Hydrogen Bonding in Phenols. VII.*
Synthesis and Intermolecular Hydrogen Bonds of
2-Hydroxy-2′,4′-disubstituted Stilbenes

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The synthesis of six 2-hydroxy-2′,4′-disubstituted stilbenes (2-hydroxy-
-2′,4′-dinitrostilbene, 2-hydroxy-2′-cyano-4′-nitrostilbene, 2-hydroxy-2′-ni-
tro-4′-aminostilbene, 2-hydroxy-2′-cyano-4′-aminostilbene, 2-hydroxy-2′-ni-
tro-4′-isothiocyanatostilbene, 2-hydroxy-2′-cyano-4′-isothiocyanatostilbene)
has been described. The infrared spectra of compounds prepared point to the
existence of unusually strong intermolecular hydrogen bonds in chloroform
solutions. All spectral measurements reveal that these compounds exist
as "dimers" containing two hydrogen bonds in the geometrically favourable
20-membered rings. Also the infrared and ultraviolet spectra of compounds
investigated are interpreted.

Phenols are known to associate in nonpolar or polar solvents by hydrogen bonding,
the aggregates so formed have no great stability [1, 2]. However, some phenols bearing
an electron-rich substituent in the *ortho* or *meta* position relative to the phenolic hydroxyl
strongly associate only in those cases where a formation of hydrogen-bonded dimers
involving fourteen- or sixteen-membered rings is spatially favoured [3—5].

We have examined phenolic compounds where intermolecular association, presumably
dimeric, is unusually persistent. The compounds under investigation are compared
with other compounds showing strong self-association in polar as well as in nonpolar
solvents [3, 4]. In our previous work [4] it was reported that strong intermolecular hyd-
rogen bonds with alkyl coumarates were due to the extended conjugated system by
hydrogen bonding, enticing us to find other compounds of a similar type. 2-Hydroxy-2′,4′-
-disubstituted stilbenes were cases in point, being discussed in more detail.

Experimental

Preparation of 2-hydroxy-2′,4′-disubstituted stilbenes

Stilbene nitro derivatives were prepared starting from substituted *p*-nitrotoluenes
with salicylaldehyde according to *Pfeiffer* [6]. The synthesis of 2-methyl-5-nitrobenzo-
nitrile as intermediate was performed by Sandmeyer reaction from 2-methyl-5-nitroanili-
ne [7]

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* For Part VI. see Ref. [4].
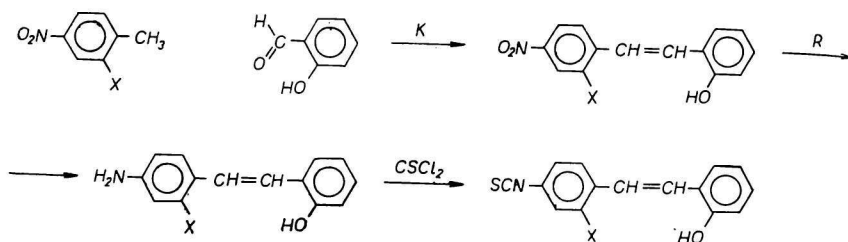
X = NO$_2$, C≡N; K — condensation; R — partial reduction.

Recrystallization of compounds *I* and *II* from ethanol afforded pure compounds *I*, m.p. 189—191°C. For C$_{14}$H$_{10}$N$_2$O$_5$ (286.23) calculated: 58.74% C, 3.52% H, 9.79% N found: 58.62% C, 3.12% H, 9.67% N. *II*, m.p. 204.5—206°C. For C$_{15}$H$_{10}$N$_2$O$_3$ (266.25) calculated: 67.66% C, 3.79% H, 10.52% N; found: 67.42% C, 3.60% H, 10.58% N

Partial reduction of 2-hydroxy-2′,4′-dinitrostilbene (I)

2-Hydroxy-2′,4′-dinitrostilbene (*I*) (0.024 mole, 7.2 g) was dissolved in ethanol (65 ml) and an aqueous solution of 25% NH$_4$OH (38 ml) was added. During two hours' heating H$_2$S was passed into the reaction mixture and a further amount of concentrated NH$_4$OH (20 ml) was added. After cooling, the precipitate obtained was filtered off, dissolved in hot ethanol (100%) and the clear solution was evaporated under reduced pressure to dryness. The amine obtained (*III*) (dark-red plates) was used without further purification in the synthesis of the appropriate isothiocyanatostilbene derivative (*V*).

Reduction of 2-hydroxy-2′-cyano-4′-nitrostilbene (II)

To glacial acetic acid (56 ml), SnCl$_2$ (16 g) was added and dry HCl was passed until the whole amount of SnCl$_2$ was dissolved. To the clear solution a fine powdered nitro compound *II* (0.01 mole, 3 g) was added with stirring. The reaction mixture was left stand overnight at room temperature, then heated on a water bath for 1 1/2 hour, and freed from HCl by the addition of 10% NaOH. The precipitate obtained was filtered off, dried, powdered and extracted with hot benzene, giving after cooling the precipitate (light-yellow plates) *IV*, which was used without further purification in the synthesis of appropriate isothiocyanatostilbene derivative (*VI*).

Preparation of 2-hydroxy-2′-X-4′-isothiocyanatostilbenes

The appropriate amine (0.01 mole, 3 g) dissolved in CHCl$_3$ was stirred into an emulsion consisting of H$_2$O (50 ml), CHCl$_3$ (20 ml) and CSCl$_2$ (0.012 mole) during 1 hour and then the stirring of the reaction mixture continued for 2 hours. The chloroform layer was separated, washed with water, dried with anhydrous CaCl$_2$ and evaporated to dryness. The product *V* was crystallized from ether—petrolether (3 : 1), giving after concentration orange crystals. For C$_{15}$H$_{10}$N$_2$O$_3$S (298.1) calculated: 60.38% C, 3.38% H, 9.39% N 10.63% S; found: 60.62% C, 3.83% H, 9.12% N, 10.73% S. In the case of compound *VI* the crude product was purified by passing ethereal solution through a column of Al$_2$O$_3$. On concentration gold-yellow crystals of *VI* were obtained. For C$_{16}$H$_{10}$N$_2$OS (278.34) calculated: 69.03% C, 3.62% H, 10.07% N, 11.50% S; found: 69.34% C, 3.38% H, 10.28% N, 11.47% S.

Spectroscopy

Infrared spectra of compounds studied were recorded on a Unicam SP 100 G double-beam instrument in the range of 650—3650 cm⁻¹ in chloroform (concentration 0.05 M, cells of 0.474 and 0.964 mm thickness, respectively) and carbon tetrachloride solution (saturated solution, cells of 20 mm thickness). The calibration was checked against the spectrum of polystyrene of 25 µm thickness. Wave number measurements are believed to be accurate to ± 1 cm⁻¹. Analar chloroform was freed from ethanol and moisture by passing it several times through a column of blue silica gel. Analar carbon tetrachloride was used directly.

Ultraviolet spectra were measured with a Perkin—Elmer 450 double-beam instrument in methanol (spectroscopic grade) (concentration 5×10^{-3}—5×10^{-5} M, cells of 0.5 and 1.0 cm thickness).

Discussion

All compounds prepared excepting 2-hydroxy-2',4'-dinitrostilbene (I) are new compounds not yet described in the literature. The low yields of compounds prepared can be caused by the fact that the resin compounds formed under the reaction conditions make the isolation of the final products difficult.

Although the yield of 2-hydroxy-2'-cyano-4'-aminostilbene obtained by reduction of the appropriate nitro derivative with SnCl₂ in acetic acid saturated with hydrogen chloride was not high, a relatively pure product was obtained, which was used without further purification in the synthesis of appropriate isothiocyanatostilbene derivative. Similarly, 2-hydroxy-2'-nitro-4'-aminostilbene obtained by a partial reduction of appropriate stilbene dinitro derivative with NH₄HS in excess of NH₄OH was used as a starting compound in the preparation of appropriate isothiocyanatostilbene derivative. The appropriate isothiocyanatostilbene derivatives were prepared by thiophosgene method in chloroform, producing good yields [8, 9].

All compounds display strong absorption bands at ~ 970 cm⁻¹ assigned to the out-of-plane bending vibrations of C—H (trans) bonds of ethylenic groups. The presence of these bands can be considered as a reliable evidence of the fact that the compounds studied are trans isomers [10]. Very strong absorption bands at ~ 1350 and ~ 1540 cm⁻¹ reveal the presence of nitro groups. The presence of the two absorption bands at ~ 1600 cm⁻¹ points to the conjugation of aromatic system with the rest of the molecule of the compounds investigated.
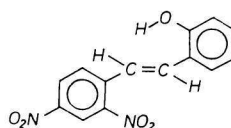
Infrared spectral data of the compounds studied are detailed in Table 1. The characteristic absorption bands of a complex shape assigned to the asymmetrical stretching vibrations of the N=C=S groups are observed in the spectra of the compounds investigated in the range of 2047—2103 cm⁻¹. Other characteristic bands assigned to the stretching vibrations of the C≡N groups of nitriles are observed at ~ 2229 cm⁻¹.

All compounds except amino derivatives (compounds III and IV) display two or three concentration dependent bands in the hydroxyl region. The band at lower wave numbers (3290 cm⁻¹) is assigned to the stretching vibrations of the OH group intermolecularly hydrogen-bonded to electron-rich groups (NO₂, C≡N).

The presence of the two absorption bands at ~ 3600 cm⁻¹, assigned to the stretching vibration of the free OH group can be ascribed to the two different conformations
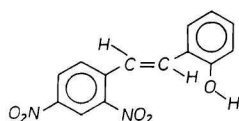
Ia

$\nu(OH) \sim 3616$ cm^{-1}

Ib

$\nu(OH) \sim 3594$ cm^{-1}

Table 1

Infrared spectral data of 2-hydroxy-2′,4′-disubstituted stilbenes in CHCl₃

Com-pound											
						$\nu(OH)$					
						free			bonded		Ɓ
	$\gamma(C-H)$	$\nu_s(NO_2)$	$\nu_{as}(NO_2)$	$\nu(C=C)$		ν	ε^a	ν	ε^a	ν	ε^a
I	970	1351	1545	1604	1624	3594	34	3608	34	3280	47 6ₒ
II	969	1354	1535	1611	1631	3594	34	3616	34	3286	44 9ₗ
V	970	1352	1538	1607	1627	3594	34	3619	34	3290	41 3ₒ
VI	972	—	—	1608	1630	3591	33	3616	33	3290	43 5ₒ
VII	—	—	—	—	—	3593	38	—	—	3326	45 1ₒ

ν in cm^{-1}; ε^a in l mole^{-1} cm^{-1}; K in l mole^{-1}.

VII — ethyl coumarate (included for comparison).

Other bands (in cm^{-1}) for $\nu(C\equiv N)$: 2229 II, 2228 VI; $\nu_{as}(NCS)$: 2047, 2083 V, 205ₒ 2103 VI.

Wave numbers of free O—H groups in CCl₄ (saturated solution) in cm^{-1}: 3602 I, 3599 II 3604 V, 3601 VI.

Table 2

Ultraviolet spectral data of 2-hydroxy-2′,4′-disubstituted stilbenes in methanol

Compound	λ_{max} [nm]	log ε	λ_{max} [nm]	log ε	λ_{max} [nm]	log ε
I	385	4.58	275	4.33	215	4.49
II	383	4.34	272	4.00	213	4.50
V	333	4.37	272	4.37	219	4.70
VI	334	4.16	303	4.16	214	4.60

Concentrations: 5 × 10^{-5} M (I, II, and V); 2 × 10^{-4} M (VI).
Cell-paths: 0.5 cm (I and VI); 1.0 cm (II and V).

In the conformer (Ib), the OH group is directed towards the ethylenic π-bond, which results in lowering the wave number of the OH group as compared with the conformer (Ia).

The existence af absorption bands at ~ 3600 cm^{-1} in the spectra of compounds studied reveal free OH groups. As can be seen from the data listed in Table 2, molar absorptivities of the bands of the bonded OH groups are relatively higher in respect to a concentration used, what indicates strong hydrogen bonds.

It is interesting to note that in these molecules, which are formally capable of considerable rotation, the self-association is so strong. The association constants calculated from the Mecke — Kempter equation [11] are several times higher (e.g. in the case of compound I, $K = 66$ 1 mole^{-1}) than those with alkyl coumarates (e.g. with ethyl coumarate, $K = 13$ l mole^{-1}) [3]. This might be ascribed to the longer conjugated system and also to steric effects
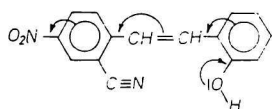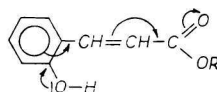

Examination of Dreiding model (Scheme 1) shows that the interacting groups can approach within bonding distance, that is the O O or O N distance ~ 3 Å. From the models it is also evident that the steric conditions for a hydrogen bond formation of a cyclic "dimeric" type are fulfilled and this is the reason why the self-association of the compounds investigated is so strong. Intramolecular hydrogen bonding within a single molecule is not possible, as can be seen on the Dreiding model of this compound, due to a close proximity of interacting groups, the O O distance is approximately ~ 2.3 Å. In respect to the slight solubility in carbon tetrachloride no absorption bands assigned to the stretching vibrations of OH group bonded are observed in the spectra
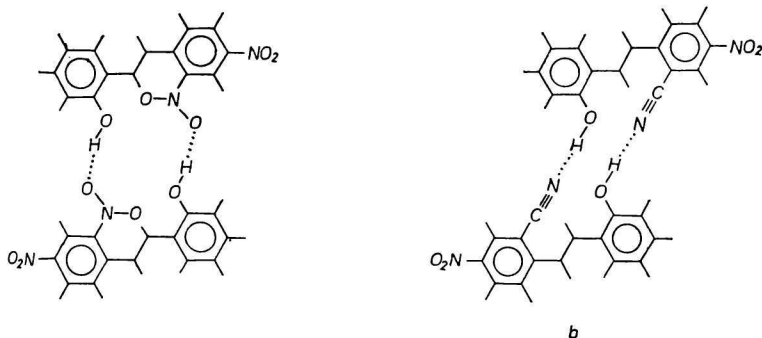
Scheme 1
Planar projection of Dreiding models.
a) cyclic dimer of I; b) cyclic dimer of II.
The dotted lines indicate the H-bonds.

of compounds investigated. The combined spectral data in CCl_4 solutions of compou. studied suggest that the bands of OH groups are concentration dependent. Unfortunatel: the solubility of the compounds investigated in nonpolar solvents was too low for UV-a. lysis. In the UV (in methanol solutions) the compounds investigated show three ba. (Table 2). The two bands at shorter wave lengths are assigned to the $\pi \to \pi^*$-transiti: of the ethylenic group and benzene rings, whilst the longer wave length band is assig. to the $\pi \to \pi^*$-transition of the whole conjugated system [12]. The highest λ_{max} are obser. with compounds *I* and *II* ($\lambda_{max} = 385$ and 383 nm). The simplest explanation seems to that the conjugated system is longer with these compounds than that with compound: and *VI* ($\lambda_{max} = 333$ and 334 nm, respectively). Evidently, in the case of isothiocyana: stilbene derivatives, as it appears from the structure of the NCS group, the mesome: interaction of the NCS group with the rest of the molecule does not take place [8].

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