to Fig. 1. But by virtue of the existing knowledge of hydrocarbon structures and the confirmation provided by the radial distribution, we believe it is reasonable to assume for the formal statement of our results that C-H/C₂-C₃ does not differ significantly from 1.08/1.48 and that $\angle HCH$ lies somewhere within the range $120 \pm 8^\circ$. With these restrictions qualitative consideration of all the theoretical scattering curves and quantitative comparison of the observed q values with the calculated q values for the best curve H as shown in Table I leads, in agreement with the radial distribution function, to the following structural parameters and probable limits of error: C-H = 1.08 Å. (assumed), $\angle HCH = 120^\circ \pm 8^\circ$ (assumed), $(C-C)_{av.} = 1.49 \pm 0.01$ Å., and $\angle C_2C_3C_1 = 61.5 \pm 2^\circ$ ($C_1-C_3 = 1.48 \pm 0.03$ Å., $C_1-C_2 = 1.51 \pm 0.04$ Å.).

TABLE I

Min.	Max.	$q_{obs.}$	q_H	$q_H/q_{obs.}$
1		5.29	6.0	(1.134)
	1	7.86	7.6	(0.967)
2		11.91	11.5	(.966)
	2	16.94	17.0	1.004
3		19.66	19.6	(0.997)
	3	22.18	21.0	(.947)
4		26.00	25.5	.981
	4	30.42	29.8	.980
5		34.87	34.9	1.001
	5	38.81	40.0	(1.031)
6		41.84	41.8	(0.999)
	6	45.03	44.7	.993
7		49.62	49.7	1.002
	7	53.58	53.4	(0.997)
8		55.47	55.5	(1.001)
	8	58.25	58.4	1.003
9		63.95	63.1	0.987
	9	68.20	68.3	1.001
10		70.73	70.6	0.998
	10	73.60	72.4	.984
11		77.91	77.1	.990
	11	81.88	81.9	1.000
12		90.64	90.7	1.001
	12	95.50	96.0	1.005
Average (fifteen features)				0.995
Average deviation				.008

By means of the radial distribution function, and with the help of theoretical scattering functions, including those calculated for the investigation of methylenecyclobutane^{6,7} and 1-methylcyclobutene,⁶ we have attempted an exhaustive consideration of the possibility that some other plausible C₅H₈ structure might be in agreement

(6) W. Shand, V. Schomaker and J. R. Fischer, *THIS JOURNAL*, **66**, 836 (1944).

(7) S. H. Bauer and J. Y. Beach, *ibid.*, **64**, 1142 (1942).

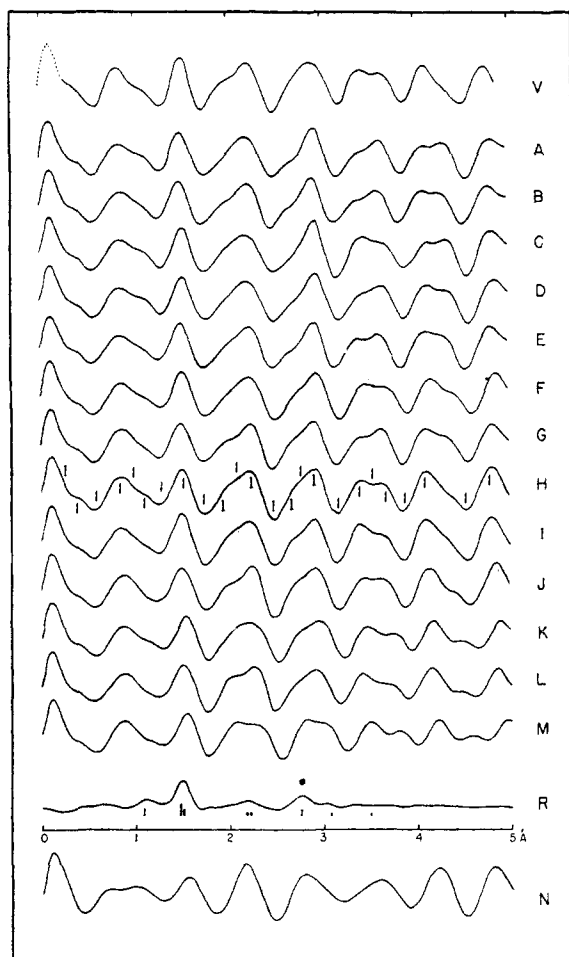


Fig. 1.—Electron diffraction curves for spiro-pentane (I):

$\angle C_2C_3C_1$	$\angle HCH$	C-H/C ₁ -C ₂	
58.5°	130°	1.09/1.49	A
	120°	1.09/1.49	B
60°	130°	1.12/1.49	C
	120°	1.09/1.49	D
	120°	1.06/1.49	E
61.5°	130°	1.09/1.49	F
	120°	1.12/1.49	G
		1.09/1.49	H
		1.06/1.49	I
	110°	1.09/1.49	J
63°	130°	1.09/1.49	K
	120°	1.06/1.49	L
64.5°	130°	1.09/1.49	M
1,1,1-Bicyclopentane (II)			N
Visual curve			V
Radial distribution curve			R

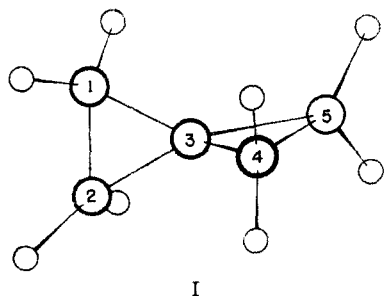
with the diffraction data. On the basis of chemical and spectral evidence, Murray and Stevenson concluded that their substance contained no multiple bonds, and must therefore be bicyclic. Among the bicyclic C₅H₈ structures there is none except spiro-pentane which can be made to agree with the diffraction data. In particular, the configuration of 1,1,1-bicyclopentane (II), which



is not definitely excluded by consideration of the Raman spectrum,⁸ is in marked disagreement with the radial distribution integral for all possible values of the bond angles. In order to illustrate the great disagreement with the observed diffraction pattern, we have calculated a theoretical scattering curve (N of Fig. 1) for a model of this molecule with all C-C-C bond angles equal. It is obvious that no reasonable variation of the angles would improve the appearance of the curve. (The stringent geometrical conditions on the C-C-C angles in the structure make it improbable that any of them could possibly differ by as much as 10° from the value 82° used for curve N.)

The radial distribution function, often merely by virtue of the large bond angle of *ca.* 138° indicated by the peaks at 1.49 and 2.77 Å., immediately excludes the other bicyclic structures, as well as all plausible C₅H₈ structures containing multiple bonds, except 1,2-dimethylcyclopropene-1, for which it is easy to set up a satisfactory planar model with C-C = 1.49 Å. and C=C = 1.34 Å. Nor is it entirely certain that agreement could not be obtained for 1-ethylcyclopropene-1. However, the evidence against a multiple bond structure presented by Murray and Stevenson seems conclusive, so that it and the electron diffraction data together afford definite proof of the spiropentane structure.

Discussion.—In spiropentane the deviations of the carbon bond angles from the normal tetrahedral values are most severe, the central carbon atom in particular being subject to the double constraint of having two of its bond angles fixed at approximately 60° by the three-rings of which it is the common member. It is of some interest to consider the structural results in relation to this condition of strain. In the first place, the average carbon-carbon bond distance, 1.49 Å., is significantly shorter than the usual single bond distance, 1.54 Å. In cyclopropane⁹ the C-C distance is 1.525 ± 0.03 Å., also less than the standard distance but not certainly so. It is possible



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(8) Private communication from Dr. Murray.

(9) L. Pauling and L. O. Brockway, *THIS JOURNAL*, **59**, 1223 (1937).

that there is indeed a general effect, correlatable with bond angle strain, which shortens the bond distances in three-membered rings by a barely detectable amount and in molecules with unusually great strain, such as spiropentane, shortens the bond distances considerably. This would be somewhat out of the ordinary (decrease in bond distance usually implies increase in bond energy or energetic stability and it is certain that these strained structures are energetically relatively unstable), but would perhaps not be entirely without precedent; ethylene with C=C = 1.353 Å.¹⁰ and allene (to be regarded as more highly strained than ethylene) with C=C = 1.330 Å.¹¹ seem to present a fair analogy. It is not likely that the bonds in highly strained cyclic compounds should be readily comparable to those in open chain compounds and it seems probable that the full explanation of the properties of the bonds in highly strained molecules with our present language will be complex, with hyperconjugation playing an important role. In the second place, the interesting question of the distribution of the shortening of the bonds between the peripheral bonds C₁-C₂ and C₄-C₅ and the central bonds, to which they are of course not equivalent, is not completely answered by our results, which indicate that the peripheral bonds are somewhat longer than the others but do not exclude either the possibility that the bonds are all of the same length or the possibility that the peripheral bonds are not shortened at all. Finally, the indicated HCH angle of 120°, being considerably greater than the normal value of 109½°, suggests that the methylene carbon atoms relieve some of their bond angle strain by widening the HCH angle. If so, then it is possible that the indicated difference in bond distances, corresponding to the greater C-C-C angle of 61.5° in the ring at the central carbon atom, represents in part the effect of the greater net angle strain on this atom relative to the methylene carbon atoms with which it competes for the total angle of the ring.

The results of Rogowski,¹² who reported that he had prepared spiropentane by the conventional debromination of pentaerythrityl bromide and identified it by an electron diffraction investigation, are still puzzling. Whitmore and Williams,¹³ repeating the preparation of Rogowski, reported that they obtained a mixture of methylene cyclobutane and 2-methyl-1-butene. Subsequent electron diffraction and chemical investigations confirmed the structure of the main product.^{6,7} Comparison of Rogowski's *g* values with ours shows that ours are 3.7 ± 0.1% higher, a difference which is much larger than is usually

(10) W. S. Gallaway and E. F. Barker, *J. Chem. Phys.*, **10**, 88 (1942).(11) E. H. Eyster, *J. Chem. Phys.*, **6**, 580 (1938). With the assumption of Gallaway and Barker's parameters for the CH₂ group (as found in ethylene) Eyster's value 97.0 × 10⁻⁴⁰ g. sq. cm. for the large moment of inertia of allene leads to C=C = 1.335 Å.(12) F. Rogowski, *Ber.*, **72**, 2024 (1939).

(13) See footnote 5 of ref. 7.

obtained in duplicate electron diffraction investigations. Moreover, if Rogowski actually did have spiro-pentane, his neglect to mention the asymmetries of the first and second minima and of the third maximum is very curious, inasmuch as these features show very clearly on our photographs. It is probably true, as would be indicated by the results of Whitmore and Williams,¹⁸ that Rogowski's preparation was a mixture of hydrocarbons.

We are indebted to Dr. E. R. Buchman for interesting discussion, and to Dr. M. J. Murray for the sample of spiro-pentane.

Summary

The results of an electron diffraction investigation of the C_5H_8 hydrocarbon prepared by Murray and Stevenson¹ confirm their assignment of the spiro-pentane structure made on the basis of the Raman spectrum. The dimensions for this molecule are C-H = 1.08 Å. (assumed), $C_1-C_3 = 1.48 \pm 0.03$ Å., $C_1-C_2 = 1.51 \pm 0.04$ Å., $\angle C_2C_3C_1 = 61.5 \pm 2^\circ$, and $\angle HCH = 120^\circ \pm 8^\circ$ ($(C-C)_{ave.} = 1.49 \pm 0.01$ Å.).

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, NORTHWESTERN UNIVERSITY DENTAL SCHOOL]

Some Alkyl and Alkamine Esters of *p*-FluorothiobenZOIC ACID¹

BY L. S. FOSDICK AND H. I. BARNES

In 1933 some alkyl and alkamine esters of *p*-aminothiobenZOIC acid were prepared.² The pharmacological activity of these compounds was compared with that of their oxygen analogs, the procaine series. It was found that the substitution of sulfur for oxygen increased the anesthetic efficiency four to six times, and increased the toxicity three to four times.³ Some clinical trials indicated that a 0.5% solution of the procaine analog, "Thiocaine," gave similar results to a 2.0% solution of procaine hydrochloride. Furthermore, unlike procaine hydrochloride, Thiocaine produced profound topical anesthesia on the cornea of the eye.

Later⁴ it was found that the esters of *p*-fluorobenZOIC acid possessed local anesthetic properties but were quite irritating to tissue. These esters were exceptionally non-toxic.

In view of the above, it was thought of interest to prepare the alkyl and alkamine esters of *p*-fluorothiobenZOIC acid.

In the present study the alkyl and chloroalkyl esters were prepared from the potassium salt of the acid and the appropriate alkyl halide or the appropriate dihalogen substituted alkane. The alkamine esters were prepared from the halogen ester and the appropriate amine.

Preliminary pharmacological data indicate that, contrary to expectations, the substitution of sulfur for oxygen does not enhance the anesthetic efficiency, but does materially increase the toxicity of these compounds.

Experimental Part

All of the compounds were prepared from *p*-toluidine by converting it to *p*-fluorotoluene according to the method of Balz and Schiemann.⁵ This was then oxidized with

neutral permanganate to *p*-fluorobenZOIC acid,^{6,7} which was subsequently converted to the acid chloride with thionyl chloride. The *p*-fluorobenZOYL chloride was then converted to the thio acid and the various esters prepared as previously indicated.

***p*-FluorothiobenZOIC ACID.**—A solution of 23.5 g. of potassium hydroxide and 300 cc. of ethyl alcohol was cooled in an ice-bath and saturated with hydrogen sulfide. To this was added slowly 32.5 g. of *p*-fluorobenZOYL chloride. A precipitate formed which was removed by filtration and the mother liquor was evaporated to dryness. The two solids were combined, dissolved in a minimum amount of cold water, and the free acid was precipitated by the addition of concentrated hydrochloric acid. The mixture was allowed to remain in an ice box overnight, after which the precipitate was removed by filtration. The acid was obtained as a light yellow solid; yield, 27 g., 86%; m. p. 36°; S, 21.9, 21.5; calcd., 20.5.

Alkyl Esters.—Fifteen grams of *p*-fluorothiobenZOIC acid was dissolved in 10–15 cc. of alcohol mixed with a saturated alcoholic solution of 5.6 g. of potassium hydroxide. An excess of the appropriate alkyl bromide was added and the mixture was refluxed on a steam-bath for two hours. The potassium bromide which had precipitated was removed by filtration and excess alcohol and alkyl bromide was removed by distillation in a vacuum. The ester was washed with water and purified by distillation *in vacuo*.

TABLE I
p-FLUOROTHIobenZOATES

Compound	Yield, %	M. p., b. p., °C.	S analyses, % Calcd. Found
Ethyl	76	224–225 at 754 mm.	17.39 17.08
<i>n</i> -Propyl	93	106–110 at 6 mm.	16.16 16.12
<i>n</i> -Butyl	80	130–133 at 8 mm.	15.60 15.52
β -Chloroethyl	67	145–148 at 8 mm.	14.64 14.51
Diethylaminoethyl-HCl	60	164–170	10.98 10.91
Di- <i>n</i> -propylaminoethyl-HCl	62	200–205	10.06 9.95
Di- <i>n</i> -butylaminoethyl-HCl	65	220–224	9.21 9.20
γ -Bromopropyl	20	165 at 7 mm.	11.55 11.50
Diethylaminopropyl-HCl	61	130	10.48 10.45
Di- <i>n</i> -propylamino-propyl-HCl	65	157	9.59 9.62
Di- <i>n</i> -butylamino-propyl-HCl	60	191	8.85 8.82

(6) Ohman. THIS JOURNAL, 16, 533 (1894).

(7) Slathower. *Rec. trav. chim.*, 33, 324 (1914).

(1) Presented before the Division of Medicinal Chemistry, New York meeting of the American Chemical Society, September 15, 1944.

(2) Hansen and Fosdick, THIS JOURNAL, 55, 2872 (1933).

(3) Fosdick and Hansen, *J. Pharmacol.*, 50, 323 (1932).

(4) Fosdick and Campaigne, THIS JOURNAL, 63, 974 (1941).

(5) Balz and Schiemann, *Ber.*, 60, 1186 (1927).