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# Carbon-13 Nuclear Magnetic Resonance Investigations of the Anionic Homoaromatic σ Adducts Formed between Liquid Ammonia and 1,2,4,5-Tetrazines[1,2]

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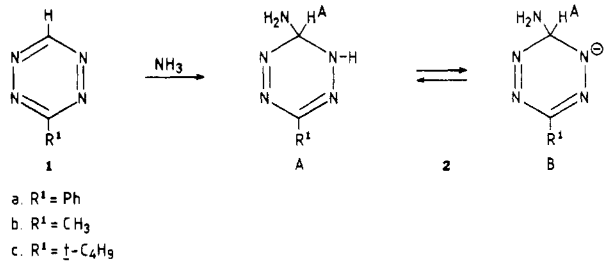
The homoaromatic σ adducts 2 formed between liquid ammonia and 3-aryl(alkyl)-1,2,4,5-tetrazines are anionic species. This is proven by (i) a study on the linear dependence between the $^{13}C$ substituent chemical shift at $C_4$ of the aryl ring (SCS-4) and the electron demand of the substituted 1,2,4,5-tetrazinyl groups in 3-(*p*-Y-phenyl)-1,2,4,5-tetrazine derivatives (Y = H, Br, $OCH_3$, $CH_3$) and (ii) a comparison of the $^{13}C$ coupling constant $J_{C_6H}$ of the σ adducts 2 with those of the deprotonated 6-$R^3$-1,6-dihydro-1,2,4,5-tetrazines (3) showing a linear relationship between $J_{C_6H}$ and the $\sigma_I$ value of the geminal group ($NH_2$ in 2 and $R^3$ = H or $CH_3$ in 3). The driving force for the deprotonation is the larger resonance stabilization of the homoaromatic anion. In the 1,6-dihydro-1,2,4,5-tetrazines the magnitude of the coupling of $C_6$ with the hydrogen above the tetrazole ring depends on the charge of the ring.

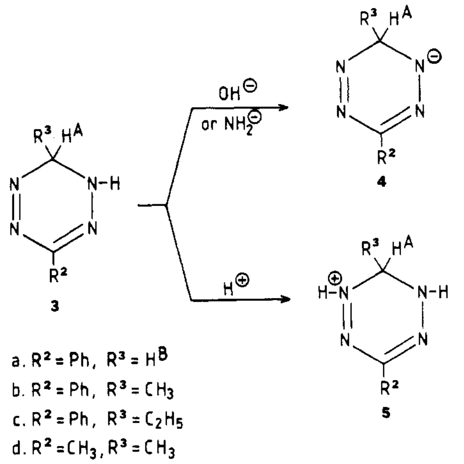
In a preceding paper[1] we proposed that 6-amino-3-phenyl-1,6-dihydro-1,2,4,5-tetrazine (**2a**) formed on addition of ammonia to 3-phenyl-1,2,4,5-tetrazine (**1a**) is a homoaromatic species (Scheme I). σ adduct **2a** is in the homotetrazole conformation, containing 6 π electrons (two double bonds and one nitrogen lone pair) in the tetrazole ring and holding the hydrogen at the $sp^3$ carbon atom above the ring and the amino group in the exo position.

It was found[1] that the delocalization stabilization in the parent compound 3-phenyl-1,6-dihydro-1,2,4,5-tetrazine (**3a**) was considerably smaller than in the conjugate base **4a** (Scheme II: **3a**, 52 kJ/mol; **4a**, 68 kJ/mol). This is ascribed to the fact that in **4a** the contribution of all possible resonance structures is of more importance than in **3a**, due to delocalization of negative charge in **4a** vs. separation of charge in **3a**. Since these data indicate that deprotonation leads to a gain of resonance energy, it induced us to investigate whether in liquid ammonia the σ adducts **2** are present as neutral species **2A** or as anionic species **2B**.[3]

Scheme I



Scheme II



## Results and Discussion

**(A) $^1H$ and $^{13}C$ Chemical Shifts.** In the $^1H$ NMR spectrum of the homoaromatic σ adduct **2a**, $H_6$ has been found at 1.51 ppm; compared with the chemical shift of $H_6$ in **1a** (10.35 ppm see Table I), it indicates that on adduct formation this hydrogen undergoes an "anomalous" large upfield shift of 8.84 ppm.

In an extension of these studies we observed that on dissolving 3-methyl-1,2,4,5-tetrazine (**1b**) or 3-*tert*-butyl-1,2,4,5-tetrazine (**1c**) in liquid ammonia, $H_6$ also undergoes an upfield shift of the same magnitude ($\Delta\delta$ = 8.55 ppm for **1b** and $\Delta\delta$ = 9.15 ppm for **1c**, Table I). These results suggest that also **2b** and **2c** are present in the homoaromatic conformation.

Further evidence for the formation of σ adduct **2a–c** was provided by comparison of the $^{13}C$ chemical shifts of $C_6$ in compounds **1a–c** when dissolved in deuteriomethanol and in liquid ammonia. In liquid ammonia, $C_6$ is found to resonate about 65–85 ppm to higher field than in methanol; this is due to adduct formation changing the hybridization of $C_6$ ($sp^2 \rightarrow sp^3$). For comparison, the $^{13}C$ chemical shifts of $C_3$ and $C_6$ in the model compounds 3-phenyl-1,6-dihydro-1,2,4,5-tetrazine (**3a**) and 3,6-dimethyl-1,6-dihydro-1,2,4,5-tetrazine (**3d**)[4] together with those of their conjugate bases **4a** and **4d** (Scheme II) are included in Table I. These chemical shifts agree reasonably well with those of $C_3$ and $C_6$ in the σ adducts **2a–c**; also, the coupling constants $J_{C_6H}$ are of the same magnitude (see Table I). Variations in the coupling constants will be discussed in section B.

For the determination of whether in liquid ammonia the σ adducts **2** are present as neutral (**2A**) or anionic species (**2B**) two approaches were taken. In a previous paper[1] we have described the preparation and $^1H$ NMR spectra of the *conjugate* bases of the 1,6-dihydro-1,2,4,5-tetrazines,

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(1) Part 4. On 1,2,4,5-Tetrazine and Its Derivatives. For part 3 see: Counotte-Potman, A.; van der Plas, H. C.; van Veldhuizen, A. *J. Org. Chem.* **1981**, *46*, 2138.

(2) Part 27. NMR Investigations of σ Adducts of Heterocyclic Systems with Nucleophiles. For part 26 see ref 1.

(3) The fact that the $pK_a$ of 6-$R^3$-3-phenyl-1,6-dihydro-1,2,4,5-tetrazines **3a–c** in water (Experimental Section) does not differ much from the $pK_a$ of the ammonium ion in water makes the assumption that the σ adducts are anionic plausible.

(4) Skorianetz, W.; Kovats, E. *Helv. Chim. Acta* **1971**, *54*, 1922.

Table I. $^1$H and $^{13}$C Chemical Shifts and the Coupling Constants $J_{C_6H}$ (in hertz) of 3-Phenyl- (1a), 3-Methyl- (1b), and 3-*tert*-Butyl-1,2,4,5-tetrazine (1c) in Deuteriomethanol, of the $\sigma$ Adducts 2a–c in Liquid Ammonia, and of the Model Compounds 3a and 4a and 3d and 4d

| compd | solvent | $\delta_{H_6}$ | $\delta_{C_6}$ | $J_{C_6H}$ | $\delta_{C_3}$ | others, $\delta$ |
|---|---|---|---|---|---|---|
| 1a | $CD_3OD$ | 10.35 | 159.5 | 215 | 168.0 | |
| 2a | $NH_3$ | 1.51 | 94.4 | 156 | 155.5 | |
| | | $\Delta\delta = 8.84$ | $\Delta\delta = 65.1$ | | | |
| 1b | $CD_3OD$ | 10.26 | 159.3 | 213 | 171.8 | $CH_3$, 3.03; $CH_3$ 21.7 |
| 2b | $NH_3$ | 1.71 | 72.8 | 156 | 156.5 | $CH_3$, 2.20; $CH_3$ 14.3 |
| | | $\Delta\delta = 8.55$ | $\Delta\delta = 86.5$ | | | |
| 1c | $CD_3OD$ | 10.45 | 158.9 | 213 | 179.5 | $CH_3$, 1.58; $CH_3$, 29.4[d] |
| 2c | $NH_3$ | 1.3[c] | 85.4 | 156 | 155.0 | $CH_3$;[c] $CH_3$, 26.4[d] |
| | | $\Delta\delta = 9$ | $\Delta\delta = 73.5$ | | | |
| 3a | $CD_3OD/D_2O$ | 4.13[e] | 66.3 | 159 | 155.2 | |
| 4a | $CD_3OD/D_2O$[a] | *f* | 78.0 | 153 | 156.3 | |
| 3d | $CD_3OD$ | 1.83 | 71.9 | 156 | 153.1 | 3-$CH_3$, 2.38; 3-$CH_3$, 17.4;<br>6-$CH_3$, 1.83; 6-$CH_3$, 14.2 |
| 4d | $NH_3$[b] | | 83.5 | 144 | 151.2 | 3-$CH_3$, 18.4; 6-$CH_3$, 17.7;<br>3-$CH_3$, 2.40; 6-$CH_3$, 1.87 |
| | $CD_3OD/D_2O$[a] | 0.87 | | | | |

[a] Sodium hydroxide, 1.5 equiv. [b] Potassium amide, 2 equiv. [c] The signals are almost under the signal of $NH_3$; the value cannot be given in two decimal places. [d] The quaternary C could not be distinguished because of aliphatic impurities. [e] Below the exchange temperature 2.13 ppm for $H^A$ and 6.13 ppm for $H^B$ (see ref 1). [f] $H^A$, 1.37 ppm; $H^B$, 6.18 ppm (see ref 1).

Table II. Chemical Shift of $H^A$ ($\delta H^A$) in 2a and 4a–c and the $\sigma_I$ Values of H, $CH_3$, $C_2H_5$, and $NH_2$

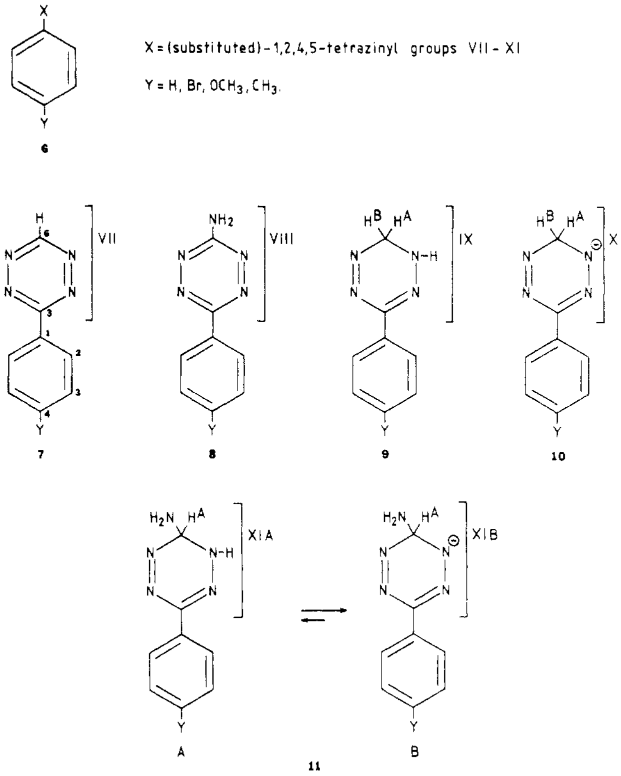
| compd | $\sigma_I$ | $\delta_{H^A}$ |
|---|---|---|
| 4a | 0.000 | 1.37 |
| 4b | −0.031 | 1.18 |
| 4c | −0.039 | 1.02 |
| 2a | 0.022 | 1.51[a] |

[a] Calculated by least-squares analysis of 4a–c: 1.56 ($r$ = 0.96, $t_\alpha$ = 3.49).

i.e., **4a–c**. The chemical shifts of $H_6$ ($\delta_{H^A}$) in these anions are linearly correlated ($r$ = 0.96, $t_\alpha$ = 3.49[5]) with the $\sigma_I$ values[6] of the geminal group (H, $CH_3$, $C_2H_5$). Substitution of the $\sigma_I$ value of 0.022 for the amino group gives a $\delta_{H^A}$ of 1.56 ppm for the $\sigma$ adduct **2a**, being nearly equal to the experimentally observed value of 1.51 ppm (Table II). These data lead to the *tentative* conclusion that $\sigma$ adduct **2a** is present in liquid ammonia as anionic species **2B**.

The second, more reliable method was based on a report[7,8] that in 1-X-4-Y-benzenes (**6**) there exists a linear dependence between the values of the substituent chemical shift of $C_4$ (SCS-4) and the electron demand of the substituent X at $C_1$. The SCS-4 values are defined as [$\delta_{C_4}$(Y $\neq$ H) − $\delta_{C_4}$(Y = H)] ppm.[7] The substituents X which have been investigated were either neutral of cationic groups. A quantitative measure of the electron-donating or -withdrawing properties of the group X was determined from the $^{13}$C chemical shift values of $C_4$ ($\delta_{C_4}$) of the 1-X-4-Y-benzenes (**6**) in which Y = H; $\delta_{C_4}$ is linearly related with the $\sigma_p{}^+$ values.[9]

Chart I



We tried to establish whether this relationship could also be applied when Y = Br, $OCH_3$, or $CH_3$ and X is the 1,2,4,5-tetrazinyl group (VII), the 6-amino-1,2,4,5-tetrazinyl group (VIII), the 1,6-dihydro-1,2,4,5-tetrazinyl group (IX), or the anionic 1,6-dihydro-1,2,4,5-tetrazinyl group (X) (see Chart I). From this relationship we wanted to extrapolate the electron demand of the substituent XIA or XIB. The electron demand of XIA will be similar to that of IX and that of XIB to X; the only difference between the pairs XIA and IX and XIB and X is the presence of the amino substituent, having an inductive influence (see Table II). Therefore we prepared the 3-($p$-Y-phenyl)-1,2,4,5-tetrazines (**7**) from which by reaction with liquid ammonia and subsequent oxidation with potassium permanganate[10] were prepared the corresponding 6-amino compounds **8**. So-

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[5] Sokal, R. R.; Rohlf, F. J. In "Biometry, The Principles and Practice of Statistics in Biological Research"; W. H. Freeman and Co.: San Francisco, 1969.

[6] Swain, C. G.; Lupton, E. C., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 4328.

[7] Hügel, H. M.; Kelly, D. P.; Spear, R. J.; Bromilow, J.; Brownlee, R. T. C.; Craik, D. J. *Aust. J. Chem.* **1979**, *32*, 1511.

[8] Membrey, F.; Ancian, B.; Doucet, J. P. *Org. Magn. Reson.* **1978**, *11*, 580.

[9] Nelson, G. L.; Levy, G. C.; Cargioli, J. D. *J. Am. Chem. Soc.* **1972**, *94*, 3089.

[10] Counotte-Potman, A. D.; van der Plas, H. C. *J. Heterocycl. Chem.* **1981**, *18*, 123.

Table III. $^{13}C$ Chemical Shifts[a] for $C_4$ ($\delta C_4$) and Substituent Chemical Shifts[b,c] (SCS-4) of 1-X-4-Y-benzenes (6)

| | substituent Y | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Br | | $OCH_3$ | | $CH_3$ | | | |
| X[d] | $\delta_{C_4}$ | SCS-4 | $\delta_{C_4}$ | SCS-4 | $\delta_{C_4}$ | SCS-4 | H, $\delta_{C_4}$ | solvent |
| VII | 128.63 | −4.61 | 164.01 | +30.77 | 143.96 | +10.72 | 133.24 | $CDCl_3$ |
| VIII | 123.98 | −6.44 | 161.28 | +30.86 | 140.15 | +9.73 | 130.42 | $Me_2SO-d_6$ |
| IX | 123.27 | −6.45 | 161.22 | +31.50 | 139.88 | +10.16 | 129.72 | $CD_3OD/D_2O$ |
| X | 120.04 | −7.13 | 159.44 | +32.27 | 136.71 | +9.54 | 127.17 | $CD_3OD/D_2O$[e] |
| XI | 116.53 | −8.22 | 157.00 | +32.25 | 133.58 | +8.83 | 124.75 | $NH_3$ |

[a] The complete spectra are in Table VII. [b] SCS-4 = [$\delta_{C_4}$ (Y ≠ H) − $\delta_{C_4}$ (Y = H)] ppm. [c] Positive values correspond to a downfield shift. [d] For an explanation of symbols VII-XI, see Chart I. [e] Sodium hydroxide 1.5 equiv.

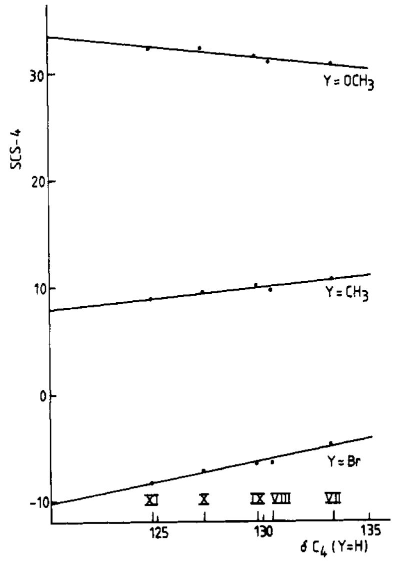


**Figure 1.** Plot of SCS-4 against $\delta_{C_4}$ (Y = H) of 1-X-4-Y-benzenes (6; Y = $OCH_3$, $CH_3$, Br).

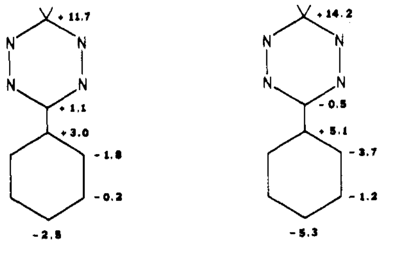
dium borohydride reduction of 7 gave the 3-(p-Y-phenyl)-1,6-dihydro-1,2,4,5-tetrazines (9), which by treatment with potassium hydroxide gave the corresponding anions 10.

In Table III the $\delta_{C_4}$ and the SCS-4 values of these compounds are collected. From these data we concluded that the substituted 1,2,4,5-tetrazinyl groups can be arranged according to decreasing electron-withdrawing properties X < IX < VIII < VII.[11]

In Figure 1 the SCS-4 values are plotted against $\delta_{C_4}$(Y = H). This plot indeed shows a linear relationship for the substituted 1,2,4,5-tetrazinyl groups VII–X, indicating that the continuity of the $C_4$ shift variations is an extended range, also for substituents in the anionic form.

The SCS-4 values of the 6-amino-1,6-dihydro-1,2,4,5-tetrazinyl group (XI) of the σ adduct 11 and its $\delta_{C_4}$(Y = H) nicely fit in these plots. From this plot it is evident that group XI resembles mostly the anionic 1,6-dihydro-1,2,4,5-tetrazinyl group (X), strongly suggesting that in σ adduct 11 the heterocylic substituent is present in the anionic form XIB. Since the $\sigma_I$ values of the hydrogen and the amino group are only slightly different (see Table II), we had expected to find that the electron demand of group XIB in the *anionic* σ adduct will be about equal to that of the anionic 1,6-dihydro group X. However, from our measurements group XIB seems to be a stronger electron donor than group X. To prove that this difference is due to a solvent effect, we compared the $^{13}C$ chemical shift data of 3-phenyl-1,6-dihydro-1,2,4,5-tetrazine (9, Y = H) when dissolved in liquid ammonia (tetrazine ring, $C_6$ 80.5, $C_3$ 154.7 ppm; benzene ring, $C_1$ 139.3, $C_2$ 121.7, $C_3$ 128.5, $C_4$ 124.4 ppm) with those of 9 (Y = H) and 10 (Y = H) in $CD_3OD/D_2O$ (see Table VII). The chemical shift differences between 10 (Y = H) and 9 (Y = H) and between 9 (Y = H) in $NH_3$ and 9 (Y = H) are shown in Chart II. From these data it is evident that 9 (Y = H) in $NH_3$ is deprotonated and present as anionic species 10 (Y = H) with more negative charge localized on the ortho and para positions; this results in a larger upfield shift in liquid ammonia than for 10 (Y = H) measured in $CD_3OD/D_2O$.

Chart II



10 (Y = H) − 9 (Y = H)

[9 (Y = H) in $NH_3$] − 9 (Y = H)

Table IV. Least-Squares Analysis of $\delta(C_4)$ as a Function of SCS-4 Comparison with Literature Values[7,8]

| Y | parameter | this work | Hügel et al.[7] | Membrey et al.[a,8] |
|---|---|---|---|---|
| Br | r | 0.977[b] | 0.984 | 0.975 |
| | slope | 0.40 ± 0.05 | 0.28 ± 0.01 | 0.24 |
| | intercept | −58 ± 10 | −42.2 ± 1.7 | −36.7 |
| | n | 5 | 24 | 25 |
| $OCH_3$ | r | 0.919[c] | 0.896 | 0.825 |
| | slope | −0.21 ± 0.05 | −0.18 ± 0.02 | −0.13 |
| | intercept | 58 ± 4 | 55.2 ± 1.6 | 48.4 |
| | n | 5 | 24 | 52 |
| $CH_3$ | r | 0.948[d] | 0.947 | 0.975 |
| | slope | 0.21 ± 0.04 | 0.30 ± 0.02 | 0.35 |
| | intercept | −17 ± 6 | −25 ± 4 | −35.1 |
| | n | 5 | 25 | 56 |

[a] The values of the intercept were converted to the same scale by substituting 128.6 (value of benzene) for $S_P{}^H$, X in Figure 2 of Membrey et al. Because of the lack of data, no standard deviations could be calculated. [b] $t_\alpha$ = 7.88. [c] $t_\alpha$ = 4.04. [d] $t_\alpha$ = 5.19.

Comparison of $\delta_{C_4}$ of 10 (Y = H) in liquid ammonia (124.4 ppm) with $\delta_{C_4}$ of the σ adduct 11 (Y = H) (124.8 ppm) shows that the effect of the 6-amino-1,6-dihydro-1,2,4,5-tetrazinyl group (XI) is very much like that of the anionic group X. All these results lead to the definitive

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[11] The 1,2,4,5-tetrazinyl group (VII) is found to be a strong electron-withdrawing group, comparable with the $NO_2$ or the COOH group.[9,12]

[12] Jackman, L. M.; Sternhell, S. In "Applications of Nuclear Magnetic Resonance Spectroscopy", 2nd ed.; Pergamon Press: Oxford and New York, 1969; p 202.

Table V. Coupling Constants $J_{\mathrm{CH^A}}$ and $J_{\mathrm{CH^B}}$ (in hertz) in the Various Homoaromatic Compounds[a]

| compd | $J_{\mathrm{CH^A}}$ | $J_{\mathrm{CH^B}}$ | $J_{\mathrm{C_6H}}$ (av)[b] | temp, K |
|---|---|---|---|---|
| 2a [11 (Y = H)] | 156 | | | 223 |
| 2b | 156 | | | 223 |
| 2c | 156 | | | 223 |
| 11 (Y = OCH$_3$) | 156 | | | 223 |
| 3d | 156 | | | 308 |
| 4d | 144 | | | 223 |
| 5d | 169 | | | 273 |
| 3a [9 (Y = H)] | 159[c] | 159[c] | 159 | 273 |
| 9 (Y = OCH$_3$) | | | 159 | 273 |
| 4a [10 (Y = H)] | 147 | 160 | 153 | 273 |
| 10 (Y = Br) | 147[d] | 159 | 153 | 273 |
| 10 (Y = OCH$_3$) | | | 153 | 273 |
| 10 (Y = CH$_3$) | 148 | 157 | 153 | 273 |
| 5a | 170[e] | | 165 | 308 |

[a] H$^A$ is above the plane of the ring; H$^B$ is in the exo position. [b] Calculated from $J_{\mathrm{C_6H}}$ (av) = ($J_{\mathrm{CH^A}}$ + $J_{\mathrm{CH^B}}$)/2. [c] Measured below the exchange temperature (223 K); irradiation of H$^A$ or H$^B$ leaves a doublet. [d] Irradiation of H$^A$ leaves a doublet with the largest coupling constant; irradiation of H$^B$ leaves a doublet with the smallest coupling constant. [e] This compound dissolved very poorly below the exchange temperature, so the coupling constants could not be determined separately.

conclusion that in the $\sigma$ adducts **11** the 1,2,4,5-tetrazinyl group is present in the anionic form (**XIB**).

A least-squares analysis of the SCS-4 as a function of $\delta_{C_4}$ is given in Table IV and compared with the literature values.[7,8] For all three substituents Y, i.e., Br, OCH$_3$, and CH$_3$, we obtained a straight line with a good degree of probability ($t_\alpha$) and a reasonable correlation coefficient. For Y = OCH$_3$ the slope and the intercept are in reasonable agreement with the data obtained by both Hügel et al.[7] and Membrey et al.,[8] for Y = CH$_3$ there is a reasonable agreement with Hügel, and for Y = Br we obtained a steeper slope.

**(B) Coupling Constants $J_{C_6H}$.** 3-Phenyl-1,6-dihydro-1,2,4,5-tetrazine (**3a** [=**9** (Y = H)]), its conjugate base **4a** [=**10** (Y = H)], and conjugate acid **5a** exist in two homotetrazole conformations, one with the CH$_2$ group pointing upward and the other with the CH$_2$ group downward. There is a rapid inversion between these two forms in these systems which is frozen on lowering the temperature.[1] This phenomenon is not changed by the presence of a substituent Y at position 4 of the aryl ring.[13]

The $^{13}$C NMR measurements of the compounds **9** (Y = H, OCH$_3$), **10** (Y = H, Br, OCH$_3$, CH$_3$), and **5a**, were carried out at 273 K. At this temperature only the conjugate bases **10** exist in one form,[1] and two different coupling constants were observed for C$_6$ of **10**. By selective decoupling in **10** (Y = Br) it was established that the smaller one (147 Hz) originates from coupling with H$^A$ (i.e., the hydrogen above the plane of the ring) and the larger one (159 Hz) from coupling with H$^B$ (i.e., the hydrogen in the exo position; see Table V). In 3-phenyl-1,6-dihydro-1,2,4,5-tetrazine (**3a**), measured at 223 K (this is below the exchange temperature), two identical coupling constants were observed ($J_{CH^A}$ = $J_{CH^B}$ = 159 Hz). The difference in $J_{CH^A}$ between the neutral and anionic species is 12 Hz and is equal to the one observed between 3,6-dimethyl-1,6-dihydro-1,2,4,5-tetrazine (**3d**) and its conjugate base **4d**. Nearly the same difference but in the *opposite* direction is found between $J_{CH^A}$ in **3d** and that in its conjugate acid **5d** (156 and 169 Hz). 3-Phenyl-1,6-dihydro-1,2,4,5-tetrazinium ion (**5a**) has an average coupling constant of 165 Hz; however, below the exchange temperature it was not soluble enough to measure the coupling constants separately. Since the positive charge in **5d** caused the coupling constant $J_{CH^A}$ to be larger and since $J_{CH^B}$ is constant in **3a** and **4a**, this average coupling constant of 165 Hz makes it plausible that $J_{CH^A}$ in **5a** is about 170 Hz.

That $J_{CH^A}$ depends on the charge of the tetrazole ring (negative, 147 Hz; uncharged, 159 Hz; positive, 170 Hz) whereas $J_{CH^B}$ remains constant can be explained as follows:[14] in case of the anionic species, H$^A$ is attracted by the negative charge, the electrons of the C–H$^A$ bond are released to carbon, leading to a decrease of the percentage of s character of the bond and a decrease of the $J_{CH^A}$. Conversely, $J_{CH^A}$ is increased in case the homoaromatic species that is positively charged. The influence through space of the charge in the tetrazole ring on H$^A$ and hardly on H$^B$ has also been observed with the $^1$H NMR chemical shift data.[1]

Comparison of $J_{CH^A}$ of the $\sigma$ adducts **2a–c** with those of **4a** and **4d** shows that there is a linear relationship[15] with the $\sigma_I$ values of the substituents (NH$_3$, H, CH$_3$) geminal to H$^A$ ($r$ = 0.93, $t_\alpha$ = 2.52) but that there is no linear dependence with the neutral compounds **3a** and **3d**. This is another additional proof of the anionic character of the $\sigma$ adducts and implies that **2b** and **2c**, when dissolved in liquid ammonia, are also present in the anionic form **2B**.

## Conclusion

From all spectroscopic data available we conclude that the $\sigma$ adducts of ammonia to substituted 1,2,4,5-tetrazines are anionic species. The driving force for the deprotonation is probably the greater resonance stabilization of the homoaromatic anion with respect to the homoaromatic neutral compound.[1]

## Experimental Section

Melting points are uncorrected. Mass spectra were determined on an AEI MS 902 mass spectrometer. $^1$H NMR spectra were recorded on a Varian EM 390 spectrometer or on a Varian XL-100-15 spectrometer. Me$_4$Si was used as internal standard ($\delta$ 0). In liquid ammonia the solvent peak was used as the standard. The spectra were converted to the Me$_4$Si scale by addition of 0.95 ppm. $^{13}$C NMR spectra were recorded on a Varian XL-100-15 spectrometer. Me$_4$Si was used as an internal standard ($\delta$ 0). In liquid ammonia, trimethylamine ($\delta$ 47.5) was used as an internal standard. The solutions were about 0.4 M. Typical spectral parameters for $^{13}$C NMR were as follows: spectral width, 5120 Hz (1.25 Hz/point); acquisition time, 0.8 s; pulse delay, 0–1.2 s; pulse width, 10–20 $\mu$s. UV spectra were measured on a Perkin-Elmer 550 spectrophotometer. Column chromatography was carried out over Merck silica gel 60 (70–230 mesh). See Tables VI and VII for the NMR data.

**Preparation of Starting Materials. 3-Phenyl-1,2,4,5-tetrazine (1a),**[17] **3-methyl-1,2,4,5-tetrazine (1b),**[18] **3-*tert*-butyl-1,2,4,5-tetrazine (1c),**[10] **3-(*p*-bromophenyl)-1,2,4,5-tetrazine (7, Y = Br),**[10] **3-(*p*-methoxyphenyl)-1,2,4,5-tetrazine (7, Y = OCH$_3$),**[17] **6-R$^3$-3-phenyl-1,6-dihydro-1,2,4,5-tetrazine (3a, R$^3$ = H;**[1] **3b, R$^3$ = CH$_3$;**[1] **3c, R$^3$ = C$_2$H$_5$),**[1] **and 3,6-dimethyl-1,6-**

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[13] That this phenomenon is indeed not changed by the presence of substituent Y on the phenyl ring is indicated by the $^1$H NMR chemical shifts of **10** (Y = Br, OCH$_3$). They both show at room temperature two different chemical shift values for H$^A$ and H$^B$, comparable with 1.37 and 6.18 ppm in **10** (Y = H);[1] see Table VI [**10** (Y = H) = **4a**].

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Table VI. $^1$H NMR Chemical Shift Data of 3-(*p*-Y-phenyl)-1,2,4,5-tetrazines 7–11 (Y = Br, $OCH_3$, $CH_3$)[a] and the Influence of the Substituted 1,2,4,5-Tetrazinyl Groups VII–XI on the Ortho and Meta $^1$H Chemical Shifts of Benzene[b]

| | chemical shift, δ | | | | | shift change, Δδ | | |
|---|---|---|---|---|---|---|---|---|
| compd | $H^A$ | $H^B$ | $OCH_3/CH_3$ | $H_2$ | $H_3$ | X | ortho[c] | meta[c] |
| 7 (Y = Br) | 10.25 | | | 8.50 | 7.75 | | | |
| 7 (Y = $OCH_3$) | 10.11 | | 3.93 | 8.55 | 7.07 | VII | −1.34 | −0.26 |
| 7 (Y = $CH_3$) | 10.16 | | 2.47 | 8.49 | 7.38 | | | |
| 8 (Y = Br) | | | | 8.18 | 7.75 | | | |
| 8 (Y = $OCH_3$) | | | 3.87 | 8.21 | 7.11 | VIII | −1.04 | −0.26 |
| 8 (Y = $CH_3$) | | | 2.40 | 8.16 | 7.36 | | | |
| 9 (Y = Br) | 4.15 | | | 7.77 | 7.57 | | | |
| 9 (Y = $OCH_3$) | 4.08 | | 3.85 | 7.82 | 7.02 | IX | −0.61 | −0.13 |
| 9 (Y = $CH_3$) | 4.11 | | 2.37 | 7.75 | 7.24 | | | |
| 10 (Y = Br) | 1.37 | 6.19 | | 7.67 | 7.47 | | | |
| 10 (Y = $OCH_3$) | 1.34 | 6.13 | 3.85 | 7.69 | 6.95 | X | −0.48 | −0.05 |
| 10 (Y = $CH_3$) | d | | 2.35 | 7.64 | 7.15 | | | |
| 11 (Y = Br) | 1.59 | | | 7.71 | 7.47 | | | |
| 11 (Y = $OCH_3$) | 1.50 | | 3.68 | 7.63 | 6.83 | XI | −0.47 | +0.01 |
| 11 (Y = $CH_3$) | 1.55 | | 2.28 | 7.65 | 7.10 | | | |

[a] Solvents as in Table VII. [b] Benzene, δ 7.27; the effects of Br, $OCH_3$, and $CH_3$ were taken from Jackman and Sternhell;[12] a negative sign denotes a downfield shift; no correction was made for the change in solvent. [c] The accuracy is ±0.05 ppm. [d] For this compound, 307 K is apparently the coalescence temperature; no signals were observed.

Table VII. $^{13}$C NMR Data[a] of Compounds 7,[b] 8,[c] 9,[d] 10,[e] 11,[f] and 5a[g]

| | tetrazine ring | | benzene ring | | | | |
|---|---|---|---|---|---|---|---|
| compd | $C_6$ | $C_3$ | $C_1$ | $C_2$ | $C_3$ | $C_4$ | others |
| 7 (Y = H) | 158.1 | 166.7 | 131.8 | 128.5 | 129.5 | 133.2 | |
| 7 (Y = Br) | 158.1 | 166.2 | 130.8 | 129.8 | 132.9 | 128.6 | |
| 7 (Y = $OCH_3$) | 157.5 | 166.1 | 124.2 | 130.3 | 115.0 | 164.0 | 55.5, $OCH_3$ |
| 7 (Y = $CH_3$) | 157.9 | 166.3 | 129.2 | 128.4 | 130.2 | 144.0 | 21.7, $CH_3$ |
| 8 (Y = H) | 159.4 | 163.1 | 133.2 | 125.7 | 129.1 | 130.4 | |
| 8 (Y = Br) | 158.7 | 162.9 | 132.4 | 127.6 | 132.1 | 124.0 | |
| 8 (Y = $OCH_3$) | 159.3 | 162.9 | 125.6 | 127.3 | 114.6 | 161.3 | 55.3, $OCH_3$ |
| 8 (Y = $CH_3$) | 159.4 | 163.0 | 130.5 | 125.6 | 129.7 | 140.2 | 21.0, $CH_3$ |
| 9 (Y = H)[h] | 66.3 | 155.2 | 134.2 | 125.4 | 129.7 | 129.7 | |
| 9 (Y = Br) | 66.6 | 154.4 | 133.9 | 127.1 | 132.8 | 123.3 | |
| 9 (Y = $OCH_3$) | 66.5 | 155.2 | 127.0 | 127.0 | 115.1 | 161.2 | 55.9, $OCH_3$ |
| 9 (Y = $CH_3$) | 66.4 | 155.4 | 131.7 | 125.5 | 130.4 | 139.9 | 21.4, $CH_3$ |
| 10 (Y = H)[i] | 78.0 | 156.3 | 137.2 | 123.6 | 129.5 | 127.2 | |
| 10 (Y = Br) | 78.2 | 155.4 | 136.6 | 125.1 | 132.3 | 120.0 | |
| 10 (Y = $OCH_3$) | 78.1 | 156.2 | 130.7 | 125.1 | 114.8 | 159.4 | 55.9, $OCH_3$ |
| 10 (Y = $CH_3$) | 78.0 | 156.4 | 134.6 | 123.7 | 130.0 | 136.7 | 21.2, $CH_3$ |
| 11 (Y = H)[j] | 94.4 | 155.5 | 138.7 | 122.1 | 128.6 | 124.8 | |
| 11 (Y = Br) | 94.9 | 154.7 | 138.3 | 123.7 | 131.2 | 116.5 | |
| 11 (Y = $OCH_3$) | 94.2 | 155.2 | 131.7 | 123.3 | 113.6 | 157.0 | 55.3, $OCH_3$ |
| 11 (Y = $CH_3$) | 94.6 | 155.5 | 136.2 | 122.2 | 129.0 | 133.6 | 20.8, $CH_3$ |
| 5a | 62.4 | 156.0 | 130.5 | 126.1 | 129.9 | 131.2 | |

[a] For each series of compounds in at least one compound the shifts were assigned by selective decoupling. The other chemical shifts could be assigned by the coupling patterns and the empirical parameters for the chemical shifts in substituted benzenes.[16] Chemical shifts are given as δ values. [b] In $CDCl_3$. [c] In $Me_2SO$-$d_6$. [d] In $CD_3OD/D_2O$, 4:1. [e] In $CD_3OD/D_2O$ (4:1) with 1.5 equiv of sodium hydroxide. [f] In $NH_3$. [g] In $CD_3OD/D_2O$ (4:1) and 0.61 M sulfuric acid. [h] 9 (Y = H) = 3a. [i] 10 (Y = H) = 4a. [j] 11 (Y = H) = 2a.

**dihydro-1,2,4,5-tetrazine (3d)**[4] were prepared according to known synthetic procedures.

**3-(*p*-Methylphenyl)-1,2,4,5-tetrazine (7, Y = $CH_3$).** This compound was prepared analogously to the procedure of Lang et al.[17] After column chromatography on silica gel with petroleum ether (bp 60–80 °C)/dichloromethane as eluant, 7 (Y = $CH_3$) was obtained: yield 8%; mp 86–88 °C (lit.[19] mp 84.5 °C); mass spectrum, *m/e* 172 ($M^+$). Anal. Calcd for $C_9H_8N_4$: C, 62.78; H, 4.68. Found: C, 62.97; H, 4.82. In addition, 5% of 3,6-bis(*p*-methylphenyl)-1,2,4,5-tetrazine was obtained: mp 248.5–249 °C (lit.[20] mp 235 °C); mass spectrum, *m/e* 262 ($M^+$). Anal. Calcd for $C_{16}N_{14}N_4$: C, 73.26; H, 5.38. Found: C, 73.41; H, 5.52.

**6-Amino-3-(*p*-Y-phenyl)-1,2,4,5-tetrazine (8, Y = H, Br, $OCH_3$, $CH_3$).** Compound 8 (Y = H, Br) was prepared as described before,[10] and compound 8 (Y = $OCH_3$, $CH_3$) was prepared according to the procedure described before[10] by dissolution of 7 (Y = $OCH_3$, $CH_3$) in liquid ammonia and subsequent oxidation with potassium permanganate. 8 (Y = $OCH_3$): yield 86%; mp 262–264 °C (lit.[21] mp 257–259 °C); mass spectrum, *m/e* 203 ($M^+$). Anal. Calcd for $C_9H_9N_5O$: C, 53.19; H, 4.40. Found: C, 53.19; H, 4.42. 8 (Y = $CH_3$): yield 82% mp 242–243 °C (lit.[21] mp 233–234 °C); mass spectrum, *m/e* 187 ($M^+$). Anal. Calcd for $C_9H_9N_5$: C, 57.74; H, 4.85. Found: C, 57.53; H, 4.89.

**3-(*p*-Y-phenyl)-1,6-dihydro-1,2,4,5-tetrazines (9, Y = Br, $OCH_3$, $CH_3$).** The compounds were prepared by sodium borohydride reduction of 7.[1] They were purified by recrystallization from benzene or by preparative thin-layer chromatography over silica gel $PF_{254}$ (2mm), eluting with 5% ether in dichloromethane. As mentioned before,[22] these compounds decompose during mass spectrometric measurements and do not show a $M^+$ peak. 9 (Y

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= Br): yield 42%; mp 115–117 °C; IR (chloroform) 3410, 3220 cm$^{-1}$ (NH stretch). Anal. Calcd for $C_8H_7BrN_4$: C, 40.19; H, 2.95. Found: C, 40.66; H, 3.12. **9** (Y = $OCH_3$): yield 35%; mp 99–101 °C; IR (chloroform) 3400, 3210 cm$^{-1}$ (NH stretch). Anal. Calcd for $C_9H_{10}N_4O$: C, 56.83; H, 5.30. Found: C, 57.02; H, 5.40. **9** (Y = $CH_3$): yield 44%; from thin-layer chromatography of the mother liquor an additional 22% was obtained; melting range 100–104 °C; IR (chloroform) 3400, 3220 cm$^{-1}$ (NH stretch). Anal. Calcd for $C_9H_{10}N_4$: C, 62.05; H, 5.79. Found: C, 62.23; H, 5.83.

**Determination of the p*K*$_a$ of 6-R$^3$-3-phenyl-1,6-dihydro-1,2,4,5-tetrazines 3a (R$^3$ = H), 3b (R$^3$ = $CH_3$), and 3c (R$^3$ = $C_2H_5$). Calculation of the p*K*$_a$ of 2a.** The p$K_a$ was determined by UV spectroscopy.[23] Each compound was measured in seven buffer solutions of different pH,[24] in a buffer solution of pH 7.5 (neutral species), and in a buffer solution of pH 12.9 (conjugate base). A stock solution in 10 mL of ethanol was prepared from which 1 mL was added to the buffer solutions. The p$K_a$ values are as follows: **3a**, 10.01 ± 0.03; **3b**, 9.77 ± 0.09; **3c**, 9.92 ± 0.08. UV data at pH 7.5: $\lambda_{max}$ for **3a** 432 nm (log $\epsilon$ 2.93), 275 (4.05); for **3b** 431 (2.86), 275 (4.06); for **3c** 433 (2.91), 277 (4.08). UV data at pH 12.9: $\lambda_{max}$ for **4a** 389 nm (log $\epsilon$ 3.28), 303 (4.15); for **4b** 385 (3.30), 303 (4.17); for **4c** 390 (3.26), 304 (4.17).

The p$K_a$ value of **2a** was approximated by averaging the p$K_a$ values of **3a–c**, which results in 9.90 ± 0.12.[25]

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**Registry No. 1a**, 36022-11-4; **1b**, 67131-36-6; **1c**, 78114-01-9; **2a**, 78199-51-6; **2b**, 78199-52-7; **2c**, 78199-53-8; **3a**, 76630-74-5; **3b**, 76630-75-6; **3c**, 76630-76-7; **3d**, 13717-81-2; **4a**, 76630-78-9; **4b**, 76630-79-0; **4c**, 76630-80-3; **4d**, 78199-54-9; **5a**, 76630-81-4; **5d**, 78199-55-0; **7** (Y = Br), 56107-99-4; **7** (Y = $OCH_3$), 56107-91-6; **7** (Y = $CH_3$), 37385-31-2; **8** (Y = Br), 72115-67-4; **8** (Y = $OCH_3$), 72115-80-1; **8** (Y = $CH_3$), 72115-68-5; **9** (Y = Br), 78199-56-1; **9** (Y = $OCH_3$), 78199-57-2; **9** (Y = $CH_3$), 78199-58-3; **10** (Y = Br), 78199-59-4; **10** (Y = $OCH_3$), 78199-60-7; **10** (Y = $CH_3$), 78199-61-8; **11** (Y = Br), 78199-62-9; **11** (Y = $CH_3$), 78199-63-0; **11** (Y = $OCH_3$), 78199-64-1; VIII (Y = H), 14418-30-5; 3,6-bis(*p*-methylphenyl)-1,2,4,5-tetrazine, 51973-26-3.

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(25) The differences in $\sigma_I$ for the geminal groups (H, $CH_3$, $C_2H_5$, and $NH_2$, Table II) are small; the Hammet equation, $\log (k/k_o) = \rho\sigma$ or $-pK_X + pK_{NH_2} = \rho(\sigma_X - \sigma_{NH_2})$ predicts a difference of 0.06p$K_a$ units (if $\rho = 1$) between **3c** and **2a**. This is below the experimental accuracy. Therefore the average value from **3a–c** was taken as the p$K_a$ of **2a**: 9.90 ± 0.12.

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# Solvomercuration–Demercuration. 10. Oxymercuration–Demercuration of Olefins with the Mercuric Salts Acetate, Trifluoroacetate, Nitrate, and Methanesulfonate[1]

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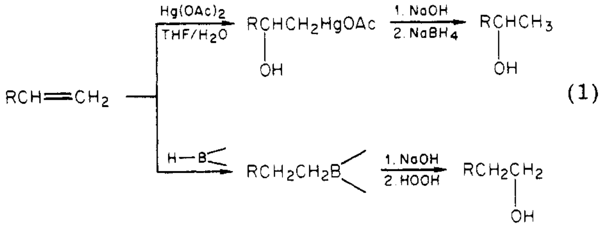
The oxymercuration–demercuration of a series of representative olefins has been examined with four mercuric salts: acetate, trifluoroacetate, nitrate, and methanesulfonate. Mono- and 1,2-disubstituted olefins undergo hydration with all four mercuric salts in 90–100% yields with a regioselectivity for the Markovnikov alcohol (from monoolefins) of ≥99.5%. Only styrene was found to be an exception. In marked contrast, only mercuric acetate is effective for the Markovnikov hydration of 1,1-di-, tri-, and tetrasubstituted olefins. The other three mercuric salts provide lower yields of the tertiary alcohols, yields which decrease rapidly with time. 1-Phenylcyclopentene undergoes only allylic oxidation with the mercuric salts trifluoroacetate, nitrate, and methanesulfonate. Mercuric acetate does give the normal hydration product but only in trace amounts. In this case, allylic oxidation is the major reaction pathway with this salt as well.

## Introduction

The oxymercuration-demercuration (OM–DM) sequence with mercuric acetate in aqueous tetrahydrofuran is a valuable method for the Markovnikov hydration of olefins (eq 1). It is characterized by an exceptionally high regioselectivity. Moreover, rerarrangements are virtually unknown. Consequently, it nicely complements hydroboration–oxidation which leads to the anti-Markovnikov alcohols (eq 1).



(1)

Mercuric acetate is highly effective in this reaction.[2] However, looking to the future, we anticipated incorporating many nucleophiles other than water into the initial mercurial. (Hence, the series was entitled "Solvomercuration–Demercuration" rather than "Oxymercuration–Demercuration".) It appeared desirable to have definite information on the behavior of a series of mercuric salts with anions of decreasing nucleophilicity. Thus, it would be easy to shift to a more favorable salt when working with a solvent of greatly reduced nucleophilic properties.

There are several reports concerning the differing behavior of various mercuric salts.[3,4] While mercuric acetate

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