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Hydrogen-bonding-based thermochromic phenol–amine complexes

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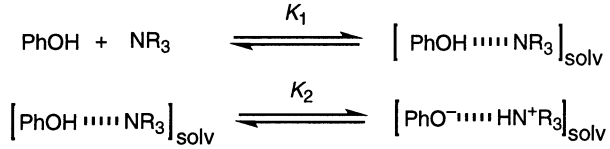
ABSTRACT: Variable-temperature UV–vis, ^{13}C NMR and IR studies showed that proton-transferred complexes were formed between phenols and amines in apolar solvents at low temperature. Upon cooling a solution of *p*-nitrophenol and diisopropylamine in toluene, the colour of the solution changed from colourless to yellow. This thermochromism was ascribed to the proton transfer in the hydrogen-bonding complex. Under UV–vis conditions, butylamine and imidazole also caused similar thermochromism upon complexation with *p*-nitrophenol, while triethylamine, quinuclidine and pyridine did not. The thermochromic behaviour was particularly dependent on the stoichiometry of the amine and the phenol: a solution of 3,3′-dibromo-5,5′-dinitro-2,2′-biphenyldiol and diisopropylamine with a molar ratio of 1:1 showed no thermochromism, while solutions with 1:2 or higher ratios showed thermochromism, indicating that excess amine is required to obtain the proton-transferred species. These results revealed that the proton-transferred species forms in apolar solvents at low temperature if an appropriate hydrogen-bonding network between the phenol and the amine can stabilize it. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: thermochromism; proton transfer; hydrogen bond; phenol; amine

INTRODUCTION

Hydrogen bonding is one of the most important non-covalent interactions in biological chemistry and its properties have been the subject of intense studies. The importance of hydrogen bonding lies not only in the ability to form secondary and tertiary structures of biopolymers, such as the α-helix of protein and the double strand of DNA, but also in the ability to cause proton transfer during enzymic catalysis. Hydrogen bonding is a non-covalent interaction but can be readily switched to a covalent interaction stabilizing a transition state by proton transfer.[1] This unique feature of hydrogen bonding plays important roles in a number of catalytic mechanisms of enzymes.[2] Model systems consisting of phenols and amines have been used to study this dual behaviour of hydrogen bonding. Several studies[3–10] showed that the proton transfer in the *p*-nitrophenol–amine hydrogen-bonding complexes is more favourable with increasing solvent polarity. In non-polar solvents, at least two equilibria should be considered in a solution of phenol and amine as shown in Scheme 1, where $[PhOH{\cdot}NR_3]_{solv}$ is a normal hydrogen-bonding complex and $[PhO{\cdot}HN^+R_3]_{solv}$ is a proton-transferred hydrogen-bonding complex.[11]



Scheme 1

Zundel and co-workers[12–14] reported that the proton transfer equilibria in the hydrogen-bonding complexes between phenols and amines are determined by their pK_a differences on the basis of their IR studies. Menger and Bathelemy[15] studied the amine–phenol proton transfer in ethanol, particularly focusing on the effects of amine structure. Less attention has been paid, however, to the effects of temperature, or thermal fluctuation, on the proton transfer equilibria in apolar solvents. To our knowledge there have been two reports on the temperature effects on the proton-transfer equilibria. Matsuyama and co-workers[4] reported that the enthalpy change in the proton transfer equilibrium in the *p*-nitrophenol–triethylcamine complex is negative from the van't Hoff plot of

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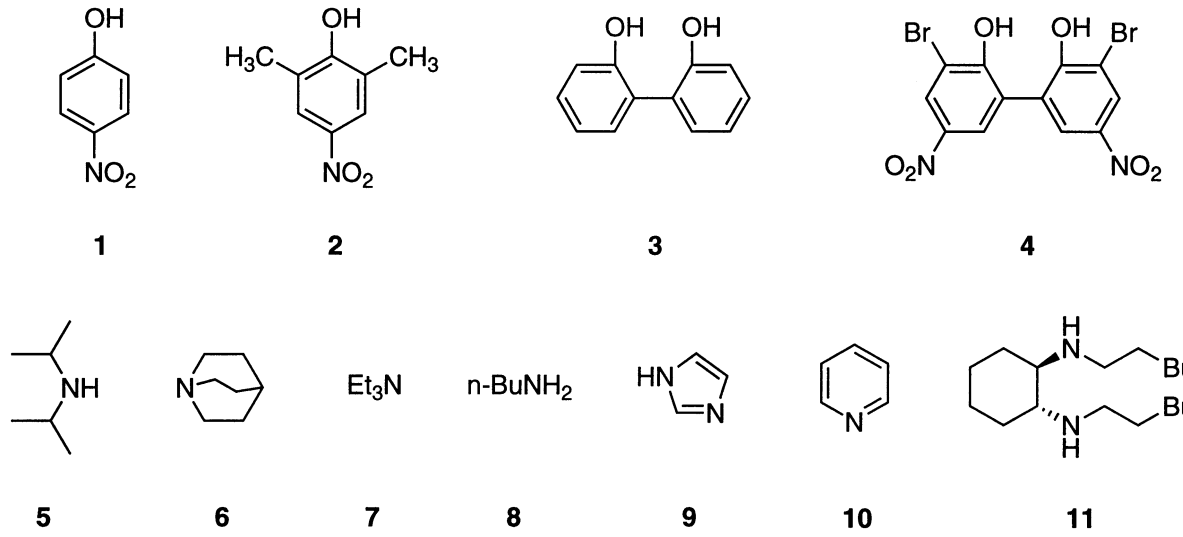

the equilibrium constants between 5 and 20 °C. Diop and Potier[16] reported that the proton was transferred in the HNO_3–Me_2SO complex in the solid state at −180 °C on the basis of their IR and Raman spectroscopic studies. Other than these studies, no systematic studies of the temperature effects on the proton transfer have been performed. This is particularly important when a simple model system is used to study hydrogen bonding, since such a system composed of host–guest molecules interacting through weak non-covalent forces is subject to greater thermal fluctuation than the hydrogen bonding in well-organized media such as proteins, in which the hydrogen-bonding sites are insulated from thermal fluctuation by the relatively rigid protein structure. In this context, studies of hydrogen bonding at low temperature may provide greater insight into the details of hydrogen bonding in biopolymers.

In this paper we focus on the new aspects of the thermochromic behaviour of hydrogen bonding between phenols and amines in non-polar solvents, which originate from the proton transfer equilibria in the hydrogen-bonding complexes. We report that the stoichiometry and the amine structure greatly influence the formation of the proton-transferred species.

RESULTS AND DISCUSSION

Effects of structures of phenols and amines on thermochromism

Before investigating the thermochromic behaviour, host–guest complexation between four phenols (**1–4**) and seven amines (**5–11**) was studied. UV–vis titration of a solution of *p*-nitrophenol (**1**) with diisopropylamine (**5**) at 25 °C resulted in a decrease in the absorbance at 300 nm with a concomitant increase in the absorbance at 328 nm, indicating that a hydrogen-bonding complex between the phenolic OH groups and the amines formed. The binding constants were determined by UV–vis titration, in which the absorbance changes in the phenol band due to increasing amine concentration were monitored and analysed by least-squares curve fitting, assuming 1:1 complex formation. The binding constants K_1 for the amine–phenol hydrogen-bonding complexes are summarized in Table 1. Biphenyldiol **4** showed particularly large binding constants for **5, 6** and **11**. This can be ascribed to the intramolecular hydrogen bonding between the two phenolic OH groups, which will promote the hydrogen donation ability of the OH group.

When a solution of 9.4×10^{-5} M of **1** in toluene was cooled to −80 °C in the presence of excess 0.42 M of **5**, a new absorption band appeared at a longer wavelength

Table 1. Binding constants (K_1) and λ_{max} of phenol–amine complexes at 25 °C

Host	Guest	K_1 (M^{-1})[a]	λ_{max} (nm)	Solvent
1	**5**	200 (10)	328	Toluene
1	**5**	2 (0.1)	328	Diethyl ether
1	**5**	10[b] (1)	342	THF
1	**5**	160 (17)	410	Acetone
1	**6**	3000 (18)	332	Toluene
1	**7**	190 (7)	329	Toluene
1	**8**	570 (5)	328	Toluene
1	**9**	1100 (23)	328	Toluene
1	**10**	150 (1)	326	Toluene
2	**5**	11 (0.6)	340	Toluene
2	**6**	230 (2)	342	Toluene
2	**7**	5 (0.2)	338	Toluene
3	**5**	280 (1)	298	Toluene
3	**6**	4600 (150)	301	Toluene
4	**5**	$> 10^6$	340	Toluene
4	**5**	$> 10^6$	368	THF
4	**6**	$> 10^6$	340	Toluene
4	**11**	$> 10^6$	340	Toluene

[a] Standard deviations are given in parentheses.
[b] $K_1 = 63$ M^{-1} from the absorbance increase at the 392 nm band.

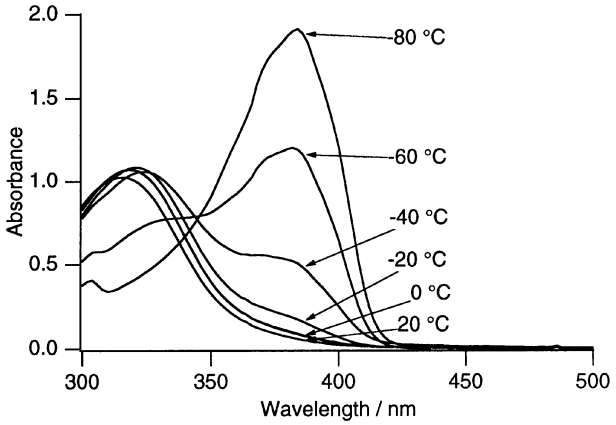

Figure 1. UV–vis spectra of a solution of **1** and **5** in toluene at temperatures from 20 to −80 °C. [**1**] = 9.41×10^{-5} M, [**5**] = 4.23×10^{-1} M

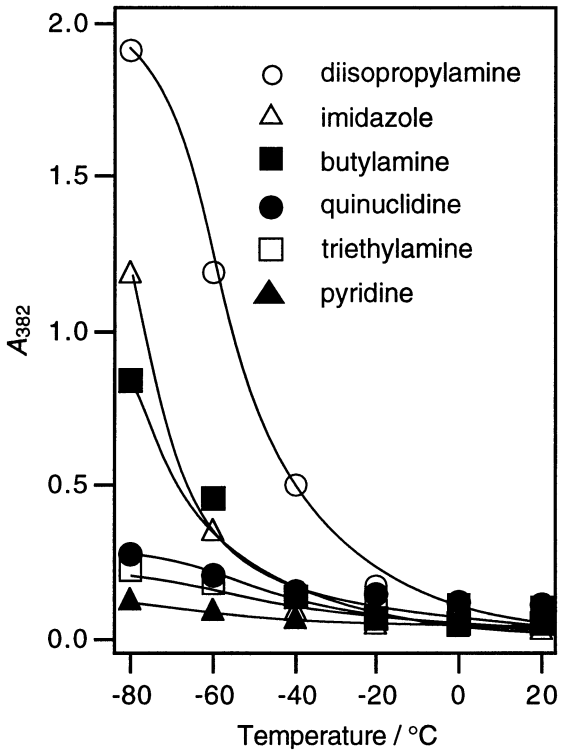

Figure 2. Plots of absorbance at 382 nm against temperature for hydrogen-bonding complexes between **1** and **5–10** in toluene. [**1**] = 9.1×10^{-5} M, [**5**] = 4.1×10^{-1} M, [**6**] = 1.8×10^{-2} M, [**7**] = 4.9×10^{-2} M, [**8**] = 1.8×10^{-2} M, [**9**] = 4.1×10^{-3} M, [**10**] = 1.5×10^{-2} M. Under these conditions more than 70% of **1** was complexed with the amines at 25 °C

and the solution became yellow (Fig. 1).[17–19] This spectral change was reversible: upon warming the solution, it became colourless again. The transition temperature was dependent on the host–guest combination, the solvent and the molar ratio of phenol to amine. Figure 2 shows plots of the absorbance at 382 nm against

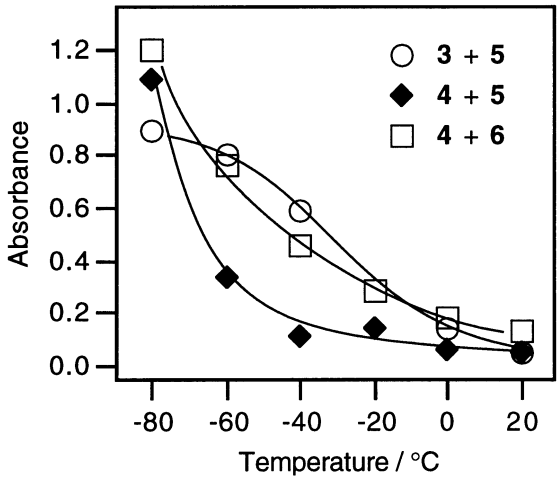

Figure 3. Plots of absorbance at 416 nm ([**4**] = 9.48×10^{-5} M, [**5**] = 1.43×10^{-4} M), 400 nm ([**4**] = 8.33×10^{-5} M, [**6**] = 1.66×10^{-4} M) and 316 nm ([**3**] = 9.08×10^{-5} M, [**5**] = 9.08×10^{-3} M) against temperature for hydrogen-bonding complexes in toluene

temperature for toluene solutions of **1** and various amines **5–10**. A solution of **1** in toluene became yellow in the presence of diisopropylamine (**5**) (pK_a = 11.13 at 21 °C),[20] butylamine (**8**) (pK_a = 10.64 at 25 °C) and imidazole (**9**) (pK_a = 6.99) upon cooling, while that in the presence of quinuclidine (**6**) (pK_a = 10.95 at 25 °C), triethylamine (**7**) (pK_a = 10.72) and pyridine (**10**) (pK_a = 5.42) remained almost colourless even at −80 °C. These results indicate that the thermochromic behaviour is greatly influenced by the amine structure, e.g. secondary amine vs tertiary amine, as well as pK_a value. It is interesting to note that tertiary amines cannot cause thermochromism even if they are strongly basic.

2,6-Dimethyl-4-nitrophenol (**2**) behaved similarly. The thermochromic curves (absorbance at 384 nm vs temperature) for the **2–5** and **2–6** complexes were almost the same as those for the **1–5** and **1–6** complexes respectively (data not shown). Biphenyldiols **3** and **4** also displayed similar thermochromic behaviour. Figure 3 shows plots of the absorbance maximum of the newly emerging band against temperature for complexes between biphenyldiols **3** and **4** and amines **5** and **6** in toluene.

The ^{13}C NMR (125 MHz) studies also confirmed the proton transfer at low temperature. Upon cooling a solution of **2** (172 mM) and **5** (344 mM) in CD_2Cl_2 from 25 to −40 °C, the resonance of C1 of **2** was shifted from 166.7 to 176.6 ppm, C4 of **2** from 137.0 to 130.2 ppm, the methyl carbon of **5** from 22.3 to 20.2 ppm and the methine carbon of **5** from 46.1 to 45.7 ppm (Fig. 4). These shifts are fully consistent with the formation of phenolate and ammonium[21] and thus the proton-transferred species at low temperature.

Under UV–vis conditions, triethylamine (**7**) cannot cause proton transfer in **1**. However, the ^{13}C NMR study indicated that even **7** can induce proton transfer at much

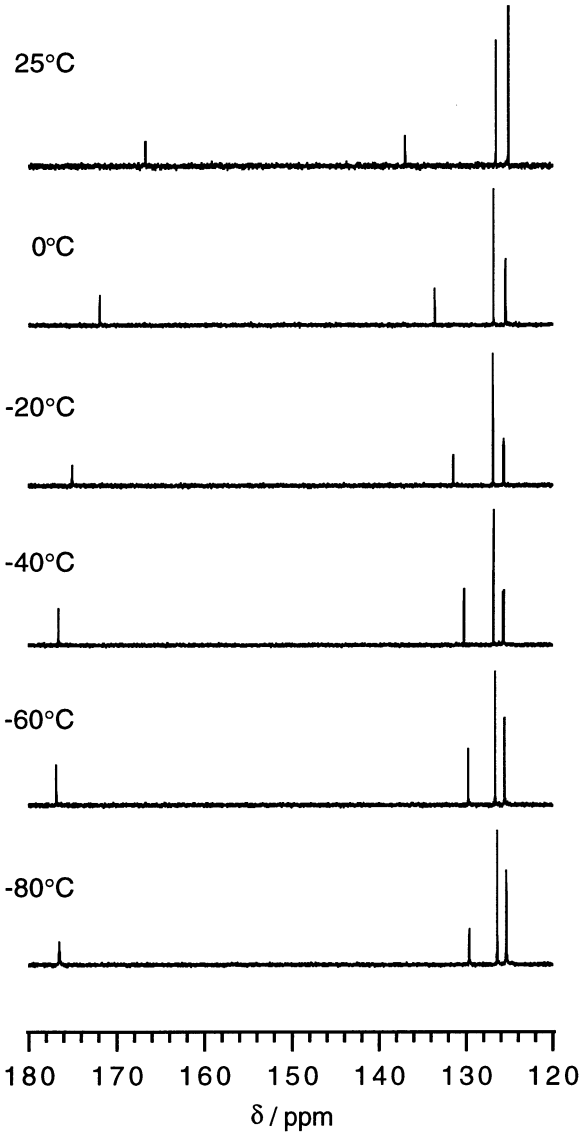

Figure 4. Variable-temperature ^{13}C NMR with complete ^{1}H decoupling of a solution of **2** and **5** in CD_2Cl_2. [**2**] = 0.172 M, [**5**] = 0.344 M

higher concentrations. For instance, the resonance of C1 of **2** in a solution of 0.175 M of **2** and 0.350 M of **7** in CD_2Cl_2 was shifted from 168.5 to 174.4 ppm by cooling from 25 to −80 °C, showing that proton transfer is facilitated by lowering the temperature. However, it should be noted that the concentration of **1** is three orders of magnitude greater than UV–vis concentrations. Under UV–vis conditions, no thermochromism was observed for tertiary amine **7**.

The variable-temperature IR spectra of a solution of **2** (6.02×10^{-2} M) and **5** (6.42×10^{-2} M) in $CDCl_3$ also supported the proton transfer in the complex. Below −40 °C, new signals appeared at 3070, 2717, 2667 and 2500 cm^{-1}, indicating the formation of an ammonium group at low temperature.

Similar thermochromism was observed for other

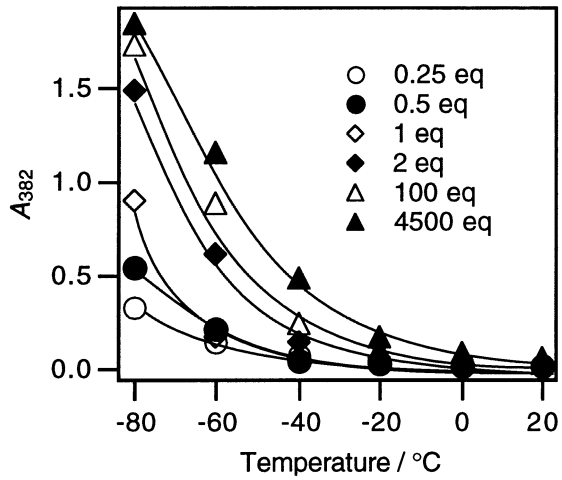

Figure 5. Plots of absorbance at 382 nm against temperature for solutions of [**1**] and [**5**] in toluene with various [**5**]:[**1**] ratios. [**1**] = 9.1×10^{-5} M, [**5**] = 4.1×10^{-1}–2.3×10^{-5} M

phenol–amine complexes. A solution of bromophenol blue and pyridine in toluene was yellow at room temperature but became blue below −50 °C. Similar behaviour was seen for both **5** and *N*-methylaniline in place of pyridine. A solution of phenolphthalein and **5** in toluene was colourless at room temperature and became pale red below −50 °C.

Stoichiometry of proton-transferred species

The variable-temperature UV–vis spectra of solutions of **1** and **5** with various ratios of **1** to **5** indicated that the thermochromism was observed at higher temperature as the molar ratio of amine to phenol became larger (Fig. 5). However, the stoichiometry of the proton-transferred species is not clear, because the small association constant between **1** and **5** makes the complex formation incomplete under UV–vis conditions. Since the binding constants K_1 between **4** and amines were large, the biphenyldiol system was suitable to elucidate the stoichiometry of the proton-transferred species. In Fig. 6 values of the absorbance at 416 nm, where the proton-transferred species showed an absorption maximum, are plotted against temperature. In the presence of 1 molar amount of **5** a toluene solution of **4** did not turn yellow at low temperature, while it turned yellow in the presence of 2 or 10 molar amount of **5**. These observations clearly demonstrate that excess **5** is necessary to obtain the proton-transferred species. Excess **5** would interact with the **4–5** complex to stabilize the proton-transferred state, probably by delocalizing the positive charge on the nitrogen of the complexed **5**. The biphenyldiol **4**–diamine **11** complex also behaved similarly. The binding constant K_1 between **4** and **11** was large and the complex formation proceeds almost quantitatively even at room

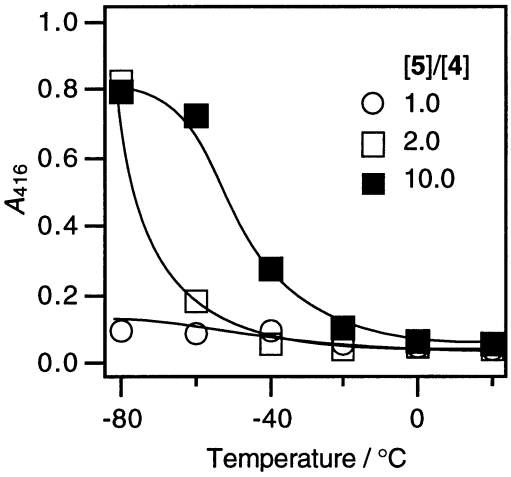

Figure 6. Plots of absorbance at 416 nm against temperature for solutions of [**4**] and [**5**] in toluene with various [**5**]:[**4**] ratios. [**4**] = 9.1×10^{-5} M, [**5**] = 9.1×10^{-5}–9.1×10^{-4} M

temperature. A solution of **4** and **11** with a 1:1 molar ratio did not exhibit thermochromism, while a solution with a molar ratio of 1:2 exhibited thermochromism. Therefore excess molar amounts of diamine **11** are again needed to obtain the proton-transferred species. These results are best explained by assuming that the formation of a 1:2 complex leads to the proton-transferred species.

Hydrogen-bonding networks and proton transfer

As described above, under UV–vis conditions, tertiary amines cannot cause thermochromism of *p*-nitrophenol, while secondary and primary amines can cause it in toluene provided that there is an excess molar amount of amine. This suggests that excess secondary and primary amines can stabilize the proton-transferred species by hydrogen-bonding network formation, where the amines act as a hydrogen donor and form a hydrogen bond to the O^- anion. For biphenyldiol, tertiary amine **6** induced thermochromism. In this case the O^- anion can be stabilized through intramolecular hydrogen bonding to the phenolic OH group. The results presented here clearly demonstrate that the proton transfer occurs even in non-polar solvents if an appropriate hydrogen-bonding network can stabilize the proton-transferred state at low temperature.[22,23]

These results imply that, when a solution was cooled and the system became ordered, a hydrogen-bonding network was formed in the amine–phenol complex, which promoted the proton transfer. The number of hydrogen atoms attached to the nitrogen of the amine and the stoichiometric ratio should be optimized to control proton transfer equilibria. These factors could form the basis for a rational design of an efficient biomimetic catalyst.

EXPERIMENTAL

Instrumentation

^{1}H NMR and ^{13}C NMR spectra were recorded using a Jeol A-500 spectrometer. ^{1}H NMR chemical shifts in acetone-d_6 were referenced to TMS (0 ppm) and ^{13}C NMR chemical shifts in CD_2Cl_2 were reported relative to CD_2Cl_2 (53.8 ppm). UV–vis spectra were recorded on a Hewlett-Packard 8452 diode array spectrometer equipped with a thermostatted cell compartment using a 1 cm path length cuvette. A cryostat (Oxford, DN1704) was used for UV–vis spectral measurements at low temperatures. IR spectra were obtained on a Perkin Elmer System 2000 FT-IR spectrometer using a cryostat with KRS-5 windows and KRS-5 cells. Mass spectra were obtained using a Jeol JMS HX110A spectrometer.

Materials

Unless otherwise noted, materials were obtained from commercial sources. Tetrahydrofuran (THF), diethyl ether, diisopropylamine and triethylamine were distilled from sodium. Pyridine was distilled from KOH. Acetone was distilled from K_2CO_3.

5,5′-Dinitro-2,2′-biphenyldiol was prepared by a modified procedure described in Ref. 24. To a solution of 2,2′-biphenol (7.00 g, 37.6 mmol) in acetic acid (20 ml) was added a mixture of nitric acid (d 1.38, 5.5 ml) and acetic acid (3 ml), then the solution was stirred overnight. The reaction mixture was poured into water. The precipitate was filtered, washed with water and dried *in vacuo*. The solid was added to ethanol-free chloroform and the suspension was sonicated for a few minutes, then the solid that remained was collected by filtration. The material was recrystallized from acetone to give the desired product as a yellow solid (1.06 g, 10.2%). ^{1}H NMR (acetone-d_6): δ 8.27 (d, J = 3 Hz, 2H), 8.20 (dd, J = 9 and 3 Hz, 2H), 7.21 (d, J = 9 Hz, 2H).

Synthesis of 3,3′-dibromo-5,5′-dinitro-2,2′-biphenyldiol (4)

5,5′-Dinitro-2,2′-biphenyldiol (0.206 g, 0.75 mmol) was dissolved in acetic acid (16 ml) at 50 °C. To the solution was added dropwise 0.24 g (1.5 mmol) of bromine, then the mixture was stirred for 3 h at 50 °C. The reaction mixture was stirred for a further 2 h at 80 °C. After cooling to room temperature, water (16 ml) was added to the mixture. The yellow crystalline product was collected by filtration and washed thoroughly with water. Recrystallization of the product from ethanol–water gave yellow crystals of **4**, yield 0.150 g (46%). ^{1}H NMR (500 MHz, acetone-d_6): δ 8.495 (d, J = 3.0 Hz, 2H), 8.250 (d, J = 3.0 Hz, 2H). FABMS (3-nitrobenzyl alcohol): *m/z*

431 $(M-1)^-$, 433 $(M+1)^-$, 435 $(M+3)^-$. Anal. calc. for $C_{12}H_6N_2O_6Br_2$: C, 33.21%; H, 1.39%. Found: C, 33.36%; H, 1.37%.

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