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RECEIVED MARCH 26, 1964

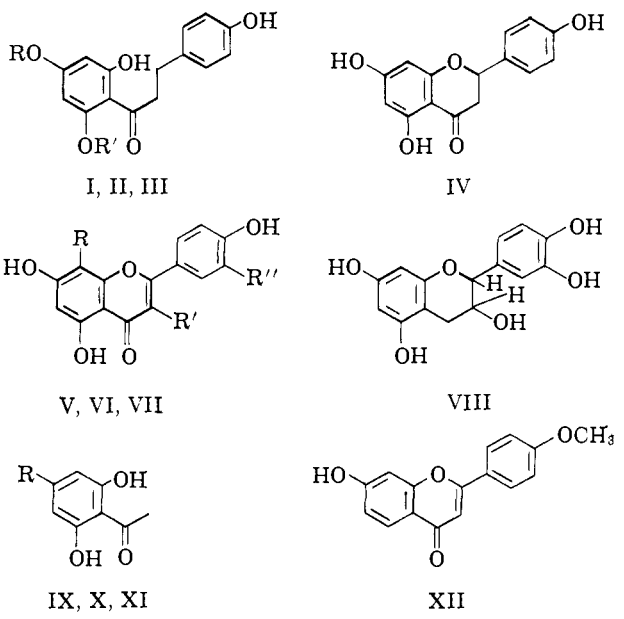
Nuclear Hydrogen–Deuterium Exchange in Resorcinols and Related Compounds in Weakly Alkaline Solution

Sir:

Under forcing alkaline conditions all hydrogen atoms of the phenoxide anion can be replaced by deuterium,[1,2] while under somewhat less stringent conditions only the *ortho* and *para* hydrogens exchange.[3] In either case the reaction is slow. We have found that the presence of a second hydroxy group, when oriented *meta*, greatly enhances the rate of exchange; mild reaction conditions then suffice for complete (*i.e.*, equilibrium) exchange of the *ortho* and *para* hydrogens.

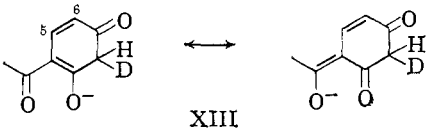
The exchange was monitored by n.m.r. spectroscopy in deuterium oxide solutions of approximate pH 9. In some cases, after the exchange was complete, the sample was diluted with water and the reappearance of the peak(s) observed.[4] The spectra of phenol, catechol, and hydroquinone in alkaline deuterium oxide did not change during several hours and were the same as their spectra in water. In contrast, the exchange of protons 2, 4, and 6 of resorcinol reached equilibrium in 1 hr. at pH *ca.* 8 and in 10 min. at pH *ca.* 11. The hydrogens in phloroglucinol also exchanged rapidly. Other compounds, listed below, showed the following behavior: (1) the combined activating effects of two or more *meta*-oriented OH groups sufficed for ready exchange of protons *ortho* and *para* to them (I–XI); (2) protons of aromatic rings containing only one OH group (I–VI) or two adjacent OH groups (VII and VIII) did not exchange; (3) the OR of the pyrone ring *meta* to an OH group did not serve in lieu of the second OH (none of the protons in XII exchanged); (4) the various protons α to a ketone (I–IV, IX–XI) exchanged, but much more slowly than the aromatic ones (see below, however).

The exchangeable nuclear protons in compounds III–V, VII, and VIII are nonequivalent and the proton absorbing at higher field exchanged more rapidly.[5] In 4-acetylresorcinol the exchangeable protons can be distinguished from each other since the signal due to H-6 exhibits the usual *ortho* coupling of ~9 c.p.s. The proton flanked by the two OH groups (H-2) exchanged readily, but H-6 was replaced rapidly only on heating; the methyl ketone protons exchanged more rapidly



I, phloretin, R = R′ = H. II, naringin dihydrochalcone, R = 2-*O*-α-L-rhamnosyl-β-D-glucosyl; R′ = H. III, phloridzin, R = H; R′ = β-D-glucosyl. IV, naringenin. V, apigenin, R = R′ = R″ = H. VI, vitexin, R = *C*-β-D-glucosyl; R′ = R″ = H. VII, quercitrin, R = H; R′ = α-L-rhamnosyloxy; R″ = OH. VIII, *d*-catechin. IX, R = H. X, R = 2-*O*-α-L-rhamnosyl-β-D-glucosyloxy. XI, R = OH. XII, pratol.

than H-6, but much more slowly than H-2. The slowness of H-6 exchange becomes understandable if delocalization of the negative charge in the intermediate XIII is greatly enhanced by the acetyl group. Formation of an sp^3 center at C-6 precludes such interactions.



XIII

In 4-carboxyresorcinol H-2 also exchanged faster than H-6, and in both compounds the peak due to H-2 was slightly upfield. However, in 4-chlororesorcinol, H-6 exchanged faster and its absorption was slightly upfield; and in 5-carboxyresorcinol H-4 and H-6 exchanged faster than H-2, although H-2 absorbed at higher field. Thus, no general direct relationship exists between the effect of substituents on the chemical shift of a particular proton and their effect on the rate of exchange.

Several naphthalenediols were examined to ascertain whether all protons that can, in principle, be activated by both OH groups do exchange. As expected, no exchange occurred in 1,5-naphthalenediol. While H-1 and H-8 in 2,7-naphthalenediol were rapidly replaced by deuterium, the other protons were unaffected even on heating.[6] In 1,6-naphthalenediol H-2, H-4, and H-5 exchanged.[7] A path for exchange is *via* ketone–enolate

(1) A. I. Shatenshtein and A. V. Vedeneev, *Zh. Obshch. Khim.*, **28**, 2644 (1958); *Chem. Abstr.*, **53**, 5836 (1959).

(2) G. E. Hall, E. M. Libby, and E. L. James, *J. Org. Chem.*, **28**, 311 (1963).

(3) A. P. Best and C. L. Wilson, *J. Chem. Soc.*, 28 (1938); C. K. Ingold, C. G. Raisin, and C. L. Wilson, *ibid.*, 1637 (1936); *cf.*, however, P. A. Small and J. H. Wolfenden, *ibid.*, 1811 (1936).

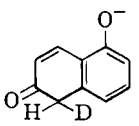
(4) For comparison, spectra of most compounds were determined in water at the same pH. The spectra varied according to the amount of anion present: signals due to protons *ortho* to an OH group were always shifted upfield as more of the anion was formed, while signals due to the *meta* protons were either unaffected or shifted downfield.

(5) In naringenin (IV) the chemical shifts of these protons coincided so that a difference in the exchange could not be ascertained. Catechin (VIII) decomposed at higher pH, but could be recovered from solution at pH 8 in which its exchange was very fast.

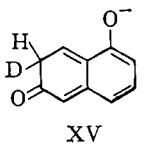
(6) Exchange occurred also in 2-naphthol. By analogy with 2,7-naphthalenediol, it was assumed that this takes place at H-1. R. F. W. Cieciuch and P. C. Morrison have analyzed the splitting pattern of the 2-naphtholate ion and determined that the exchange does occur at H-1. We thank Dr. Cieciuch for permission to cite these results in advance of publication.

(7) The positions of exchange were deduced as follows: after exchange the spectrum showed a typical AB system ($J \sim 9$ c.p.s.) as well as a singlet. Since the low-field part of the AB system was also apparent prior to exchange (the high-field part overlapped with the complex multiplet due to the other protons except H-2 which appeared as a quartet at higher field) and since H-8 is the only proton in the nondeuterated compound that would ordinarily be expected to couple with only one proton, *i.e.*, H-7, the AB system in the spectrum of the deuterated compound must be due to H-7 and H-8. The singlet is assigned to the *meta* hydrogen, H-3.

intermediates. That such intermediates are feasible is shown by the fact that the anion of 1,3-naphthalenediol exists entirely as a ketone–enolate.[8] In intermediates postulated for the exchangeable protons, the aromaticity of one ring is retained in at least one of the resonance hybrids (*e.g.*, XIV); the failure of the other *ortho* protons to exchange can be attributed to loss of the benzenoid character of both rings (*e.g.*, XV).[9]



XIV



XV

Regardless of mechanism, the exchange described above should be useful in structural elucidations of complex phenols and is, of course, suitable for the preparation of various deuterated aromatic compounds.

(8) E. S. Hand and R. M. Horowitz, unpublished results. It is of interest that H-2 and H-4 of 1,3-naphthalenediol exchange rapidly in deuterium oxide solution even in the absence of base.

(9) The fact that 5-nitro-1-naphthol has a pK_a not very different from that of 1-naphthol itself has been rationalized in similar terms: K. C. Schreiber and M. C. Kennedy, *J. Am. Chem. Soc.*, **78**, 153 (1956).

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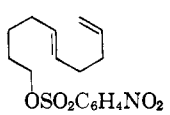
ELLI SMAKULA HAND[10]
ROBERT M. HOROWITZ

RECEIVED MARCH 9, 1964

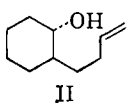
Cationic Cyclizations Involving Olefinic Bonds. V.[1] Solvolysis of *cis*-5,9-Decadienyl *p*-Nitrobenzenesulfonate

Sir:

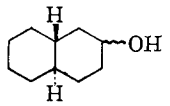
In the formolysis of *trans*-5,9-decadienyl *p*-nitrobenzenesulfonate (I),[2] the processes resulting in the formation of cyclic products were highly stereoselective, possibly stereospecific. Thus (after cleavage of formate esters) *trans*-2-(Δ^3-butenyl)cyclohexanol (II) was formed to the exclusion of the *cis* isomer, while the decalols were exclusively those with *trans*-fused rings (III). It was not possible to decide whether this stereochemical consequence was the result of a synchronous process or of a stereoselective equatorial attack of nucleophile on a cationic intermediate like IV.[3] We now wish to present evidence which supports the former mechanism.



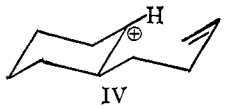
I



II



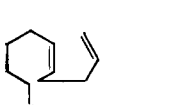
III



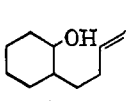
IV

The formolysis of *cis*-5,9-decadienyl *p*-nitrobenzenesulfonate (V) has now been examined. If this reaction, as well as that of the *trans* isomer, were to proceed by a stepwise mechanism involving the intermediacy of a common cation like IV, both isomeric substrates would yield the same cyclic products.

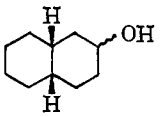
5,9-Decadiynol[2] was selectively hydrogenated over Lindlar catalyst to yield *cis*-5,9-decadienol which was purified by preparative vapor phase chromatography, n^{20}D 1.4637. *Anal.* Found: C, 77.9; H, 11.8. The *p*-nitrobenzenesulfonate V, m.p. 26.5–27° (*Anal.* Found: C, 56.5; H, 6.4; N, 4.4), was solvolyzed by heating a 0.02 *M* solution in anhydrous formic acid containing pyridine (0.04 *M*) for 1 hr. at 75°. The formate esters were reductively cleaved by treatment with lithium aluminum hydride, and the resulting product was analyzed by vapor phase chromatography.[2] The products were identified by peak enhancement experiments and by infrared spectral comparison with authentic specimens.[2] Since the solvolysis of the *trans* sulfonate ester had not been carried out previously under these conditions, it was re-examined for direct comparison with the *cis* isomer. The relative proportions of alcohols from the *trans* sulfonate ester were as follows: 3% of 1-(Δ^3-butenyl)cyclohexanol, 10% of Δ^3-butenylcyclopentylcarbinol, 57% of *trans*-2-(Δ^3-butenyl)cyclohexanol (II), 8% of *trans*-5,9-decadienol, 5% of *trans-anti*-2-decalol, 14% of *trans-syn*-2-decalol, and 3% total of several unidentified components. *There was no detectable amount of the cis monocyclic alcohol VI or the cis decalols VII among the products.* These results are quite comparable to those obtained with 80% formic acid.[2] Formolysis of the *cis* sulfonate ester V gave the following relative proportions of alcohols: 3% of 1-(Δ^3-butenyl)cyclohexanol, 8% of Δ^3-butenylcyclopentylcarbinol, 56% of *cis*-2-(Δ^3-butenyl)-cyclohexanol (VI), 16% of *cis*-5,9-decadienol, 13% of an inseparable mixture of *cis-syn-* and *cis-anti*-2-decalol, and 4% total of several unidentified components. *There was no detectable amount of the trans monocyclic alcohol II or of the trans decalols III among the products.* *cis*-2-(Δ^3-Butenyl)cyclohexanol (VI) was identified by comparison with an authentic specimen, n^{20}D 1.4770 (*Anal.* Found: C, 77.8; H, 11.75), which was prepared by reduction of the corresponding ketone with lithium tri-*t*-butoxyaluminum hydride followed by preparative vapor phase chromatographic separation from the predominant *trans* isomer II.



V



VI



VII

Since the cyclizations of I and V proceed stereochemically in exactly the opposite sense, a common cationic intermediate IV cannot possibly be involved. If the solvolyses of both I and V proceed by the same basic mechanism—an assumption which is reasonable, particularly in view of the strikingly similar type of product distribution—then it follows that the cyclizations must either be concerted processes or involve cationic intermediates (*e.g.*, bridged carbonium ions) which retain the stereochemical integrity of the respective substrates. A decision between these latter two

(1) Paper IV of this series: W. S. Johnson, W. H. Lunn, and K. Fitzi, *J. Am. Chem. Soc.*, **86**, 1972 (1964).

(2) W. S. Johnson, D. M. Bailey, R. Owyang, R. A. Bell, B. Jacques, and J. K. Crandall, *ibid.*, **86**, 1959 (1964).

(3) W. S. Johnson, S. L. Gray, J. K. Crandall, and D. M. Bailey, *ibid.*, **86**, 1966 (1964).