and CHF (ϕ 191, 194.5, 201, 206; area $\approx$ 1), but no –CHFI.[11] The 3:1 fractions in ethanol showed $\lambda_{max} \approx 256$ mμ, $\epsilon \approx 370$.

Anal. Calcd. for $C_7H_6F_6I$: C, 25.1; H, 2.69; F, 34.2; I, 38.0. Found: C, 24.9; H, 2.58; F, 34.1; I, 37.8.

The elimination reaction of 3b–3c was carried out by dissolving the mixture (18.0 g., 0.054 mole) in ethanol (60 ml.) containing triethylamine (10.0 g., 0.099 mole) and refluxing. After 7 days, v.p.c. analysis indicated almost complete reaction with formation of a single, new peak (retention time 7.8 min. at 125°, helium flow rate 150 ml./min. with analytical column described above). The reaction mixture was poured into water (200 ml.) causing separation of a red oil which was washed with cold water (3 × 25 ml.), dilute hydrochloric acid (2 × 25 ml.), and dilute sodium carbonate solution (2 × 25 ml.). The organic layer was steam distilled and the colorless oil which separated in the distillate dried over anhydrous sodium carbonate to yield an olefin, $C_7H_5F_6$ (6.8 g., 62% yield); C=C in infrared spectrum at 5.9 μ.

Anal. Calcd. for $C_7H_8F_6$: C, 40.7; H, 3.89; F, 55.4. Found: C, 40.7; H, 4.05; F, 55.2.

Ozonization was carried out by dissolving the olefin (0.50 g., 2.43×10^{-3} mole) in a mixture of chloroform (10 ml.) and methylene chloride (2 ml.), cooling to −78° in a Dry Ice trap, and passing in O_3 (3% in O_2) until the solution turned blue (40 min.). The solution of ozonide was poured slowly into water (10 ml.) and stirred 45 min. To the solution was added sodium hydroxide (0.2 g., 4.0×10^{-3} mole) and silver oxide (2.0 g., 5.0×10^{-3} mole) and the mixture heated in a steam bath for 1 hr. After filtering the reaction mixture, the organic solvents were removed under vacuum and the aqueous solution strongly acidified with hydrochloric acid. The filtrate was extracted with ether (3 × 50 ml.), the ether solution dried ($CaCl_2$) and evaporated to yield an acid, $C_6H_7F_5O_2$ (0.45 g., 90% yield), which was recrystallized from chloroform; m.p. 97–95° (partly), >285° (remainder). The infrared spectrum showed carbonyl absorption at 5.70 μ indicating an α-fluoro substituent.[12] The F^{19} n.m.r. spectrum was consistent with this assignment but was not in itself definitive.

Anal. Calcd. for $C_6H_7F_6O_2$: C, 34.9; H, 3.4; F, 46.1; neut. equiv., 206. Found: C, 35.3; H, 3.5; F, 45.8; neut. equiv., 210.

Telomerization in the Presence of CF_3CH_2CHFI.—This run was carried out as run 5, Table I, except that 10.0 g. of 1:1 telomer CF_3CH_2CHFI was also added. Fractionation yielded 8.6 g. of 1:1 telomer compared to control runs yielding 4–7 g. Therefore, at least half of the initial 10.0 g. of telomer must have reacted, presumably by chain transfer.

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[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY AND PHARMACEUTICAL CHEMISTRY, UNIVERSITY OF FLORIDA, GAINESVILLE, FLA.]

Hydrogen Chemical Shifts of 3-Alkyl and 3-Phenyl Sydnones

BY K. D. LAWSON, WALLACE S. BREY, JR., AND L. B. KIER

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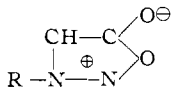
Proton resonance spectra of five 3-alkyl sydnones and 3-phenyl sydnone have been determined in acetone and in chloroform solution. The ring hydrogen chemical shifts in chloroform solution are strongly concentration dependent in a manner which indicates that the chloroform solvent is breaking down aggregates of solute molecules. The resonances of the hydrogens in the substituent group which are α to the sydnone ring fall strikingly far downfield, indicating an unshielding by the aromatic ring current as well as by the electronegative effect of the nitrogen atom in the ring.

The sydnone ring system is an unusual one, for it cannot be represented satisfactorily by any canonical structure which does not place formal charges somewhere in the ring. The conventional formulation of a 3-substituted sydnone is



The chemical and spectroscopic properties of molecules containing the sydnone ring have been interpreted to indicate a six-electron aromatic system, delocalized over the five atoms of the ring.[1] It appeared of importance to determine the relationship of the n.m.r. chemical shifts in various sydnones substituted in position 3 to the behavior of these compounds as aromatic molecules. Of interest also is the relation of the physical properties of these materials to their pharmacological activity as central nervous system stimulants.[2–4]

Experimental

Preparation of the materials was described in an earlier paper,[3] and various physical properties of the compounds which had not been previously reported were tabulated there. Nuclear magnetic spectra of solutions of several sydnones substituted in position 3 were determined for the compounds in solution in acetone and in deuterated chloroform, using a Varian HR-60 Model V4300-2 spectrometer operating at 60.0 Mc. The shift of the ring hydrogen in each of the compounds was very carefully determined by superimposing the audiofrequency sideband of the internal reference, tetramethylsilane (TMS), on the appropriate sydnone resonance peak, and observing the superimposed peaks on the oscilloscope. The audiofrequency used was measured simultaneously with an electronic counter. The average of replicate measurements was computed; the average deviation of ten replications was 0.2 to 0.3 c.p.s. The shifts were extrapolated to infinite dilution from results on solutions of varying concentration. Some determinations were also made of the shifts of hydrogens in the substituent alkyl and phenyl groups, and of the resonance position of the proton in $CHCl_3$ as the solvent for isopropyl syndone.

Figures 1 and 2 show the data for the ring hydrogen chemical shifts in the two solvents. In these figures, the frequency difference from TMS is plotted as measured, in order to represent accurately the numerical values obtained. The extrapolated values are compiled in Table I. In the discussion which follows, and in Table II, which represents the data for the shifts of the substituent groups, the results are given for convenience as τ-values,[5] although it is to be noted that this is not quite legitimate, since the τ-scale was originally defined in terms of the shift at low concentrations in carbon tetrachloride as the solvent.

TABLE I

CHEMICAL SHIFTS OF THE RING HYDROGENS OF 3-SUBSTITUTED SYDNONES, EXTRAPOLATED TO INFINITE DILUTION

Substituent	Shift from TMS in acetone, c.p.s.	Shift from TMS in $CDCl_3$, c.p.s.
Methyl	−401.5	−382.5
Ethyl	−405.5	−381.5
Isopropyl	−405.9	−379.3
t-Butyl	−407.9	−377.0
t-Octyl[a]	−413.2	−376.5
Phenyl	−438.9	−405.8

[a] $\alpha,\alpha,\gamma,\gamma$-Tetramethylbutyl.

Discussion

The first feature of the spectra to be considered is the general location of the ring hydrogen resonance.

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(3) L. B. Kier and D. Dhawan, *J. Pharm. Sci.*, **51**, 1058 (1962).

(4) D. Dhawan and L. B. Kier, *ibid.*, in press.

(5) G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

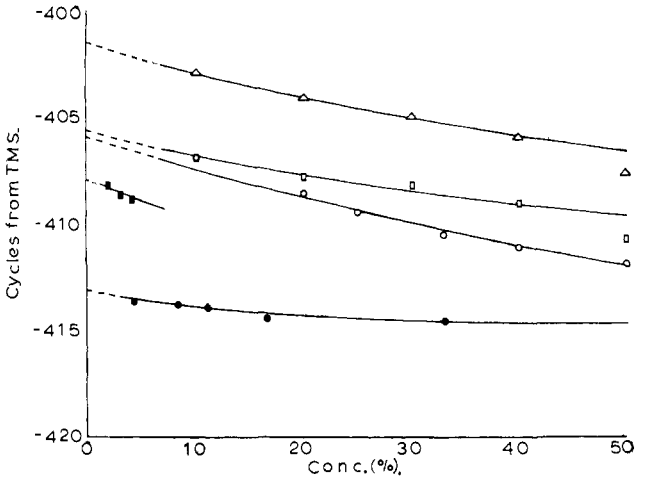

Fig. 1.—Chemical shifts of ring hydrogens of sydnones in acetone. Concentrations are expressed in per cent by weight. Symbols: △, methyl; □, ethyl; ○, isopropyl; ■, *t*-btuyl; ●, *t*-octyl.

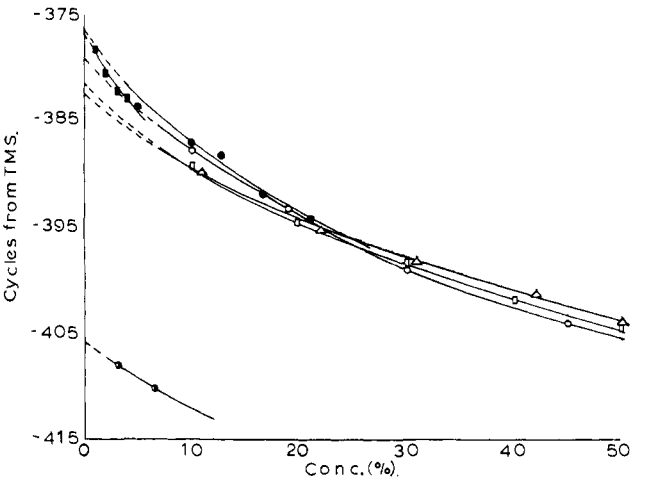

Fig. 2.—Chemical shifts of ring hydrogens of sydnones in $CDCl_3$. Concentrations are expressed in per cent by weight. Symbols: △, methyl; □, ethyl; ○, isopropyl; ■, *t*-butyl; ●, *t*-octyl; ◑, phenyl.

Because of the anisotropy of the aromatic ring in benzene, the ring hydrogens in that compound have a τ-value of 2.73, somewhat downfield from the resonance for hydrogens attached to doubly-bonded carbons in nonaromatic molecules. The range of values for the hydrogen in position 4 in the 3-alkyl sydnones is from about τ = 3.1 to 3.7. This is consistent with aromatic character of the sydnone ring; however, the electron-withdrawing effects of the nearby nitrogen and oxygen atoms might be sufficient to shift the resonances downfield from the usual location for olefinic hydrogens to the position observed. Thus the magnitude of the ring hydrogen shift is not clear evidence for the aromatic character of the ring; other evidence for aromaticity will, however, be discussed later.

TABLE II

CHEMICAL SHIFTS OF HYDROGENS IN SUBSTITUENT GROUPS IN 3-SUBSTITUTED SYDNONES

Group	Solvent	Concn., per cent by weight	Shift, τ
CH_3	$CDCl_3$	12.5	5.90
	Acetone	50.0	5.80
CH_3CH_2	$CDCl_3$	10.0	8.48
	Acetone	50.0	8.37
CH_3CH_2	$CDCl_3$	10.0	5.66
	Acetone	50.0	5.38
$(CH_3)_2CH$	$CDCl_3$	7.5	8.40
$(CH_3)_2CH$	$CDCl_3$	7.5	5.29
$CH_3CH_2CH(CH_3)$	$CDCl_3$	20.0	8.33
	Acetone	10.0	8.35
$CH_3CH_2CH(CH_3)$	$CDCl_3$	20.0	9.02
	Acetone	10.0	9.07
$CH_3CH_2CH(CH_3)$	$CDCl_3$	20.0	8.02
	Acetone	10.0	8.00
$CH_3CH_2CH(CH_3)$	$CDCl_3$	20.0	5.46
	Acetone	10.0	5.40
$(CH_3)_3C$	$CDCl_3$	Satd.	8.33
$(CH_3)_3CCH_2C(CH_3)_2$	$CDCl_3$	25.0	9.06
$(CH_3)_2CCH_2C(CH_3)_2$	$CDCl_3$	25.0	8.24
$(CH_3)_3CCH_2C(CH_3)_2$	$CDCl_3$	25.0	7.99
C_6H_5	Acetone	8.0	2.12[b]

[a] Shift given is for italicized *H*. [b] Position of tallest peak in multiplet.

The hydrogen on the sydnone ring of the 3-phenyl compound is considerably unshielded compared to the corresponding hydrogens in the other compounds. This is strong evidence for the near coplanarity of the phenyl ring with the sydnone ring,[6] since the effect of the phenyl would, in this geometry, be an anisotropic unshielding of hydrogens attached to the other ring. Data for the shift of the ring hydrogen of this compound in acetone fall outside the range of Fig. 1. Determinations at 8, 6, and 4% concentration all fall between 438.5 and 438.8 c.p.s. below the reference, so that the effect of phenyl *vs.* alkyl is about the same in acetone as it is in chloroform.

The next significant aspect of the results is the relatively large concentration dependence of the chemical shift in $CDCl_3$ solution, particularly as compared with the comparatively small dependence in acetone solution. Since the use of an internal standard corrects for all but perhaps a few tenths of a cycle of the shift produced by changing magnetic susceptibility of the solution, the concentration dependence must be related to intermolecular interactions in the solution. These may include interactions between solute molecules or between solvent and solute. To determine whether the solvent was involved, the chemical shift of the hydrogen in $CHCl_3$ was measured as a function of the concentration of isopropyl sydnone as solute. As the concentration of sydnone is increased from 0 to 50% by weight, the solvent peak moves from τ = 2.74 to 2.25. This downfield shift is a very strong indication that the chloroform is forming hydrogen bonds to the solute; the expected point of attachment of the hydrogen bond to the sydnone is at the relatively negative, exocyclic oxygen atom. Acetone as a solvent would not be able to form a hydrogen bond of this sort.

The upfield shift of the sydnone hydrogen as the amount of $CDCl_3$ in the solution increases cannot be explained as the result of hydrogen bonding of this ring hydrogen to the $CDCl_3$ solvent, because this would lead to a downfield shift with increasing concentration of solvent. Presumably the formation of the hydrogen bond between the hydrogen of the solvent and the negative part of the ring would draw electron density away from the ring and likewise produce a downfield shift. The only remaining alternative explanation is that the sydnone is aggregated in concentrated solutions in chloroform and in all solutions in acetone, and that the chloroform, by forming hydrogen bonds, can break up the aggregates when it is

(6) H. Bärnighausen, F. Jellinek, and A. Vos, *Proc. Chem. Soc.*, 120 (1961).

present in excess. The hydrogen bond of the sydnone to the solvent would then withdraw less electron density from the sydnone ring than does the linkage to another sydnone molecule. In confirmation of this picture, we note that the sydnone ring chemical shifts seem to be approaching common values in both solvents at high concentrations; these would be the values characteristic of the aggregates.

We next examine the effect of the substituent alkyl group on the chemical shifts of the ring hydrogens. Using the values extrapolated to zero concentration we find for the solutions in acetone one order, as shown in Table I, and for the solutions in chloroform almost exactly the reverse order. The order found in the acetone solutions is that expected from the electron-releasing properties of the alkyl groups concerned, and is similar to that found in monoalkylbenzenes: the more hydrogens attached to the carbon α to the aromatic ring, the more shielded is the hydrogen attached to the adjacent carbon in the aromatic. The reversal of the order in chloroform solutions would then be connected with the relative tendency of the chloroform to break up the aggregates of the molecules of differing size rather than with any property of the sydnone. In this respect, it must be emphasized that there is some latitude in the extrapolation of points in the case of the chloroform solutions, although the order of extrapolated shifts should be correct. It would appear that the aggregates of the molecules with larger side chains are more easily disrupted than those with smaller side chains, which is quite reasonable.

The final point in discussion of the spectra concerns the shifts of the hydrogens in the side chains. The most striking feature is the low field at which the hydrogens on the carbon α to the sydnone ring appear in the spectrum. For a methyl group in an aliphatic compound,[7] the usual value is $\tau = 9.1$; for a methyl group in toluene, 7.7; and for the methyl group attached to nitrogen in an amine, 7.8–7.9. But for methyl sydnone, the methyl peak appears below τ of 6, the exact position depending on the solvent. The methylene hydrogen chemical shift is about $\tau = 8.75$ in an aliphatic hydrocarbon, 7.38 in ethyl benzene, 7.4 to 7.6 for the α-hydrogens in alkyl amines, and approximately 5.5 in ethyl sydnone. For the methine hydrogens in isopropyl and *sec*-butyl sydnone, the shifts are in the range of $\tau = 5.3$ to 5.4, compared with a value in isopropylamine of 7.13. Finally, the phenyl protons in phenyl sydnone give a complex pattern with an average shift quite a bit below the normal position of unsubstituted benzene. The value of $\tau = 2.1$ may be compared with a value of 3.4 for the ring hydrogens in aniline.

All these data represent, then, a very strong unshielding of those protons of the substituent group which are located near the sydnone ring. This may best be interpreted as representing the combined unshielding effects of the electronegative nitrogen atom to which the group is attached, with the electronegativity accentuated by the positive charge on the ring, and of the ring current in the aromatic sydnone structure. This result represents the strongest proof, from the n.m.r. investigation, of the aromaticity of sydnones.

Acknowledgment.—This investigation was supported in part by PHS Research Grant Number GM-09343-02 from the Institute of General Medical Sciences, Public Health Service.

(7) Chemical shifts cited here are taken from other work in these laboratories and from G. V. D. Tiers, "Characteristic Nuclear Magnetic Resonance Shielding Values," Minnesota Mining and Manufacturing Company, 1958.

[JOINT CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF STANFORD UNIVERSITY, STANFORD, CALIF., AND OF COLUMBIA UNIVERSITY, NEW YORK 27, N. Y.]

Optical Rotatory Dispersion Studies. XCII.[1] Some Observations on the Conformation of *cis*-10-Methyl-2-decalones[2]

BY CARL DJERASSI, J. BURAKEVICH, J. W. CHAMBERLIN, D. ELAD, T. TODA, AND GILBERT STORK

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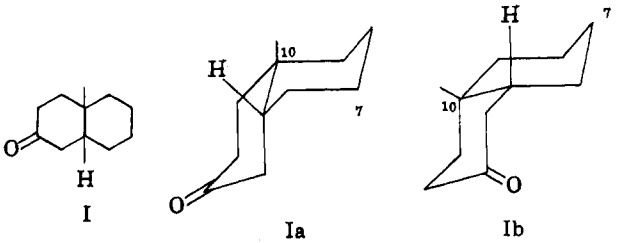
cis-Decalones can exist in two all-chair conformations, commonly termed the "steroid" and "nonsteroid" forms. The latter conformation has been proposed for certain *cis*-10-methyl-2-decalones substituted at C-7 (*e.g.*, 7,7-dimethyl), since the generally accepted tenets of conformational analysis clearly favor such conformations. In the present work, optically active antipodes of known absolute configuration of such *cis*-decalones have been synthesized and it has been demonstrated by optical rotatory dispersion measurements that, contrary to the earlier held views, the "nonsteroid" conformation cannot play an important role.

The conformational problem among *cis*-2-decalones is a vexing one. Taking the bicyclic analog of the 3-keto 5β-steroids, *cis*-10-methyl-2-decalone (I) as an example, two all-chair forms (Ia and Ib) are possible, of which only the former can exist among steroids because of the additional B/C ring juncture.

Initially, it had been suggested[3] that *cis*-2-decalone would assume the "nonsteroid" conformation Ib, but on the basis of subsequent optical rotatory dispersion measurements[4] it was suggested that in *cis*-10-methyl-2-decalone, the "steroid" form predominates. This



I Ia Ib

latter conclusion was based on the similarity in shape of the O.R.D. curves of the rigid model 3-keto 5β-steroid and that of *cis*-10-methyl-2-decalone (I) as well as on an analysis of the data by the octant rule.[5]

(1) Paper XCI: K. M. Wellman, R. Records, E. Bunnenberg, and C. Djerassi, *J. Am. Chem. Soc.*, **86**, 492 (1964).

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