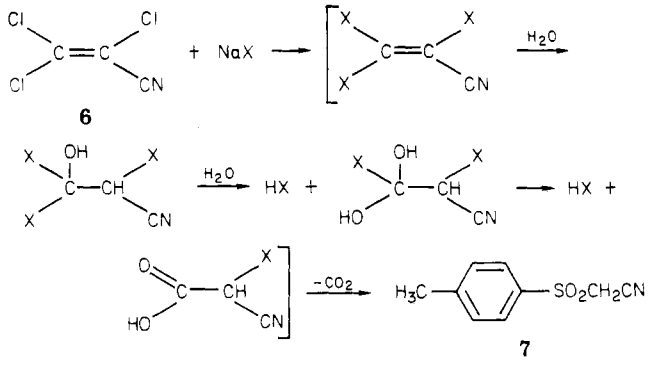
Scheme II[a]



[a] X = $H_3CC_6H_4SO_2$.

coated plates and chloroform–*n*-heptane (1:1) as a developing phase, we were able to obtain clear separation of *E* and *Z* isomers of **3a** and **5**. The R_f values of (*Z*)-**3a**, (*Z*)-**5**, and also (*Z*)-**3b** were in very close range and had higher value than R_f of (*E*)-**3a** and (*E*)-**5**. Furthermore, in contrast with **3a** and **5**, TLC analysis of **3b** showed the presence of only one component. Infrared spectra of (tolylsulfonyl)acrylonitriles showed extremely weak absorption of the cyano group at 2210 cm^{-1} for **3b** and **5** and of moderate intensity at 2218 cm^{-1} for **3a**.

The reaction of trichloroacrylonitrile (**6**) with sodium *p*-toluenesulfinate in a 1:1 or 1:3 molar ratio gave *p*-(tolylsulfonyl)acetonitrile (**7**) as the only product (Scheme II). In this case, the extensive substitution of all chlorine atoms renders the double bond of the intermediate product susceptible for addition of water, which results in the formation of **7** as the stable end product.

Experimental Section

Melting points are uncorrected. Sodium *p*-toluenesulfinate dihydrate (Aldrich Chemical Co.) was used as received. Elemental analyses were performed by Huffman Laboratories, Wheatridge, CO. The mass spectra were obtained on a DuPont 21-491 instrument, and the IR spectra were obtained on a Perkin-Elmer 1320 IR instrument. The ^1H NMR spectra were obtained on a Perkin-Elmer R-12A (60 MHz) spectrometer as solutions in deuteriochloroform with Me_4Si as an internal standard. The TLC separations were carried out on Eastman 13181 silica gel plates with fluorescent indicator and a mixture of chloroform–*n*-heptane (1:1) as a developing phase.

(*Z*)-3-Chloro-2-methyl-3-(*p*-tolylsulfonyl)acrylonitrile (3a). The acrylonitrile **1a**[9,10] (1.0 g, 7 mmol) was dissolved in 4 mL of DMF in a flask equipped with a magnetic stirrer, an addition funnel, and a thermometer. The solution was cooled to 10 °C, and a slurry of sodium *p*-toluenesulfinate dihydrate (1.6 g, 7 mmol) in 20 mL of DMF was added while stirring for 15 min. The mixture was stirred for an additional 3 h at room temperature and then poured into 200 mL of cold water. The colorless precipitate was filtered off, washed with water, dried in a dessicator, and sublimed under reduced pressure. Recrystallization from petroleum ether (bp 65–75 °C) afforded 1.2 g (64%) of **3a** as colorless plates: mp 93–95 °C; IR(KBr) 2920, 2218, 1596, 1450, 1342, 1158, 1088, 928, 837, 813, 703 cm^{-1}; ^1H NMR δ (*Z*)-**3a** 7.87 (d, 2 H, *J* = 8 Hz, Ar H), 7.43 (d, 2 H, *J* = 8 Hz, Ar H), 2.52 (s, 3 H, Ar CH_3), 2.48 (s, 3 H, CH_3), the resonance of the vinylic methyl group of (*E*)-**3a** appeared at δ 2.23; MS (70 eV), *m/e* 257, 255 (M^+), 240, 155, 139, 124, 92, 91 (base).

Anal. Calcd for $C_{11}H_{10}ClNO_2S$ (255.7): C, 51.66; H, 3.94; Cl, 13.86; N, 5.68; S, 12.54. Found: C, 51.16; H, 3.99; Cl, 14.07; N, 5.46; S, 12.13.

(*Z*)-3-Chloro-2-phenyl-3-(*p*-tolylsulfonyl)acrylonitrile (3b). A solution of **1b**[3,13] (0.6 g, 3 mmol) in 8 mL of DMF was cooled to 10–15 °C and while stirring a slurry of sodium *p*-toluenesulfinate **2**, 1.3 g, 6 mmol) in 15 mL of DMF was slowly added. The mixture was stirred at room temperature for 2 days and then poured into 300 mL of water. The precipitated product was collected, washed with water, sublimed in vacuo, and recrystallized from petroleum ether (bp 65–75 °C) to give 0.65 g (67%) of **3b** as colorless fluffy clusters: mp 122 °C; IR (KBr) 2910, 2210, 1592, 1448, 1350, 1163, 1090, 900, 811, 763, 702 cm^{-1}, ^1H NMR δ 7.43 (m, 9 H, Ar H), 2.47 (s, 3 H, Ar CH_3); MS (70 eV), *m/e* 319, 317 (M^+), 253, 218, 155, 149, 141, 140, 139 (base), 127, 126, 124, 100, 92, 91, 89.

Anal. Calcd for $C_{16}H_{12}ClNO_2S$ (317.8): C, 60.47; H, 3.81; Cl, 11.16; N, 4.41; S, 10.09. Found: C, 60.71; H, 3.98; Cl, 11.17; N, 4.36; S, 10.26.

2-(*tert*-Butyl)-3-chloro-2-(*p*-tolylsulfonyl)acrylonitrile (5). A slurry of **2** (1.2 g, 6 mmol) in 15 mL of DMF was slowly added to the stirred and cooled (10 °C) solution of the acrylonitrile **4**[9,10] (0.5 g, 3 mmol) in 5 mL of DMF. The suspension was then stirred at room temperature overnight and poured into 200 mL of water. After standing overnight, the precipitated solid was filtered off, washed with water, and sublimed in vacuo. Recrystallization from petroleum ether (bp 35–50 °C) furnished 0.46 g (55%) of a *E* and *Z* mixture of **5** as colorless crystals: mp 68–70 °C; IR (KBr) 2973, 2922, 2210, 1590, 1336, 1162, 1081, 888, 810 cm^{-1}; ^1H NMR δ (*Z*)-**5**, 7.87 (d, 2 H, *J* = 8 Hz, Ar H), 7.42 (d, 2 H, *J* = 8 Hz, Ar H), 2.48 (s, 3 H, Ar CH_3), 1.60 (s, 9 H, $C(CH_3)_3$), (*E*)-**5**, 1.37 (s, $C(CH_3)_3$) (the (*Z*)-**5**:(*E*)-**5** ratio was 5:2); MS (70 eV), *m/e* 298,297(M^+), 282, 218, 191, 157, 155, 144, 142, 139, 107, 92, 91 (base), 79.

Anal. Calcd for $C_{14}H_{16}ClNO_2S$ (297.8): C, 56.46; H, 5.41; Cl, 11.90; N, 4.70; S, 10.77. Found: C, 56.31; H, 5.56; Cl, 11.79; N, 4.74; S, 10.66.

Reaction of 2,3,3-Trichloroacrylonitrile (6) with Sodium *p*-Toluenesulfinate. A slurry of **2** (4.1 g, 19 mmol) in 20 mL of DMF was added during 20 min to the stirred and cooled (10 °C) solution of trichloroacrylonitrile **6**[3,14] (1.0 g, 6 mmol) in 4 mL of DMF. Stirring was continued for additional 3 h at room temperature, and the mixture was poured into 200 mL of water. After the usual isolation procedure the precipitate was sublimed in vacuo and recrystallized from benzene to give 0.8 g (64%) of *p*-(tolylsulfonyl)acetonitrile (**7**) as colorless crystals: mp 149–150 °C [lit.[6] mp 149.5–150.5 °C]; IR (KBr) 2980, 2925, 2257, 1595, 1380, 1318, 1152, 1082, 813, 736 cm^{-1}; ^1H NMR δ 7.94 (d, 2 H, *J* = 8 Hz, Ar H), 7.44 (d, 2 H, *J* = 8 Hz, Ar H), 4.05 (s, 2 H, CH_2), 2.50 (s, 3 H, CH_3); MS (70 eV), *m/e* 195 (M^+), 155, 139, 124, 123, 92, 91 (base), 77.

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Registry No. **1a**, 31413-58-8; **1b**, 31413-60-2; (*Z*)-**3a**, 88703-71-3; (*E*)-**3a**, 88703-72-4; **3b**, 88703-73-5; **4**, 42867-44-7; (*Z*)-**5**, 88703-74-6; (*E*)-**5**, 88703-75-7; **6**, 16212-28-5; **7**, 5697-44-9; sodium toluenesulfinate, 824-79-3.

(13) Soulen, R. L.; Carlson, S. C.; Lang, F. *J. Org. Chem.* **1973**, *38*, 479.

(14) Boeseken, J.; Du Jardin, P. *Recl. Trav. Chim. Pays-Bas* **1913**, *32*, 97.

Structure and Dynamics of Tröger's Base and Simple Derivatives in Acidic Media

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Tröger's base (**1**)[1–4] was the first amine, dissymmetric solely due to pyramidal geometry about nitrogen, to be

(1) IUPAC name: 2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]-[1,5]diazocine.

(2) Troger, J. *J. Prakt. Chem.* **1887**, *36*, 227.

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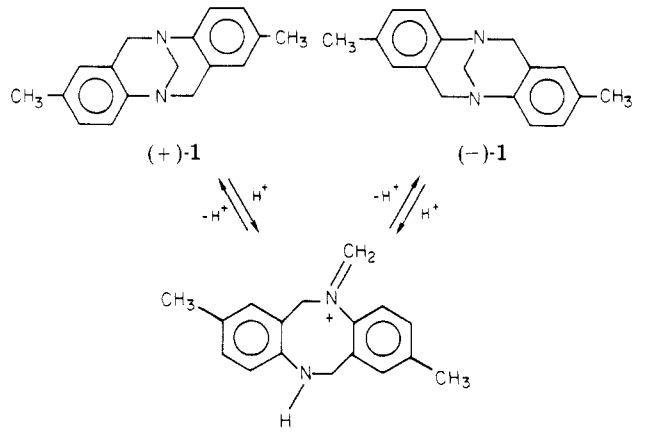
optically resolved.[5-7] Dilute acid causes racemization of 1, postulated[5] to proceed through the intermediacy of iminium ion 2. Crude published racemization data[5] lead to

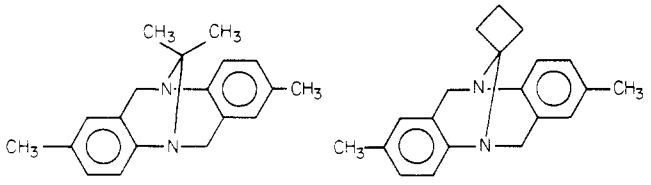


(+)-1 (−)-1

2

$\Delta G^{\ddagger}$ of racemization in the range 18.9–22.6 kcal/mol.[8] This is similar to the eight-membered-ring inversion barrier of 5,11-diacetyl-5,6,11,12-tetrahydro-2,8-dimethyldibenzo[*b*,*f*][1,5]diazocine,[9] a reasonable model for 2.

The structure of protonated Tröger's base has not been previously reported. If iminium ion 2 is stable in dilute acid, it should manifest vastly different spectral properties than those of the neutral base. In the present study, selected spectroscopic properties of Tröger's base in neutral and acidic media, its monohydrochloride, and the 13,13-dimethyl and 13,13-spirocyclobutyl derivatives 3 and 4 are compared in order to deduce the structure of the mono- and diprotonated derivatives.



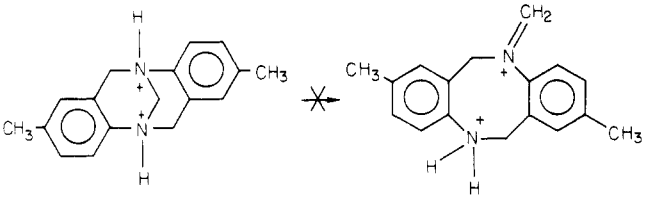
3 4

Tröger's base and its monohydrochloride (monohydrate) were synthesized according to published procedures.[3] Selected proton NMR and UV spectral properties of 1 in neutral, dilute, and concentrated acidic media as well as spectral data for the monohydrochloride are as follows:

	NMR, δ N-CH_2-N	NMR, δ Ar-CH_2-N	UV, nm
base (1, acetone-d_6)	4.18	4.03, 4.57	230, 283
monocation (2% D_2SO_4)	4.92	4.30, 4.92	complex centered at 273
monohydrochloride (D_2O)	4.92	4.41, 4.92	complex centered at 273
dication (35% DCl)	5.69	4.84, 5.42	264

(3) Spielman, M. A. *J. Am. Chem. Soc.* **1935**, *57*, 583–585.
(4) Wagner, E. C. *J. Am. Chem. Soc.* **1935**, *57*, 1296–1298.
(5) Prelog, V.; Wieland, P. *Helv. Chim. Acta* **1944**, *27*, 1127–1134.
(6) Eliel, E. L. "Stereochemistry of Carbon Compounds"; McGraw-Hill: New York, 1962; pp 391–392.
(7) Hesse, G.; Hagel, R. *Chromatographia* **1973**, *6*, 277–280.
(8) This assumes that the specific rotation at $t = 0$ is similar to that of Tröger's base, not unreasonable in light of the structure of 7. In any case, $\Delta G^{\ddagger}$ is fairly insensitive to the value chosen.
(9) Crossley, R.; Downing, A. P.; Nogradi, M.; de Oliveira, A. B.; Ollis, W. D.; Sutherland, I. O. *J. Chem. Soc., Perkin Trans 1* **1973**, 205–217.

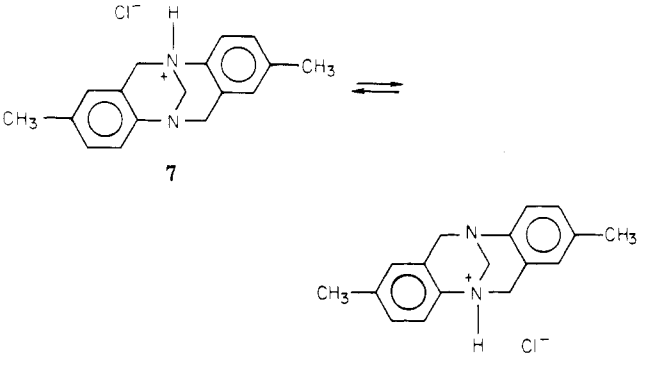
The changes in chemical shifts of the benzylic hydrogens, upon protonation of the base, are essentially the same as that observed in the spectrum of *N*,*N*-dimethylbenzylamine on going from chloroform to trifluoroacetic acid.[10] Clearly, an imminium ion is not present in significant concentration since one would expect chemical shifts on the order of δ 8.4 for the exocyclic methylene protons.[11,12] Furthermore, the UV spectrum in concentrated HCl (as well as in concentrated H_2SO_4) is simply that of an anilinium ion and corresponds to structure 5. This ion shows



5 6

no change in its NMR spectrum up to ca. 180 °C (except for exchange of deuterium for the aromatic protons in D_2SO_4 above 140 °C). If 5 had any tendency to ring open to iminium ion 6, one would have anticipated exchange of the nonequivalent benzylic hydrogens through inversion of the eight-membered ring. At higher temperatures, decomposition occurs. The UV spectrum in dilute acid shows aspects of the spectra of both the neutral compound and 5, with a complex peak centered around 273 nm and is identical with the spectrum of the monohydrochloride.

The above UV and NMR data indicate that the monoprotonated form of Tröger's base maintains bicyclic structure 7. The fact that the NMR spectrum of 7 relfects



7

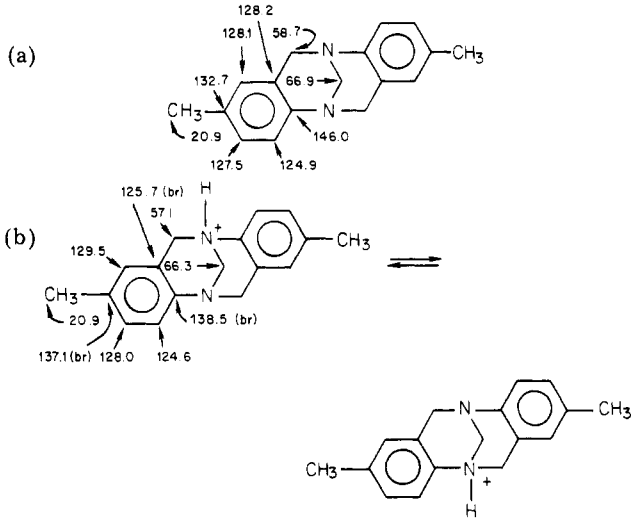
7

C_2 symmetry indicates that proton exchange between the two bridgehead nitrogens is rapid on the NMR time scale at room temperature. At low temperatures (ca. −40 to −50 °C) in dilute acid (1:1 concentrated DCl/CD_3OD and 1:2 CF_3CO_2D/CD_3OD), the benzylic hydrogens broaden and exhibit coalescence patterns. If one makes the approximation that the benzylic proton chemical shifts in Tröger's base (1) and dication 5 represent the limiting chemical shifts of the nonequivalent benzylic positions in monocation 7, then the chemical shift difference (66 Hz at 79.5 MHz) can be employed to calculated an approximate rate constant $K = 150\ s^{-1}$ at ca. −50 °C, corresponding to $\Delta G^{\ddagger}$ of 10–11 kcal/mol. This is not inconsistent with the observed barriers to proton exchange between protonated and unprotonated anilines.[13] Thus, $\Delta G^{\ddagger}$ for proton exchange

(10) Ma, J. C. N.; Warnhoff, E. W. *Can. J. Chem.* **1965**, *43*, 1849–1869.
(11) Jensen, K. A.; Henriksen, L. *Acta Chem. Scand., Ser. B.* **1975**, *B29*, 877–883.
(12) Merenyi, R. In "Advances in Organic Chemistry: Methods and Results"; Taylor, E. C., Ed.; Wiley: New York, 1976; pp 23–105.
(13) Reynolds, W. F.; Schaefer, T. *Can. J. Chem.* **1964**, *42*, 2641–2656.

should be lower for Tröger's base than the experimental value for *N,N*-dimethylaniline ($\Delta G^{\ddagger}$ = 16.9 kcal/mol[13]) since the former is a weaker base by ca. 0.9 pK unit[14] and the acid medium investigated is more dilute than in the published study.[13]

Carbon-13 NMR spectroscopy should be a very sensitive probe for small amounts of **2** since the chemical shift of an iminium ion carbon should be fairly far downfield (e.g., chemical shift in $CH_2{=}N(CH_3)_2^+$ is 168 ppm downfield from Me_4Si[12]). Below, one sees the carbon-13 chemical shifts (relative to Me_4Si) of Tröger's base (a) as well as its monohydrochloride (b), both in dimethyl sulfoxide. The



chemical shift of the methylene carbon (C_{13}) bridging the two nitrogen atoms in Tröger's base is 66.9 ppm, almost identical with the corresponding value in the monohydrochloride (66.3 ppm). Thus, the latter has no detectable iminium ion. Similar results are found in benzene solution. The chemical shift assignments were made by using a published table.[15]

An interesting feature in the carbon-13 spectrum of **7** is the broadness of three of the aromatic peaks noted above. These three peaks correspond to three carbons which undergo the greatest chemical shift changes upon protonation of Tröger's base and they support the aforementioned proton exchange. The broad peaks observed in dimethyl sulfoxide solution are sharp in methanol solution.

It is clear that in the dilute acid conditions studied by Prelog and Wieland,[5] only the monoprotonated "closed" structure **7** should exist in measurable quantity. Under these conditions, **2** would be an intermediate present in undetectable amounts.

Replacement of the C_{13} hydrogens in Tröger's base by methyl substituents yielding **3** causes profound changes in the behavior of this molecular system. This derivative was synthesized from 2,8-dimethyl-5*H*,6*H*,11*H*,12*H*-dibenzo[*b*,*f*][1,5]diazocine and acetone by using a published procedure.[16] Compound **3** is considerably more labile than the parent compound, tending to decompose within days while in a vial unprotected from the air. In dilute HCl, **3** rapidly reverts to starting material. However, in concentrated DCl or D_2SO_4 it is immediately clear that the twofold axis present in the diprotonated form of the parent is now lost. This is clear from the observation of two

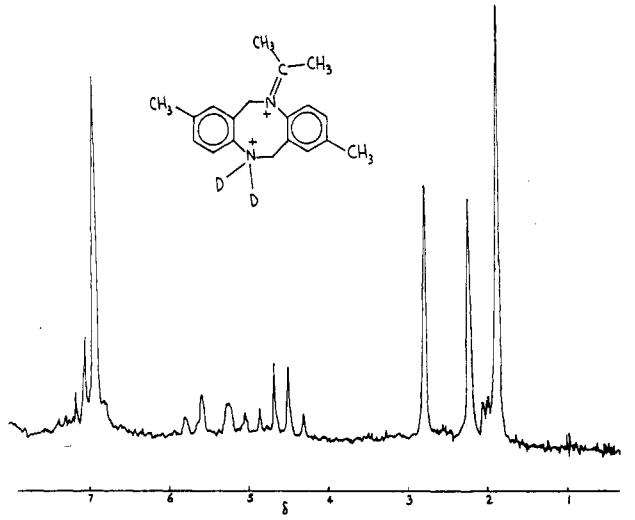
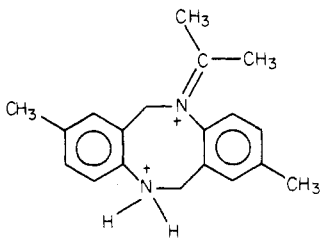
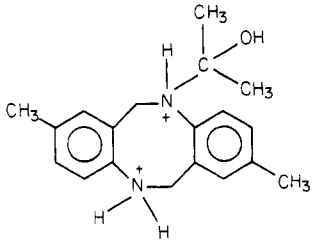


Figure 1. Proton NMR of compound **3** (the 13,13-dimethyl derivative of Tröger's base) in concentrated D_2SO_4.

distinct benzylic H_{AB} patterns in the 4–6-ppm region of the proton NMR spectrum (see Figure 1), while only one such H_{AB} pattern is seen for **5**. The two C_{13} methyl peaks are nonequivalent while the aromatic methyl peak is broadened. These observations are consistent with the presence of iminium ion **8**. It is known that the C=N



8



9

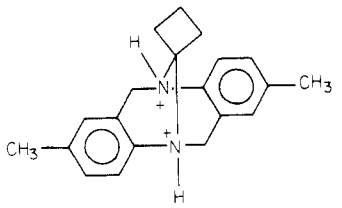
rotational barriers in iminium ions are quite high.[17] However, methyl nonequivalence could also arise in structure **9** since this ion has C_1 symmetry and diastereotopic methyls.

Carbon-13 NMR spectroscopy readily resolves the question of whether **8** or **9** is present. While the chemical shifts of iminium ion carbons are quite high, the shift of the corresponding carbon in **9** should be much lower. An upper limit for this chemical shift can be assumed to be about 95 ppm (i.e., C_2 in 1,3-dioxane; see ref 15, p 71; a tetracoordinate carbon attached to one oxygen, one nitrogen, and two carbons should not be shifted as far downfield even if the nitrogen is quarternary: compare the C_{13} chemical shifts displayed above for Tröger's base and its monohydrochloride). However, the experimental chemical shift is found to be 201.4 ppm (assuming 20.7 ppm for the aromatic CH_3), consistent only with iminium ion **8**. This is a reasonable chemical shift considering the fact that a value of 168 ppm is recorded for $CH_2{=}N(CH_3)_2^+$,[12] and that **8** should be further downfield since it has more carbonium ion character.[18] Although one might be tempted to assume that the downfield chemical shift arises from acetone, a potential hydrolysis product, this is clearly not the case since the chemical shift of the carbonyl carbon is about 244 ppm in concentrated sulfuric

(14) Wepster, B. M. *Recl. Trav. Chim. Pays-Bas* **1953**, *72*, 661–672.
(15) Levy, G. C.; Lichter, R. L.; "Carbon-13 Nuclear Magnetic Resonance Spectroscopy", 2nd ed.; Wiley: New York, 1980; Table 4.3, pp 111–112.
(16) Cooper, F. C.; Partridge, M. W. *J. Chem. Soc.* **1957**, 2888–2893.
(17) Kollman, P. A. In "Advances in Organic Chemistry: Methods and Results"; Taylor, E. C., Ed.; Wiley: New York, 1976; pp 1–21.
(18) From Table 6.1, p 173, of ref 15, the following chemical shifts are obtained: $(CH_3)_2COH^+$, 250.3 ppm; CH_3CHOH^+, 237.2 ppm; CH_2OH^+, 223.8 ppm.

acid rather than 205 ppm found in neutral media.[19]

The 13,13-spirocyclobutyl derivative of Tröger's base (4), synthesized by the procedure used for 3, has also been studied. In dilute acid, this molecule readily loses cyclobutanone. However, in contrast to 3, a concentrated sulfuric acid solution of 4 indicates the presence of "closed" structure 10. This is clear from the single H_{AB} pattern



10

at 4.3 and 5.0 ppm and a spectrum fully consistent with C_2 symmetry. Unlike the dimethyl derivative, the spirocyclobutyl compound is stable in a vial unprotected from air.

In summary, dilute acidic solutions of Tröger's base contain the protonated amine in its closed form 7 with no detectable iminium ion 2. In concentrated acid, Tröger's base exists as the closed structure 5. In contrast, the 13,13-dimethyl derivative 3 rapidly loses acetone in dilute acid but forms the open iminium ion 8 in concentrated acid. One would therefore expect Tröger's acid to racemize in dilute acid only while the dimethyl derivative would racemize in concentrated acid. The tendency to form 8 undoubtedly reflects the added stability of a tertiary iminium ion relative to a primary iminium ion. The 13,13-spirocyclobutyl derivative 4, which also hydrolyzes rapidly in dilute acid, remains in the closed structure 10 in concentrated acid. Although a tertiary iminium carbon is present, the ring strain of the carbonium ion inhibits ring opening of the diprotonated ion.

Experimental Section

NMR spectra were obtained on a Varian 360L NMR spectrometer, a Bruker WM-360 widebore 8.5 Tesla Multi-Nuclear NMR spectrometer, or an IBM WP200SY Multinuclear Fourier Transform NMR spectrometer.

Tröger's base[1] (mp 135 °C, lit.[3] mp, 135–136 °C) and its monohydrochloride (mp 211–212 °C, lit.[31] mp 213 °C) were prepared by the published procedure.[3]

2,8,13,13-Tetramethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (3) was synthesized according to the published procedure, using chromatographic purification of 2,8-dimethyl-5*H*,6*H*,11*H*,12*H*-dibenzo[*b*,*f*][1,5]diazocine with basic silica gel eluted with benzene–methanol and a trace of *p*-toluenesulfonic acid to catalyze the reaction with acetone. The melting point agreed with the literture value:[16] ^{1}H NMR (acetone-d_6) δ 1.34 (s, 6 H), 2.16 (s, 6 H), 4.00 (d, 2 H), 4.64 (d, 2 H), 6.84 (br s, 2 H), 6.92 (br s, 4 H).

13,13-Spirocyclobutyl-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (4) was synthesized by using cyclobutanone (Aldrich) in the manner of 3: mp 185–187 °C; ^{1}H NMR ($CDCl_3$) δ 1.91 (m, 4 H), 2.19 (s, 6 H), 2.31 (m, 2 H), 3.96 (d, 2 H), 4.69 (d, 2 H), 6.62 (s, 2 H), 6.89–7.31 (m, 4 H). Anal. Calcd C, 82.72; H, 7.64; N, 9.65. Found: C, 82.63; H, 7.67; N, 9.38.

Acknowledgment. We acknowledge Mr. Joseph Flisak and Drs. Frank Jordan, David Craik, and Maria Konienczny for obtaining some of the NMR spectra as well as Dr. David Kristol for obtaining some of the UV spectra used in this study. Helpful conversations with Drs. Joel Liebman and Howard Perlmutter are gratefully acknowledged. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the support of this research.

Registry No. 1, 529-81-7; 3, 88703-13-3; 4, 88703-14-4; 5, 88703-15-5; 7, 88703-16-6; 8, 88703-17-7; 10, 88703-18-8.

(19) From Table 5.6 of ref 15, p 143.

The Amino Blocking Reagent 1-Isopropyl-3-ethoxy-4-nitro-2-oxo-3-pyrroline and the *N*-Hydroxysuccinimide Esters of *N*-(1-Cyclohexyl- and 1-Isopropyl-4-nitro-2-oxo-3-pyrrolin-3-yl)glycine. Reagents for the Introduction of *N*-Glycyl Residues

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A previous paper[2] described the preparation of the reactive nitro enol ether 1-cyclohexyl-3-ethoxyl-4-nitro-2-oxo-3-pyrroline (**6a**), as well as some applications of this compound as a reagent for the introduction of a reversible amino protecting group (the 1-cyclohexyl-4-nitro-2-oxo-3-pyrrolin-3-yl or "NOPY" group). Applications of the NOPY blocking group in simple examples of peptide synthesis[2] and protein modification[3] have been described. Advantages of the NOPY group are its ease of introduction (short reaction times in partially aqueous media at ca. 25 °C and pH 7.5–9), ease of removal (treatment with ammonia or aqueous base at ca. 25 °C), and the convenience with which it is monitored through its high absorptivity at 367–385 nm and visibility on thin-layer chromatography plates with 254-nm fluorescent indicator. For many applications, however, it would be useful to have a new blocking reagent that would be more water soluble and which would introduce a blocking group that adds only minimally to the hydrophobic character of a resulting protected amino acid or peptide derivative. A reagent of the NOPY type with cyclohexyl replaced by a smaller group was thought likely to have such properties. The corresponding 1-isopropyl reagent has been obtained and found to meet these expectations. (Efforts to prepare methyl and ethyl reagents did not succeed.) The new reagent is quite water soluble, and has yielded an N-protected glycine active ester with solubility appropriate for reaction with both peptides and proteins. The acronym NOPYE (for nitrooxopyrrolinyl ethyl ether) had been applied to compound **6a**;[2] we propose henceforth to call this original cyclohexyl reagent "c-NOPYE" and **6b**, the new isopropyl-containing reagent, "i-NOPYE." The derived NOPY groups would similarly be distinguished as "c-NOPY" and "i-NOPY".

Synthesis of the i-NOPYE Reagent (6b). A synthetic sequence based on a different type of starting material was

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