An Instance of a Stereoselective Isotopic Exchange Reaction

By E. BULLOCK, J. M. W. SCOTT, and P. D. GOLDING

(*Memorial University of Newfoundland, St. John's, Newfoundland, Canada*)

RECENTLY Wolfe and his co-workers[1,2] have reported some observations concerning the reactivity of the methylene protons of benzyl methyl sulphoxide (BMSO) towards isotopic exchange in 1M-NaOD/D_2O and have shown that the methylene protons in this compound differ in reactivity by a factor of fourteen.

In conjunction with another study we have examined qualitatively the kinetics of deuterium–hydrogen exchange of [$\alpha\alpha$-$^2H_2$]phenylsulphoxyacetic acid in pure water. This reaction shows

$$\underset{\text{(I)}}{PhSO{\cdot}CD_2{\cdot}CO_2H} \rightarrow \underset{\text{(II)}}{PhSO{\cdot}CHD{\cdot}CO_2H} \rightarrow PhSO{\cdot}CH_2{\cdot}CO_2H \quad \text{(III)}$$

certain features in common with the studies mentioned above, but since the discrepancy in the reactivity of the methylene deuterons in (I) appears to be less than in the case of the methylene protons of BMSO, the n.m.r. spectra of the partially exchanged acid provide some further information which was lacking in the previous study.

The kinetics of the above reaction were followed by examining the n.m.r. spectra of samples of the deuterated acid which had been left in contact with pure water for various periods of time at room temperature. Samples of the partially exchanged acid were isolated from the solvent by freeze-drying, to minimise further exchange during re-isolation. The n.m.r. spectra of the recovered samples were examined in D_2O, $(CD_3)_2SO$ (DMSO), and slightly moist $CF_3{\cdot}CO_2H$(TFA)/C_6H_6. The methylene absorption of (III) in D_2O is a singlet, but in the other solvents mentioned above this group appears as an AB quartet. The coupling constants and chemical shifts on the τ-scale for this compound are reported in the Table.

Examination of the n.m.r. spectrum of the partially exchanged acid in the nonaqueous solvents revealed the four peaks appropriate to the protium acid together with two further relatively broad peaks of *unequal* intensity, the chemical shifts of which were close to, but did not exactly

TABLE

The chemical shifts and coupling constant of the methylene protons appropriate to isotopically substituted phenylsulphoxyacetic acid

Acid	Solvent	τ-Value		J_{AB}
		CH_2 (A)	CH_2 (B)	
$PhSO{\cdot}CH_2{\cdot}CO_2H$	$CF_3{\cdot}CO_2H/C_6H_6$	6·36	6·56	15·0 c./sec.
(I)	$(CD_3)_2SO$	5·99	6·10	14·5 c./sec.
		†CH (a)		
*$PhSO{\cdot}CHD{\cdot}CO_2H$ (a)	$CF_3{\cdot}CO_2H/C_6H_6$	6·32		—
(IIa)	$(CD_3)_2SO$	6·13		—
		†CH (b)		
	$CF_3{\cdot}CO_2H/C_6H_6$	6·62		—
*$PhSO{\cdot}CHD{\cdot}CO_2H$(b) (IIb)	$(CD_3)_2SO$	5·98		—

* The two diastereoisomers of $PhSO{\cdot}CHD{\cdot}CO_2H$ are arbitrarily designated (a) and (b).

† The relative position of the n.m.r. peaks of CHD (a) and CHD (b) appear to invert in the two nonaqueous solvents used in the investigation. In a wide range of TFA/DMSO mixtures the n.m.r. spectrum of (I) is a singlet. The AB quartet appears only at the DMSO-rich or TFA-rich compositions.

correspond with, the shifts of the methylene hydrogens of protium acid. Furthermore, the intensity of the broad peaks varied with time reaching a maximum and then disappearing as the conversion of the deuterium into the protium acid became complete (see Figure).

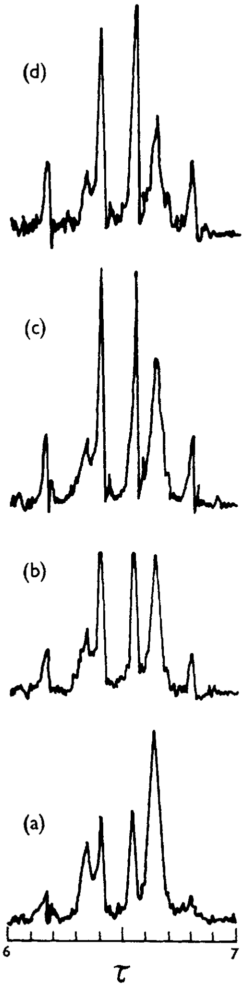

FIGURE. *N.m.r. spectra of partially exchanged* $PhSO{\cdot}CD_2{\cdot}CO_2H$ *at various times*; (a) 29 *hr.*, (b) 42 *hr.*, (c) 54 *hr.*, (d) 66 *hr.*

We consider that the two n.m.r. absorptions superimposed on the spectrum of the protium acid correspond to the diastereoisomers of $PhSO{\cdot}CHD{\cdot}CO_2H$, since the protium acid (III) can be resolved[3] and the group $CHD{\cdot}CO_2H$ is asymmetric, *i.e.*, (II) contains two directly linked asymmetric tetrahedral groups. The peaks appropriate to each of the diastereosiomers are broadened, presumably by an unresolved (triplet) coupling to deuterium in each case (*cf.* ref. 1) and the unequal intensity is a consequence of differing exchange rates for the two methylene deuterons. Although we have not attempted a quantitative assessment of the relative reactivities of the deuterons in (I) it is probable that the discrepancy in rates is less than in the case of the methylene protons of BMSO. We draw this conclusion from the following considerations. The difference in the chemical shifts of the methylene protons in both (III) and BMSO are similar, and the coupling constants are also of a similar magnitude. Hence the only other factor which can influence the possible observation of both diastereoisomers by proton resonance experiments is the relative rates of exchange of the two protons or deuterons. The most favourable situation for the observation of both diastereoisomers is when the protons or deuterons are of equal reactivity, since this implies that the diastereoisomers will be formed and removed (neglecting secondary isotope effects on the exchange of the second proton or deuteron) at equal rates. As the difference in reactivity of the methylene protons or deuterons increases the diastereoisomer formed by the "fast–slow" sequence will be the only isomer detected by proton resonance experiments, irrespective of whether the exchange is from D to H or *vice versa.* We therefore conclude that the methylene deuterons in (I) are closer in reactivity than the methylene protons in BMSO, since both diastereoisomers can be observed with the former compound, whereas only one diastereoisomeric proton resonance peak was observed in the case of BMSO, when this substance was treated with 1M-$NaOD/D_2O$.[1]

A conformational analysis of the exchange process (see ref. 1 and 2) suggests that the following factors may be important in determining the relative reactivity of the methylene deuterons in (I): (a) incipient carbanion–sulphur lone-pair interactions; (b) the relative orientation of the phenyl and carboxyl groups; and (c) hydrogen bonding between the carboxyl proton and the sulphoxide group. Any further discussion of the mechanism of the exchange requires a structural assignment of the "slow" and "fast" deuterons. The observation that the protons of (III) are magnetically equivalent in D_2O* and that the positions of the CHD absorption peaks for the diastereoisomers (II) are reversed on passing from perdeutero-DMSO to TFA/C_6H_6 demonstrates that structural assignments based on n.m.r. evidence

---

* The deuterons of (I) are presumably magnetically equivalent in H_2O.

alone are uncertain, since solvent effects appear to determine the chemical shifts. Hence further mechanistic discussion of this reaction based on the available evidence is unwarranted.

(*Received, January* 12*th*, 1967; *Com.* 038.)

---

[1] S. Wolfe and A. Rauk, *Chem. Comm.*, 1965, 778.

[2] A. Rauk, E. Buncel, R. Y. Moir, and S. Wolfe, *J. Amer. Chem. Soc.*, 1965, **87**, 5498.

[3] W. Piechulek and J. Suszko, *Roczniki Chem.*, 1933, **13**, 520.