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The cations and anions of cyclobutanetetraone poly(phenylhydrazones)

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This paper is dedicated to the memory of Horace S. Isbell on the occasion of the tenth anniversary of his death. Isbell made significant contributions in all fields of Carbohydrate Chemistry, including many on the topic of the present paper. A few years after receiving his Ph.D., a co-author of this paper (M.A.S.) died in an auto accident.

Abstract

Six cyclobutanetetraone poly(arylhydrazones) have been treated with acids and bases, and the structures of the resulting anions and cations studied by UV–Vis absorption and NMR spectroscopy. In acid media, all the hydrazones studied formed cations, which exhibited bathochromic shifts due to the extension of their resonance systems. However, in bases, only some (those which could enolize) formed anions that exhibited hypsochromic shifts; the others were unaltered.

Keywords: Anions; Bathochromic shift; Cations; Cyclobutanetetraone poly(phenylhydrazones); Enolization; Hypsochromic shift; NMR spectroscopy; UV–Vis spectrophotometry

1. Introduction

It was shown by Isbell and Fatiadi[1] that the electronic absorption spectra of many phenylazo-phenylhydrazones show bathochromic shifts on protonation with strong acids. Such shifts occur because the cations formed contain significantly more conjugated double bonds than their parent compounds. The research of Isbell on the tautomerism of cyclitol poly(phenylhydrazones)[1–3] prompted other authors, including the present ones, to study the tautomerism and properties of vicinal polycarbonyls and their polyhydrazones.[4–13] The present work deals with a spectroscopic study of the cations and anions formed when cyclobutanetetraone poly(arylhydrazones) are treated with acids and bases, respectively.

2. Results and discussion

The cyclobutanetetraone poly(arylhydrazones) obtained in previous studies,[10,12] were treated with acids and bases and the resulting cations and anions studied by UV–Vis spectrophotometry (see Fig. 1) and NMR spectroscopy (see Figs. 2–6). The study involved

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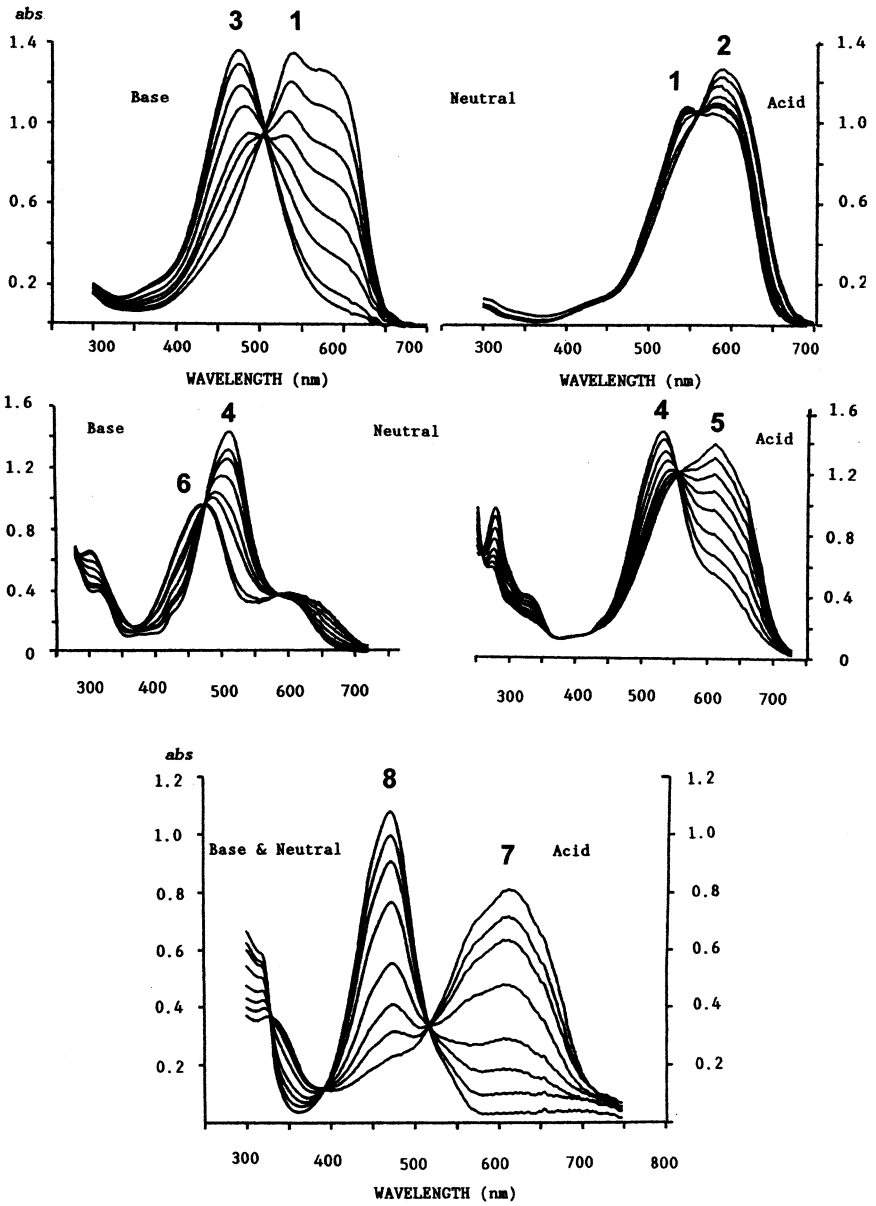


Fig. 1. Electronic absorption spectra of cyclobutanetetraone poly(phenylhydrazones). Top, spectra of the bis(phenylhydrazone) in basic (**3**), neutral (**1**) and acid media (**2**); middle, spectra of the tris(phenylhydrazone) in basic (**6**), neutral (**4**) and acid media (**5**); bottom, spectrum of the tetrakis(phenylhydrazone) in neutral or basic media (**8**) and acid medium (**7**). The curves show the effect of gradually increasing concentrations of acid or base.

three poly(*N*-phenylhydrazones) (**1**, **4**, and **7**) and three poly(*N*,*N*-disubstituted-hydrazones) (**10**, **11**, and **12**). The structures of these compounds have been confirmed by ^{1}H and ^{13}C NMR, a count of the number of types of phenyl ^{1}H and ^{13}C resonances in the spectra being particularly revealing of the symmetry or lack of symmetry in the structures.

Initially, solutions of the different polyhydrazones in dichloromethane were treated with ethanolic solutions of either acid or base, and the UV–Vis spectra were compared with the spectra of the untreated compounds. In acid media, bathochromic shifts occurred for all of the compounds (**1**, **4**, **7**, **10**, **11**, and **12**), with the first three compounds showing larger shifts (see Table 1), whereas in basic media, a hypsochromic shift occurred in the spectra of some compounds, while the spectra of others remained unchanged. This prompted us to carry out a closer study of the ions formed at different pH. Each compound was treated with increasing amounts of acid or base, and the successive UV–Vis spectra were recorded.

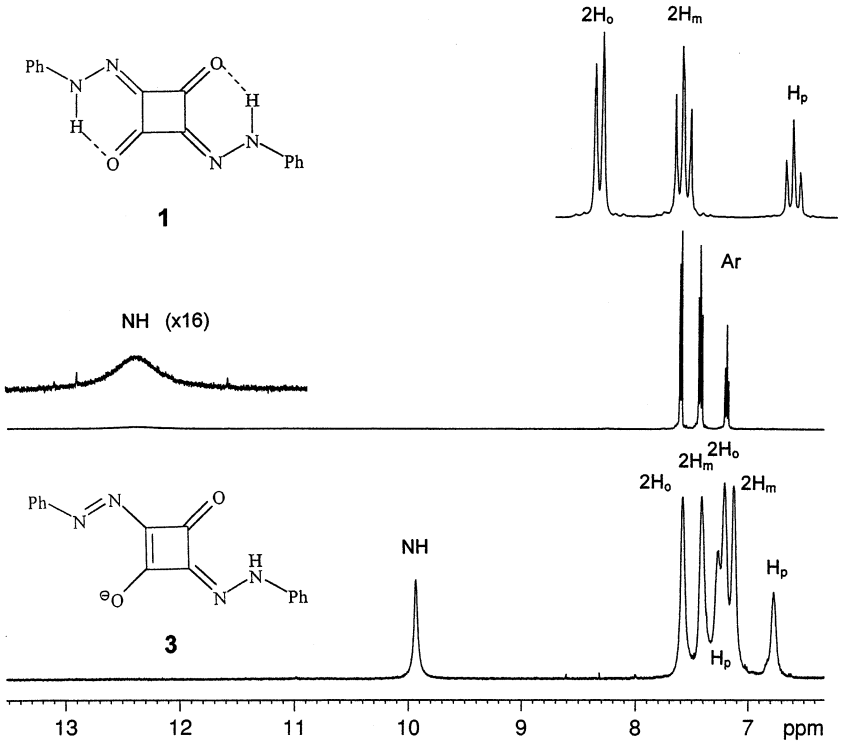


Fig. 2. Top, ^{1}H NMR spectrum of a solution of cyclobutanetetraone 1,3-bis(phenylhydrazone) (**1**) in Me_2SO-d_6 measured at 500 MHz, and showing a single type of phenyl group. Bottom, with Et_3N added, showing the generation of two types of phenyl signals for **3**, as well as a significant upfield shift ($\Delta\delta$ −2.45) and sharpening of the NH signal on disengagement of the hydrogen bonding.

When superimposed, these spectra revealed the number of species in equilibrium. Compounds **1** and **4** showed two isosbestic points, denoting the presence of three species in equilibrium, while compounds **7**, **10**, **11**, and **12** showed only one, thus demonstrating that only two species were in equilibrium (the neutral species was unaffected by bases; see Fig. 1 for the superimposed spectra of compounds **1**, **4**, **7**).

The bathochromic shifts exhibited by compounds **1**, **4**, **7**, **10**, **11**, and **12** in strong acid were reversible and quite similar to those observed by Isbell for cyclic and acyclic phenylazo-ene- (and enol-) phenylhydrazones.[1] Their cations were accordingly assigned analogous structures. For example, cyclobutanetetraone 1,3-bis(phenylhydrazone), which we previously found[10,12] to exist in a dichelated oxo-phenylhydrazone form (**1**), readily formed a pair of resonance-stabilized phenylazo-enol-phenylhydrazone cations (**2**) on treatment with ethanolic sulfuric acid. The hybrid of this resonance pair contains a string of 19 atoms in conjugation (12 in the two phenyl rings and seven in the azo-enol-hydrazono group that separates them), instead of only 11 atoms in the starting bishydrazone (**1**). This large increase in conjugation accounts for the bathochromic shift observed, the change in color, and the stability of the cations. Similarly, when cyclobutanetetraone tris(phenylhydrazone), which was found[10,12] to exist in a phenylazo-ene-phenylhydrazino-keto-phenylhydrazone form (**4**), was protonated, it formed several tautomeric pairs of keto–enol resonance-stabilized cations, depending on the position of the hydrazone residue protonated; to avoid repetition, only one of the possible keto-hydrazine forms is depicted (**5**). Likewise, cyclobutanetetraone tetrakis-(phenylhydrazone) (**7**), which was found to exist[10,12] in the all-hydrazone form, upon protonation formed a resonance pair (**8**) (see Schemes 1–3).

When cyclobutanetetraone poly(phenylhydrazones) **1**, **4**, and **7** were treated with a base (KOH or ethylamine) in ethanol, they did not behave uniformly; those compounds that possessed keto groups, such as cyclobutanetetraone bis- and tris-(phenylhydra-

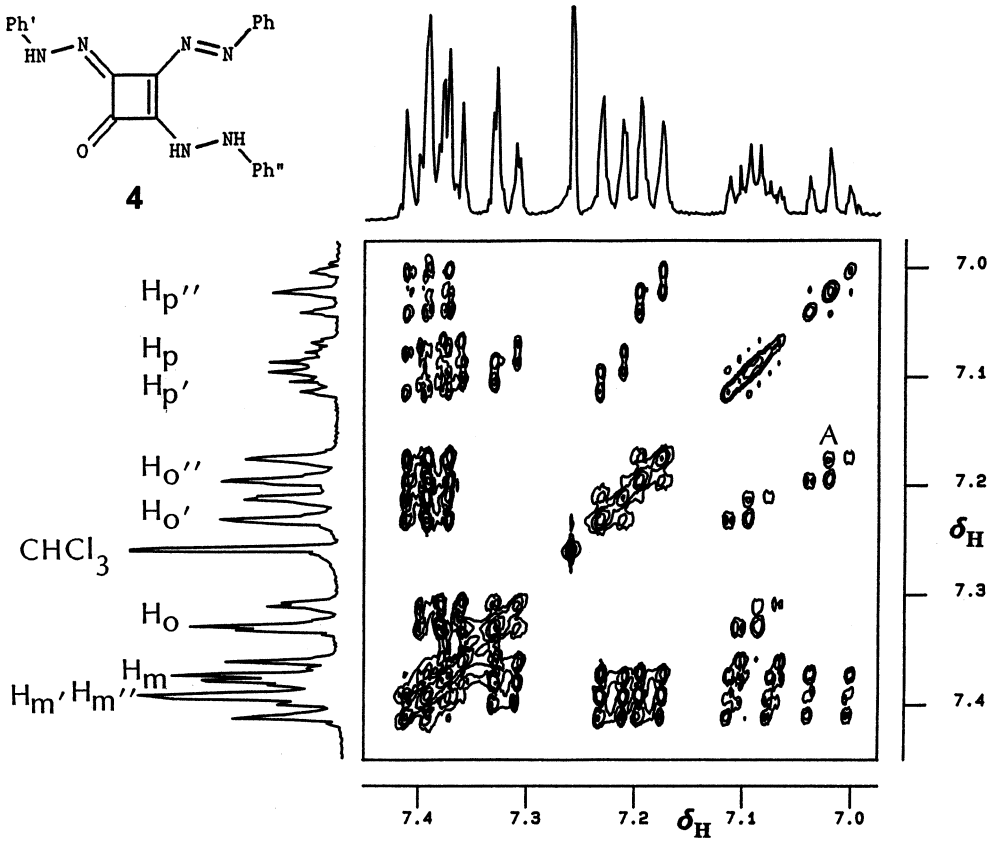


Fig. 3. 2D COSY-45 ^{1}H NMR spectrum of cyclobutanetetraone bis(phenylhydrazone)-2-phenylhydrazone (**4**) in $CDCl_3$ solution at 400 MHz, showing three types of phenyl group.

zones) (**1** and **4**), exhibited reversible hypsochromic shifts, whereas cyclobutanetetraone tetrakis(phenylhydrazone (**7**), which lacks any keto groups, was unaffected by this treatment (see Fig. 1). A likely reason for the hypsochromic shift of **1** and **4** is their ability to form enolates in bases, which compounds like **7** are unable to produce. This was confirmed by comparison of the ^{1}H NMR spectra of compound **1** and anion **3** (see Fig. 2). Compound **1** shows a broad, chelated NH signal at δ 12.38 and one type of H_o, H_m, and H_p signals for the phenyl ring, whereas **3** shows a one-proton, unchelated NH signal at δ 9.93, and two types of H_o, H_m, and H_p signals for the phenyl rings.[†] To test this hypothesis, we studied the spectra of cyclobutanetetraone bis(*N*-methyl-*N*-phenylhydrazone) (**10**) and bis(*N*,*N*-diphenylhydrazone) (**12**) in base. The UV–Vis spectra of both compounds were unchanged in base, suggesting that the hypsochromic shift observed for compounds **1** and **4** was indeed due to their enolization. The unsymmetrical structure of **4** was confirmed by its 2D COSY ^{1}H NMR (see Fig. 3) and 2D HMBC NMR spectra (see Fig. 4), which each showed evidence for the presence of three different types of phenyl groups, in either ^{1}H or ^{13}C dimensions.

The lack of chelation in compound **10** was apparent in a comparison of its carbonyl IR absorption with that of compound **1** (see Table 1), and its greater affinity towards nucleophiles. For example, **10** reacts with phenylhydrazine to yield an analog of compound **4**, namely 1-*N*-methyl-*N*-phenylhydrazono-2-*N*-methyl-*N*-phenyl-hydrazino-3-phenylazo-cyclobut-2-ene-4-one (**11**) (see Scheme 4).

Cyclobutanetetraone 1,3-bis(phenylhydrazone) (**1**) and sugar osazones do not react readily with excess phenylhydrazine, because of their chelation.[10–12] The structure of com-

[†] The loss of the splittings due to spin coupling of the aromatic protons of **3** is an interesting feature of its ^{1}H NMR spectrum (see Fig. 2), which appears to be due to chemical exchange of the tautomers of **3** under basic conditions.

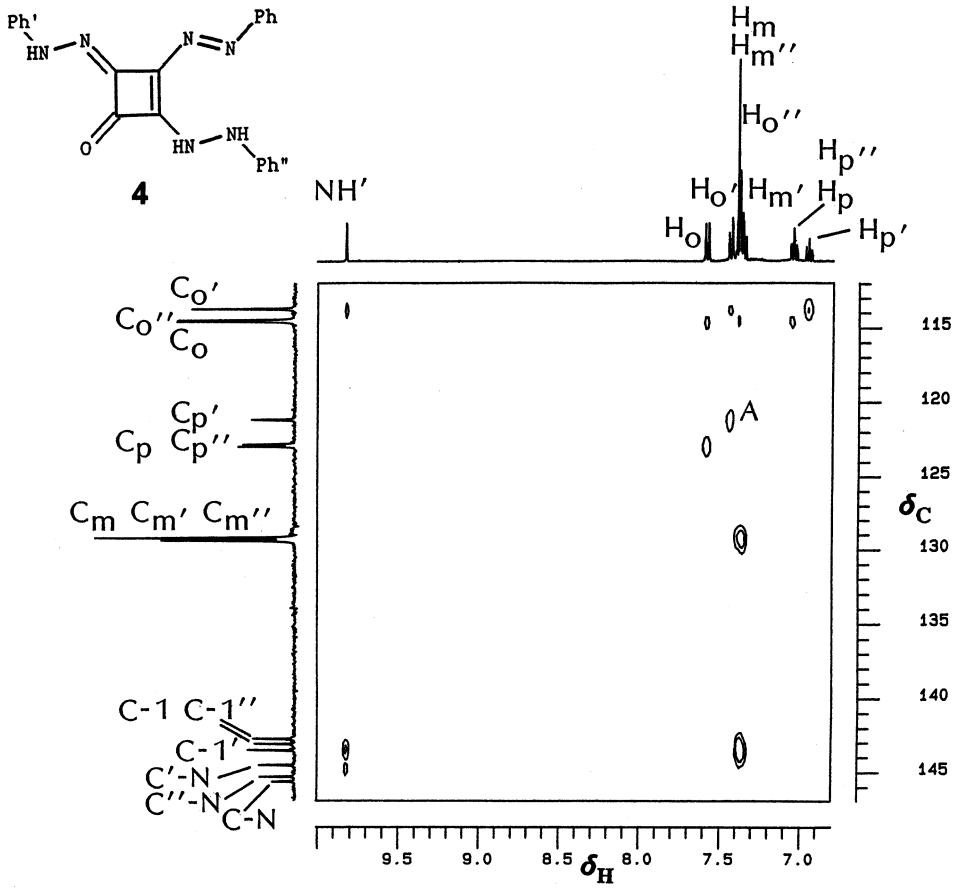


Fig. 4. 2D HMBC NMR spectrum of cyclobutanetetraone bis(phenylhydrazone)-2-phenylhydrazone (**4**) in Me_2SO-d_6 solution at 400/100.6 MHz, showing the chemical shift correlation of three sets of phenyl ^{13}C nuclei with three sets of phenyl protons.

pound **10** was confirmed by its ^1H and ^{13}C NMR spectra (see Fig. 5), which clearly revealed only one type of phenyl group and one type of methyl group in both ^1H and ^{13}C spectra, and one type of C=O and C=N in the ^{13}C NMR spectrum. In contrast, the ^1H and ^{13}C NMR spectra of unsymmetric compound **11** showed three different types of phenyl groups and two different methyl groups in their ^1H and ^{13}C NMR spectra, and one type of NH in the ^1H NMR spectrum, and one C=O in the ^{13}C NMR spectrum. A 2D COSY ^1H NMR spectrum of **11** in $CDCl_3$ (see Fig. 6), further confirmed its structure by showing the expected ^1H–^1H connectivities within the three sets of aromatic protons.

A literature survey showed that some phenylazo-ene-phenylhydrazones form resonance-stabilized ions that show bathochromic shifts in both acidic and basic media.[1,13] However, such bathochromic shifts in bases were not reported by Isbell in his study of phenylazo-enol-hydrazones,[1] nor were they observed in the cyclobutanetetraone poly(phenylhydrazones) studied here. The reason for this is that NH groups form cations more easily than anions (For example ammonia, a weak base, is readily protonated in acidic media, but is very difficult to dissociate, because it is one of the weakest acids). Accordingly, when cyclobutanetetraone poly(phenylhydrazones) **1**, **4**, **7**, **10**, **11**, and **12** are treated with strong acids, their NH groups are readily protonated, and they afford the observed pairs of canonical forms which stabilize the resulting phenylazo-enol-phenylhydrazone cations, and induce bathochromic shifts. However, when compounds **1** and **4** are treated with a strong base, they overcome the difficult dissociation of their NH groups by enolizing, and then dissociating the more acidic enolate proton. This pathway is not only more facile than the direct dissociation of the NH group, but it also produces anions having the negative charge on the more electronegative oxygen

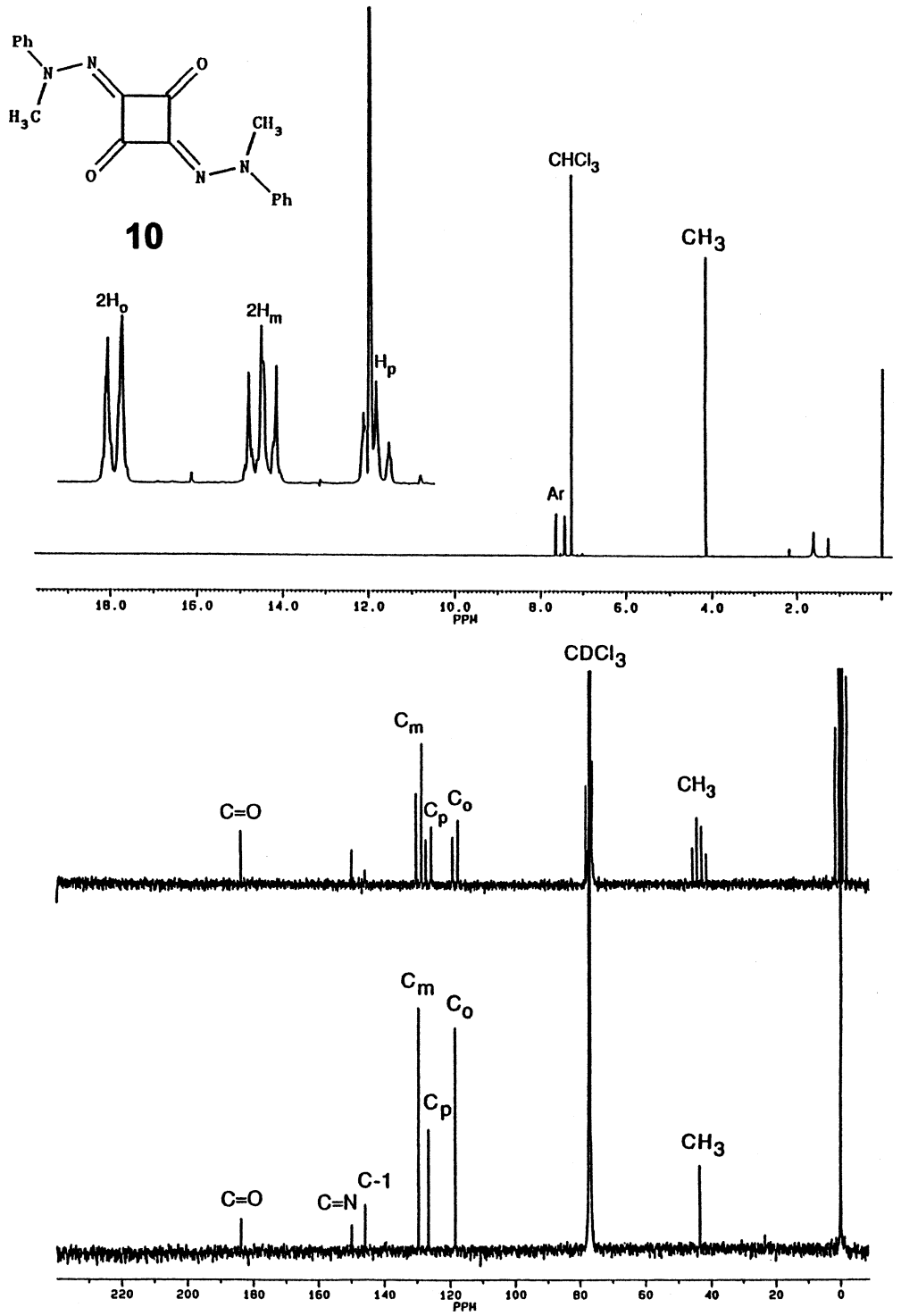


Fig. 5. NMR spectra of cyclobutanetetraone 1,3-bis(*N*-methyl-*N*-phenylhydrazone) (**10**) in $CDCl_3$ solution, showing the presence of one type of phenyl group and one type of methyl. Top, ^1H NMR spectrum at 400 MHz; middle, ^1H coupled ^{13}C NMR spectrum at 100.6 MHz; bottom, ^1H decoupled ^{13}C NMR spectrum.

atom, instead of on the less electronegative nitrogen (see Scheme 1). The absence of a keto group in compound **7**, and the inability of compounds **10**–**12** to enolize (because of a lack of available protons) necessitates the direct removal of NH protons by base. This process is difficult to achieve and requires the use of strong base in aprotic solvents.[1,13]

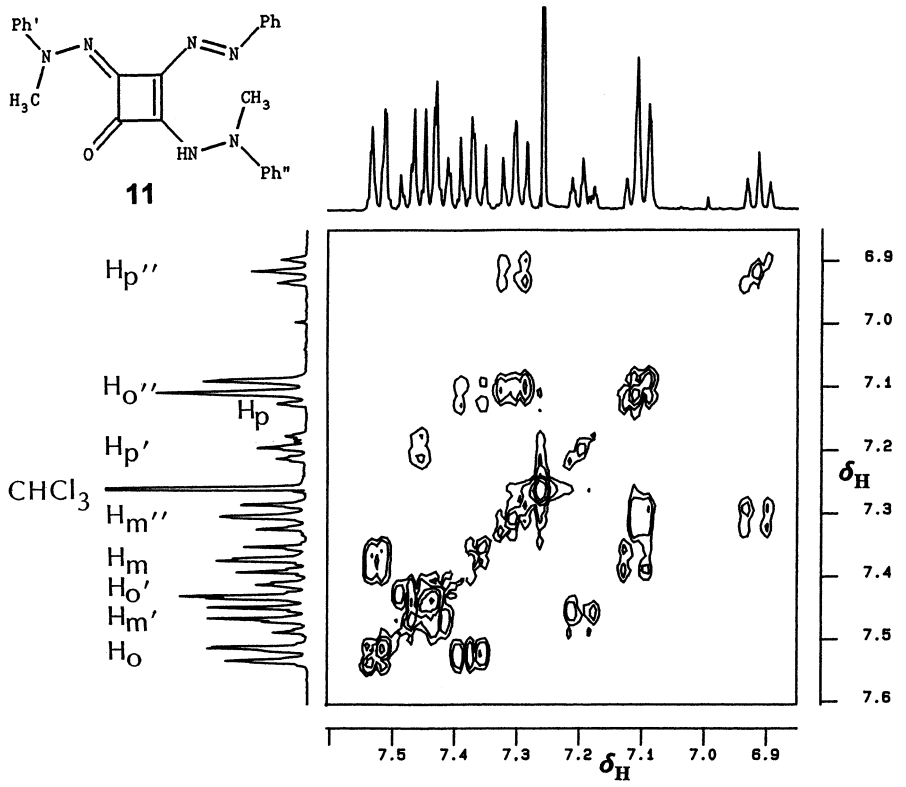


Fig. 6. 2D COSY-45 ^{1}H NMR spectrum of cyclobutanetetraone bis(*N*-methyl-*N*-phenylhydrazone)-2-phenylhydrazone (**11**) in $CDCl_3$ solution, showing the expected ^{1}H–^{1}H connectivities of the aromatic protons.

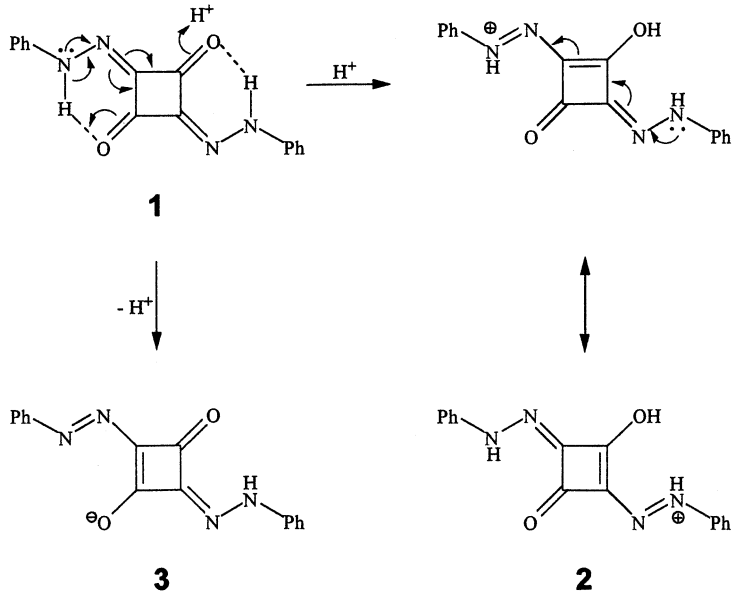
Anions **3** and **6** do not exhibit bathochromic shifts because their conjugation has not been altered by ionization; the number of conjugated double bonds in the enolate is the same as in the starting phenylazo-enol-phenylhydrazones or its keto tautomer. It is possible of course to draw non-equivalent resonance pairs of phenylazo-phenylhydrazone enolates having negative charges on oxygen in one form, and on nitrogen in the other form. Because the first anion is more stable (oxygen is more electronegative than nitrogen), such resonance would contribute little to the stability of the anion. This explains why phenylazo-phenylhydrazones and phenylazo-ene-phenylhydrazones, but not phenylazo-enol- (or keto-) phenylhydrazones, exhibit bathochromic shifts in bases.

3. Conclusions

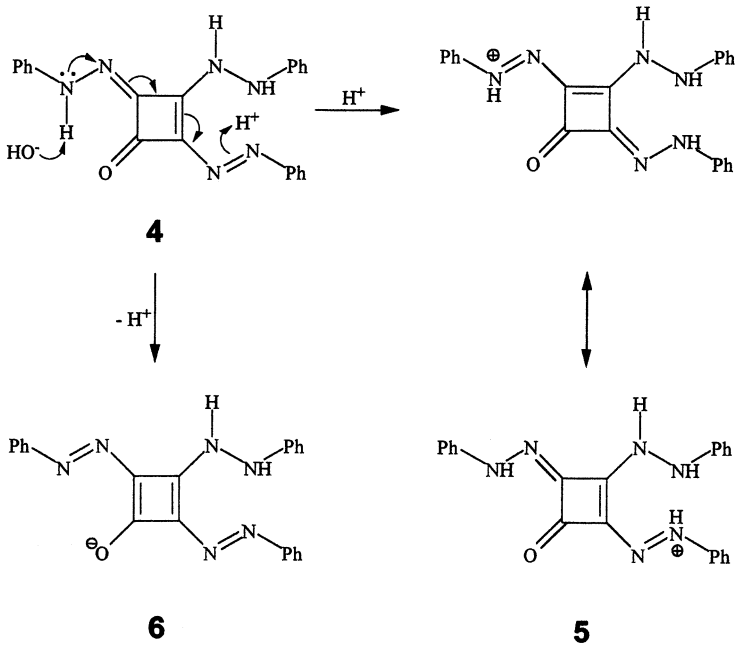
Studies of the UV–Vis absorption spectra of cyclobutanetetraone poly(phenylhydrazones) in the presence of acids and bases and a review of the literature on cyclopentene and cyclohexene poly(phenylhydrazones)[1] have led us to the following conclusions regarding the cations and anions of cycloalkanone poly(phenylhydrazones):

Table 1
UV–Vis and IR spectrophotometric data for cyclobutanetetraone poly(phenylhydrazones)

Compound	Color	λ_{max} (nm)	ν_{max}C=O (cm^{-1})	Media
1	blue	540; (570 sh)	1680	neutral
2	deep blue	590		acidic
3	red	460		basic
4	violet	526; (620 sh)	1740	neutral
5	dark blue	625		acidic
6	lavender	460		basic
7	red	474	–	neutral and basic
8	blue	620		acidic
10	magenta	514	1672	neutral and basic
	violet	518		acidic
11	violet	503	1760	neutral and basic
	indigo	538		acidic
12	green	538	1685	neutral and basic
	olive	546		acidic



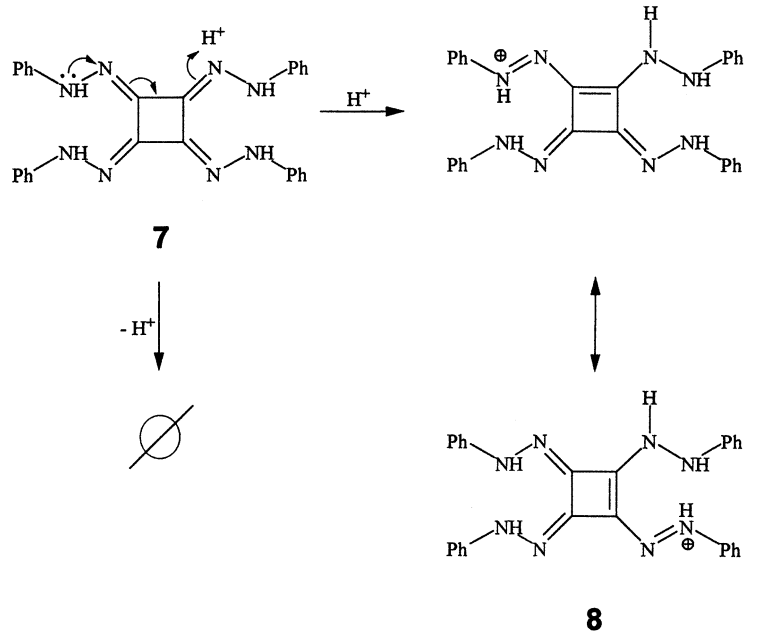
Scheme 1.



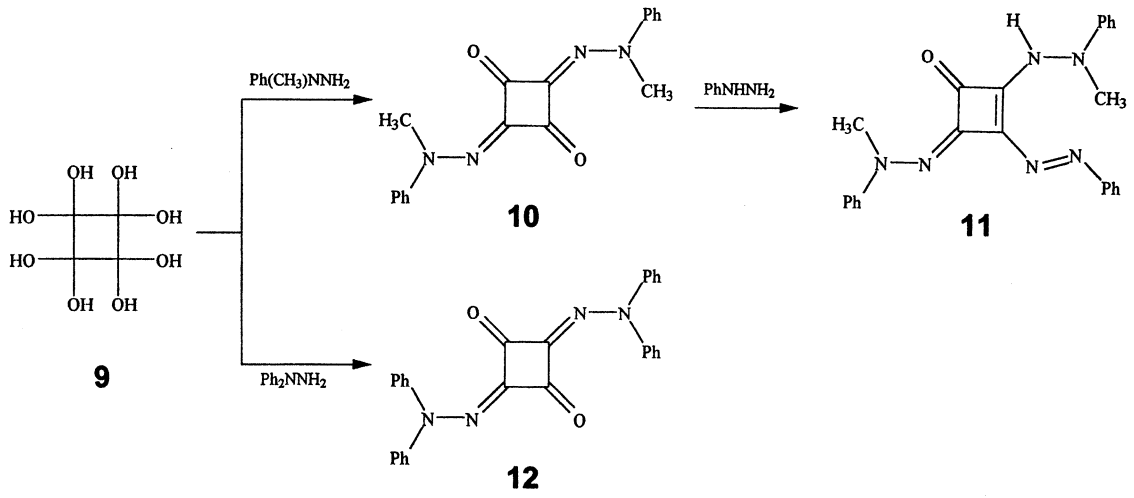
Scheme 2.

1. Bathochromic shifts are observed in resonance-stabilized phenylazo-enol-phenylhydrazone cations produced when poly-(phenylhydrazones) are treated with strong acids. The groups needed to form such resonance-stabilized cations include phenylazo- and phenylhydrazono groups linked directly (as in formazans), or through ene, enol, or ene-hydrazine groups (–C=C–, –C=C–OH, or –C=C–NH–NH–Ph).

2. Phenylazo-keto-phenylhydrazones do not exhibit bathochromic shifts in basic media, because the OH groups they can form by enolization are stronger acids than their NH groups, and the anions formed have negative charges on oxygen instead of on nitrogen. They exhibit hypsochromic shifts because the enolate ions formed have weaker chromophores than the starting keto-phenylhydrazones.



Scheme 3.



Scheme 4.

3. Polyhydrazones lacking protons in their hydrazone residues (for example oxo-bis(*N*,*N*-diphenylhydrazones) can enolize in acids, but not in bases. They therefore show bathochromic shifts in acids, but remain unchanged in bases.
4. Phenylazo-ene-phenylhydrazones exhibit bathochromic shifts in acids and bases, but their ionization in acid requires milder conditions than in base (NH groups are more readily protonated than dissociated). The hydrazones can be protonated in either protic or aprotic solvents, but are dissociated in aprotic solvents only (protic solvents will dissociate in base).

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

‡ Certain commercial equipment, instruments, or materials are identified in this paper to adequately specify the experimental procedure. Such identification does not imply recommendation by the National Institute of Standards and Technology, nor does it imply that the materials are necessarily the best available for the purpose.

spectra were measured with a BIORAD FTS-7 FTIR spectrophotometer.

Materials.—Cyclobutanetetraone was prepared as described in the literature.[14] Compounds **1**, **4**, **7**, **10**, **11**, and **12** were prepared as described in previous papers,[10,12] and their structures were then confirmed by C, H, and N combustion analysis, as well as MS and NMR spectral analyses.

UV–Vis spectrophotometry.—UV–Vis spectra of the compounds shown in Table 1 and Fig. 1 were recorded by use of an HP 8452A diode-array spectrophotometer. Stock solutions of each of compounds **1**, **4**, **7**, **10**, **11**, and **12** (5 mg) in CH_2Cl_2 (10 mL) were treated with abs EtOH (10 mL) and diluted to 50 mL with a 'neutral diluent' (1:1 v/v CH_2Cl_2–EtOH) The stock solutions were then used in all of the experiments. For Table 1, the spectra of the neutral species were acquired by diluting the stock solutions as necessary, with more of the 'neutral diluent'. For spectra of the anions and cations, the stock solutions were diluted with either an 'acid diluent' (1:2:2 v/v concd H_2SO_4–CH_2Cl_2–EtOH), or a 'basic diluent' (1:2:2 v/v ethylamine–CH_2Cl_2–EtOH), respectively. Superimposed spectra such as those shown in Fig. 1 were acquired by recording on a printed spectrum of the neutral species (diluted with the neutral diluent), the spectra of either their cations or anions measured in increasing amounts of acidic or basic diluents. The desired concentrations of acid or base were achieved by increasing the ratio of the acid or the basic diluents to that of the neutral diluent. The pH of the various solutions was measured to confirm the conditions.

NMR spectroscopy.—NMR spectra were acquired at 300 K by using either Bruker Instruments WM 400 or DRX 500 spectrometers. 1D ^{1}H NMR spectra were measured at either 400 or 500 MHz, by using either 30° (3.3 μs at 400 MHz) or 90° (9 μs at 500 MHz) pulses, spectral widths of 8 kHz, pulse recycle times of 4 s (400 MHz) or 4.8 s (500 MHz), and 32,768 point data sets. 1D ^{13}C NMR spectra were recorded at 100.6 MHz, either in the ^{1}H decoupled mode (WALTZ-16), or in the ^{1}H coupled mode with the nuclear Overhauser effect, by use of gated decoupling. 2D COSY ^{1}H NMR spectra were acquired at 400 MHz by use of a 45° (3.3 μs) mixing pulse, with 2048 (t_2) × 128 (t_1) point data sets zero-filled to 256 points in the t_1 dimension. One-bond and multiple bond ^{1}H–^{13}C chemical shift correlations were performed at 400–100.6 MHz by the 2D HMQC and HMBC methods, respectively, as described previously.[10]

Microanalyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, MI. Squaric acid and the substituted hydrazines were purchased from Aldrich Chemical Co. Milwaukee, WI.

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