Å. Great motion of the radicals with respect to each other upon loss of nitrogen is not expected, because of the good alignment of the C(1)–N(7) bond with the aryl π cloud in the tetrazene. Our ESR data is not good enough to measure the actual amount of motion of the radicals from their positions in the tetrazene precursor, as McBride and co-workers[19,23] have done for several crystals. As a qualitative way of gauging motion, we calculated the D' and E' expected using the spin densities estimated from the doublet ESR spectrum ($\rho_N = 0.489$, $\rho_o = 0.234$, $\rho_m = -0.080$, $\rho_p = -0.284$; these are only estimates, and ignore spin density in the *tert*-butyl group) and the atom positions of the tetrazene, obtaining $D' = -146$, $E' = 10$ G, both rather higher than the observed values.

The axes for the anisotropic g tensor coincided, with our rather wide experimental error, with those for the D tensor, and the observed values were $g_{zz} = 2.0058$, $g_{yy} = 2.0003$, $g_{xx} = 2.0044$, $g_{iso} = 2.0035$, close to the 2.0033 observed for the doublet in solution.

Hyperfine splittings caused by the nitrogen atoms were observed in some orientations of the triplet, but we have not been able to analyze them. No splittings were observed in the dipolar lines for orientation about the axis nearly coincident with the z axis of the triplet, although the line width varied from about 6.5 to 15 G, but in rotations about the other axes, each half of the doublet for species I varied from appearing as a singlet (splitting under 2 G) to appearing as a five to nine line pattern with apparent line separation of up to 12 G.

Quantitative study of these triplets was hampered by the presence of species I and II, which frequently merged with each other, disrupting our ability to accurately measure the line positions of either one. Preparation of deuterated **2A** would allow study of the nitrogen hyperfine splittings without this difficulty, but such a study has not been carried out.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation for partial financial support of this research. The funds used for purchasing the diffractometer came partly from the Major Instrument Program of the NSF. We thank Professor J. M. McBride for extensive discussions and the program used for calculation of D' and E', and W. C. Hollinsed for assistance in calculations from the x-ray data.

Registry No.—**2A,** 63641-20-3; **2B,** 63641-21-4; aniline-2,4,6-d_3, 7291-08-9; aniline, 62-53-3; D_2O, 7789-20-0.

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Telesubstitution and Other Transformations of Imidazo[1,2-a]- and s-Triazolo[4,3-a]pyrazines[1]

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Received May 23, 1977

Imidazo[1,2-a]pyrazine is brominated to give either the 3-bromo- or the 3,5-dibromo derivative. The 6,8-dibromo compound, prepared from 2-amino-3,5-dibromopyrazine, is brominated to 3,6,8-tribromoimidazo[1,2-a]pyrazine. With sodium methylate only the bromine atom at position 8 is substituted, and from the 6,8-dibromo compound 6-bromo-8-methoxyimidazo[1,2-a]pyrazine is prepared. Quaternization of imidazo[1,2-a]pyrazine gives a mixture of the 1-methyl and 7-methyl derivatives. s-Triazolo[4,3-a]pyrazine afforded upon bromination the 5-bromo derivative. This and other 5-halo compounds reacted with nucleophiles to give either the anticipated 5-substituted derivative or at position 8 telesubstituted product, or both. Mechanistic aspects of telesubstitution are outlined.

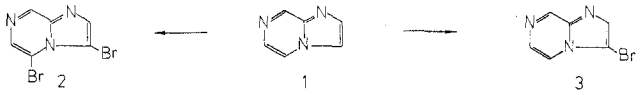
As part of our interest in the chemistry of azolopyrazines we would like to report some new transformations of imidazo[1,2-a]- and s-triazolo[4,3-a]pyrazines.

A general method for the synthesis of imidazo[1,2-x]azines consists of the reaction between the corresponding 2-aminoazines and α-halocarbonyl compounds. In the pyrazine

series this method gives less satisfactory results and only a few 2- or 3-substituted imidazo[1,2-*a*]pyrazines were synthesized.[2,3] In connection with the isolation of luciferins, new and better synthetic approaches have been devised. Imidazo[1,2-*a*]pyrazines were prepared from aminopyrazines and α-keto aldehydes or formaldehyde and hydrogen cyanide.[4-10] In another method 2-formylimidazoles were used as starting material and at position 1 quaternized derivatives were thus accessible.[11] Although the first derivative of this bicyclic system was reported in 1957,[12] the parent system has so far not been described in the free form but was obtained as the perchlorate[13] in low yield.

We have recently reported the synthesis of imidazo[1,2-*a*]pyrazine[14] and have examined its reaction with hydrazine to give a mixture of 2-methylimidazole and 1-ethyl-2-methylimidazole. It was established that these compounds arise from an initial attack of hydrazine on the pyrazine part of the bicycle, either at position 5 or at position 8.

The ready availability of the parent heterocycle (**1**)[14] prompted us to investigate in more detail the reactivity of this system, in particular, electrophilic and nucleophilic substitutions. Bromination of **1** with bromine in glacial acetic acid

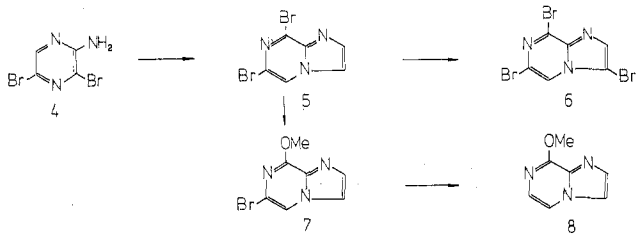


2 **1** **3**

afforded the 3,5-dibromo compound **2**, whereas with *N*-bromosuccinimide the 3-bromo derivative **3** was obtained. The structure of this monobromo derivative follows from the following observations. The compound was resistant to nucleophilic substitution and no reaction with either sodium alcoholate, or sodium thiophenolate, hydrazine hydrate, or liquid ammonia could be observed. Such unreactivity toward nucleophiles is incompatible with structure of a 5-bromo compound, since because of theoretical considerations[15] as well as practical experience[16] a halogen atom at position 5 should be easily replaced. The NMR parameters of this monobromo compound did not allow unambiguous assignment of the peaks. However, when the spectrum was recorded after addition of a shift reagent, assignment became possible. In the normal NMR spectrum a broad singlet at δ 8.19 was observed, assignable to H_5 and H_6 protons. After addition of some Eu(fod)$_3$ a doublet for H_6 at δ 9.43 and a doublet of doublets at δ 8.79 for H_5 were clearly separated. Moreover, coupling constants, $J_{5,6}$ = 5.5 and $J_{5,8}$ = 2.0 Hz, could be observed. This excludes other possible structures with the bromide atom either at positions 5, 6, or 8. The structure as a 2-bromo derivative is also excluded if we compare chemical shifts for H_2 and H_3 in the unsubstituted compound[14] and the monobromo derivative, since the signal for H_3 appears at lower field. Such spectral characteristics were observed also with pyrroloazines or imidazo[1,2-*b*]pyridazines.[17-21] All this evidence favors the structure of 3-bromoimidazo[1,2-*a*]pyrazine (**3**).

The structure of the dibromo compound **2** is also in agreement with NMR data. The signal for H_2 appears as a singlet at δ 7.73 and is almost at the same position as that of the unsubstituted compound[14] or the 3-bromo derivative **3**. Moreover, two other singlets at δ 7.95 and 8.96 appear in the NMR spectrum of **2**, and this excludes substitution at position 8. In this case a $J_{5,6}$ should be observable. Substitution at position 6 is also excluded, since in this case one should observe a $J_{5,8}$, observed so far in all 5,8-unsubstituted imidazo[1,2-*a*]pyrazines, such as the parent compound[14] or compounds **3**, **9**, and **10**.

Other bromo derivatives were prepared as follows. 6,8-Dibromoimidazo[1,2-*a*]pyrazine (**5**) was synthesized from 2-amino-3,5-dibromopyrazine (**4**) and bromoacetaldehyde, and after bromination with *N*-bromosuccinimide a tribromo derivative was obtained. Because of the NMR spectral evi-



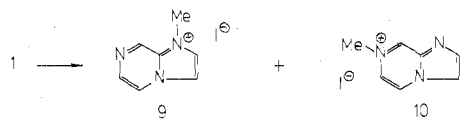
4 **5** **6** **7** **8**

dence for this compound the structure of 3,6,8-tribromoimidazo[1,2-*a*]pyrazine (**6**) could be assigned. These findings agree with theoretical predictions of reactivity of imidazo[1,2-*a*]pyrazine, based on calculated electron densities.[15] These indicate that the most reactive position for electrophilic attack should be position 3, followed by position 5, whereas nucleophilic substitutions should take place predominantly at positions 5 and 8.

In a nucleophilic substitution, 6,8-dibromoimidazo[1,2-*a*]pyrazine (**5**) exchanged only one bromine atom with a methoxy group. For the purpose of structural assignment the obtained compound was catalytically dehalogenated to give the monomethoxy derivative. Since this compound revealed in its NMR spectrum a coupling constant of 5.0 Hz, corresponding to two ortho protons, its structure can be only 8-methoxyimidazo[1,2-*a*]pyrazine (**8**) and the precursor is 6-bromo-8-methoxy compound **7**.

Imidazo[1,2-*a*]pyrazine does not undergo hydrogen–deuterium exchange under neutral or acid conditions. In an alkaline solution of aqueous NaOD in dimethyl sulfoxide exchange of protons 3 and 5 was complete in 19 min at room temperature (50% of H_5 is exchanged in <2 min, whereas 50% of H_3 is exchanged in 2 min). Other protons were not exchanged even at 100 °C after 75 min. This contrasts the more reactive *s*-triazolo[1,2-*a*]pyrazine system.[16]

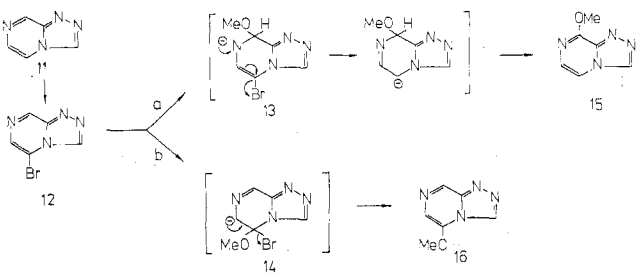
Quaternization of imidazo[1,2-*a*]pyrazine with methyl iodide at room temperature afforded after 5 days a mixture of 7-methyl (**10**) and 1-methyl quaternary compounds (**9**) in a



9 **10**

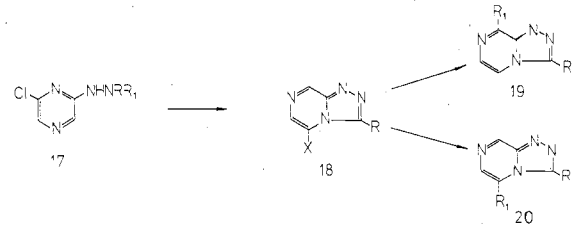
ratio of 1:1.6, as determined from NMR evidence. The structure assignment to both quaternary compounds follows from the following observations. The most important feature which allows the structure assignment to **10** is the appearance of $J_{6,8}$ = 1 Hz, this coupling constant being otherwise not observable with all azolopyrazines.[14,19] In the last case the quadrupole effect of N_7 is responsible for the fact that $J_{6,8}$ does not appear or is very small. The same effect, when blocking the free electron pair on the ring nitrogen, has been observed also with some azine *N*-oxides.[22] In addition, the signals for H_6 and H_8 in **10** are sharper in comparison to those of **9** or all other azolopyrazines, again because of the absence of the quadrupole effect of N_7.

As a continuation of our investigations on *s*-triazolo[1,5-*a*]- and *s*-triazolo[4,3-*a*]pyrazine,[14,16,23-25] we now report some new findings. 5-Bromo-*s*-triazolo[4,3-*a*]pyrazine (**12**) was



12 **13** **14** **15** **16**

obtained from the parent compound 11 upon bromination with bromine in acetic acid. Its structure follows from the following considerations. In the NMR spectrum appear three singlets and this excludes substitution at either position 3 or 8, since in these cases a $J_{5,6}$ would be observed. Substitution at position 6 is also excluded, since in this case a $J_{5,8}$ would be observed. Moreover, the NMR spectrum of **12** is very similar to that of the analogous 5-chloro compound (**18**, R = H, X = Cl, three singlets for protons H_3, H_6, and H_8), whose structure follows unequivocally from its synthesis from the corresponding chloropyrazine (**17**, R = R_1 = H).



Compound 12 reacted with sodium methylate at room temperature to give a mixture of 5-methoxy (**16**) and 8-methoxy compounds (**15**). The structure assignment follows from NMR spectroscopic data. One of the isomers showed a $J_{5,6}$ = 5 Hz, which is characteristic for two ortho protons and therefore only structure **15** is acceptable. To the other compound the structure of the 5-methoxy isomer **16** was assigned, since its NMR spectrum revealed three singlets for ring protons. The possibility of a 6-methoxy derivative is excluded because of reasoning which is presented above for the related 5-bromo compound **12**. The formation of the 8-methoxy isomer is another example of telesubstitution which we have observed previously.[16] On the other hand, 5-bromo-*s*-triazolo[4,3-*a*]pyrazine (**12**) or its 3-phenyl analogue (**18**, R = Ph, X = Br) reacted with hot sodium thiophenolate to give only the corresponding 5-phenylthio derivatives (**20**, R_1 = SPh, R = H or Ph). So far, we have no adequate explanation for the specific reactivity of sodium thiophenolate; yet it should be mentioned that we have observed similar specificity also with *s*-triazolo[1,5-*a*]triazine.[16]

From 2-hydrazino-6-chloropyrazine (**17**, R = R_1 = H) and diethoxymethyl acetate 5-chloro-*s*-triazolo[4,3-*a*]pyrazine (**18**, R = H, X = Cl) was obtained in low yield. Cyclization was attempted also with triethyl orthoformate or a mixture of the latter and acetic anhydride, but without success. However, the 3-phenyl analogue (18, R = Ph, X = Cl) could be prepared in good yield from the benzylidene derivative of 2-hydrazino-6-chloropyrazine (**17**, RR_1 = CHPh) by oxidative cyclization with lead tetraacetate. We have attempted also another approach for the synthesis of *s*-triazolo[4,3-*a*]pyrazines, which proved to be successful in the pyridazine series.[26] From hydrazinopyrazines and *N,N*-dimethylformamide dimethyl acetal the corresponding *N,N*-dimethylaminomethylenehydrazine derivatives were prepared, but attempts to cyclize these were unsuccessful.

3-Phenyl-5-chloro-*s*-triazolo[4,3-*a*]pyrazine (**18**, R = Ph, X = Cl) reacted with sodium methoxide either at room temperature or under reflux to give only the telesubstituted product, the 8-methoxy derivative (**19**, R = Ph, R_1 = OMe). With sodium ethoxide under reflux the same chloro compound afforded again only the 8-ethoxy derivative (**19**, R = Ph, R_1 = OEt) in moderate yield. On the other hand, this compound is obtainable also from the 8-methoxy derivative (**19**, R = Ph, R_1 = OMe) with hot sodium ethoxide. Telesubstitution occurred also when **18** (R = Ph, X = Cl) reacted at room temperature with methanolic ammonia to give the 3-phenyl-8-amino derivative (**19**, R = Ph, R_1 = NH_2), formed also from the corresponding 8-methoxy compound (**19**, R = Ph, R_1 = OMe).

For telesubstitution one can postulate the following reaction mechanism. In view of the electron-withdrawing property of the 7-aza group, position 8 of imidazo[1,2-*a*]- or *s*-triazolo[4,3-*a*]pyrazines is activated for nucleophilic attack. Accordingly, besides the normal addition–elimination process at position 5 (**14**) (path b), a competitive addition of the nucleophile at position 8 (**13**) can take place (path a). These and previous results[14] appear to be consistent with this mechanism, although by monitoring the reaction in a NMR probe the anticipated σ complex could not be detected. To the best of our knowledge, there are no previous examples of telesubstitution in the azoloazine series with a bridgehead nitrogen atom.

Experimental Section

Melting points were determined on a Kofler hot plate melting point apparatus. The NMR spectral measurements were performed on a JOEL JNM C-60 HL spectrometer with Me_4Si as internal standard. Mass spectra were recorded on a Hitachi Perkin-Elmer RMU-6L spectrometer.

Materials. 2-Chloropyrazine was prepared from glyoxal and formamide according to the described procedure[27] and was transformed further into 2-hydrazinopyrazine.[28] *s*-Triazolo[4,3-*a*]pyrazine[29] (^{1}H NMR (Me_2SO-d_6) δ 9.55 (s, H_3), 8.71 (dd, H_5), 8.01 (d, H_6), 9.55 (d, H_8), $J_{5,6}$ = 5.0, $J_{5,8}$ = 2.0 Hz), 2-amino-3,5-dibromopyrazine,[30] and imidazo[1,2-*a*]pyrazine[14] were reported previously.

3,5-Dibromoimidazo[1,2-*a*]pyrazine (2). A solution of **1** (0.2 g) in glacial acetic acid (4 mL) was cooled on ice, and a solution of bromine (0.5 mL) in glacial acetic acid (2 mL) was added dropwise with stirring. The separated orange-colored product was filtered and crystallized from water: mp 150–151 °C (yield 75 mg, 16%); MS *m/e* 273 (M); ^{1}H NMR ($CDCl_3$) δ 7.73 (s, H_2), 7.95 (s, H_6), 8.96 (s, H_8).

Anal. Calcd for $C_6H_3Br_2N_3$: C, 26.02; H, 1.09; N, 15.17. Found: C, 26.33; H, 1.35; N, 15.07.

3-Bromoimidazo[1,2-*a*]pyrazine (3). A mixture of 1 (2.0 g), *N*-bromosuccinimide (2.94 g), and chloroform (100 mL) was heated under reflux for 2 h. Upon cooling, the solution was treated with a saturated aqueous solution of sodium carbonate (200 mL) and shaken. The chloroform layer was separated and upon evaporation of the solvent the residue was crystallized from chloroform–petroleum ether: mp 193–194 °C (1.9 g, 58% yield); MS *m/e* 197 (M); ^{1}H NMR ($CDCl_3$) δ 7.84 (s, H_2), 8.19 (br s, H_5 and H_6), 9.15 (s, H_8); ^{1}NMR (after addition of 15 mg of Eu(fod)$_3$ in 0.5 mL of $CDCl_3$) δ 10.6 (s, H_2), 9.82 (dd, H_5), 11.0 (d, H_6), 13.2 (d, H_8), $J_{5,8}$ = 2.0, $J_{5,6}$ = 5.5 Hz.

Anal. Calcd for $C_6H_4BrN_3$: C, 36.39; H, 2.04; N, 21.22. Found: C, 36.72; H, 2.14; N, 21.45.

6,8-Dibromoimidazo[1,2-*a*]pyrazine (5). A mixture of bromoacetaldehyde diethyl acetal (1.4 g), concentrated hydrobromic acid (0.38 mL), and water (0.38 mL) was heated under reflux for 1 h. Upon cooling the reaction mixture was poured into ethanol (15 mL) and neutralized with solid sodium bicarbonate. To the filtrate 2-amino-3,5-dibromopyrazine (1 g) was added and the reaction mixture was stirred for 3 days at room temperature. The separated product was filtered and crystallized from water: mp 165–166 °C (yield 0.40 g, 33%); MS *m/e* 275 (M); ^{1}H NMR ($CDCl_3$) δ 8.26 (s, H_5), 7.80 (m, H_3 and H_2).

Anal. Calcd for $C_6H_3Br_2N_3$: C, 26.02; H, 1.09; N, 15.17. Found: C, 26.44; H, 1.33; N, 14.99.

The hydrobromide salt, prepared with concentrated hydrobromic acid, revealed the following: ^{1}H NMR (Me_2SO-d_6) δ 8.00 (d, H_2), 8.37 (d, H_3), 9.17 (s, H_5), $J_{2,3}$ = 1.2 Hz.

3,6,8-Tribromoimidazo[1,2-*a*]pyrazine (6). A mixture of 6,8-dibromoimidazo[1,2-*a*]pyrazine (0.24 g), NBS (151 mg), and chloroform (10 mL) was heated under reflux for 1 h and a white precipitate was formed. The reaction mixture was shaken with a saturated aqueous solution of sodium carbonate (15 mL), and the chloroform layer was separated and evaporated to dryness. The residue was sublimed in vacuo to give the pure product: mp 161–165 °C (yield 0.135 g, 44%); ^{1}H NMR ($CDCl_3$) δ 7.83 (s, H_2), 8.23 (s, H_5).

Anal. Calcd for $C_6H_2Br_3N_3$: C, 20.25; H, 0.57; N, 11.81. Found: C, 20.39; H, 1.06; N, 11.50.

6-Bromo-8-methoxyimidazo[1,2-*a*]pyrazine (7). A methanolic solution of sodium methylate was prepared from sodium (20 mg) and methanol (15 mL) and to this 6,8-dibromo compound **5** (0.25 g) was added. The reaction mixture was heated under reflux for 2 h and evaporated to dryness, and the residue was crystallized from water: mp 208–210 °C (yield 0.147 g, 72%); MS *m/e* 228 (M); ^{1}H NMR

($CDCl_3$) δ 7.50 (d, H_2), 7.56 (d, H_3), 7.83 (s, H_5), 4.14 (s, OMe), $J_{2,3}$ = 1.0 Hz.

Anal. Calcd for $C_7H_6BrN_3O$: C, 36.86; H, 2.65. Found: C, 37.06; H, 2.77.

8-Methoxyimidazo[1,2-*a*]pyrazine (8). To a solution of the above compound (7) (0.265 g) in methanol (40 mL) palladized carbon (60 mg of 10%) was added and the mixture was shaken in an atmosphere of hydrogen for 15 h. Upon filtration the filtrate was evaporated to dryness and the hydrobromide salt was crystallized from methanol–ether: mp 244–245 °C (yield 92%); MS *m/e* 149 (M − HBr); ^1H NMR (Me_2SO-d_6) δ 7.89 (d, H_6), 8.25 (d, H_2), 8.53 (d, H_3), 8.60 (d, H_5), 4.17 (s, OMe), $J_{5,6}$ = 5.0, $J_{2,3}$ = 2 Hz.

Anal. Calcd for $C_7H_8N_3OBr$: C, 36.54; H, 3.51. Found: C, 36.45; H, 3.41.

5-Chloroimidazo[1,2-*a*]pyrazine. A mixture of bromoacetaldehyde diethyl acetal (0.4 g), hydrobromic acid (0.12 mL of 48%), and water (0.12 mL) was heated under reflux for 1 h. Upon cooling the reaction mixture was diluted with ethanol (5 mL), neutralized with sodium bicarbonate, and filtered. The filtrate was treated with 2-amino-6-chloropyrazine (0.3 g) and the mixture was stirred at 40 °C for 30 h. The solvent was evaporated in vacuo and the residue was dissolved in water (1 mL). The solution was neutralized with sodium bicarbonate, and the aqueous layer was separated and extracted with chloroform. Upon evaporation of the solvent the residue was crystallized from cyclohexane (yield 14 mg, 4%) and had mp 88–95 °C; ^1H NMR ($CDCl_3$) δ 7.99 (s, H_2 and H_3), 8.06 (s, H_6), 9.20 (s, H_8).

Anal. Calcd for $C_6H_4ClN_3$: C, 46.93; H, 2.63. Found: C, 47.02; H, 2.90.

Methylation of Imidazo[1,2-*a*]pyrazine. A solution of imidazo[1,2-*a*]pyrazine (0.24 g) in methanol (4 mL) was treated with methyl iodide (0.48 g), and the reaction mixture was left in a sealed tube in the dark at room temperature for 5 days. The separated crystals (0.181 g, 35%) were filtered and dissolved in hot methanol, and upon cooling the separated crystals of the 7-methyl derivative **10** were filtered: mp 270–280 °C dec (55 mg, yield 11%); ^1H NMR δ 4.36 (s, Me), 8.25 (dd, H_5), 8.43 (d, H_2), 8.77 (d, H_3), 9.25 (dd, H_6), 9.98 (dd, H_8), $J_{5,8}$ = 1.5, $J_{2,3}$ = 1.0, $J_{6,8}$ = 1.0, $J_{5,6}$ = 5.6 Hz.

Anal. Calcd for $C_7H_8IN_3$: C, 32.20; H, 3.09. Found: C, 32.61; H, 3.28.

The filtrate, when evaporated to dryness, afforded the 1-methyl isomer **9:** mp 199–200 °C (from methanol) (0.107 g, 21%); ^1H NMR (Me_2SO-d_6) δ 8.50 (d, H_2), 8.55 (d, H_3), 8.50 (dd, H_5), 9.05 (d, H_6), 9.55 (d, H_8), 4.28 (s, Me), $J_{2,3}$ = 1.0, $J_{5,6}$ = 5.6, $J_{5,8}$ = 1.5 Hz. (In the literature, however, 1-methylimidazo[1,2-*a*]pyrazinium bromide, mp >330 °C, has been reported.[11])

2-Hydrazino-6-chloropyrazine (17, R = R_1 = H). A solution of 2,6-dichloropyrazine (10 g) in ethanol (30 mL) was treated with hydrazine hydrate (15 mL of 98%) and the reaction mixture was heated under reflux for 3 h. The solvent was evaporated in vacuo and the residue was crystallized from water and toluene: mp 136–139 °C (yield 6.7 g, 69%); MS *m/e* 144 (M); ^1H NMR (Me_2SO-d_6) δ 8.10 (s, H_3 or H_5), 7.74 (s, H_3 or H_5), 8.45 (br s, NH), 4.40 (br s, NH_2).

Anal. Calcd for $C_4H_5ClN_4$: C, 33.23; H, 3.48; N, 38.76. Found: C, 33.34; H, 3.50; N, 39.18.

The compound formed the benzylidene derivative in the usual manner: mp 223 °C; MS *m/e* 232 (M).

Anal. Calcd for $C_{11}H_9ClN_4$: C, 56.78; H, 3.90; N, 24.08. Found: C, 56.97; H, 3.75; N, 23.94.

If 2-hydrazino-6-chloropyrazine (1 g), *N,N*-dimethylformamide dimethyl acetal (1.5 mL), and absolute ethanol (7 mL) were heated under reflux for 30 min, upon cooling the corresponding *N,N*-dimethylaminomethylenehydrazino derivative (**17**, R, R_1 = $CHNMe_2$) was separated (0.5 g, 36%): mp 168–170 °C (from ethanol); MS *m/e* 199 (M).

Anal. Calcd for $C_7H_{10}ClN_5$: C, 42.11; H, 5.05; N, 35.08. Found: C, 42.17; H, 5.25; N, 35.10.

In a similar manner 2-*N,N*-dimethylaminomethylenehydrazinopyrazine was prepared, mp 141 °C (from cyclohexane), in 67% yield: MS *m/e* 165 (M).

Anal. Calcd for $C_7H_{11}N_5$: C, 50.89; H, 6.71; N, 42.40. Found: C, 50.90; H, 6.90; N, 42.72.

5-Bromo-*s*-triazolo[4,3-*a*]pyrazine (12). A solution of **11** (3.0 g) in glacial acetic acid (90 mL) was treated with bromine (4.0 g in 25 mL of glacial acetic acid) at room temperature. The separated product was filtered and crystallized from ethanol: mp 214–217 °C (yield 1.70 g, 34%); MS *m/e* 198 (M); ^1H NMR (Me_2SO-d_6) δ 8.24 (s, H_6), 9.67 (s, H_3 or H_8), 9.49 (s, H_3 or H_8).

Anal. Calcd for $C_5H_3BrN_4$: C, 30.17; H, 1.52; N, 28.15. Found: C, 30.40; H, 2.02; N, 28.02.

5-Chloro-*s*-triazolo[4,3-*a*]pyrazine (18, R = H, X = Cl). A mixture of 2-hydrazino-6-chloropyrazine (1 g) and diethoxymethyl acetate (3 mL) was heated under reflux for 10 h. The solvent was evaporated in vacuo to dryness and the residue was sublimed. The compound had mp 167–172 °C (yield 0.125 g, 12%); MS *m/e* 154 (M); ^1H NMR ($CDCl_3$) δ 7.94 (s, H_6), 9.06 (s, H_3 or H_8), 9.27 (s, H_3 or H_8).

Anal. Calcd for $C_5H_3ClN_4$: C, 38.85; H, 1.96. Found: C, 38.89; H, 2.30.

3-Phenyl-5-chloro-*s*-triazolo[4,3-*a*]pyrazine (18, R = Ph, X = Cl). A suspension of 2-benzylidenehydrazino-6-chloropyrazine (1.1 g) in benzene (15 mL) was treated with lead tetraacetate (2.5 g, washed with benzene before use) with stirring. The reaction mixture was left at room temperature for 6 h, the solid was filtered, and the filtrate was evaporated in vacuo to dryness. The residue was crystallized from ethanol: mp 176 °C (yield 0.7 g, 64%); MS *m/e* 230 (M); ^1H NMR (Me_2SO-d_6) δ 7.65 (m, Ph), 8.10 (s, H_6), 9.52 (s, H_8).

Anal. Calcd for $C_{11}H_7ClN_4$: C, 57.28; H, 3.06; N, 24.29. Found: C, 57.50; H, 3.21; N, 24.31.

5-Phenylthio-*s*-triazolo[4,3-*a*]pyrazine (20, R = H, R_1 = SPh). To a solution of sodium thiophenolate in ethanol, prepared from 12 mg of sodium, 55 mg of thiophenol, and 5 mL of absolute ethanol, the 5-bromo compound **12** (0.1 g) was added. The reaction mixture was heated under reflux for 1 h and upon cooling poured on ice. The product which separated (14 mg) was filtered and the filtrate was evaporated in vacuo to dryness. Some water was added and the residue was filtered (65 mg). Both products were found to be identical, and they were combined and crystallized from water: mp 95–96 °C (yield 26 mg, 23%); MS *m/e* 228 (M); ^1H NMR (Me_2SO-d_6) δ 8.26 (s, H_6), 10.57, 10.47 (s, H_3 and H_8), 7.5 (m, Ph).

Anal. Calcd for $C_{11}H_8N_4S$: C, 57.89; H, 3.53; N, 24.55. Found: C, 58.08; H, 3.80; N, 24.50.

3-Phenyl-5-phenylthio-*s*-triazolo[4,3-*a*]pyrazine (20, R = Ph, R_1 = SPh) was prepared in a similar manner in 52% yield: mp 194–198 °C; MS *m/e* 304 (M); ^1H NMR (Me_2SO-d_6) δ 7.9 (s, H_6), 9.25 (s, H_8), 7.43 (m, Ph), 6.8, 7.23 (m, 3-Ph).

Anal. Calcd for $C_{17}H_{12}N_4S$: C, 67.09; H, 3.98; N, 18.41. Found: C, 66.79; H, 4.28; N, 18.69.

Reaction between 5-Bromo-*s*-triazolo[4,3-*a*]pyrazine and Sodium Methylate. A methanolic solution of sodium methylate (prepared from 8 mL of ethanol and 25 mg of sodium) was treated with **12** (0.2 g) and the reaction mixture was left at room temperature overnight. The solvent was evaporated in vacuo and the residue was extracted with chloroform. Upon evaporation of the solvent the product was crystallized from chloroform and petroleum ether. There were obtained 40 mg of a mixture of 8-methoxy- (**15**) and 5-methoxy-*s*-triazolo[4,3-*a*]pyrazine (**16**): mp 131–134 °C; MS *m/e* 150 (M); ^1H NMR (Me_2SO-d_6) 8-methoxy isomer δ 4.15 (s, 8-OMe), 7.49 (d, H_6), 9.17 (s, H_3), 8.17 (d, H_5), $J_{5,6}$ = 5 Hz; 5-methoxy isomer δ 4.25 (s, 5-OMe), 7.66 (s, H_6), 9.55 (s, H_3), 9.49 (s, H_8).

Anal. Calcd for $C_6H_6N_4O$: C, 48.00; H, 4.03. Found: C, 47.69; H, 3.70.

3-Phenyl-8-methoxy-*s*-triazolo[4,3-*a*]pyrazine (19, R = Ph, R_1 = OMe). Compound **18** (R = Ph, X = Cl) (231 mg) was dissolved in methanol (14 mL) and a solution of sodium methylate (23 mg of sodium in 3 mL of methanol) was added. The progression of the reaction was followed by TLC and when reaction was complete, the solvent was evaporated and the residue crystallized from aqueous methanol: mp 190–193 °C (yield 89 mg, 39%). However, if the reaction was conducted under reflux for 30 min the product was obtained in 17% yield: MS *m/e* 226 (M); ^1H NMR (Me_2SO-d_6) δ 4.25 (s, OMe), 7.45 (d, H_5), 7.90 (d, H_6), 8.0-7.5 (m, Ph), $J_{5,6}$ = 4.5 Hz.

Anal. Calcd for $C_{12}H_{10}N_4O$: C, 63.70; H, 4.46; N, 24.77. Found: C, 63.42; H, 4.90; N, 24.66.

3-Phenyl-8-ethoxy-*s*-triazolo[4,3-*a*]pyrazine (19, R = Ph, R_1 = OEt). (A) The compound was prepared in an analogous manner as the 8-methoxy compound from **18** (R = Ph, X = Cl), but under reflux: mp 172–173.5 °C (yield 76 mg, 31%); MS *m/e* 240 (M); ^1H NMR (Me_2SO-d_6) δ 7.37 (d, H_5), 7.82 (d, H_6), 7.95–7.46 (m, Ph), 1.55 (t, CH_2CH_3), 4.70 (CH_2CH_3), $J_{5,6}$ = 4.5, J_{Et} = 7.2 Hz.

Anal. Calcd for $C_{13}H_{12}N_4O$: C, 64.98; H, 5.03; N, 23.32. Found: C, 64.71; H, 5.29; N, 23.15.

(B) A solution of the 8-methoxy compound **19** (R = Ph, R_1 = OMe) (10 mg) in 50% aqueous ethanol was treated with ethanolic sodium ethylate (prepared from 2.9 mg of sodium in 1 mL of ethanol). The reaction mixture was heated under reflux for 30 min, the solvent was evaporated in vacuo to dryness, and the residue was treated with some water. The product was filtered (yield 1.5 mg, 14%) and had mp 171 °C. The compound has been identified by its IR spectrum and mixture melting point as the above 8-methoxy compound, prepared as described under A.

3-Phenyl-8-amino-*s*-triazolo[4,3-*a*]pyrazine (19, R = Ph, R_1 = NH_2). (A) Compound **18** (R = Ph, X = Cl) (231 mg) was added to

a saturated methanolic solution of ammonia (30 mL) and the reaction mixture was left to stand at room temperature for 20 h. The separated product was filtered off, the filtrate was evaporated to dryness and treated with water (5 mL), and the residue was filtered. The combined products were crystallized from ethanol: mp 247–248.5 °C (yield 53.5 mg, 30%); MS *m/e* 211 (M); ^{1}H NMR (Me_2SO-d_6) δ 7.26 (d, H_5), 7.74 (d, H_6), 8.0–7.4 (m, Ph), 3.33 (s, NH_2), $J_{5,6}$ = 4.5 Hz.

Anal. Calcd for $C_{11}H_9N_5$: C, 62.55; H, 4.30; N, 33.16. Found: C, 62.77; H, 4.55; N, 33.36.

(B) Compound **19** (R = Ph, R_1 = OMe) (50 mg) was added to a saturated methanolic solution of ammonia (10 mL) and the reaction mixture was heated in an autoclave at 100 °C for 5 h. Upon evaporation of the solvent, the residue was crystallized from ethanol. The compound was found to be identical in all respects with product obtained as described under A.

Acknowledgment. We thank the Boris Kidrič Fund for partial support of the research.

Registry No.—**1,** 274-79-3; **2,** 63744-21-8; **3,** 57948-41-1; **4,** 24241-18-7; **5,** 63744-22-9; **5** HBr, 63744-23-0; **6,** 63744-24-1; **7,** 63744-25-2; **8** HBr, 63744-26-3; **9,** 63744-27-4; **10,** 63744-28-5; **11,** 274-82-8; **12,** 63744-29-6; **15,** 63744-30-9; **16,** 63744-31-0; **17** (R = R_1 = H), 63286-29-3; **17** (RR_1 = PhCH=), 63744-32-1; **17** (RR_1 = =CHNMe$_2$), 63744-33-2; **18** (R = H, X = Cl), 63744-34-3; **18** (R = Ph, X = Cl), 63744-35-4; **19** (R = Ph, R_1 = OMe), 63744-36-5; **19** (R = Ph, R_1 = OEt), 63744-37-6; **19** (R = Ph, R_1 = NH_2), 63744-38-7; **20** (R = H, R_1 = SPh), 63744-39-8; **20** (R = Ph, R_1 = SPh), 63744-40-1; 5-chloroimidazo[1,2-*a*]pyrazine, 63744-41-2; 2-amino-6-chloropyrazine, 33332-28-4; 2,6-dichloropyrazine, 4774-14-5; 2-*N*,*N*-dimethylaminomethylenehydrazinopyrazine, 63744-42-3; sodium thiophenolate, 930-69-8; ammonia, 7664-41-7; *N*,*N*-dimethylformamide dimethyl acetal, 4637-24-5; hydrazinopyrazine, 54608-52-5.

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Deuterium Isotope Effects in the Thermochemical Decomposition of Liquid 2,4,6-Trinitrotoluene: Application to Mechanistic Studies Using Isothermal Differential Scanning Calorimetry Analysis

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Received April 22, 1977

The thermochemical decomposition of liquid 2,4,6-trinitrotoluene (TNT) produces a primary kinetic deuterium isotope effect when its methyl moiety is deuterium labeled. The novel integration of the deuterium isotope effect with isothermal differential scanning calorimetry analysis provides the first directly measured mechanistic evidence that carbon–hydrogen bond rupture in the TNT methyl group constitutes the rate-determining step of the thermochemical decomposition reaction. This thermochemical reaction possesses an induction period during which a single species forms from TNT and catalyzes a sustained exothermic decomposition. An expression was derived that correlated deuterium/hydrogen induction time ratios with inaccessible hydrogen/deuterium rate constant ratios during this induction period. Direct induction time measurement allowed deuterium isotope effect evaluation before interfering side reactions diluted the magnitude of the isotope effect during the latter stages of exothermic decomposition. Hydrogen donor effects suggest that the rate-determining carbon–hydrogen bond rupture proceeds homolytically. A large negative entropy of activation reveals a high degree of orderliness during the decomposition.

The kinetic deuterium isotope effect has proved to be a powerful tool in mechanistic elucidations of gaseous and solvolyzed chemical reactions. Recently, isothermal differential scanning calorimetry (isothermal DSC) proved its value as a rapid and elegant technique for determining kinetic parameters (e.g., reaction rate, rate constant, reaction order, activation energy) in thermochemical decomposition reactions of liquified nitrated organic compounds.[2-4] Because liquid organic compounds constitute a homogeneous phase, and because an isothermal DSC curve is directly proportional to a reaction rate that is easily converted into a rate constant, we felt the deuterium isotope effect concept could be integrated