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3d-ORBITAL RESONANCE IN DIVALENT SULPHIDES—IV

ACIDITY OF HYDROGEN ATOM ADJACENT TO MERCAPTO GROUPS[1,2]

S. OAE, W. TAGAKI and A. OHNO[3]
Department of Applied Chemistry, Faculty of Engineering, Osaka City University,
Japan

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Abstract—The rates of base-catalysed hydrogen-isotope exchange reactions of various sulphides and their corresponding oxygen analogues have been measured in order to compare the relative acidifying effects of mercapto and alkoxy groups toward α-hydrogen atoms. Practically no exchange reaction was observed in the oxygen compounds, whereas, with the sulphur compounds, the reaction readily takes place, the rate being increased several powers of ten by the substitution of one additional mercapto group. Furthermore, dramatic rate increase was observed when an open chain compound, orthothioformate was cyclized to the corresponding bicyclic compound. These observations are interpreted in terms of the 3d orbital resonance of the sulphur atom.

THE ability of the sulphur atom to expand its valence shell beyond the octet has been displayed in numerous examples. Especially, when the central sulphur atom bears a positive charge (or charges) such as in sulphoxides, sulphonium salts and sulphones, there is sufficient evidence to indicate the resonance between unsaturated groups (i.e., double bond, lone electron pair) and the charged sulphur atom involving its vacant 3d orbitals. Thus, insofar as positively charged sulphur groups are concerned, the 3d orbital resonance is accepted as a general concept.[4]

On the other hand, in the case of uncharged divalent sulphur compounds, theoretical studies on possible 3d orbital resonance have been made only in very few cases, such as in thiophene.[5] Here, 3d orbital resonance is assumed to be considerably weaker than that in positively charged sulphur groups, because 3d orbitals of a neutral sulphur atom are so diffused that the overlapping with p orbitals of adjacent atoms would not be efficient. Although resonance of divalent sulphur groups when the sulphur atom is attached to a carbanion or an unsaturated group is well supported,[1c]

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[1] [a] Part I, S. Oae, W. Tagaki and A. Ohno, *J. Amer. Chem. Soc.* **83**, 5036 (1961); [b] Part II, S. Oae, A. Ohno and W. Tagaki, *Chem. & Ind.* 304 (1962); [c] Part III, S. Oae, "*3d Orbital Resonance Involving the Sulfur Atom in Organic Sulfides* in *Organic Sulfur Compounds*" (Edited by N. Kharasch) Vol. 4. Pergamon Press, in press.

[2] A part of this work was done at the Radiation Center of Osaka Prefecture and the preliminary results and discussions were reported elsewhere.[1a,1c]

[3] Present address, Department of Chemistry, Massachusetts Institute of Technology.

[4] [a] G. Cilento, *Chem. Revs.* **60**, 147 (1960); [b] C. C. Price and S. Oae, *Sulfur Bonding*. Ronald Press Co., New York (1962); [c] H. H. Jaffe and M. Ohchin, *Theory and Application of Ultraviolet Spectra* Chap. 17. John Wiley, New York (1962).

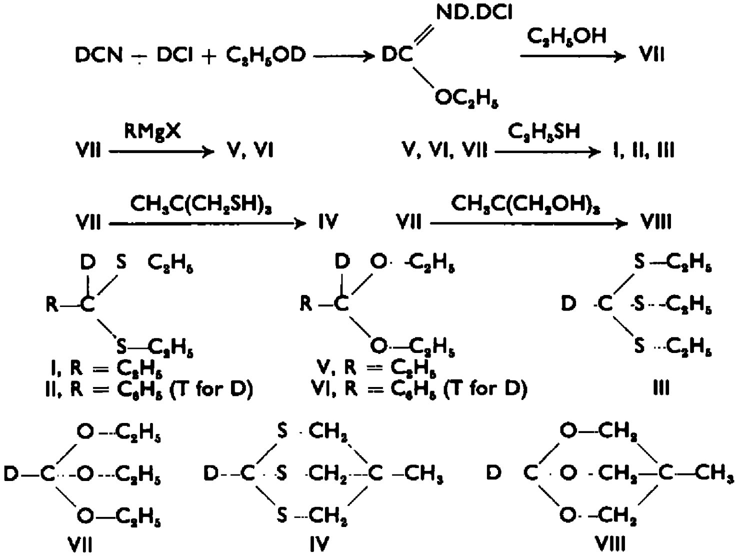
[5] [a] V. Schomaker and L. Pauling, *J. Amer. Chem. Soc.* **61**, 1769 (1939); [b] H. C. Longuet-Higgins, *Trans. Faraday Soc.* **45**, 173 (1949); [c] M. J. S. Dewar and E. A. C. Lucken, *J. Chem. Soc.* 426 (1959); [d] A. Mangini and C. Zauli, *J. Chem. Soc.* 2210 (1960); [e] K. Maeda, *Bull. Chem. Soc., Japan* **33**, 304 (1960); [f] M. M. Kreevoy, *J. Amer. Chem. Soc.* **80**, 5543 (1958).

most of the work is either uncritical or only qualitative in nature explaining a certain reaction pathway by means of 3d orbital resonance. Therefore, quantitative and critical investigations with well-defined systems are necessary in order to elucidate the 3d orbital resonance in divalent sulphur groups.

The contribution of 3d orbital resonance may be assessed by determination of the acidities of α-hydrogen atoms adjacent to the divalent sulphur groups in comparison with those of the corresponding oxygen analogues. Thus, several divalent sulphur compounds and their oxygen analogues were synthesized and subjected to the base-catalysed hydrogen isotopic exchange reactions.

RESULTS

Synthesis of the compounds. An equimolecular mixture of deuterium cyanide, deuterium chloride and ethanol-d_1 gave the deuterated formiminoester hydrochloride in a yield exceeding 80%. Use of a non-deuterated compound in place of any one of the above three deuterated compounds resulted in a considerable loss of deuterium content of the formiminoester. Since no hydrogen exchange was observed in the subsequent ethanolysis of formiminoester hydrochloride, ordinary ethanol, necessary in a large excess, could be used. The other compounds were all prepared starting from VII: (1) The acetals (V and VI) were obtained by the Grignard reaction. (2) The mercaptals (I and II) and triethyl orthothioformate (III) were obtained by the acid catalysed equilibration reactions of the corresponding oxygen analogues with ethyl mercaptan. (3) Of the bicyclic compounds, IV was prepared by the acid catalysed equilibration reaction of VII with trithiapentaglycerine, while VIII was obtained by the thermal condensation of VII with 1,1,1-trishydroxymethylethane. Successful deuterations were shown by the complete lack of NMR α-proton resonance peaks in the deuterated compounds, for example, VII (δ benzene = 1·74 p.p.m.) and IV (δ benzene = 2·89 p.p.m.). Meanwhile, a number of different absorption bands in the IR spectra were observed between the protium and deuterium compounds, of which relatively intense and well-separated bands are shown in Table 1, footnote (a).



Among them, the following three pairs are worthy of mention in view of their frequency ratios lying near the predicted value, 1·363, of H *vs.* D frequency ratio, though the assignments are difficult; 3030 cm^{-1} (H-VIII) and 2280 cm^{-1} (D-VIII), 1150 cm^{-1} (H-III) and 872 cm^{-1} (D-III), and 1177 cm^{-1} (H-I) and 893 cm^{-1} (D-I).

Hydrogen exchange reactions. Table 1 lists kinetic data obtained in t-butoxide and ethoxide catalysed exchange reactions. The deuterium–hydrogen exchange kinetics were followed by IR spectroscopic analyses and the tritium-hydrogen exchange kinetics were followed by the determination of the loss of tritium activity during the reaction using a liquid scintillation counter. Typical kinetic examples are shown in Table 2 and 3.

TABLE 1. KINETICS FOR THE BASE-CATALYSED D–H AND T–H EXCHANGE REACTIONS

Compound	Base	Solvent	Temp., °C	First order reaction rate constant, $k_1 \times 10^6$ sec.$^{-1}$ [a]	Rel. rate
I	t-BuOK[b]	t-BuOH	138	4·73	1·00
II	EtONa[c]	EtOH	50	3·52	$1·38 \times 10^{6}$
VI	t-BuOK[b]	t-BuOH	120	0·405	0·24
III	t-BuOK[b]	t-BuOH	120	24,980[d]	
III	t-BuOK[b]	t-BuOH	138	69,950[d]	$1·48 \times 10^{4}$
III	t-BuOK[b]	t-BuOH	60	364	
III	t-BuOK[b]	t-BuOH	50	155	
III	t-BuOK[b]	t-BuOH	40	62	
III	EtONa[c]	EtOH	50	0·375[d]	
III	EtONa[c]	EtOH	80	17·4	
III	EtONa[c]	EtOH	90	58·2	
III	EtONa[c]	EtOH	100	159	
IV	EtONa[c]	EtOH	50	452	$1·78 \times 10^{7}$
VII	t-BuOK[b]	t-BuOH	112	No exchange (in 20 hr)	
VIII	t-BuOK[b]	t-BuOH	138	No exchange (in 5 hr)	

[a] From measurement at 862 cm^{-1} and 713 cm^{-1} for IV, 1150 cm^{-1} and 872 cm^{-1} for III, 1177 cm^{-1} and 893 cm^{-1} for I, 3030 cm^{-1} and 2280 cm^{-1} for VIII, and 1735 cm^{-1} and 1700 cm^{-1} for VII. Tritium activities were measured by Tri-carb liquid scintillation counter for II and VI. [b] 0·097M. [c] 0·107M. [d] Extrapolated values.

DISCUSSIONS

As shown in Table 1, practically no exchange reactions of oxygen compounds were observed under the conditions listed. Under more drastic conditions, considerable decompositions were observed for oxygen compounds. Whereas α-deuterated propylidenediethyl mercaptal (I) was found to undergo a considerable D–H exchange in t-butanol at 138°, as anticipated from previous work,[6] in which diethylthioformal, in the presence of lithium amide in liquid ammonia, was shown to react with alkyl halide to give α-alkylated thioformal. The substitution of one additional ethylmercapto group, e.g., in III, increased the reactivity by more than ten thousand fold as compared with I, which corresponds to a difference in free energy of activation of about 7·8 Kcal $mole^{-1}$. Although the inductive effect of an alkyl group would destabilize,[7] whilst that of the mercapto group would stabilize the carbanion as

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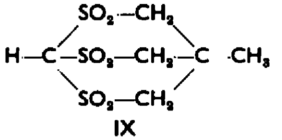
[6] J. F. Arens, M. Fröling and A. Fröling, *Rec. Trav. Chim.* **78**, 663 (1959).

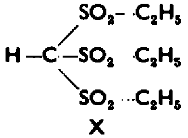
[7] [a] D. E. Applequist and D. F. O'brien, *J. Amer. Chem. Soc.* **85**, 743 (1963); [b] G. S. Hammond, *Steric Effects on Equilibrated Systems* in M. S. Newman's *Steric Effects in Organic Chemistry*, Chap. 9. John Wiley, New York (1959).

compared with hydrogen, it is unlikely that an inductive effect alone can cause such a large rate difference.[8] In this case, undoubtedly 3d orbital resonance is the major contributing factor in the facile isotopic hydrogen exchange reactions of the sulphur compounds, while the electron-withdrawing inductive effect contributes little, since the latter effect should be larger for alkoxy than for mercapto groups. A phenyl group in α-position is also known to have a considerable conjugative stabilization effect for a carbanion.[9] In fact exchange rate of II in t-butanol was so fast that it was only measurable in sodium ethoxide-ethanol solution. Apparently, a phenyl group has a larger conjugating ability with carbanion than an ethylmercapto group by a factor of about nine (the ratio of the rate of II *vs.* of III). This strong acidifying effect of a phenyl group helps to estimate the small acidifying effect of an alkoxy group: namely, although the acidifying effect of an alkoxy group is so weak that it cannot be determined by the direct comparison of the rates of VII and VIII, it could be estimated by the comparison of the rates of two phenyl substituted compounds (II and VI), II being about six powers of ten more reactive than VI, and this difference may be taken as the relative magnitude of acidifying effects of alkoxy and mercapto groups. This value agrees with that of Slaugh and Bergman[10] who recently measured the rates of T–H exchange reactions of chloroform, orthoformate and orthothioformate.

Since earlier work[11] on various positively charged sulphur compounds indicates that there is no strict angular requirement for d–p overlap of the C–S π-bond as there is for p–p overlap, one would expect the rate of hydrogen isotopic exchange of IV to be of the same order of magnitude as that of III or possibly somewhat lower than that of III because of its less favoured solvation. However, it was found that the rate of IV was about three powers of ten larger than that of III in ethanol at 50°; the difference of rates corresponds to a difference of free energy of activation of about 4·6 Kcal mole^{-1}. This seems rather strange when one recalls the well-known work by Doering and Levy[12] that the bicyclic trisulphide (IX) was less acidic than the acyclic trisulphone (X).



IX



X

The large rate difference between III and IV seems likely to be caused by two main factors. One factor is that an effective 2p–3d overlap between a carbanion and sulphur atoms could be attained by constraining the sulphur atoms at some fixed positions as in IV. In IV, the α-C–H bond or the resulting non-bonded lobe of the carbanion which would be of sp^3 configuration is coplanar with the adjacent three C–S–C planes. While in III, a considerable steric crowding is expected around the three mercapto groups which would hinder the coplanarity of non-bonded lobe with

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[8] See the results for the acidities of cyclic mercaptals, where the alkyl groups were varied from methyl to t-butyl, cited in ref. 1*c*.

[9] For example, see A. Streitwieser, Jr., *Molecular Orbital Theory for Organic Chemists*, Chap. 14. John Wiley, New York (1961).

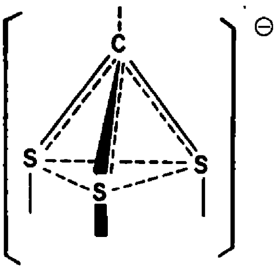
[10] L. R. Slaugh and E. Bergman, *J. Org. Chem.* **26**, 3158 (1961).

[11] [a] Ref. 4*b*; [b] G. E. Kimball, *J. Chem. Phys.* **3**, 188 (1940); [c] D. P. Craig, A. Maccoll, R. S. Nyholm, L. E. Orgel and L. E. Sutton, *J. Chem. Soc.* 332 (1954); [d] E. J. Corey, H. Koenig and T. H. Lowry, *Tetrahedron Letters* 515 (1962).

[12] W. E. von Doering and L. K. Levy, *J. Amer. Chem. Soc.* **77**, 509 (1955).

C–S–C planes. This interesting difference between the geometrical configurations of III and IV seems to be partly responsible for the large rate-enhancement in the cyclic compound, IV, in view of our other kinetic observations on the hydrogen exchange reactions of various cyclic mercaptals of varing ring sizes *vs.* those of the corresponding open chain mercaptals.[8] This may be related to the fact that a sulphur atom confined in an unsaturated ring system displays a strong conjugative effect. For instance, the resonance energy of thiophene (31 Kcal mole^{-1}) is greater than that of furan (23 Kcal mole^{-1})[13]. "Thiabenzenes" and the related compounds have been recently shown to have considerable degrees of aromaticity due to the 3d orbital resonance of the sulphur atom,[14] the resonance energy of 1,4-dithiadiene (15–30 Kcal mole^{-1})[15a] is very large despite of its non-planar structure,[15b] and the mesomeric moment of γ-thiopyrone is larger than that of γ-pyrone.[16]

The second factor is that the three sulphur atoms of IV retain their lone electron pairs which could be used for 3p–3d overlapping between three sulphur atoms. Such non-bonded interaction has been suggested earlier to explain the apparent red shifts of UV absorption maxima of mercaptals,[17] α-ketosulphides,[17] allyl sulphide[4b,18] and polysulphides.[4b,18] Although the precise geometrical structure of IV is yet to be determined,[19] it is obvious that the interatomic distances between three sulphur atoms are identical because of the symmetrical structure[20] and would be smaller than the average interatomic distance between three sulphur atoms of the open chain analogue, e.g. III, in which the three sulphur atoms are not held in a symmetrical fixed geometry. Hence, the non-bonded interaction between three sulphur atoms through the overlappings of 3p and 3d orbitals of three sulphur atoms would be greater in IV than in III. This added resonance may enhance the stability of the carbanion that is already enjoying a resonance stabilization through 2p–3d overlapping between bridgehead non-bonded lobe and the three sulphur atoms. Thus, the structure, XI seems a likely representation of the intermediate carbanion of IV in this exchange reaction.



XI

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[13] L. Pauling, *The Nature of the Chemical Bond*, P. 197. Cornell Univ. Press, Ithaca, N.Y. (1960).

[14] [a] G. Suld and C. C. Price, *J. Amer. Chem. Soc.* **84**, 2094 (1962), and the preceding papers; [b] C. C. Price, M. Hori, T. Parasaran and M. Polk, *J. Amer. Chem. Soc.* **85**, 2278 (1963).

[15] [a] Ref. 5*f*; [b] P. A. Howell, R. M. Curtis and W. N. Lipscomb, *Acta Cryst.* **7**, 498 (1954), and W. E. Parham, *The Chemistry of 1,4-Dithiadiene and Related Compounds* Chapt. 22; in *Organic Sulfur Compounds*, (Edited by N. Kharasch) Pergamon Press, New York (1961).

[16] Ref. 4*b*, p. 19-22.

[17] E. A. Fehnel and M. Carmack, *J. Amer. Chem. Soc.* **71**, 89 (1949).

[18] H. P. Koch, *J. Chem. Soc.* 387 (1949).

[19] Being investigated by Prof. T. Watanabe and his group at Osaka University.

[20] IV has been found to be of C_{3v} symmetry by Dr. G. Zerbi who is now making a detailed spectroscopic study of IV.

Table 2. Kinetic for 4-methyl-2,6,7-trithiabicyclo(2,2,2)octane-α-d_1 (IV)
EtONa-EtOH (0·107M.); Temp. 50 + 0·02°

Time, sec.	T_D/T_H[a]	% D-compound	$k_1 \times 10^4$
0	2·57	87·2	—
120	1·67	82·6	4·53
300	1·26	76·8	4·25
540	0·989	67·2	4·80
960	0·713	55·5	4·71
1,260	0·635	50·8	4·29
			av. 4·52 ± 0·18

[a] The ratio of intensities for D- and H-peaks.

Table 3. Kinetic for benzaldehyde diethylmercaptal-α-t_1 (VI)
EtONa-EtOH (0·107M.); Temp. 50 ± 0·02°

Time, sec.	$X \times 10^4$ c.p.m.	$X/Xo \times 100$	$k_1 \times 10^6$
run 1			
0	1·852	100	—
3,600	1·829	98·76	3·48
7,200	1·806	97·52	3·50
10,800	1·783	96·27	3·51
run 2			
0	1·962	100	—
7,200	1·913	97·50	3·51
14,400	1·864	95·01	3·49
25,200	1·798	91·23	3·64
			av. 3·52 ± 0·04

The sulphone (IX) having no unbonded 3p orbitals, is incapable of forming a similar interaction as in XI. Recently, the higher acidity of IV over that of III has been suggested to be due to the increased acidity of hydrogen atom attached to a strained cyclic system over that of the corresponding acyclic analogue, referring cyclopropyl system as the supporting evidence.[21] However, this explanation can hardly be accepted, since there is substantial evidence that the cyclopropyl carbanion is exceptional and quite different from other cyclic carbanions.[7a,22] Other cyclic carbanions, such as cyclobutyl and cyclopentyl have recently been shown to be less stable than the open chain carbanions.[7a].

Seeking additional supporting evidence, the UV spectra of a number of mercaptals were taken[23] and parts of them are shown in Table 4. The absorption maxima of the bicyclic compound (IV) is shifted toward substantially longer wave length ($\Delta\nu = 16$) as compared with that of the acyclic compound (III), the absorption spectrum and the maximum of which are not very different from those of the open chain mercaptal (I). This would imply that IV has a different chromophore which is characteristic only for such compounds (IV) that have three mercapto groups constrained in a fixed geometry.

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[21] C. Y. Meyers, *Tetrahedron Letters* No. 24, 1125 (1962).

[22] [a] C. A. Coulson and W. F. Moffitt, *J. Chem. Phys.* **15**, 151 (1947); [b] N. Muller and D. E. Pritchard, *J. Chem. Phys.* **31**, 768 (1959); [c] L. L. Ingraham in Newman's *Steric Effects in Organic Chemistry* p. 518. John Wiley, New York, N.Y., [d] H. M. Warborsky, *Record of Chemical Progress* **23**, No. 2, June (1962).

[23] The UV spectra have been presented at the *International Symposium on Molecular Structure and Spectroscopy*, Tokyo, Japan, Sept. 13 (1962) and will be published elsewhere.

TABLE 4. THE ULTRAVIOLET SPECTRA AND THE RELATIVE RATES OF HYDROGEN EXCHANGE REACTIONS OF SULPHIDES

Compounds	λmax (mμ) in EtOH	ε	Relative rates of hydrogen exchange reaction
I	231	834	1·00
III	235	954	$1·48 \times 10^4$
IV	251	1,242	$1·78 \times 10^7$
2-Methyl-1,3-dithian	252	449	1·393[a]

[a] Ref. 8.

However, this bathochromic shift in IV was found not necessarily to be associated with three fixed symmetrical mercapto groups of the bicyclic compound (IV), but was a commonly observable phenomenon in cyclic mercaptals. In fact, some cyclic mercaptals, such as 2-methyl-1,3-dithian, have an absorption maximum at a slightly longer wavelength and yet the exchange rate is far smaller when compared with the bicyclic compound, IV. Therefore, although it seems that there is a distinct nonbonded interaction between sulphur atoms in the photoexcitation of mercaptals or of trisulphides and such an interaction is definitely larger in cyclic sulphur compounds than their open chain analogues, UV absorption maxima are not directly related to the hydrogen exchange rates. This may be in part due to the fact that the latter involves the α-C–H bond rupture but the former does not.

EXPERIMENTAL

All the m.ps and the b.ps were uncorrected. The IR spectra were recorded with Perkin–Elmer Model 221 Infrared Spectrophotometer and the NMR spectra were recorded with Varian NMR Spectrophotometer at either 40 Mc or 60 Mc.

Triethyl orthoformate-α-d_1 (VII)

(a) *Deuterium cyanide.* Into a 100 ml. three-necked flask containing 18 g phosphorous pentoxide was added dropwise 20 g deuterium oxide (99·8 % D) under ice cooling. The resulting colourless clear solution of deuterated phosphoric acid in excess deuterium oxide was connected through a water cooled trap and a drying tube ($CaCl_2$) to an efficient trap which was cooled below −40°. A L-shaped side tube filled with 25 g well dried potassium cyanide was attached to the flask. The whole apparatus was evacuated in order to remove the trace of light water before replacing it with deuterium oxide. Potassium cyanide was added portionwise and deuterium cyanide gas evolved was collected in the trap. The yield was 7·5 g (70 %, based on potassium cyanide).

(b) *Deuterium chloride.* Into a three-necked flask attached with a L-shaped side tube which contained 3·5 g deuterium oxide was placed 43 g phosphorus pentachloride. The flask was connected through an ice-cooled trap and a drying tube ($CaCl_2$) to a flask which contained 60 ml anhydrous ether and was cooled below −10°. The whole apparatus was evacuated as in (a) for the same purpose. The deuterium oxide was added dropwise under constant shaking of the flask to avoid a violent evolution of the gas. The yield of deuterium chloride trapped into anhydrous ether was 12 g (91 % based on deuterium oxide).

(c) *Ethanol-*d_1. Freshly cut clean sodium metal was dissolved in excess anhydrous ethanol under nitrogen atmosphere. The excess ethanol was removed until no more liquid remained in a trap cooled with liquid nitrogen in a high vacuum line. In the same vacuum line, 20 g deuterium oxide was transferred to a large excess of dried sodium ethoxide and the two were allowed to react by repeating the cooling and the heating of the reaction tube, then deuterated ethanol was collected in another trap cooled with liquid nitrogen and dried over molecular sieve 4A, yield 22 g (47 %, based on deuterium oxide).

(d) *Deuterated formiminoester hydrochloride.*[24] The above deuterium cyanide (7·5 g) in 20 me anhydrous ether, 18 g ethanol-d_1 and 12 g deuterium chloride in 60 ml anhydrous ether were reacted below −10° in an ice–salt bath for about 24 hr. Formiminoester hydrochloride was separated as crystalline mass, washed with anhydrous ether thrice and dried (KOH and P_2O_5), yield 25 g (84%). The IR absorption maxima of D-compound (Nujol): 2300, 1242 cm.$^{-1}$

(e) *Ethanolysis of deuterated formiminoester hydrochloride.*[24] In a three-necked flask was dissolved 24 g of the above deuterated formiminoester hydrochloride in 200 ml anhydrous ethanol under stirring at room temp. Anhydrous ether was (250 ml) then added to the resulting almost clear solution. The reaction mixture was refluxed and stirred on a steam bath for 10 hr. The ammonium chloride was filtered off and the filtrate concentrated and fractionally distilled to give a colourless fraction of pure VII boiling at 145–146°, yield 22 g (70%). The product was further purified by gas chromatography through silicone impregnated firebrick column for the uses in the kinetic and the spectroscopic measurements. The IR absorption maxima (in CCl_4): 2160, 2100, 1700, 963, 890 cm^{-1} for D-VII; 1735, 840 cm^{-1} for H-VII. The NMR spectra of H-VII showed three kinds of proton signals in CCl_4 solution, centered at : δ benzene = 1·74 (doublet) for α-proton, δ benzene = 3·27 (quartet) for methylene protons and δ benzene = 5·71 p.p.m (triplet) for methyl protons, of which α-proton signal was completely absent in the spectra of D-VII.

Triethyl *ortho*formate-α-t_1 was prepared by the same procedure as for the above deuterium compound using tritiated water instead of using deuterium oxide. The tritium activity of the product, for example, was 7·19 μc/mM.

Propionaldehyde diethylacetal-α-d_1 (V) was prepared by the Grignard reaction of triethyl orthoformate-α-d_1 (VII) with ethylmagnesium iodide in anhydrous ether[25] to give a colourless liquid, b.p. 122–124° (reported for H-V, 123° [25]), yield 60–70%. The IR absorption maxima of V purified by gas chromatography on silicone column: 2140, 1730, 1705, 1400, 1345, 1280, 1200, 1020, 855 cm^{-} for D-V; 1740, 1380, 1350, 1315, 1040, 1015, 910, 835 cm^{-1} for H-V.

By the same method, benzaldehyde diethylacetal-α-t_1 (VI) was prepared from the tritiated VII and phenylmagnesium bromide to give a colourless liquid, b.p. 103–105°/15 mm. (reported for H-VI, 93°/10 mm.[25]), yield 65%, tritium activity 9·45 μc/mM.

Triethyl orthothioformate-α-d_1 (III)[25,26] was prepared by treating triethyl orthoformate-α-d_1 (VII) with more than three times excess of ethyl mercaptan using fused anhydrous zinc chloride or *p*-toluenesulphonic acid as the catalyst to give a pale yellow liquid, b.p. 136°/16 mm, yield 80%. The IR absorption maxima (in CCl_4): 1650, 1150, 895, 880, 865 cm^{-1} for D-III; 1680, 1180, 1145, 1135, 872 cm^{-1} for H-III.

By the same method, propionaldehyde diethylthioacetal-α-d_1 (I) and benzaldehyde diethylthioacetal-α-t_1 (II) were prepared from the corresponding oxygen compounds, V and VI respectively. I, b.p. 98–100°/26 mm, yield 60%. The IR absorption maxima (in CCl_4): 1130, 1070, 943, 893 cm^{-1} for D-I; 1290, 1230, 1177, 1080, 905, 820 cm^{-1} for H-I. II, colorless liquid, b.p. 110°/2 mm, yield 85%, tritium activity 9·40 μc/mM.

4-*Methyl*-2,6,7-*trioxabicyclo*(2,2,2)*octane*-α-d_1 (VIII).[12] To a distillation flask with a fractionating column, 2·6 g (0·025 mole) 1,1,1-trishydroxymethylethane and 3·3 g (0.002 mole) triethyl orthoformate α-d_1 (VII) were added and the mixture heated at 140°. During the heating, ethanol was slowly distilled off and the residue distilled (red. press.), and the distillate sublimed to give colorless needles m.p. 106° (reported for H-VIII, 105·5–106°[12]), yield 1·2 g (42%). The IR absorption maxima (in CCl_4): 2690, 2280, 2210, 2130, 1840, 1690, 1340, 1125, 1065, 920, 840 cm^{-1} for D-VIII; 3030, 1940, 1900, 1850, 1360, 1150, 940, 905 cm^{-1} for H-VIII.

4-*Methyl*-2,6,7-*trithiabicyclo*(2,2,2)*octane*-α-d_1 (IV)[12]. A solution of 4 g (0·024 mole) trithiapentaglycerine and 3·6 g (0·024 mole) triethyl orthoformate-α-d_1 (VII) in 70 ml anhydrous benzene was added to a refluxing solution of 1·3 g *p*-toluenesulphonic acid in 20 ml anhydrous benzene. This amount of the acid seems to be essential for a better yield, and smaller amounts give lower yields. The reaction mixture was refluxed 6 hr, cooled, washed, and the benzene layer dried and concentrated. The residual crystalline mass was chromatographed through an alumina column and the crystals eluated recrystallized from n-hexane to give colourless needles, m.p. 131° (reported for H-IV,

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130–131°[12]), yield 2 g (46·5%). The IR absorption maxima (in CCl_4): 2205, 900, 862 cm^{-1} (in CS_2) for D-IV; 2280, 885, 713 cm^{-1} (in CS_2) for H-IV. The NMR spectra of H-IV showed the following three kinds of proton signals (each was singlet) in CCl_4: δ benzene = 2·89 for α-proton, δ benzene = 5·19 for methylene protons and δ benzene = 7·78 p.p.m. for methyl protons, of which the α-proton signal was completely absent in D-IV.

Exchange kinetics

Base solutions, 0·097M potassium t-butoxide in t-butanol, and 0·107M and 0·214M sodium ethoxide in ethanol were prepared by dissolving the corresponding clean metals in the anhydrous alcohols respectively under a nitrogen atmosphere.

(a) *Deuterium-hydrogen exchange kinetics.* Each compound except IV, 0·004 mole, was dissolved in 20 ml base solution at room temp, the concentration of a compound being kept at approximately 0·2M. Two ml aliquots of the sample solution (each 2 ml contained 0·0004 mole of the compound) were pipetted into 8–9 ampoules, sealed, immersed into a constant temp bath and withdrawn at suitable time intervals. The content of the ampoule was poured into a cooled quenching solution of 0·1N HCl in anhydrous methanol which was used in excess to make the solution slightly acidic. The salt (NaCl or KCl), was immediately precipitated. From the resulting clear supernatant of this quenching solution, the product was isolated by the following procedures.

For the sulphur compounds (I and III) the supernatant was decanted into a small distillation flask attached with a small side tube trap, concentrated and distilled under a stream of nitrogen to give a colourless liquid, yield 0·00025–0·00035 mole (60–80%). The product was shown to be pure by IR spectra, not contaminated with any impurity such as the solvent. The product contaminated with the solvent was redistilled. For the oxygen compound (VII) the supernatant was directly fractionated by gas chromatography to give a colourless liquid, yield 0·00012–0·00024 mole (30–60%). For the oxygen compound (VIII) the supernatant was decanted into a distillation flask, concentrated, and the residue was sublimed to give colourless needles, yield 0·00008–0·0002 mole (20–50%).

Since the solubility of the cage compound, IV was low and it easily crystallized during the pipetting, the concentration was lowered and the sampling was modified; namely, each 20 mg of IV was weighed into an ampoule and to this was added 2 ml ethanol and the compound dissolved. Then to this solution was added 2 ml of the above 0·214M solution of sodium ethoxide in ethanol and henceforth the treatments till the quenching were the same as before. The quenching was done by pouring the content of the ampoule into cooled 20 ml aqueous 0·1N HClaq and the resulting needles were filtered, washed with distilled water and dried (P_2O_5).

The above kinetic products were analysed for deuterium by Perkin-Elmer Model 211 Infrared Spectrophotometer. The products from I, III and VII were analysed in liquid phase, IV in CS_2 and VIII in CCl_4. The calibration curves were obtained by plotting the ratios of transmittance for H- and D-peaks against the standard compositions of H- and D-compounds. The well-separated absorption peaks selected for the analysis are shown in Table 1, footnote (a). The pseudo-first order rate constants thus obtained are shown in Table 1. Typical kinetic example is shown in Table 2.

(b) *Tritium-hydrogen exchange kinetics.* The compounds (II and VI) described before were diluted with H-compounds so as to make the tritium activities fall in a range of 10^4-10^5 d.p.m.

The sample solutions were prepared by dissolving 900 mg of each II and VI in 18 ml of the base solution [the same as in (a)]. Three ml of each solution was pipetted into ampoules. After the reaction, the content of the ampoule was transferred into a 200 ml separating funnel which contained 20 ml toluene and 50 ml distilled water, and the content of the ampoule was washed (4 times) into the flask with 2 ml portions of acetic acid. The flask was shaken, and the toluene layer further washed with 50 ml distilled water (3 times) and dried ($CaCl_2$). Five ml of this toluene solution was pipetted into a counting tube supplied from Packard Co., diluted with 10 ml POPOP-PPO scintillator solution of toluene and the tritium activity measured by Packard Model 314A Tri-carb liquid scintillation counter with the reference of known activity of tritiated water. Typical kinetic example is shown in Table 3.

In the separate experiments using H-compounds, it was confirmed that the compounds could be recovered quantitatively without any detectable decomposition or side reaction under the conditions of the exchange kinetics listed in Table 1.

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