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Deprotonation Equilibrium of 5-Tropolonediazonium Salt Strongly Favors 1,2,5-Tropoquinone-5-diazide Structure in Certain Solvents

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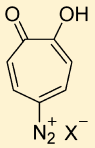
Supporting Information

ABSTRACT: 5-Tropolonediazonium salt **1** is a well-known intermediate for the preparation of 5-substituted tropolone derivatives, but 1,2,5-tropoquinone-5-diazide **2**, which is expected to be formed by deprotonation of **1**, has not been reported. We synthesized **2**, and the structures of **1** and **2** were investigated and compared. NMR and UV spectral data indicated that **1** is easily deprotonated in water, methanol, DMSO, and DMF and exists in the form of **2** in these solvents (but not in acetone or acetonitrile) because of its strong acidity (estimated pK_a −2.07). Thus, the acid−base equilibrium shows strong solvent-dependence. Compound **2** may be synthetically available as a carbene precursor.



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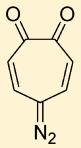

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INTRODUCTION

Tropolone (2-hydroxy-2,4,6-cycloheptatrien-1-one), which contains an unsaturated seven-membered ring, is a nonbenzenoid aromatic compound.[1] Its chemical behavior is intermediate among those of β-diketone, vinylogous carboxylic acid, and phenol: it is readily halogenated and nitrosonated like phenol, but electrophilic substitution reactions, such as the Friedel−Crafts and Gattermann reactions, do not take place because of its basicity.[1,2] Furthermore, although tropolone's carbonyl group is not reactive, its hydroxy group, which can be regarded as a vinylogous carboxylic acid, can be easily converted into a halo or methoxy group.[3−5] The acidity of tropolone (pK_a = 6.92)[6] is intermediate between those of benzoic acid (pK_a = 4.2)[7] and phenol (pK_a = ca. 9.9).[8]

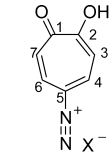
On the basis of its chemical properties, the tropolone moiety is of interest as a pharmacophore in place of benzoic acid or phenol.[9] Further, the natural products colchicine and hinokitiol, which contain a tropolone ring, have potent antitumor and antimicrobial activities.[10,11] Thus, we have been investigating the structural and medicinal chemistry of tropolone and its derivatives.

Diazotization of 5-aminotropolone is an important reaction for tropolone derivative synthesis.[1] Because 5-tropolonediazonium salt **1** (Scheme 1), which is obtained by treatment of 5-aminotropolone with sodium nitrite in acid in situ, can be derivatized to various 5-substituted tropolone compounds, including 5-halo, 5-cyano, 5-hydroxy, and 5-alkoxy derivatives, via Sandmeyer reaction.[12,13]

On the other hand, diazotization of arylamines having a *para* hydroxy group is well-known; an example is the formation of 4-hydroxybenzenediazonium salt **3**, which has properties quite different from those of a typical diazonium salt.[14,15] Deprotonation of **3** affords 1,4-benzoquinonediazide (4-diazo-2,5-cyclohexan-1-one) **4**, which can be regarded as a cyclic vinylogue of α-diazo ketones and is used as a carbene reaction precursor (see Table 1 for structures).[16] Recently we showed that 5-nitrosotropolone exists in the tropoquinone-5-monoxime form, rather than the 5-nitroso form, by means of NMR and UV studies.[17] The diazo group is known to be powerful electron-withdrawing group, like the nitroso group. Therefore, we speculated that if 5-tropolonediazonium salt **1** is deprotonated, it may exist in the diazo form **2** (Scheme 1), which might be available as a carbene precursor, as in the case of **4**.[16,18] However, little information is available about the structure of **2** and its relationship to **1**, to our knowledge.

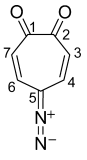
Therefore, in this paper, we carefully investigated the structures of 5-tropolonediazonium salt **1** and 1,2,5-tropoquinone-5-diazide **2** by means of NMR and UV spectral measurements. Our results indicate that **1** exists predominantly in the form of **2** in solvents such as water, methanol, DMSO and DMF, because of its very strong acidity (estimated pK_a −2.07).

Scheme 1. 5-Tropolonediazonium salt 1 and 1,2,5-Tropoquinone-5-diazide 2



diazonium form **1**

1a: X=Cl **1b**: X=BF_4



diazo form **2**

RESULTS AND DISCUSSION

Synthesis of 5-Tropolonediazonium Salt 1 and 1,2,5-Tropoquinone-5-diazide 2. Diazotization of 5-aminotropolone in hydrochloric acid with sodium nitrite gave 5-tropolonediazonium chloride (**1a**: X = Cl) in situ. The reaction mixture was extracted, and the product was purified by chromatography, giving a brown powder **2**. We could not crystallize **2** for X-ray analysis because **2** was unstable under the crystallization conditions. In order to determine the structure of

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2, 5-tropolonediazonium salt **1** was also prepared for comparison. Generally, diazonium salts are very unstable and explosive in dry form. However, it is known that the stability of diazonium salts depends upon the counteranion; for instance, diazonium compounds can be isolated as tetrafluoroborate salts and stored at room temperature.[19]

Therefore, 5-tropolonediazonium tetrafluoroborate (**1b**: X = BF_4) was prepared from 5-aminotropolone in tetrafluoroboric acid diethyl ether complex (HBF_4·Et_2O) with isoamyl nitrite or from **2** with HBF_4·Et_2O.

Structural Determination of 1 and 2 Using IR, NMR, and UV Spectroscopy. In order to confirm the structures of **1b** and **2**, the IR spectra (neat) were analyzed (see the Experimental Section and Supporting Information). The IR spectra of quinone diazides have two characteristic strong bands in the N═N absorption (2250−2000 cm^{-1}) and C═O absorption (1650−1600 cm^{-1}) regions.[15] On the other hand, diazonium salts showed the characteristic $^{+}N{\equiv}N$ absorption at 2294−2110 cm^{-1}.[15] The N═N absorption of **2** at 2016 cm^{-1} was shifted to lower wavenumber as compared with the $^{+}N{\equiv}N$ absorption of **1b** at 2255 cm^{-1}. These bands of **2** and **1b** are similar to the corresponding N═N absorption of **4**[20] at 2076 cm^{-1} and $^{+}N{\equiv}N$ absorption of **3**[21] at 2224 cm^{-1}, respectively.

The C═O absorptions of **1b** and **2** appeared at 1618 and 1542 cm^{-1}, respectively. The C═O absorption of **1** at 1618 cm^{-1} is similar to that of tropolone-5-carboxylic acid[22] having electron-withdrawing group at 1618 cm^{-1}. In contrast, the C═O absorption of **2** was shifted considerably to lower wavenumber (1542 cm^{-1}) than that of 3,6-cycloheptadiene-1,2,5-trione (1672, 1650, 1613 cm^{-1}).[23] In general, the C═O absorption of quinone diazides is shifted to lower wavenumber as compared with that of the corresponding quinones: the most extreme example is the C═O absorption of 2,6-dichloro-1,4-benzoquinone diazide (4-diazo-2,6-dichloro-2,5-cyclohexadienone) at 1580 cm^{-1}, which is shifted by 122 cm^{-1} compared with that of 2,6-dichloro-1,4-benzoquinone at 1702 cm^{-1}.[20] These results indicated that **1b** and **2** exist in the diazonium form and the diazo form, respectively, in the solid state.

The ^1H NMR spectrum of **2** was compared with that of **1b** in absolute CD_3CN (Figure 1). The ^1H NMR spectrum of **1b** in CD_3CN (Figure 1, spectrum A) showed only two doublet signals at δ 8.18 ppm (H4 and H6) and δ 7.35 ppm (H3 and H7). This is because signal averaging between H4 and H6 and signal averaging between H3 and H7, occurs as a result of rapid proton migration between the two oxygens of tropolone.[24] In the ^1H NMR spectrum of **2** (Figure 1, spectrum B), the H4 and H6 proton signal, and H3 and H7 proton signal were found at δ 7.23 and 6.30 ppm, respectively, and these two signals were shifted to higher field by ca. 1 ppm compared with those of **1b**. Addition of HBF_4·Et_2O/CD_3CN to **2** in CD_3CN caused lower field shifts (Figure 1, spectrum C), and further addition of Na_2CO_3/D_2O restored the signals of **2** in CD_3CN (Figure 1, spectrum D).

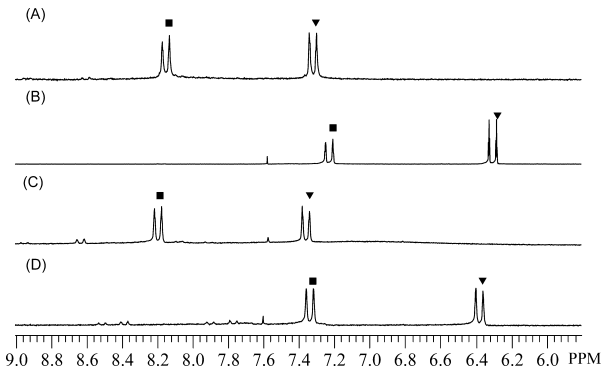
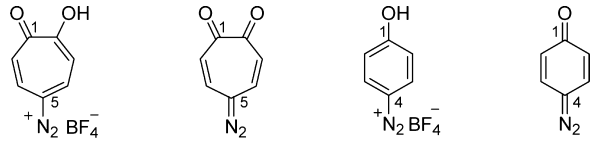


Figure 1. ^1H NMR spectra of **1b** and **2** in CD_3CN: (A) **1b**; (B) **2**; (C) **2** after addition of 1 M HBF_4·Et_2O (1.6 equiv); (D) spectrum after addition of 1 M Na_2CO_3/D_2O (2.5 equiv) to (C). Squares (■) show H4 and H6. Triangles (▼) show H3 and H7.

Next, the ^{13}C NMR spectra of **1b** and **2** were measured, and signals were assigned on the basis of ^1H/^{13}C correlation experiments (see the Supporting Information). Table 1 compares the chemical shifts of the carbonyl carbon (C1) and the N_2^+-bearing carbon (C4 or C5) in **1b**, **2**, **3**,[25] and **4**.[20]

As mentioned above, ^{13}C NMR spectra of tropolone in solution always exhibit averaged signals due to the two tautomeric forms: for example, the signal due to C1 (C═O) and C2 (C−OH) of tropolone are observed at 172 ppm ($CDCl_3$).[26] On the other hand, the signal of C1 (C═O) and C2 (C═O) of *p*-tropoquinone structure, such as in 3,6-cycloheptadiene-1,2,5-trione, is found at much lower field, at δ 186 ppm ($CDCl_3$).[23] In the ^{13}C NMR spectra of **1b** and **2** in CD_3CN, C1 (δ 185.0 ppm) of **2** similarly appeared at lower field than C1 (δ 177.3 ppm) of **1b**, but the difference was not sufficient to allow unequivocal structure determination. However, the difference of chemical shift between C5 (δ 83.6 ppm) as the N_2^+-bearing carbon of **2** and C5 (112.7 ppm) of **1b** was very large, and these signals are close to those of corresponding benzene derivatives, i.e., C4 (δ 75.2 ppm[20] in DMSO-d_6) as the N_2^+-bearing carbon of **4** and C4 (99.7 ppm[25] in DMSO-d_6) of **3**, respectively.

Table 1. ^{13}C NMR Data for 1b, 2, 3, and 4



compd	solvent	C_1 (ppm)	$C_{4\ or\ 5}$ (ppm)
1b	CD_3CN	177.3	111.0[a]
1b	CF_3COOD	178.9	114.0[a]
2	CD_3CN	185.0	83.6[a]
2	CF_3COOD	179.3	112.7[a]
3	DMSO-d_6[c]	169.5	99.7[b]
4	DMSO-d_6[d]	180.8	75.2[b]
4	CF_3COOD[d]	173.4	101.7[b]

[a]Chemical shift of C_5. [b]Chemical shift of C_4. [c]Reference 25. [d]Reference 20.

In CF_3COOD, the chemical shifts C1 and C4 of **2** are close to those of the corresponding carbons of **1b**, as in the spectrum of **4** in CF_3COOD,[20] which showed good agreement with that of **3**. The signals were assigned on the basis of ^1H/^{13}C correlation experiments (see the Supporting Information). These shift changes can be considered as the result of protonation at the oxygen atom of **2** and consequent structural change from diazo form **2** to diazonium form **1**.

The UV spectra of **1b** and **2** were analyzed in acetonitrile (Figure 2). The UV spectrum of **2** in absolute acetonitrile showed an absorption maximum at 384 nm, which coincides with that of **2** under basic conditions [in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO)]. However, in the spectrum of **2** under acidic conditions (in the presence of

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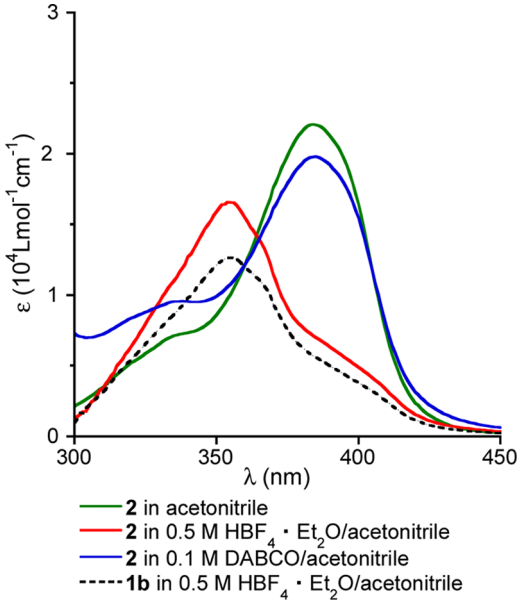

Figure 2. UV spectra of **1b** and **2**. Concentrations were as follows: **1b** in 0.5 M HBF_4·Et_2O/acetonitrile (1.1×10^{-4} M), **2** in acetonitrile (6.8×10^{-5} M), **2** in 0.5 M HBF_4·Et_2O/acetonitrile (1.7×10^{-4} M), **2** in 0.1 M DABCO/acetonitrile (6.8×10^{-5} M).

HBF_4·Et_2O), the absorption maximum was observed at 356 nm, which coincides with that of **1b** under acidic conditions. These results are consistent with the above NMR results, indicating that **2** is protonated to **1** under acidic conditions; that is, **2** is the conjugate base of **1**. The UV spectra of **3** and **4** show similar phenomena to those described above.[14]

Thus, it can be concluded that the structures of **1b** and **2** in acetonitrile are the diazonium form and the diazo form, respectively.

Deprotonation of 1 in Various solvents. As discussed above, the spectrum of **2** in acetonitrile is distinguishable from that of **1b** by NMR and UV measurements. In contrast, the signals of **1b** in D_2O were shifted to higher field and coincided with those of **2** (Figure 3).

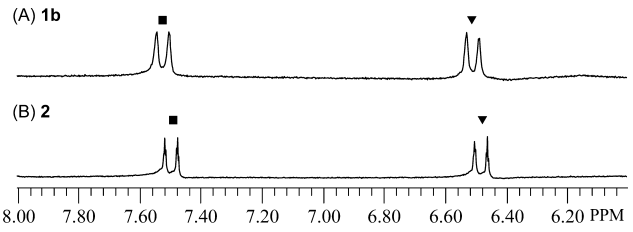

Figure 3. ^{1}H NMR spectra of **1b** and **2** in D_2O: (A) **1b**; (B) **2**. Squares (■) show H4 and H6. Triangles (▼) show H3 and H7.

Furthermore, the UV spectra of **1b** and **2** in aqueous solution were measured. The maximum absorptions at 392 and 410 nm of **1b** coincided with those of **2** (Figure 4), in accordance with the above NMR results. These results thus indicated that structural change from **1b** to **2** takes place in aqueous solution.

To investigate the structure of **1b** in solution, we measured the ^{1}H NMR spectra of **1b** and **2** in various solvents, such as acetone-d_6, CD_3OD, DMSO-d_6, and DMF-d_7. The ^{1}H NMR spectra of **1b** in CD_3OD,[27] DMSO-d_6, and DMF-d_7 are similar to those of **2**, but that in acetone-d_6 is not. These results indicate that **1b** takes

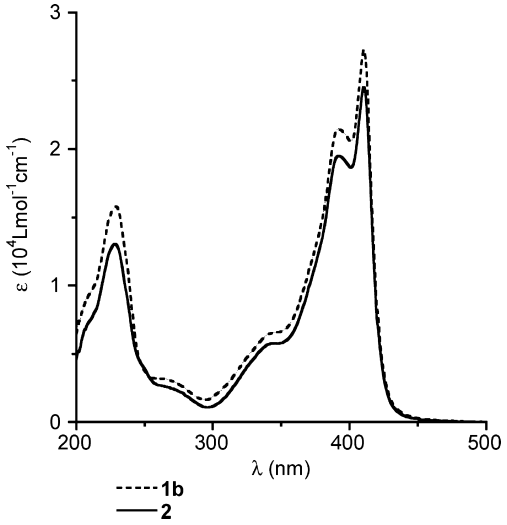

Figure 4. UV spectra of **1b** (4.2×10^{-5} M) and **2** (3.4×10^{-5} M) in aqueous solution.

the diazo form **2** in D_2O, CD_3OD, DMSO-d_6, and DMF-d_7, but not in CD_3CN or acetone-d_6.

In order to examine the solvent-dependent structural change of **1b**, the ^{1}H NMR spectra of **1b** were measured in CD_3CN containing various amounts of D_2O (Figure 5).

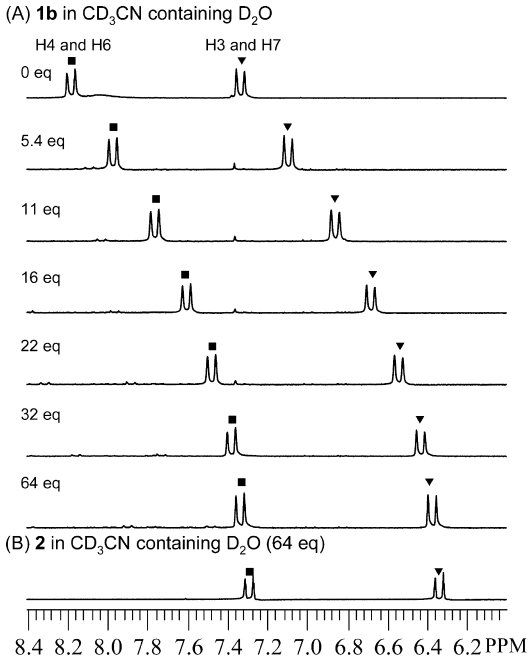

Figure 5. ^{1}H NMR spectra of **1b** and **2** in CD_3CN with D_2O: (A) **1b** with D_2O (0, 5.4, 11, 16, 22, 32, 64 equiv); (B) **2** with D_2O (64 equiv). A square (■) shows the signals of H4 and H6, and a triangle (▼) shows those of H3 and H7.

Figure 5 shows that a shift of NMR spectral signals accompanies the addition of D_2O. The addition of D_2O to **1b** in CD_3CN increased the ratio of **2** and the two signals (■ and ▼) were shifted toward high field. Finally, the ^{1}H NMR spectrum of **1b** in CD_3CN containing sufficient D_2O coincided almost exactly with that of **2** in CD_3CN containing D_2O (Figure 5, spectrum B). These higher-field shifts are essentially the same as those caused by addition of base (Na_2CO_3/D_2O, Figure 1,

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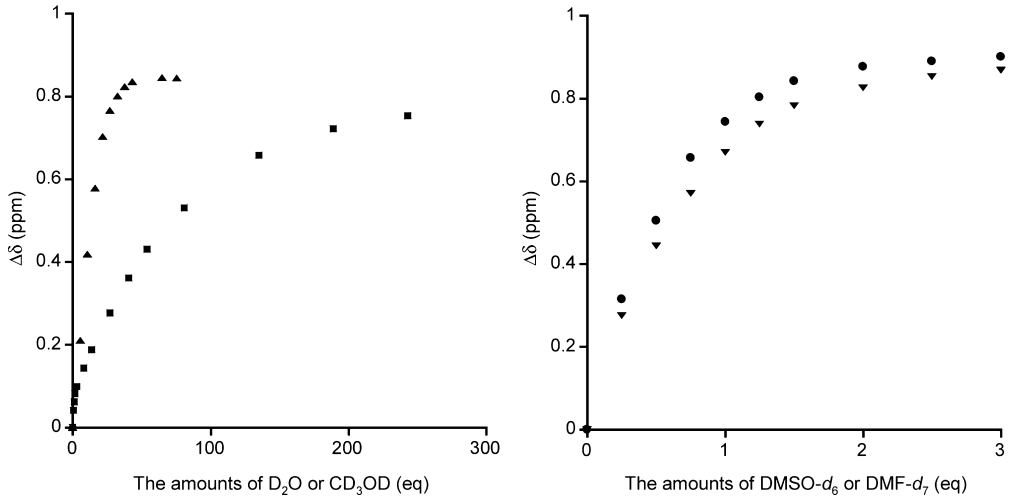
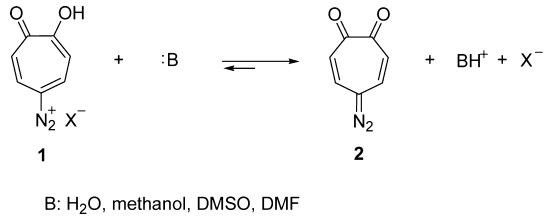


Figure 6. Chemical shift changes of H4 and H6 of **1b** in CD_3CN in the presence of various amounts of D_2O (▲), CD_3OD (■), DMSO-d_6 (●), or DMF-d_7 (▼). $\Delta\delta$ (ppm) = $\delta_{\text{additive free}} - \delta_{\text{observed}}$; $\delta_{\text{additive free}}$ is the chemical shift of H4 and H6 in the absence of additive (0 equiv), and δ_{observed} is the chemical shift in the presence of the indicated amount of the indicated additive. The amounts of added solvent (D_2O, CD_3OD, DMSO-d_6, or DMF-d_7) are shown as the ratio of base to **1b**.

spectrum D). When CD_3CN solution of **1b** was titrated with CD_3OD, DMSO-d_6 or DMF-d_7, similar behavior to that in the case of D_2O was observed. Figure 6 shows the chemical shift changes of H4 and H6 of **1b** in the presence of increasing amounts of D_2O, CD_3OD, DMSO-d_6 or DMF-d_7.

The deprotonation process required a much larger amount of CD_3OD as compared with D_2O. In contrast, the deprotonation process required only small amounts of DMSO-d_6 or DMF-d_7, so that the solvent effects were very marked. These results indicate that the structural change from **1** to **2** is due to water, methanol, DMSO, or DMF acting as a Brønsted base (Scheme 2).

Scheme 2. Structural Preference of 1 in Solution



The pK_a Value of 5-Tropolonediazonium Salt 1. The UV spectrum of **1b** in aqueous solution was measured over the pH range of −0.26 to 11.0 (see the Supporting Information, Figure S1). The spectrum of an acid solution at pH −0.26 was close to both that of a basic solution at pH 11.0 and that of **2** in aqueous solution (see Figure 4 and the Supporting Information, Figure S1). Therefore, the absorption at pH −0.26 can be assigned to **2**.

In order to estimate the acidity of **1**, we calculated the pK_a using the Hammett equation. It is known that the dissociation constants of tropolone derivatives are linearly correlated with Hammett's constants obtained in benzenoid compounds.[6,28−30] Therefore, it can be considered that 4- and 5-substituted tropolones correspond approximately to 3- and 4-substituted benzenoids, respectively. Thus, we estimated the pK_a value of **1** using the Yukawa−Tsuno equation (eq 1),[31] as in the case of phenol or aniline derivatives.

$$\log(k/k_0) = \rho[\sigma^0 + r(\sigma^- - \sigma^0)] \quad (1)$$

Substituent constants σ_m^0, σ_p^0, and σ_p^- and 4- and 5-substituted tropolone pK_a values were taken from the literature (see the Supporting Information, Table S1). The ρ value (2.39) was obtained from the correlation line for 4-substituted tropolones, and using this ρ value, the r value was calculated to be 1.64 (for details, see the Supporting Information, Figure S2). Therefore, the pK_a value of substituted tropolone can be expressed by eq 2.

$$pK_a = 6.92 - 2.39[\sigma^0 + 1.64(\sigma^- - \sigma^0)] \quad (2)$$

The applicability of eq 2 was supported by the linear correlation shown in Figure 7. Accordingly, the pK_a value of **1** was estimated

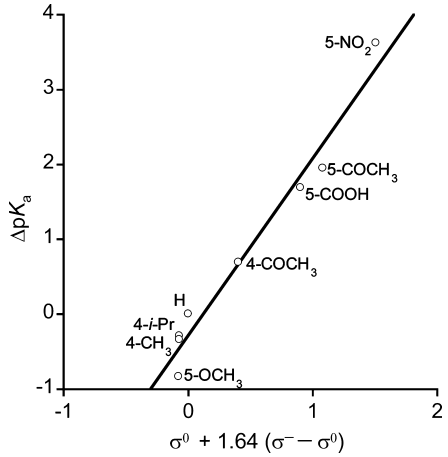


Figure 7. Application of eq 2 to the dissociation of 4- and 5-substituted tropolones. $\Delta pK_a = pK_{a0} - pK_a$; pK_{a0} is the pK_a value of unsubstituted tropolone and pK_a is that of 4- or 5-substituted tropolone ($R^2 = 0.968$).

to be −2.07. This result is consistent with the UV measurements, which indicated that **1b** exists in the form of **2** at pH −0.26 (see the Supporting Information, Figure S1). Thus, **1** is a strong acid, presumably due to the strong resonance effect of **1** with the diazonium ion group at the *para* position and the important contribution of **2**. This would be consistent with the contribution

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of **4** to the ionization of **3**: i.e., the pK_a value of **3** is ca. 3.4, being larger by a factor of about 10^6 than that of phenol (pK_a = ca. 9.9).[8]

Why Is the Equilibrium between 1 and 2 Solvent-Dependent? Overall, our results indicated that the structure change from **1b** to **2**, i.e., the dissociation equilibrium between **1b** and **2**, is due to the high acidity of **1b** and the properties of the solvent. As the basicity of a solution increases, and/or as the dielectric constant (ε)[32] increases, acidic substances are more easily ionized. In addition, solvation effects are involved in the acid−base equilibrium because as the proton (cation) and the conjugate base (anion) of an acid become more strongly solvated, the ions are increasingly stabilized, and the equilibrium moves in the direction favoring production of ions.[33,34] The most widely used basicity parameter, which serves as a measure of the ability of a solvent to solvate cations, is the donor number (DN) of Gutmann.[35] The larger the DN of the solvent, the greater is the basicity, and consequently the cation is increasingly stabilized. On the other hand, the solvent acidity and the ability of a solvent to solvate anions are characterized by acceptor number (AN).[36] The larger the AN of the solvent, the stronger is the acidity, and consequently the anion is increasingly stabilized.

We suggest that the structural change from **1b** to **2** is dependent on the pK_a value of the conjugate acid of the solvent, and the solvent properties (dielectric constant ε, DN, and AN). These parameters of the solvents used are shown in Table 2.

Table 2. pK_a of Conjugated Acid, Dielectric Constants (ε), Donor Number (DN), and Acceptor Number (AN) of Various Solvents from Literature

solvent (BH)	pK_a value of conjugated acid (BH^+)[a]	dielectric constant (ε)[b,c]	DN[e]	AN[f]
acetonitrile	−10	37.5[d]	14.1	18.9
acetone	−3.1	20.5	17.0	12.5
methanol	−2.2	32.6	(19)	41.3
H_2O	−1.7	78.5	18.0	54.8
DMSO	−1.5	48.9[d]	29.8	19.3
DMF	−1.1	36.7	26.6	16.0

[a]Reference 37. [b]Reference 32. [c]Value at 25 °C. [d]Value at 20 °C. [e]Reference 35. [f]Reference 36.

Polar aprotic solvents, such as acetonitrile or acetone, have low basicity and very low ability to solvate (DN and AN values are both low), so that **1b** cannot be easily dissociated, and consequently the diazonium form **1b** is favored in such solvents. Furthermore, in this equilibrium, the acids (proton donors) are **1b** and the conjugate acid (BH^+) of the solvent, and the conjugate acid (BH^+) of acetonitrile or acetone has a lower pK_a than **1**; that is, the conjugate acid (BH^+) of acetonitrile or acetone is a far stronger acid than **1**. For example, acetonitrile is only 20−50% protonated in 100% sulfuric acid.[37] Therefore, the equilibrium favors **1**. On the other hand, polar aprotic solvents, such as DMSO or DMF, are much more basic and are stronger H-bond acceptors[38] than acetonitrile or acetone, so that **1b** can be more easily dissociated, favoring the diazo form **2**. The estimated pK_a value of **1** is indeed lower than that of the conjugate acid of DMSO or DMF. Protic solvents, such as water or methanol, have high dielectric constants and strongly solvate anions, so these solvents also favor the diazo form **2**. It is of interest to note that much larger amounts of these protic solvents are required for the structure change from **1b** to **2**, as compared with DMSO or DMF (see Figure 6). We think the main reason for this is that although protic solvents favor the dissociation of **1b**, the basicity and the H-bond-accepting ability of these solvents are considerably weaker than those of DMSO or DMF (for example, the order of DN is H_2O or methanol ≪ DMF or DMSO, while the order of AN is H_2O or methanol ≫ DMF or DMSO).

CONCLUSION

We synthesized **2**, investigated its structure, and compared it with the structure of **1**. NMR and UV spectral data indicated that 5-tropolonediazonium salt **1** is easily deprotonated in water, methanol, DMSO and DMF and consequently exists predominantly as 1,2,5-tropoquinone-5-diazide **2** in those solvents (but not in acetonitrile or acetone) because of its very high acidity (the pK_a value of **1** was estimated to be −2.07). The acid−base equilibrium is highly solvent-dependent, being influenced by the pK_a of the conjugate acid, the dielectric constant, the donor number and the acceptor number of the solvent. We are currently investigating the chemistry of **2** as a carbene precursor.

EXPERIMENTAL SECTION

5-Tropolonediazonium Tetrafluoroborate 1b. A solution of 5-aminotropolone (274 mg, 2.0 mmol) and HBF_4·Et_2O (1.5 mL, 11 mmol) in EtOH (5 mL) was stirred at 0 °C, and then isoamyl nitrite (0.34 mL, 2.5 mmol) was added at 0 °C over 1 h. To the reaction mixture was added Et_2O (50 mL), and the precipitate was collected by filtration to give **1** (299 mg, 63%). Brown powder, mp 96−98 °C. ATR-FTIR (neat) cm^{-1}: 3058, 2255, 1618, 1487, 1421, 1334, 1010 (see the Supporting Information). ^1H NMR spectra were determined in various deuterated solvents (CD_3CN, acetone-d_6, CF_3COOD, D_2O, CD_3OD, DMSO-d_6, and DMF-d_7) and ^{13}C NMR spectra in CD_3CN and CF_3COOD. ^1H NMR (300 MHz, CD_3CN, Figure 1, spectrum A) δ: 8.18 (2H, d, J = 12.3 Hz), 7.35 (2H, d, J = 12.3 Hz). ^1H NMR (300 MHz, acetone-d_6) δ: 8.21 (2H, d, J = 12.3 Hz), 7.02 (2H, d, J = 12.3 Hz). ^1H NMR (500 MHz, CF_3COOD) δ: 8.49 (2H, d, J = 12.5 Hz), 7.60 (2H, d, J = 12.5 Hz). ^1H NMR (300 MHz, D_2O, observed as **2**) δ: 7.52 (2H, d, J = 12.6 Hz), 6.50 (2H, d, J = 12.6 Hz). ^1H NMR (300 MHz, CD_3OD, observed as **2**) δ: 7.53 (2H, d, J = 12.6 Hz), 6.45 (2H, d, J = 12.6 Hz). ^1H NMR (300 MHz, DMSO-d_6 observed as **2**) δ: 7.55 (2H, d, J = 12.6 Hz), 6.28 (2H, d, J = 12.6 Hz). ^1H NMR (300 MHz, DMF-d_7 observed as **2**) δ: 7.67 (2H, d, J = 12.6 Hz), 6.34 (2H, d, J = 12.6 Hz). ^{13}C NMR (500 MHz, CD_3CN) δ: 177.2, 141.1, 123.0, 111.0. ^{13}C NMR (500 MHz, CF_3COOD) δ: 178.9, 143.3, 125.1, 114.0. UV (0.5 M HBF_4·Et_2O/acetonitrile, see Figure 2) λ_{max} nm (ε): 356 (12600 L mol^{-1} cm^{-1}). UV (H_2O, see Figure 4) λ_{max} nm (ε): 391 (21400 L mol^{-1} cm^{-1}), 410 (27200 L mol^{-1} cm^{-1}). MS (ESI) m/z: 149 $[M - HBF_4 + H]^+$. HRMS (ESI-TOF) m/z: $[M - HBF_4 + Na]^+$ calcd for $C_7H_4N_2O_2Na$ 171.0165, found 171.0163.

1,2,5-Tropoquinone-5-diazide 2. 5-Aminotropolone (411 mg, 3.0 mmol) was dissolved in concd HCl (1.6 mL) and ice−water (2.0 mL) and stirred at 0 °C for 10 min. A solution of sodium nitrite (311 mg, 4.5 mmol) in H_2O (6.0 mL) was added dropwise to the above solution at 0 °C. The mixture was stirred for 0.5 h, poured into water (10 mL), and extracted with 10% methanol−$CHCl_3$ (×6). The organic layer was washed with brine (10 mL), dried over sodium sulfate (Na_2SO_4), and evaporated in vacuo. The residue was flash-chromatographed [silica gel, ethyl acetate−hexane (1:1) → 10% methanol−$CHCl_3$] to give **2** (251 mg, 57%). Brown powder, 110−115 °C dec. ATR-FTIR (neat) cm^{-1}: 2189, 2106, 1542, 1451, 1319, 1082, 810 (see the Supporting Information). ^1H NMR spectra were determined in various deuterated solvents (CD_3CN, CD_3CN + HBF_4·Et_2O, CD_3CN + HBF_4·Et_2O + Na_2CO_3, acetone-d_6, CF_3COOD, D_2O, CD_3OD, DMSO-d_6, and DMF-d_7) and ^{13}C NMR spectra in CD_3CN and CF_3COOD. ^1H NMR (300 MHz, CD_3CN, see Figure 1, spectrum B) δ: 7.23 (2H, d, J = 12.6 Hz), 6.30 (2H, d, J = 12.6 Hz). ^1H NMR (300 MHz, CD_3CN+HBF_4·Et_2O, Figure 1, spectrum C) δ: 8.20 (2H, d, J = 12.3 Hz), 7.36 (2H, d, J = 12.3 Hz). ^1H NMR (300 MHz, CD_3CN + HBF_4·Et_2O + Na_2CO_3/D_2O, see Figure 1, spectrum D) δ: 7.35 (2H, d, J = 12.6 Hz), 6.38 (2H, d, J = 12.6

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Hz). ^{1}H NMR (300 MHz, acetone-d_6) δ: 7.46 (2H, d, J = 12.3 Hz), 6.27 (2H, d, J = 12.3 Hz). ^{1}H NMR (500 MHz, CF_3COOD) δ: 8.45 (2H, d, J = 12.0 Hz), 7.56 (2H, d, J = 12.0 Hz). ^{1}H NMR (300 MHz, D_2O) δ: 7.53 (2H, d, J = 11.7 Hz), 6.51 (2H, d, J = 11.7 Hz). ^{1}H NMR (300 MHz, CD_3OD) δ: 7.52 (2H, d, J = 7.52), 6.45 (2H, d, J = 11.4 Hz). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.55 (2H, d, J = 12.6 Hz), 6.28 (2H, d, J = 12.6 Hz). ^{1}H NMR (300 MHz, DMF-d_7) δ: 7.67 (2H, d, J = 12.6 Hz), 6.34 (2H, d, J = 12.6 Hz). ^{13}C NMR (500 MHz, CD_3CN) δ: 185.0, 132.1, 123.0, 83.6. ^{13}C NMR (500 MHz, CF_3COOD, observed as **1**) δ: 179.3, 142.9, 125.1, 112.7. UV (acetonitrile) λ_{max} nm (ε): 384 (22000 L mol^{-1} cm^{-1}). UV (0.1 M DABCO/acetonitrile) λ_{max} nm (ε): 384 (19800 L mol^{-1} cm^{-1}). UV (0.5 M HBF_4·Et_2O/acetonitrile, see Figure 2) λ_{max} nm (ε): 356 (12600 L mol^{-1} cm^{-1}). MS (EI, 70 eV) m/z: 120 (M^+−28, 2), 92 (9), 63 (100). MS (ESI) m/z: 149 $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_7H_4N_2O_2Na$ 171.0165, found 171.0159.

Preparation of 1b from 2. HBF_4·Et_2O (27 μL, 0.20 mmol) was added to **2** (30 mg, 0.20 mmol) in CH_2Cl_2 (3.0 mL), and the solution was stirred at 0 °C for 1 h. The precipitate was collected by filtration to give **1b** (37 mg, 79%).

■ ASSOCIATED CONTENT

Supporting Information

General experimental procedures; IR, ^{1}H, ^{13}C and C−H COSY spectra for **1b** and **2**; UV spectra for **1** in aqueous solution at various pH values; table of substituted constants σ_m^0, σ_p^0, and σ_p^-, and pK_a values of 4-and 5-substituted tropolones. Details of estimation of the acidity of **1b** using the Yukawa−Tsuno equation. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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