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Resonance-stabilized phenylazo-ene-phenylimine cations of cyclobutanetetraone derivatives

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Dedicated to Professor Derek Horton on the occasion of his 70th birthday

Abstract

Cyclobutenedione phenylazo-phenylamines were found to exhibit bathochromic shifts in acidic media and hypsochromic shifts in basic media, like phenylazo-phenylhydrazones. The bathochromic shifts are due to the formation of resonance-stabilized cations and the hypsochromic shifts to enolization. The phenylazo-phenylamines and their cations and anions have been studied by NMR spectroscopy.

Keywords: Anions; Bathochromic shift; Cations; Chiral shift reagents; Cyclobutenedione phenylazo-phenylamines; Enolization; Hypsochromic shift; NMR spectroscopy; UV–Vis spectrophotometry

1. Introduction

Cyclitol poly(phenylhydrazones) have been used as model compounds in the study of saccharides and carba-sugar osazones.[1] In 1969 Isbell and Fatiadi[2] showed that the electronic spectra of cyclitol phenylazo-phenylhydrazones undergo bathochromic shifts upon protonation with strong acids and attributed this to the formation of resonance-stabilized phenylazo-phenylhydrazone cations that have more extended conjugation than their parent compounds. The extra conjugation was caused by the participation of an additional phenyl ring in their resonance hybrids.[2–4] In a recent publication,[5] we reported bathochromic shifts for the cations of cyclobutanetetraone poly(phenylhydrazones) and were able to confirm that they were indeed due to the protonation of phenylazo-phenylhydrazone groups. The same compounds exhibited hypsochromic shifts in bases, which were attributed to their enolization, because compounds lacking keto groups, or the necessary protons to enolize, did not show such shifts in moderately strong basic solutions.[5]

In the present paper, we have expanded our study to include the cations and anions of cyclobutane derivatives having phenylazo-ene-phenylamine groups, which were found to exhibit bathochromic shifts in acid media and hypsochromic shifts in basic media. Their shifts are analogous to the bathochromic[2–5] and hypsochromic[5] shifts observed in the phenylazo-phenylhydrazones studied earlier, which suggests a similarity in their chromophores and in the cations and anions they form. The present work continues investigations[5–8] aimed at using the phenylhydrazones of squaric acid as effective models for saccharide osazones, since these phenylhydrazones lack the hydroxyalkyl chains that are often involved in concurrent reactions of osazones. Squaric acid derivatives are also of interest as linkers for the preparation of potential conjugate vaccines.[9,10]

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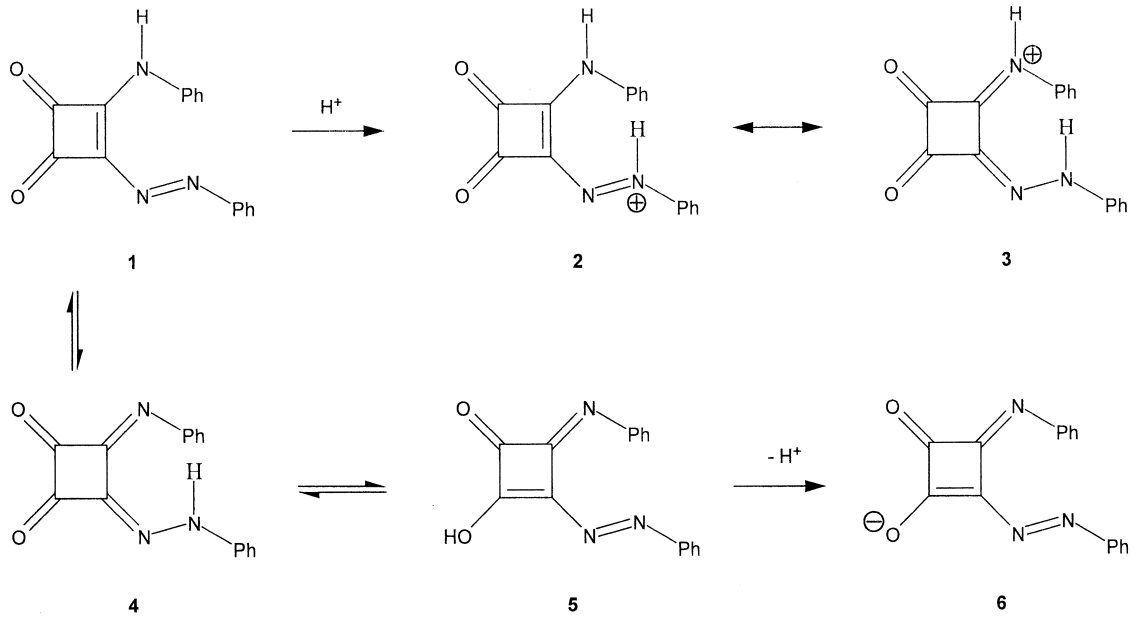


Scheme 1.

2. Results and discussion

One of the aims of this study was to explore the similarity between phenylazo-phenylamines and phenylazo-phenylhydrazones. For example, a goal was to find out whether phenylazo-phenylamino-cyclobutenes would exhibit bathochromic shifts in acid media and hypsochromic shifts in basic media similar to the shifts observed in the phenylazo-phenylhydrazones studied earlier.[2–5] To test this, we studied the cations and anions of two cyclobutene derivatives having phenylazo-cyclobutene-phenylamino groups. The first ions were obtained from a previously prepared[6,7] 1-phenylamino-2-phenylazo-cyclobut-1-ene-3,4-dione (**1**) (Scheme 1), which was found to exhibit bathochromic shifts in acid and hypsochromic shifts in basic media (see Fig. 1(a)). The study was then extended to another known[8] cyclobutene derivative, namely 2-(phenylazo)-8a-(2-phenylhydrazino)-cyclobuta[*b*]quinoxalin-1(8a*H*)-one (**11**) (Scheme 2), which also possesses phenylazo-ene-phenylimine groups. It exhibited bathochromic shifts in acid solution, but remained unchanged in the presence of base (see Fig. 1(b)). In order to shed light on the difference in behavior of these two compounds, we have studied the structures of the ions they form in acidic and basic media, especially by the use of UV–Vis spectrophotometry and ^{1}H NMR spectroscopy (for NMR data, see Tables 1 and 2). The shifts observed in the UV–Vis and NMR spectra could be reversed by timely neutralization (like the shifts observed in the spectra of cyclobutanetetraone polyphenylhydrazones[5]), but over the course of hours or days, examination of the spectra revealed that other products were being formed.

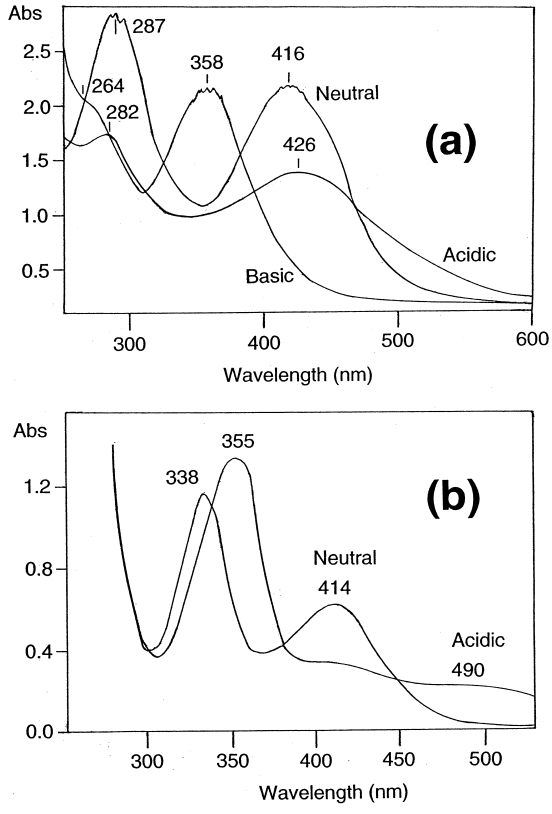
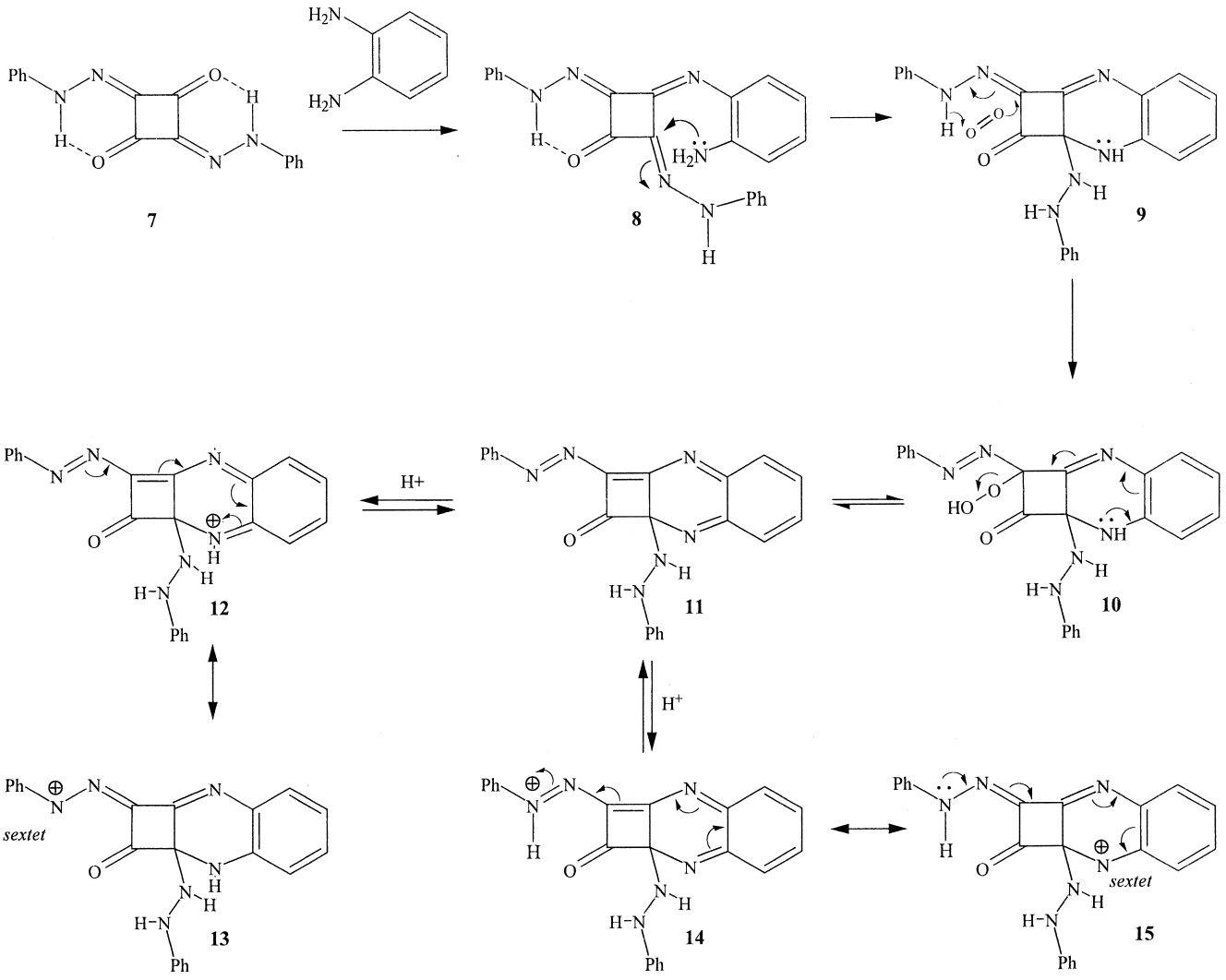


Fig. 1. UV–Vis absorption spectra. (a) 1-Phenylamino-2-phenylazo-cyclobut-1-ene-3,4-dione (**1**) showing the bathochromic and hypsochromic shifts in acidic and basic solutions, respectively (for conditions, see Section 4). (b) 2-(Phenylazo)-8a-(2-phenylhydrazino)-cyclobuta[*b*]quinoxalin-1(8a*H*)-one (**11**) showing a bathochromic shift in acid, but no hypsochromic shift in base.



Scheme 2.

Cations of 1-phenylamino-2-phenylazo-cyclobut-1-ene-3,4-dione (**1**).—A detailed ^{1}H NMR spectral analysis[6] of the previously prepared 1-phenylamino-2-phenylazo-cyclobut-1-ene-3,4-dione (**1**)[6,7] revealed that it exists as an unresolved pair of tautomers (Scheme 1, **1** and **4**) in the ratio of 92:8 in chloroform-*d* solution and 45:55 in methyl sulfoxide-d_6. The tautomers showed two sets of signals for their phenyl and NH protons, which integrated for the given ratios.[6] This was confirmed by their ^{13}C NMR spectra that showed two separate sets of signals for the phenyl, CO, and CN carbons, also in the same ratio.[6] Treatment of compound **1** with strong acids caused a dramatic change in its absorption spectrum and a bathochromic shift of the longer wavelength absorption (see Fig. 1(a)), which may be attributed to the formation of a resonance-stabilized cation having an extended conjugation. The formation of the cation probably proceeds by protonation of the azo group of **1** to give a phenylazo-ene-phenylamine cation (**2**), which is in resonance with a phenylhydrazono-*N*-phenylimine form (**3**). The resonance hybrid of these forms has two phenyl rings involved in conjugation instead of only one phenyl group in the starting compound (**1**). The conjugation of the resonance system **2**↔**3** is strikingly similar to that of formazan cations, as may be seen from the structures depicted in Scheme 3.

When a solution of compound **1** in chloroform-*d* was treated with CF_3CO_2H, there was no significant color change, and ^{1}H NMR spectroscopy revealed only minor changes in the chemical shifts of the aromatic protons (see Table 1). However, the addition of CF_3SO_3H to **1** in chloroform-*d* caused an immediate color change from red-amber to dark purple, accompanied by relatively large downfield shifts ($+0.09$ to $+0.59$ ppm) of all of the aromatic proton signals (see Table 1). Dilution of a solution of **1** in methyl sulfoxide-d_6 with an equal volume of CF_3CO_2H produced a color change of dark amber to red-amber, but only moderate deshielding ($+0.04$ to $+0.09$ ppm) of the

ortho protons of both tautomers, together with smaller positive and negative shifts of their *meta* and *para* proton signals (see Table 1). Clearly, the magnitudes of the shifts are related to the strength and concentration of the acid added, and they correlate well with the absorption shifts of the solutions. The deshielding effects observed in the ^{1}H NMR spectra of the cations formed in acid media are consistent with the presence of the positive charges in the resonance structures **2**↔**3** (see Scheme 1).

Anions of 1-phenylamino-2-phenylazo-cyclobut-1-ene-3,4-dione (**1**).—Treatment of compound **1** with base induces a significant hypsochromic shift of its longer wave length absorption (see Fig. 1), similar to the

Table 1
^{1}H NMR chemical shifts[a,b] of 1-phenylamino-2-phenylazo-cyclobut-1-ene-3,4-dione (**1**) in neutral solvents, acids, and basic mixtures

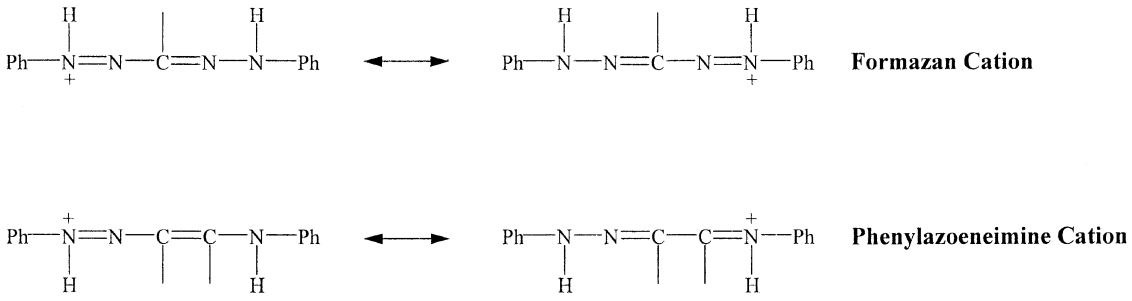
Solvent	Color of solution	Tautomer	*ortho*	*meta*	*para*	NH
$CDCl_3$–Et_3N (one drop)[b]	red-amber	major	7.993	7.573	~7.583	–
			7.559	7.472	7.297	
$CDCl_3$	red-amber	major	7.995	7.558	7.590	10.041
			7.583	7.478	7.304	
$CDCl_3$–CF_3CO_2H (two drops)	red-amber	major	7.977	7.587	7.635	9.451, 10.054
			7.560	7.501	7.354	10.054
$CDCl_3$–CF_3SO_3H (one drop)	dark purple	major	8.099	7.755	7.889	10.912, 11.851
			7.677	7.605	7.565	12.001
$(CD_3)_2SO$–Et_3N (one drop)	dark red	major	7.051	7.216	6.996	–
			7.448	7.415	7.343	–
		minor	7.769	7.514	7.411	–
			7.416	–	–	–
$(CD_3)_2SO$	dark amber	major	7.763	~7.597	~7.597	11.866
			7.688	7.496	7.322	
		minor	8.052	~7.645	~7.645	~11.686
			7.569	7.469	7.308	
$(CD_3)_2SO$–CF_3CO_2H (1:1 v/v)	red-amber	major	7.847	~7.568	~7.568	11.924
			7.780	7.486	7.332	
		minor	8.094	~7.613	~7.616	11.062
			7.605	7.479	7.332	

[a] Measured at 500 MHz.
[b] For solutions containing $CDCl_3$. Only data for the predominant tautomer are reported.

Table 2
^{1}H NMR chemical shifts[a,b] of the ring protons of 2-(phenylazo)-8a-(2-phenylhydrazino)-cyclobuta[*b*]quinoxalin-1(8a*H*)-one (**11**) in neutral solvents, acids, and base

Solvent	Color of solution	Phenylazo ring			Quinoxaline ring				Phenylhydrazino ring		
		ortho	*meta*	*para*	*ortho*	*ortho′*	*meta*	*meta′*	*ortho*	*meta*	*para*
$CDCl_3$–Et_3N	yellow	8.510	7.593	7.405	8.343	8.284	7.938	7.873	7.050	7.261	6.929
$CDCl_3$	yellow	8.505	7.604	7.418	8.348	8.292	7.949	7.884	7.061	7.273	6.948
$(CD_3)_2SO$–Et_3N (two drops)	yellow	8.511	7.709	7.487	8.409	8.312	8.066	7.985	6.934	7.206	6.770
$(CD_3)_2SO$	yellow	8.501	7.711	7.490	8.406	8.310	8.065	7.984	6.928	7.209	6.774
CD_3CO_2D	yellow	8.551	7.666	7.474	8.420	8.341	8.030	7.960	7.083	7.270	6.932
CF_3CO_2H–CD_3CO_2H (9:1 v/v)	red	8.373	7.772	7.697	8.806	8.744	8.513	8.423	7.400	7.511	7.360
CF_3SO_3H	deep red	7.372	7.298	7.350	8.502	8.265	8.399	8.321	7.253	7.155	7.205

[a] Measured at 500 MHz.
[b] *ortho′* and *meta′* indicate the *ortho* and *meta* protons of the quinoxaline ring resonating at higher field than the *ortho* and *meta* protons, respectively. The *ortho′* proton could also be labeled as a *para* proton.



Scheme 3.

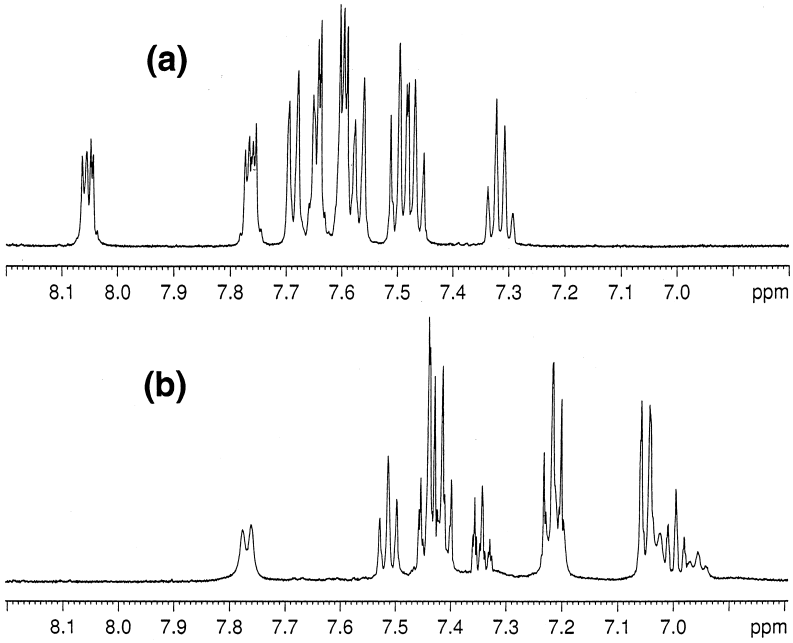


Fig. 2. ^{1}H NMR spectra of 1-phenylamino-2-phenylazo-cyclobut-1-ene-3,4-dione (**1**) at 500 MHz. (a) In methyl sulfoxide-d_6. (b) The same solution with one drop of triethylamine added showing the marked upfield shift of many of the aromatic proton signals due to enolization of **1**. For assignments in (a) and (b), see Table 1; for (a), also see Ref. 6.

hypsochromic shifts of phenylazo-phenylhydrazones studied earlier.[5] This behavior is attributed to enolization. A plausible mechanism for the enolization of compound **1** starts with a prototropic rearrangement to form the phenylimine–hydrazone tautomer (**4**), which as mentioned earlier, is formed in small amounts during the preparation of **1**. A second prototropic rearrangement produces the enol–phenylazo form **5**, which readily dissociates in the presence of base, to form an enolate anion **6** (see Scheme 1). The latter species is quite similar to the enolate anions obtained by treating phenylazo-phenylhydrazones with base.[5] The enols formed in both reactions can dissociate in base much more readily than the keto forms (an enolic OH group is much more acidic than the NH group of its keto form). In addition, the enolate anion has a negative charge on the more electronegative oxygen instead of on the less electronegative nitrogen, and is therefore more stable. The enolate anions formed exhibit hypsochromic shifts because the C=C group of an enol is a weaker chromophore than the C=O group of its keto form (the first undergoes $\pi \rightarrow \pi^*$ transitions, whereas the second can undergo both $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions).

The formation of anions in basic media was also monitored by studying the ^{1}H NMR spectra of compound **1** in the presence of triethylamine. When a chloroform-*d* solution of **1** was treated with triethylamine, there was no color change, and only small changes in the ^{1}H chemical shifts of **1** were observed (see Table 1). On the other hand, when a solution of **1** in methyl sulfoxide-d_6 was treated with triethylamine, the color of the solution changed from dark amber to dark red, and the observable aromatic proton signals of both tautomers underwent substantial upfield shifts in the range of -0.08 to -0.71 ppm (see Table 1 and Fig. 2). This difference may be attributed to enhanced ease of formation of the anion of **1** by enolization in the

polar solvent, compared with that in the nonpolar chloroform-*d*. Increased shielding of the aromatic protons on enolization of **1** (Fig. 2(b)) is most likely due to delocalization of the negative charge of the enolate anion **6** into the aromatic rings by resonance, particularly at the *ortho* and *para* positions, whose protons do indeed display the larger upfield shifts (Table 1). Due to strong coupling of some *meta* and *para* protons for **1** in methyl sulfoxide-d_6 solution, the two *ortho* proton signals at lowest field (see Fig. 2(a)) still show virtual coupling effects[11,12] at 500 MHz, as they did at 400 MHz.[6] This phenomenon is manifested here by additional resonances within the *ortho* proton doublets. The effect disappears when triethylamine is added, producing greater dispersion of the *meta* and *para* protons (see Fig. 2(b)) and, therefore, weaker coupling in terms of a smaller J/δ ratio.

Formation of quinoxaline **11**.—This quinoxaline was prepared from cyclobutanetetraone 1,3-bis(phenylhydrazone) (**7**) by treatment with *o*-phenylenediamine. Combustion[7,8] and mass spectral analysis revealed that this product possessed two protons less than expected for a condensation product of an NH_2 group of *o*-phenylenediamine with a carbonyl group and the addition of the other NH_2 onto the C=N group of a phenylhydrazone residue. This means that an oxidation must have occurred during the reaction. A review of the possible oxidants that could produce such a reaction suggested that atmospheric oxygen in the basic medium of the reaction was the most likely candidate. In basic solution, aldehyde and ketone phenylhydrazones,[13–16]

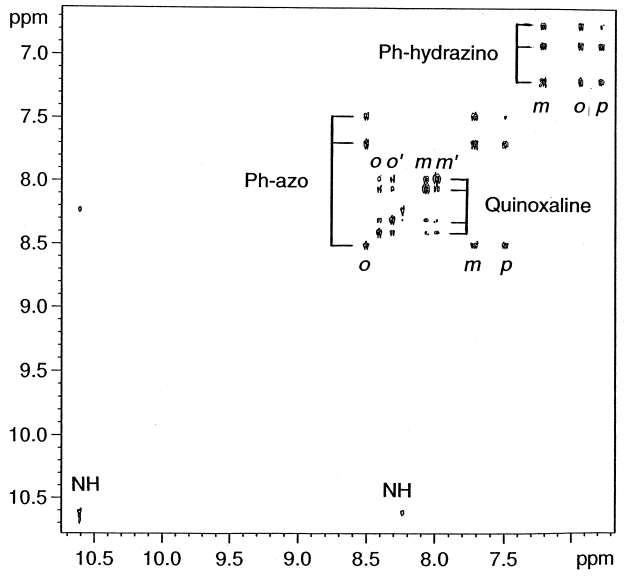


Fig. 3. 2D TOCSY ^{1}H NMR spectrum of 2-(phenylazo)-8a-(2-phenylhydrazino)-cyclobuta[*b*]quinoxalin-1(8a*H*)-one (**11**) in methyl sulfoxide-d_6 at 500 MHz showing the internal connectivities in the four separate proton spin systems in the HNNH, phenylazo, phenylhydrazino, and quinoxaline groups.

saccharide phenylhydrazones,[17,18] and osazones[1] readily undergo rapid peroxidation in air, even at room temperature.

These reactions are initiated by the free radicals generated by atmospheric oxygen, which add onto the C=N group of phenylhydrazones to form phenylazo-hydroperoxides. The phenylazo-hydroperoxides formed by peroxidation of benzaldehyde and other aromatic aldehyde phenylhydrazones can be readily isolated,[13] but those produced by peroxidation of saccharide phenylhydrazones and osazones undergo a further elimination by nucleophilic substitution to form phenylhydrazono lactones.[17,18] An analogous peroxidation of compound **9** formed by the condensation of bishydrazone **7** with *o*-phenylenediamine would produce product **11** (see Scheme 2). A probable mechanism would start with the condensation of one of the amino groups of *o*-phenylenediamine with the carbonyl groups of **7**, and the addition of the other onto the C=N group of an adjacent hydrazone residue, to close the quinoxaline ring and form a hydrazine **9**. Peroxidation of the unreacted phenylhydrazone group would then result in the formation of a phenylazo-hydroperoxide **10**, which eliminates a hydroperoxide anion to form the product isolated **11**.

Previously reported NMR evidence[8] that this structure is 2-(phenylazo)-8a-(2-phenylhydrazino)-cyclobuta-[*b*]quinoxalin-1(8a*H*)-one (**11**) is supported by additional data from the present study in which 2D TOCSY spectra (see Fig. 3) gave a good indication of the connectivities within the four independent proton spin systems represented by the HNNH moiety and the phenylazo, phenylhydrazino, and quinoxaline rings.

Cations of quinoxaline **11**.—Treatment of quinoxaline **11** with strong acids resulted in the formation of cations that exhibit significant bathochromic shifts and a weak absorbency at their longer wavelength maxima (see Fig. 1(b)). The bathochromic shifts in acid are probably the result of protonation of either the phenylazo group of compound **11**, or of its quinoxaline ring to form resonance-stabilized cations such as **12**↔**13** or **14**↔**15** (Scheme 2), which are similar to the cations of phenylazo-phenylhydrazones studied earlier.[5] It should be noted, however, that the protonated and unprotonated nitrogen atoms in these cations are not of equal stability; the first are always surrounded by an octet of electrons, whereas the unprotonated nitrogens have an electron sextet in one of their resonance forms (see Scheme 2). This probably causes the weak absorbency of the maximum at λ 490 nm in the cation spectrum (see Fig. 1).

NMR experiments showed that the presence of acids (CD_3CO_2H, CF_3CO_2H, CF_3SO_3H, etc.) frequently causes substantial downfield protonation shifts for quinoxaline **11**. The extent of the shifts, which depend on the position of the proton and the strength of the

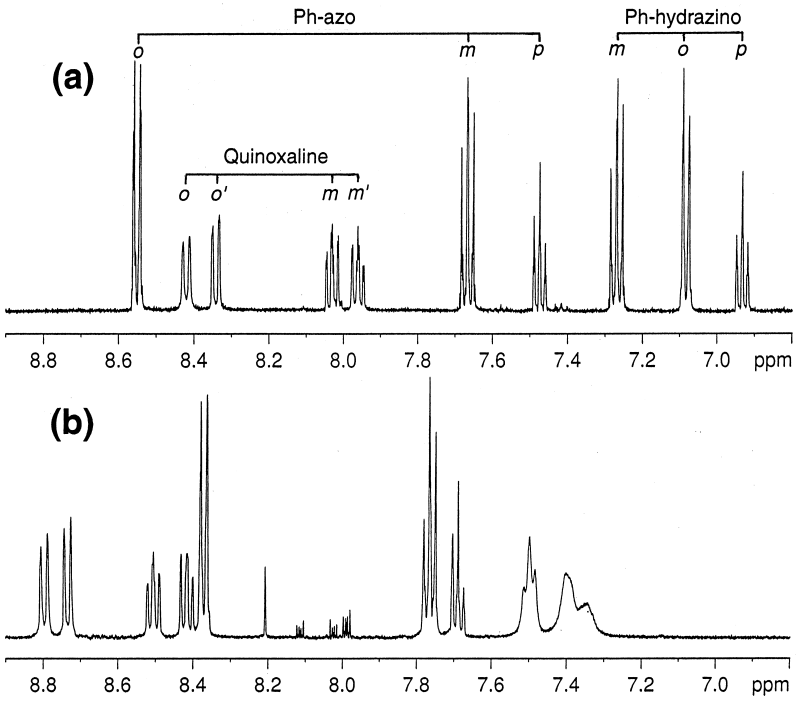


Fig. 4. ^{1}H NMR spectra of 2-(phenylazo)-8a-(2-phenylhydrazino)-cyclobuta[*b*]quinoxalin-1(8a*H*)-one (**11**) at 500 MHz. (a) In CD_3CO_2D solution. (b) in 9:1 CF_3CO_2H–CD_3CO_2H (v/v) showing the downfield shift of many of the proton signals on protonation of **11**, and also specific broadening of the aromatic proton signals of the phenylhydrazino group, due possibly to acid catalysis of an intermediate rate of chemical exchange of the NH protons.

acid, correlate well with the colors of the solutions. Thus, the weaker acid, CD_3CO_2H gave a yellow solution together with negligible ^{1}H chemical shift changes for the phenylazo and quinoxaline protons, and larger protonation shifts ($+0.06$ to $+0.16$ ppm, see Table 2) for the phenylhydrazino ring protons. The stronger acid CF_3CO_2H gives a red solution, together with substantial protonation shifts ($+0.30$ to $+0.59$ ppm) for both the quinoxaline and phenylhydrazino ring protons (see Fig. 4 and Table 2). The even stronger acid CF_3SO_3H gave a deep red solution, and similar downfield shifts for several of the quinoxaline and phenylhydrazino ring protons (see Table 2). Deshielding of the aromatic protons probably arises from protonation of the different nitrogen atoms of compound **11**, and the data shown in Table 2 suggest that a phenylhydrazino nitrogen protonates first.

Only protonation of a nitrogen atom of the quinoxaline or phenylazo groups will result in the resonance depicted by structures **12**↔**13** and **14**↔**15**, while protonation of the hydrazino group of **11** will not increase the resonance, and cannot, therefore, be responsible for the bathochromic shift observed. Deshielding of all four quinoxaline protons could result from protonation of one of the nitrogens of the quinoxaline ring, because the presence of a positive charge on either of the two nitrogens will induce a partial charge on the other by resonance. The effect of distribution of charge among the large number of competing sites that could undergo protonation (six imino groups) is clearly evident in the ^{1}H NMR spectra of quinoxaline **11** in neutral and acid media, as well as in the data in Table 2, which show that the majority of the protons of all three aromatic rings adjacent to nitrogen atoms are significantly deshielded upon acidification.

Action of bases.—When 1-phenylamino-2-phenylazocyclobut-1-ene-3,4-dione (**1**) and 2-(phenylazo)-8a-(2-phenylhydrazino)-cyclobuta[*b*]quinoxalin-1(8a*H*)-one (**11**) were treated with base, they behaved differently. The first was able to enolize by two consecutive sigmatropic rearrangements, then dissociate to give an anion that exhibits a strong hypsochromic shift, whereas the second remained unchanged in the moderately basic medium used in both reactions, because it lacks the necessary proton to enolize. The minimal changes observed in the ^{1}H NMR chemical shifts of **11** on the addition of triethylamine to its chloroform-*d* or methyl sulfoxide-d_6 solutions (see Table 2) are consistent with the inability of **11** to enolize in base.

Action of chiral shift reagents.—The general effect of the six chiral shift reagents investigated (see Section 4) was to promote HNNH proton–proton spin coupling in chloroform-*d* solutions of **11**. For example, the coupling $^3J_{HNNH}$ 2.8 Hz, observed[8] in methyl sulfoxide-d_6 but not in chloroform-*d* solution (see Fig. 5(a)) can be observed in the latter solvent after the addition of a

(chiral) shift reagent (Fig. 5(b)). For such chloroform-*d* solutions, homonuclear spin decoupling and 2D COSY experiments provided proof that the splittings (4.8 Hz) in the NH proton signals (for example, in Fig. 5(b)) are due to HNNH spin–spin coupling and not to diastereomeric interactions with the chiral shift reagents. These observations confirmed the presence of the phenylhydrazino group.

The apparent slowing of the rates of NH proton exchange of **11** by (chiral) shift reagents in chloroform-*d* suggests hydrogen bonding or association of the NH protons with the shift reagents, by analogy with observation[8] of the HNNH proton coupling in methyl sulfoxide-d_6 solutions, in which NH proton exchange is undoubtedly diminished by NH hydrogen bonding with the solvent. Support for this concept is provided by the

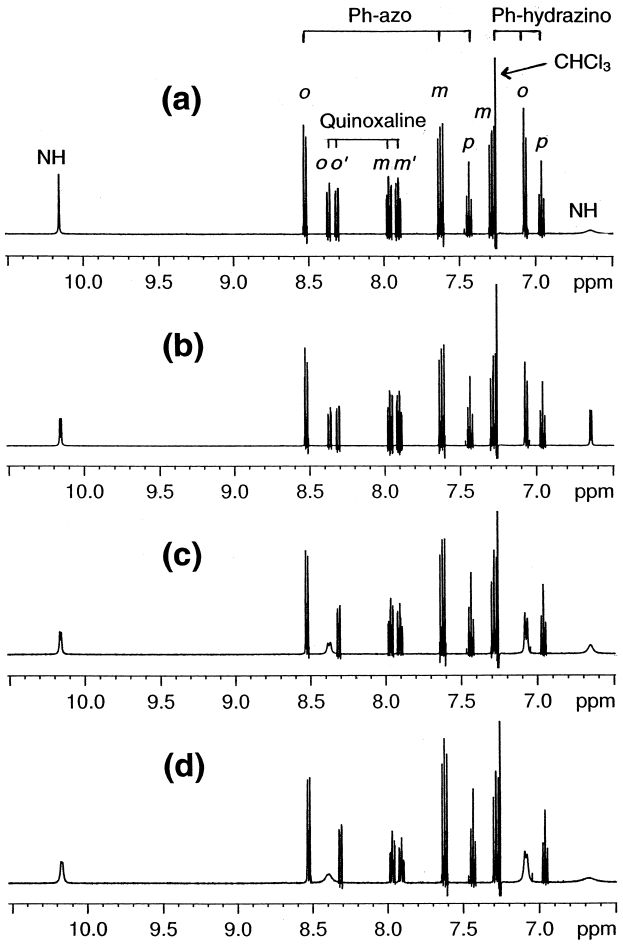


Fig. 5. ^{1}H NMR spectra of 2-(phenylazo)-8a-(2-phenylhydrazino)-cyclobuta[*b*]quinoxalin-1(8a*H*)-one (**11**) at 500 MHz. (a) In chloroform-*d* showing the NH signals as singlets, (b)–(d) with increasing quantities of europium tris[3-(trifluoromethyl-hydroxymethylene)-(+)-camphorate] added, showing in (b) the presence of the HNNH proton–proton spin coupling constant in the NH doublets, and in (c)–(d) selective broadening of the *ortho* proton signals of the phenylhydrazino ring, one *ortho* proton signal of the quinoxaline ring, and the NH signals.

observation that the six chiral shift reagents studied produced selective broadening of the *ortho* proton signals of the phenylhydrazino ring and one *ortho* proton of the quinoxaline ring (for example, see Fig. 5(c, d)), indicating association of the shift reagents with the α-face of structure **11** to form complexes in the vicinity of the NH protons and one nitrogen atom of the quinoxaline ring.

Increasing concentration of shift reagents also caused broadening of the NH proton signals, and the eventual obscuring of their splittings (see Fig. 5(d)). The resonances that displayed selective broadening by the europium complex used for the spectra in Fig. 5 were also shifted downfield to the greatest extent. Over a range of seven experiments involving the dropwise addition of shift reagent solution, these shifts ($\Delta\delta$) amounted to $+0.023$ to $+0.064$ ppm. By contrast, the resonances that were not noticeably broadened were shifted downfield by only $+0.003$ to $+0.011$ ppm. As a control, the chemical shift of the residual chloroform signal was unaffected by the shift reagent ($\Delta\delta < 0.001$). The selective broadening of the quinoxaline *ortho* proton signal at lower field (δ 8.348, see Table 2) allows the specific assignment of this resonance to the quinoxaline *ortho* proton on the underside of structure **11**.

For two chiral shift reagents containing praseodymium (see Section 4) broadening of the proton signals of **11** was less selective, and the initial broadening of the *ortho* proton signals of the phenylhydrazino ring and one *ortho* proton of the quinoxaline ring was soon followed by broadening of all proton signals, except those of the *meta* and *para* protons of the phenylazo and phenylhydrazino groups.

It should be noted that attempts to resolve the signals of the diastereomeric complexes that might be formed by treating chloroform-*d* solutions of **11** with different chiral NMR shift reagents proved unsuccessful. No splittings of the resulting ^{1}H NMR spectra were observed that could be attributed to diastereomeric interactions with the chiral shift reagents. These observations should not be attributed to the absence of an asymmetric carbon atom in **11**, but rather to weak diastereomeric interactions that are too small to be detected.

3. Conclusions

The results obtained in the study of the cations and anions of phenylazo-phenylamines and in our previous studies of the ions of cyclobutanetetraone phenylazo-phenylhydrazones,[5–8] as well as in Isbell and Fatiadi's studies on the cations of cyclohexane poly(phenylhydrazones)[2–4] can be explained as follows.

1. The NMR results obtained in this paper show that when compounds **1** and **11** are acidified, a number of

their aromatic protons become deshielded, evidently by the positive charges on the adjacent protonated nitrogens that withdraw electrons from the rings. Since aliphatic amines are much more basic than aromatic amines, one could assume that the remaining nitrogens (those not attached to aromatic rings) are also protonated. It should be noted, however, that not all of the protonated nitrogen atoms in the molecule contribute to the bathochromic shifts observed on acidification. Only protonation of the nitrogen atoms of the azo group or the imino nitrogens of **1**, and the azo or quinoxaline nitrogens of **11** will produce expanded conjugation systems that are needed for bathochromic shifts.

2. Bathochromic shifts exhibited in strong acid by the cations of phenylazo-ene-phenylamines and phenylazo-phenylhydrazones are caused by their ability to form resonance-stabilized hybrids that involve both phenyl rings in the conjugated system of their chromophores, instead of only one ring in the chromophores of the starting compounds. The groups needed to form such extended resonance-stabilized hybrids include phenylazo groups linked through double bonds to phenyl imines, or to phenylhydrazone groups. The newly observed bathochromic shifts in phenylazo-ene-phenylamines treated with acids confirm Isbell and Fatiadi's explanation that similar shifts of phenylazo-phenylhydrazones are caused by the extension of their resonance systems.[2]

3. α-Keto phenylhydrazones and phenylazo-ene-phenylamines do not exhibit bathochromic shifts in basic media because they form enolates instead of resonance-stabilized anions. The OH groups they form by enolization are stronger acids than their original NH groups and readily dissociate to form anions that have a negative charge on oxygen instead of on nitrogen. These anions exhibit hypsochromic shifts because the C=C groups of the enolate ions are weaker chromophores than the C=O of the starting keto forms (they can only undergo $\pi \rightarrow \pi^*$ transitions, whereas C=O groups can undergo $n \rightarrow \pi^*$, as well as $\pi \rightarrow \pi^*$ transitions).

4. Phenylazo-ene-phenylamines and phenylazo-ene-phenylhydrazones lacking keto groups or protons to form enols by sigmatropic rearrangements remain unchanged in moderately strong bases.

5. Isbell and Fatiadi mentioned that to dissociate the NH group of phenylazo-phenylhydrazones, aprotic solvents and very strong bases are needed.[2] The anions formed have extended conjugation and are stabilized by resonance, so they exhibit bathochromic shifts like their cations. However, the presence of enolizable keto groups preferentially leads to enolate anions that exhibit hypsochromic shifts instead.

4. Experimental

General.—Melting points are uncorrected. Mass spectra were recorded in the EI mode by use of an HP 5995 GC–MS spectrometer. IR spectra were measured using a BIO-RAD FTS-7 FTIR spectrophotometer. Microanalyses were performed by Spang Microanalytical Lab, Eagle Harbor, MI.

UV–Vis absorptions.—UV–Vis spectra of the compounds shown in Fig. 1 were recorded by means of an HP 8452A diode array spectrophotometer. Stock solutions of compounds **1** and **11** (5 mg in 10 mL) in dichloromethane were treated with 10 mL of absolute EtOH and diluted to 50 mL with a 'neutral diluent' (a 50% soln of CH_2Cl_2–EtOH). The spectra of neutral media were acquired by diluting the stock solutions as necessary with the 'neutral diluent'.[2] For spectra of the anions and cations, the stock solutions were diluted with either an 'acid diluent' (20% concd H_2SO_4 in EtOH), or a 'basic diluent' (20% Et_3N or KOH in EtOH).

NMR spectroscopy.—The spectra were acquired at 300 K by using a Bruker DRX 500 spectrometer. 1D ^1H NMR spectra were acquired by use of either 5-mm triple resonance, triple gradient (HCN) or broad band (BBO) probes, with a spectral width of 6.01 kHz, 32768 point data sets, and a pulse recycle time of 6 s. The ^1H 90° pulse width was 7.0 μs for the HCN probe and 9.2–10.5 μs for the BBO probe.

Spectral assignments were confirmed for **1** by 2D COSY-45, *J*-resolved, and TOCSY experiments using the BBO probe. 2D COSY-45 was performed with 2048 (F_2) × 512 or 1024 (F_1) point data sets zero-filled to 2048 × 2048 points, a spectral width of 3 kHz in each dimension, 4–32 scans, 16 dummy scans, and a minimum pulse recycle time of 1–2 s. 2D *J*-resolved spectra were acquired with 8192 (F_2) × 128 or 256 (F_1) point data sets zero-filled to 16384 × 512 points, respectively, spectral widths of 3 kHz (F_2) and 50 Hz (F_1), 16–32 scans, 16 dummy scans, and a minimum pulse recycle time of 1.36–2 s. 2D TOCSY experiments were conducted in the sensitivity-improved, gradient-selected mode, using rectangular data sets[19] of 4096 (F_2) × 128 (F_1) points zero-filled to 8192 × 512 points, respectively, 16 scans, 16 dummy scans, spectral widths of 2 kHz in both dimensions, and a pulse recycle time of 1.12 s. All 2D data sets were processed with a sine-bell squared window function shifted by π/2 rad. 2D COSY-45 and *J*-resolved spectra were processed using magnitude calculations, whereas 2D TOCSY spectra were acquired and processed in the phase-sensitive, echo/anti-echo mode.

NMR studies of the effect of acids, base, and neutral solvents on compounds **1** *and* **11**.—Solutions of **1** or **11** (1 mg) in aliquots (0.4 mL) of various solvents and their mixtures with organic acids and bases were prepared

from chloroform-*d*, methyl sulfoxide-d_6, acetic acid-d_4, 9:1 v/v trifluoracetic acid–acetic acid-d_3, trifluoracetic acid, trifluoromethanesulfonic acid, and triethylamine. The ^{1}H NMR spectra of the mixtures were recorded immediately, and then again during the several hours following preparation of the solutions. For solutions that contained no deuterium, methyl sulfoxide-d_6 (one drop) was added to provide a field-frequency lock. The color of the solutions was noted.

NMR studies of the effect of chiral shift reagents on quinoxaline derivative **11**.—Stock solutions of the chiral shift reagents europium tris[3-(heptafluoropropyl-hydroxymethylene)-(+)-camphorate], europium tris[3-(heptafluoropropyl-hydroxymethylene)-(−)-camphorate], praseodymium tris[3-(heptafluoropropyl-hydroxymethylene)-(+)-camphorate], ytterbium tris[3-(heptafluoropropyl-hydroxymethylene)-(+)-camphorate], europium tris[3-(trifluoromethyl-hydroxymethylene)-(+)-camphorate], and praseodymium tris[3-(trifluoromethyl-hydroxymethylene)-(+)-camphorate] (1 mg of each) in aliquots of chloroform-*d* (1 mL) were prepared. Each solution was added dropwise (up to a maximum of seven drops) to solutions of **11** (1 mg) in chloroform-*d* (0.4 mL), and the ^{1}H NMR spectra of the mixtures were recorded after each addition. The NMR shift reagents were obtained in a kit from Aldrich Chemical Co., Milwaukee, WI.

1-Phenylamino-2-phenylazo-cyclobut-1-ene-3,4-dione (**1**).—To a solution of 1-anilino-2-phenylhydrazino-cyclobut-1-ene-3,4-dione[6] (1.40 g) in 50 mL of THF was added 0.55 g of benzoquinone, and the mixture was refluxed for 10 min. Evaporation and extraction with EtOH afforded the desired product that crystallized from THF in red needles: mp and mixed mp 175–176 °C; ν_{max} (KBr) 1775; 1740 (C=O) cm^{-1}; MS *m*/*z* 277 (40% M$^+$).

2-(Phenylazo)-8a-(2-phenylhydrazino)-cyclobuta[b]-quinoxalin-1(8aH)-one (**11**).—To a solution of cyclobutanetetraone 1,3-bis(phenylhydrazone) (2 g) in 10 mL of DMF was added *o*-phenylene diamine (0.75 g), and the mixture was refluxed for 1 h. The syrup that separated on evaporation was crystallized from chloroform in yellow needles: mp and mixed mp 222–223 °C; MS *m*/*z* 380 (90% M$^+$); 273 (100% M − PhNHNH); ν_{max} (KBr) 3260 (NH) 1680 (C=O) cm^{-1}.

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