Acyclic Trialkyldiazenium Cation Chemistry. Thermolysis and Solvolysis of 1,2-Di-*tert*-butyl-1-ethyldiazenium Perchlorate

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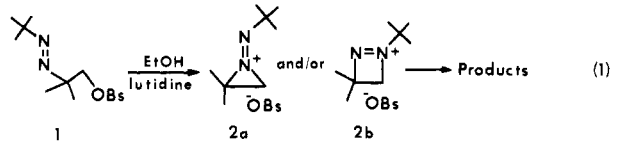
Abstract: The thermolysis, ethanolysis, and ethanolysis with 2,6-lutidine reactions of 1,2-di-*tert*-butyl-1-ethyldiazenium perchlorate (**3**) are reported. Clean first-order kinetics were observed for these reactions. The reactivity of **3** was found to be nearly the same for the various reaction conditions. Thermolysis of **3** yielded acetaldehyde *tert*-butylhydrazonium perchlorate (**4**) and isobutylene (**5**) as products. Ethanolysis gave **4**, **5**, ethyl *tert*-butyl ether (**6**), acetaldehyde diethyl acetal (**7**), and mono-*tert*-butylhydrazinium perchlorate (**8**). For ethanolysis with lutidine, the products were **5**, **6**, **7**, *trans*-1,1-dimethylazoethane (**10**), and 1,2-di-*tert*-butylhydrazinium perchlorate (**11**). The kinetic and product results for both thermolysis and ethanolysis are rationalized by a mechanistic sequence involving as key first steps a prototropic rearrangement of diazenium cation **3** to an iminium cation **14**, which subsequently ionizes to *tert*-butyl cation (**13**) and acetaldehyde *tert*-butylhydrazone (**12**). For ethanolysis with lutidine, two separate competing mechanistic processes are indicated. One pathway involves direct ionization of **3** to **10** and **13**. The second pathway involves the rearrangement of **3** to **14** followed by direct reaction of **14** with ethanol.

The chemistry of azoalkanes has been intensively investigated during the last 15 years.[1-18] The studies show that a remarkable variety of mechanistic pathways are available for reaction of the —N=N— functional group. Cases of reaction by radical,[1-7] zwitterion,[8,9] carbene,[10-12] and cationic intermediates[13,14] have been reported. Examples of concerted reaction processes without formation of reactive intermediates[15-17] and reverse Diels–Alder processes[18] also have appeared. In contrast, only recently has the chemistry of the —N=N⁺< group in alkyldiazenium cations become the target of mechanistic investigation.[19-21] The handful of available reports are directed mainly at probing the oxidation–reduction interrelationships of bicyclic diazenium cations, iminium ions, and related N=N systems.

We became aware of the overall scarcity of information about diazenium cation chemistry during our investigation of the new mode of neighboring-group participation by the azo group as shown in eq 1.[13] A need of additional basic information to guide



1 2a 2b (1)

this research and our expectation that a general study of the chemical properties of diazenium cations might afford some interesting new facts concerning structure, bonding, and reactivity prompted us to initiate exploratory work in the area.

In order to establish a basis for future comparisons of chemical behavior, we have used **3** as a model system for our preliminary studies. Reasons for this choice include easy accessibility of **3**, substitution about the —N=N⁺< moiety, which limits the potential reaction processes, and close structural similarity of **3** and **2b**. In this paper we report the results of the investigations of the thermolysis and solvolysis reactions of **3** and discuss the mechanistic implications.

Table I. Rate Data[a] for the Reactions of Trialkyldiazenium Salt **3**

solvent	[**3**], M	[2,6-lutidine], M	10^4k, s^{-1}	temp, °C
CD_2Cl_2	0.15		0.32	55.0
	0.15		1.2	65.0
	0.15		3.8	75.0
$CDCl_3$	0.15		4.0	75.0
$CD_3CD_2OD/CDCl_3$[b]	0.07		0.28	50.0
	0.07		0.85	60.0
	0.07		5.2	75.0
	0.20		5.1	75.0
$CD_3CD_2OD/CDCl_3$[b]	0.10	0.45	5.8	75.0

[a] The rates were determined by the NMR method. Reaction samples were contained under an N_2 atmosphere in sealed NMR tubes. The progress of the reaction was followed by periodically monitoring NMR integration changes of the δ 1.80 signal of **3** against Me_4Si internal standard. [b] $CD_3CD_2OD/CDCl_3$ (ca. 2:1 v/v).

Results

Trialkyldiazenium salt **3** was synthesized in a straightforward fashion from 1,2-di-*tert*-butylhydrazine as outlined in eq 2.

(1) During this time well over 500 references dealing with the chemistry of azo compounds have appeared. Citations 2–18 are given for direct access to the mechanistic area listed. For an excellent recent summary overview of the decomposition of azoalkanes, see: Engel, P. S. *Chem. Rev.* **1980**, *80*, 99–150.
(2) Crawford, R. J.; Tahagi, K. *J. Am. Chem. Soc.* **1972**, *94*, 7406.
(3) Porter, N. A.; Dubay, G. R.; Green, J. G. *J. Am. Chem. Soc.* **1978**, *100*, 920.
(4) Garner, A. W.; Timberlake, J. W.; Engel, P. S.; Melaugh, R. A. *J. Am. Chem. Soc.* **1975**, *97*, 7377.
(5) Cichra, D. A.; Duncan, C. D.; Berson, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 6527.
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(7) Allred, E. L.; Smith, R. L. *J. Am. Chem. Soc.* **1969**, *91*, 6766.
(8) McGreer, D. E.; Masters, I. M. E.; Liu, M. T. H. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1791.
(9) Begley, M. J.; Dean, F. M.; Hoghton, L. E.; Johnson, R. S.; Park, B. K. *J. Chem. Soc., Chem. Commun.* **1978**, 461.
(10) Franck-Neumann, M.; Lohmann, J. J. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 323.
(11) Schneider, M.; Csacsko, B. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 816.
(12) White, D. H.; Condit, P. B.; Bergman, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 1348.
(13) Allred, E. L.; Oberlander, J. E.; Ranken, P. F. *J. Am. Chem. Soc.* **1978**, *100*, 4910.
(14) Allred, E. L.; Flynn, C. R. *J. Am. Chem. Soc.* **1975**, *97*, 614; **1972**, *94*, 5891; **1970**, *92*, 1064.
(15) Allred, E. L.; Voorhees, K. J. *J. Am. Chem. Soc.* **1973**, *95*, 620. Allred, E. L.; Johnson, A. L. *Ibid.* **1971**, *93*, 1300. Allred, E. L.; Hinshaw, J. C. *J. Chem. Soc., Chem. Commun.* **1969**, 1021.
(16) Snyder, J. P.; Olsen, H. *J. Am. Chem. Soc.* **1978**, *100*, 2566.
(17) For a nice summary, see: Berson, Olin, S. S.; Petrilla, E. W.; Bickart, P. *Tetrahedron* **1974**, *30*, 1639.
(18) Hinshaw, J. C.; Allred, E. L. *Chem. Commun.* **1969**, *72*. Lay, W. P.; Mackenzie, K.; Telford, J. R. *J. Chem. Soc. C* **1971**, 3199. Adam, W.; DeLucci, O. *J. Am. Chem. Soc.* **1980**, *102*, 2109.
(19) (a) Nelsen, S. F.; Parmelee, W. P.; Göbl, M.; Hiller, K.-O.; Veltwisch, D.; Asmus, K.-D. *J. Am. Chem. Soc.* **1980**, *102*, 5606. (b) Nelsen, S. F.; Laudis, R. T., II, *Ibid.* **1974**, *96*, 1788.
(20) Snyder, J. P.; Heyman, M.; Gundestrup, M. *J. Org. Chem.* **1978**, *43*, 2224.
(21) Snyder, J. P.; Heyman, M. L.; Gundestrup, M. *J. Chem. Soc., Perkin Trans. 1* 1977, 1551.

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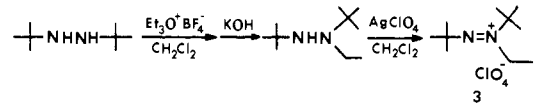
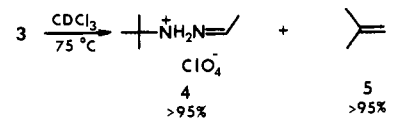


(2)

Elemental analyses were in agreement with the molecular formula of **3**. The 90-MHz ^1H NMR spectrum of the salt showed a single set of signals as an overlaid composite of a methyl triplet and two *tert*-butyl singlets (21 H) in the δ 1.65–1.90 region, and a methylene group quartet (2 H) at δ 4.95. The alkyl groups of **3** will be oriented as the *Z* or *E* configuration. Since only one other acyclic trialkyldiazenium salt has been reported,[19b] there is not sufficient information available at this time to make the configuration assignment. For this reason we show the structural formula in a nonspecific way.

Thermolysis in CD_2Cl_2 and $CDCl_3$. Thermolysis studies with **3** were conducted in CD_2Cl_2 and in $CDCl_3$. Kinetic measurements were made by ^1H NMR spectroscopy. Sealed NMR tubes containing ca. 0.15 M solutions of **3** under an N_2 atmosphere were held at constant temperatures, and the progress of thermolysis was followed over a reaction range covering 10–90% by periodically monitoring NMR integration changes of the δ 1.80 signals of **3** against Me_4Si internal standard. All rate constants were nicely first order. Table I summarizes the results.

Product formation in $CDCl_3$ at 75 °C was followed during the kinetic experiments by observing the appearance of new NMR signals. Analysis of the results showed formation of only two major products, which were discernible in a 1:1 ratio from the onset to the finish of thermolysis. The products indentified as acetaldehyde *tert*-butylhydrazonium cation (**4**) and isobutylene (**5**) by NMR spectral comparisons with authentic specimens are shown in eq 3. Yields of **4** and **5** are high (>95%) based on NMR integration



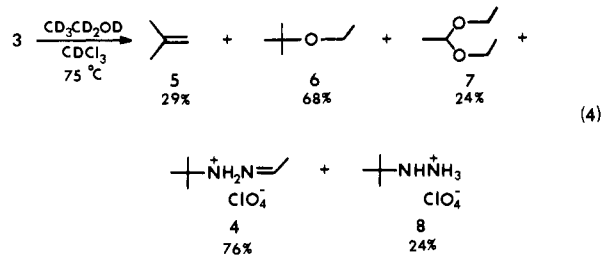
(3)

values. A small amount of unidentified product with NMR signals partially overlapped by *tert*-butyl and methyl resonances of **4** developed throughout thermolysis. These latter signals integrate to <5% of the total product.

Considerations of mechanistic pathways that could lead from **3** to **4** and **5** suggested that 1,1-dimethylazoethane (**10**) is a possible intermediate in the reaction. To test this possibility, a mixture of **3** and **10** in a 2.5:1 mol ratio in $CDCl_3$ was thermolyzed at 75 °C. The rates of disappearance of both **3** and **10** were determined by the above NMR method. A reactivity ratio of ca. 0.9:1 for **3**:**10** was observed. Treatment of this result on the basis of a series first-order reaction (**3** → **10** → **4**) indicates that if **10** is an important thermolysis intermediate from **3**, **10** will build up to a maximum concentration of ca. 0.35 relative to the initial value of **3** during the first 40 min of reaction and then slowly decrease. We did not detect any formation or accumulation of **10** during the thermolysis kinetic studies listed in Table I. As a second check on this reactivity result, the rate of disappearance of **10** in $CDCl_3$ in the presence of the *p*-toluenesulfonate salt of **4** at 75 °C was measured. This reactivity comparison was ca. 0.8:1 for **3**:**10**.

Ethanolysis in $CDCl_3$. Ethanolysis of **3** (ca. 0.07 M) was investigated in a mixture of $CD_3CD_2OD/CDCl_3$ (ca. 2:1 v/v). Kinetic measurements were carried out by ^1H NMR spectroscopy as described for thermolysis. The rate constants, which were strictly first order, are listed in Table I.

Inspection of the ethanolysis kinetics NMR spectra showed formation of a variety of products. For identification and yield determinations, it was necessary to resort to the use of a combination of analytical methods. At time infinity the NMR spectrum showed the vinyl multiplet of isobutylene (**5**) and the *tert*-butyl singlet of ethyl *tert*-butyl ether (**6**) free of interference from other signals. Integration of these signals gave 29% and 68% yields for **5** and **6**, respectively. The volatile part of the reaction solution was transferred under vacuum to a dry ice–acetone-cooled trap. Gas chromatographic (GC) analysis of this material showed the presence of **6** and acetaldehyde diethyl acetal (**7**) on the basis of retention-time comparisons with authentic samples. The GC and NMR yields were in agreement for **6** and the GC yield of **7** was 24%. NMR comparisons of authentic specimens with samples of **6** and **7** isolated by preparative GC confirmed the structure assignments. The NMR spectrum ($CDCl_3$) of the salt residue remaining from the vacuum treatment showed the presence of **4** (76%) and mono-*tert*-butylhydrazinium cation (**8**) (24%). These structure assignments were verified by spectral comparisons with authentic compounds. Mechanistic considerations suggested that diethyl ether (**9**) might be an ethanolysis product. However, GC control experiments indicated that **9** is not formed in the reaction. The ethanolysis products and distribution are summarized in eq 4.



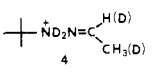
(4)

The possibility that the ethanolysis of **3** might involve 1,1-dimethylazoethane (**10**) as a reaction intermediate was investigated by determining the relative reactivity of **3** and **10** under the ethanolysis conditions of eq 4. Ethanolysis of a mixture of **3** and **10** in a 3.5:1 mol ratio gave a relative rate ratio of ca. 1:0.4. Analysis of the ratio as a series first-order reaction shows that if **10** is an ethanolysis intermediate, it will build up to a maximum concentration of ca. 0.54 relative to the initial value of **3** after 50-min reaction and then slowly diminish. Examination of the NMR spectra obtained for the ethanolysis kinetic studies listed in Table I did not show any detectable formation or accumulation of **10**.

The NMR spectra obtained as a result of the kinetic measurements for the ethanolysis of **3** are of interest for other reasons. It was observed from integration results that both methyl and methine proton signals of product **4**[22] contained fewer H atoms than should be present for the amount of **4** formed from **3**. This discrepancy increased as the ethanolysis of **3** proceeded. In addition, the doublet and quartet peaks gradually became broadened multiplets with increase in reaction time. These observations are suggestive of H–D exchange at both sites of **4**. To test this, ethanolysis of the perchlorate salt of **4** in CD_3CD_2OD at 75 °C was examined. The ^1H NMR integration ratios of the methyl:*tert*-butyl and the methine:*tert*-butyl signals each decreased with increasing time.[22] Both methyl and methine peaks slowly changed to broadened multiplets during the same time period. It also was observed that formation of acetal **7** and hydrazinium cation **8** from **4** accompanied the H–D exchanges. All reaction processes appeared to approach equilibrium. As a check on this last point, a mixture of **7** and **8** (1:1 mol ratio) in CD_3CD_2OD at 75 °C was shown to form **4** (NMR) and approach equilibrium from the opposite side.

Observation of H–D exchange during ethanolysis of **4** suggested the possibility that the ethyl group diazenium cation **3** might also exhibit a similar exchange reaction via tautomerism and reversal from an intermediate iminium ion **14** (see Scheme I). Inspection of ^1H NMR spectra from the ethanolysis kinetic study of **3** showed that the integration ratio of the methylene:*tert*-butyl signals had the correct value, which remained constant throughout the course

(22) The methyl and methine sites of D incorporation into **4** are shown in the following structure:

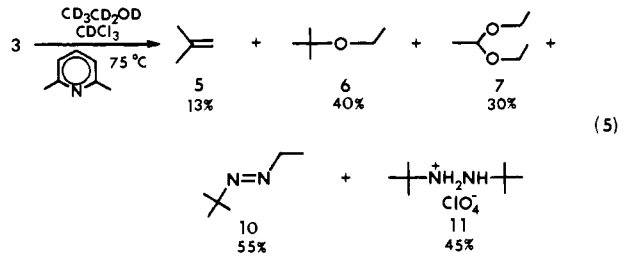


Under the reaction conditions, D also is incorporated on N. For reasons of simplicity, D inclusion is not shown in eq 4 or Scheme II.

of ethanolysis.[23] No H–D exchange was detectable during these time intervals.

Ethanolysis with Added Lutidine Base in $CDCl_3$. Buffered ethanolysis of **3** (ca. 0.1 M) was investigated in a mixture of $CD_3CD_2OD/CDCl_3$ (ca. 2:1 v/v) that contained 2,6-lutidine (ca. 0.45 M). Kinetic measurements were carried out as described in the previous sections. The first-order rate constants are collected in Table I.

Examination of the NMR spectra from the ethanolysis/lutidine kinetic study showed the formation of a varied assortment of reaction products. It was necessary for identification and yield determinations to use a combination of analytical methods. At the completion of reaction, the NMR vinyl signals of isobutylene (**5**), the methylene quartet of *trans*-1,1-dimethylazoethane (**10**), and the *tert*-butyl peak of 1,2-di-*tert*-butylhydrazinium cation (**11**) were free of interference from other signals. Integration of these peaks gave yields of 13%, 55%, and 45%, respectively. The volatile part of the reaction solution was transferred under vacuum to a cold trap. Treatment of a sample of this material with aqueous $HClO_4$ converted **10** to hydrazonium ion **4** and moved the NMR signal of the *tert*-butyl group of **10** downfield and away from the corresponding signal of ethyl *tert*-butyl ether (**6**). Integration of each of these *tert*-butyl signals showed a yield of **10** in accord with the above value and a yield of 40% for **6**. GC analysis of the volatile part showed the presence of **6**, **7**, and **10**. The GC and NMR yields of **6** and **10** were in agreement, and the GC yield of acetaldehyde diethyl acetal (**7**) was 30%. Structure assignments are based on NMR spectra and GC retention time comparisons with authentic samples of the products or their derivatives. Products **6**, **7**, and *trans*-**10** isolated by preparative GC showed NMR signals in agreement with those of authentic specimens. Evidence for the structure of **11** was obtained by treating the nonvolatile salt residue with aqueous KOH. This caused the *tert*-butyl signal of **11** to move upfield to the same chemical shift as that of the *tert*-butyl peak of authentic 1,2-di-*tert*-butylhydrazine. After the sample of freed hydrazine had been allowed to stand in air (O_2), the *tert*-butyl signal moved downfield to the exact chemical shift of authentic 2,2′-azobis(isobutane). GC analysis of this oxidized sample showed a retention time identical with that of known 2,2′-azobis(isobutane). The ethanolysis/lutidine products and distribution are summarized in eq 5.

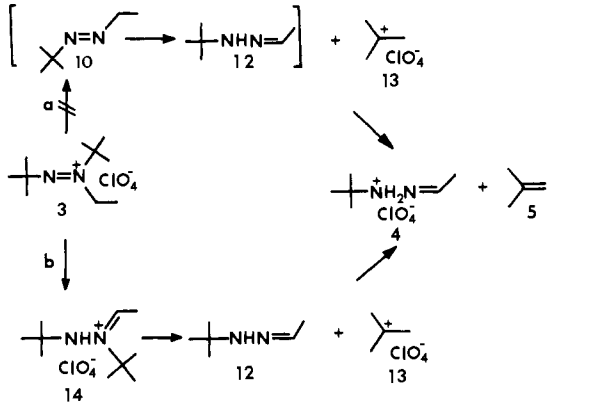


(5)

The question of **7** and **11** undergoing a reversible reaction was examined by observing the behavior of **7** and the *p*-toluenesulfonate salt of **11** (1:1 mol ratio) in $CD_3CD_2OD/CDCl_3$ with lutidine at 75 °C. ^1H NMR integration ratios of the various signals in the mixture had correct initial values, and these remained unchanged for 4 h at 75 °C. No reaction was detectable during this time period. This finding also is indicative that **7** does not undergo H–D exchange.

Mechanistic hypotheses based on the kinetic and product results cited in this and the preceding sections strongly implicate the iminium cation **14** as a key intermediate in the thermal and solvolytic reactions of **3**. In this regard, the NMR spectra collected as a part of the kinetic studies did not provide any spectral evidence for **14**.

Scheme I



Discussion

Some general comments about the nature of the mechanism(s) of the reactions of acyclic diazenium cation **3** are in order. Conversion of the rate data in Table I to a reactivity sequence ratio of 1:1:1.4:1.5 for the solvent ionizing power order $CDCl_3 \sim CD_2Cl_2 < EtOH/CDCl_3 \sim EtOH/CDCl_3$/lutidine[25] shows only a very small response to the change. This result is open to more than one kind of mechanistic description. One possibility is a reaction process that involves radical or radical-like intermediates. In the one literature report[21] of reaction of bicyclic trialkyldiazenium ions via a solvolysis step, the question of the intermediacy of radicals has been examined in detail. A variety of observations and control experiments excluded radical formation as a part of the major reaction pathway. All of these results pointed to a mechanism involving cations.[21] For the case of salt **3**, the products shown in eq 3, 4, and 5 are not the ones expected from radical pathways. Instead, these observations clearly indicate mechanistic processes that proceed through reactions of cation intermediates. The relative insensitivity of the above reactivity ratio to change in solvent polarity is also consistent with this. Positively charged substrates that react by heterolytic processes are expected to be affected only to a small degree.[26]

Thermolysis. Considerations of the nature of the products formed from the thermolysis of **3** (eq 3) suggest two different plausible ionization processes that could rationalize the observations. These possibilities are formulated in Scheme I. A comparison of the mechanistic features of pathways a and b shows that the intrinsic difference between them occurs in the initial steps. For pathway a, ionization proceeds directly to azo compound **10** and *tert*-butyl cation (**13**). Since **10** is of low basicity,[21,24a] an elimination reaction with **13** to give **5** is unlikely. Well-known facile tautomerization of **10** to hydrazone **12**[27] provides the base that could effect elimination of carbonium ion 13 and account for the observed products. In the case of the pathway b, tautomerism of **3** to the iminium ion **14** is the first step. Ionization of **14** affords **12** and **13**, which react as in path a to give products.

The thermolysis reactivity comparison of **3** and **10** provides a criterion for choosing between pathways a and b. The fact that both **3** and **10** react at comparable rates under the conditions of eq 3 and the observation that **10** is not detectable during thermolysis of **3** rule out pathway a as the major process for forming products. This leaves pathway b as the best working hypothesis for the mechanism. Failute to detect, isolate, or otherwise obtain iminium cation **14** made it inaccessible for study and suggests, at this point, that it is a labile and transient intermediate.[24] Evidence of an indirect kind linking **14** to the reactions of **3** is

(23) Unfortunately, the methyl signal of **3** is obscured by other peaks in the spectrum, and it could not be used for this analysis.

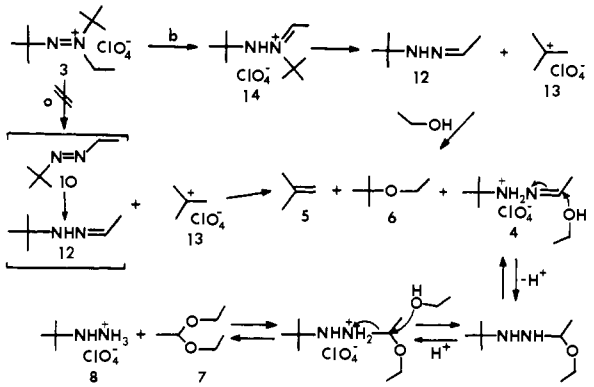
(24) This result is not surprising in view of the paucity of acyclic hydrazonium structures like **12** reported in the literature. See: (a) Hegarty, A. F. In "The Chemistry of the Hydrazo, Azo, and Azoxy Groups"; Patai, S., Ed.; Wiley-Interscience: New York, 1975; Part 2, p 665. (b) Elguero, J.; Marzin, C. In "Iminium Salts in Organic Chemistry", Böhme, H., Viehe, H. G., Eds.; Wiley-Interscience: New York, 1976; Part 1, pp 538–539, 546, 548, 552.

(25) Based on relative rates of ionization data from: Smith, S. G.; Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1961**, *83*, 618.

(26) Ingold, C. K. "Structure and Mechanism in Organic Chemistry", 2nd ed.; Cornell University Press: Ithaca, NY, 1969; pp 457–463.

(27) Reference 24a, pp 687–688.

Scheme II



found in the complexity of products from ethanolysis (vide infra).

Ethanolysis. A wider range of products from ethanolysis (eq 4) than from thermolysis (eq 3) of **3** is suggestive of mechanistic differences in the two reaction types. However, considerations of the genealogy of the product sets clearly indicate that there are mechanistic features that are common to both processes. It is evident that **5** + **6** quantitatively corresponds to the t-C_4H_9-N^+ moiety of **3**. For both reactions, **4** represents the remainder of **3**. In the case of ethanolysis, **7** and **8** are secondary products that arise from **4**. The nature of the products points to pathways a and b as possible initial steps in the ethanolysis mechanism. These possibilities along with that for the secondary process are illustrated in Scheme II. The observations that **3** and **10** show closely similar reactivity under the conditions of eq 4 and that **10** is not detectable during ethanolysis of **3** exclude pathway a as an important source of products and single out pathway b as the principal operating process.

Additional mechanistic detail about the steps in pathway b is provided by the H–D exchange observations. The finding that D incorporation into **3** does not occur during the course of ethanolysis is suggestive that equilibration of cations **14** and **3** (**14** ⇄ **3**) is not competitive with ionization of **14**. In this connection, it is interesting that facile tautomeric equilibrations are manifest as D inclusion at the methyl and methine sites[22] of **4** in the same reaction medium.

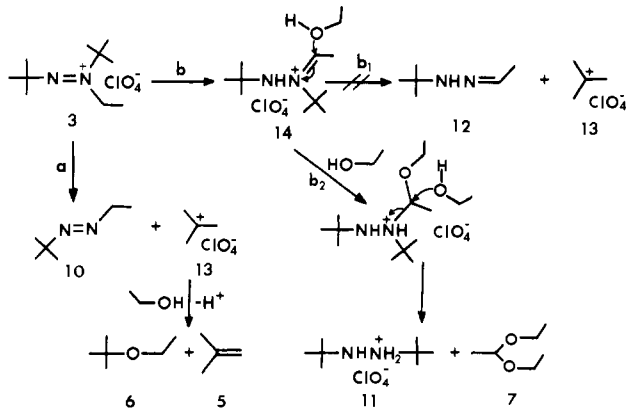
As shown in Scheme II, the reaction steps between **4** and **7**, **8** are reversible. Unambiguous evidence for this is found in the experiments that demonstrate that **4** + ethanol yields **7** and **8**, while **7** + **8** forms **4**.

Ethanolysis with Added Lutidine Base. From comparison of the product data summarized in eq 4 and 5, it is readily apparent that ethanolysis of diazenium cation **3** differs significantly in mechanistic detail depending on whether or not lutidine is present. In both reactons, *tert*-butyl cation **13** is the intermediate that is the source of products **5** and **6**. In the case of eq 4, all observed products are linked to formation of **13** and arise subsequent to this step (Scheme II). For eq 5, it is evident from the product distribution that part of the reaction is not coupled to formation of **13**. The occurrence of azo compound *trans*-**10** in eq 5 but not in eq 4 makes it clear that different ionization steps are involved in the two reactions. On the basis of these considerations, a plausible interpretation of the ethanol (lutidine) results is that both pathways a and b operate simultaneously. In this regard, a product ratio of 1.2:1 for **10** and **11** is indicative that pathways a and b contribute about equally as sources of product. The formation of **11** requires that iminium ion intermediate **14** of pathway b takes a reaction course different (b_2 not b_1) than that in Scheme II. The necessary series of mechanistic events are outlined in Scheme III.

Conclusions

Although the reaction possibilities of diazenium cation system **3** were limited by design, two observed transformations stand out and are of general mechanistic interest in regard to the chemistry of the —N=N⁺< group. Both thermal decomposition and reaction with ethanol show exclusive isomerization to iminium cation

Scheme III



14 in the initial mechanistic step. In contrast, reaction with ethanol (lutidine) proceeds with almost equal partition between isomerization of **14** and ionization to **10** and *tert*-butyl cation **13**. It is clear that prototropic rearrangement of the H of an α-H–C moiety of diazenium cation species to iminium cations is a reaction process of high driving force. The difference produced in the first reaction step of ethanolysis by inclusion of the weak base lutidine establishes the rearrangement as acid catalyzed. It is striking that, for **3**, ionization of the C–N⁺ bond in pathway a is competitive with isomerization pathway b (Scheme III).

The roles played by cation **14** in the conversion of **3** to reaction products (Schemes I, II, and III) also are of mechanistic interest since little is known about the chemistry of *N*-heteroiminium species like **14**.[24] Ready transformation of **3** → **14** shows cation **14** to be the favored structure of the two. This is similar to observations for aliphatic bicyclic diazenium and iminium cations.[21] The most salient feature of the chemistry of the *N*-heteroiminium group of **14** is the facile ionization of the C–N⁺ bond to **12** and *tert*-butyl cation **13**. It is interesting that the rates of ionization (Scheme II) and attack of ethanol at =C (path b_2, Scheme III) are comparable. The indications are that noncyclic aliphatic *N*-heteroiminium cations are species of high chemical reactivity.

Experimental Section

Melting points are uncorrected. ^{1}H NMR spectra were obtained with either a Varian EM-360, EM-390, or SC-300 spectrometer with Me_4Si as an internal standard. UV spectra were recorded with a Cary 14 spectrophotometer. Preparative gas chromatography (GC) separations were carried out with an Aerograph Autoprep Model A-700 chromatograph fitted with either a 10 ft × 0.375 in. column packed with 15% Carbowax 20M in Chromosorb W 60/80 mesh (column A) or a 10 ft × 0.375 in. column packed with 20% SE-30 on Chromosorb W 60/80 mesh (column B). Some analytical GC measurements were made with a Varian Hi-Fi III Model 1200 instrument equipped with a flame-ionization detector and an Autolab 1300 digital integrator. The columns used were either 10 ft × 0.125 in. 5% Carbowax 20M on Chromosorb P 60/80 mesh (column C) or 10 ft × 0.125 in. 20% SE-30 on Chromosorb W 60/80 mesh (column D). Other analytical GC data were obtained with a Hewlett-Packard 5880A instrument fitted with a thermoconductivity detector and equipped with a 20 × 0.125 in. column packed with 2% OV-101 on 100/120-mesh Chromosorb W-HP (column E). Yields were calculated by comparing the chromatogram integrations against those for standard known samples. Elemental analyses were obtained from M-H-W Laboratories, Phoenix, AZ.

Chemicals for Kinetics. Chloroform-*d* (99.8% isotopic purity, Stohler Isotope Chemicals), dichloromethane-d_2 (99.5% isotopic purity, Chemical Dynamics Corp.), and ethanol-d_6 (99% isotopic purity, Stohler Isotope Chemicals or Merck Sharp & Dohme) were used as purchased. 2,6-Lutidine was triple distilled and stored over type 4A molecular sieves.

Some Authentic Compounds. Isobutylene (**5**) was purchased from Matheson Chemical Co; NMR (CD_3CD_2OD) δ 1.77 (6 H, m, two CH_3), 4.77 (2 H, m, $=CH_2$). Ethyl *tert*-butyl ether (**6**) was prepared by a known method;[28] NMR ($CDCl_3$) δ 1.12 (3 H, t, J = 7 Hz, CH_3), 1.15 (9 H, s, three CH_3), 3.50 (2 H, q, J = 7 Hz, $-CH_2-$). Acetaldehyde diethyl acetal (**7**) was purchased from Matheson Coleman and Bell; NMR (CCl_4) δ 1.18 (6 H, J = 7 Hz, two CH_3), 1.23 (3 H, d, J = 6 Hz,

(28) Norris, J. F.; Riby, G. W. *J. Am. Chem. Soc.* **1932**, *54*, 2088.

CH_3), 3.53 and 3.60 (4 H, two q, J = 7 Hz, two $-CH_2-$), 4.73 (1 H, q, J = 6 Hz). A sample of mono-*tert*-butylhydrazinium perchlorate (**8**) was prepared from mono-*tert*-butylhydrazine hydrochloride (purchased from Polysciences) by anion exchange with $AgClO_4$; NMR ($CDCl_3$ + 5% Me_2SO) δ 1.40 (9 H, s, three CH_3). In a similar manner, 1,2-di-*tert*-butylhydrazinium perchlorate (**11**) was prepared from 1,2-di-*tert*-butylhydrazine hydrochloride (obtained from 1,2-di-*tert*-butylhydrazine[29]) by anion exchange with $AgClO_4$ (in ethanol); NMR ($CDCl_3$) δ 1.36 (18 H, s, six CH_3). Also, 1,2-di-*tert*-butylhydrazinium *p*-toluenesulfonate was prepared by treatment of 1,2-di-*tert*-butylhydrazine with anhydrous *p*-toluenesulfonic acid; NMR ($CDCl_3$) δ 1.30 (18 H, s, six CH_3).

1,2-Di-*tert*-Butyl-1-ethyldiazenium Perchlorate (3). A mixture of 0.84 g (5.8 mmol) of 1,2-di-*tert*-butylhydrazine[29] and 1.13 g (5.9 mmol) of triethyloxonium fluoroborate[30] in 10 mL of dichloromethane was stirred at room temperature for 2 h. After this period, the solvent was removed under vacuum, and the reaction mixture was treated with 40% aqueous KOH. Liberated **1,2-di-*tert*-butyl-1-ethylhydrazine** was recovered by extraction with two 50-mL portions of ether. The combined extracts were dried over K_2CO_3. Removal of the ether followed by distillation at 45 °C (8 mm) yielded 0.7 g (70%) of the trialkylhydrazine; NMR ($CDCl_3$) δ 1.02 (9 H, s, three CH_3), 1.04 (9 H, s, three CH_3), 1.10 (3 H, t, J = 7 Hz, CH_3), 2.72 (2 H, q, J = 7 Hz, $-CH_2-$), 3.60 (1 H, br s, -NH).

To a solution of 0.65 g (3.8 mmol) of the above trialkylhydrazine in 15 mL of dichloromethane (dried with 4A molecular sieves) was added, with stirring, 0.85 g (4.1 mmol) of anhydrous $AgClO_4$. The solution was allowed to stand for 10 min as a Ag^0 mirror developed on the walls of the flask. The precipitated Ag^0 was removed by filtration and the solvent by evaporation under vacuum. A crude yield of 0.79 g (77%) of **1,2-di-*tert*-butyl-1-ethyldiazenium perchlorate (3)** was obtained. This salt was washed with ether (dried over Na ribbon) and then recrystallized three times from dry THF (distilled from $LiAlH_4$) to give purified **3**, which was used for mechanistic studies; mp 117–118 °C dec; UV ($CHCl_3$) 326 nm (ϵ 60); NMR ($CDCl_3$) δ 1.69 (3 H, t, J = 8 Hz, CH_3), 1.74 (9 H, s, three CH_3), 1.75 (9 H, s, three CH_3), 4.89 (2 H, q, J = 8 Hz, $-CH_2-$). Anal. ($C_{10}H_{23}N_2ClO_4$): C, H.

Acetaldehyde *tert*-Butylhydrazonium Salts (4). A 2.0 g (45 mmol) sample of freshly distilled acetaldehyde was added to a stirring solution of 4.0 g (45 mmol) of distilled *tert*-butylhydrazine in 10 mL of anhydrous ether. The reaction mixture was stirred for 2 h at room temperature, 1 g of K_2CO_3 was added, and stirring was continued for another 4 h. After this the mixture was filtered, and the solvent was removed under vacuum to yield 3.5 g (61%) of **acetaldehyde *tert*-butylhydrazone (12)**: NMR ($CDCl_3$) major isomer δ 1.18 (9 H, s, three CH_3), 1.83 (3 H, d, J = 6 Hz, CH_3), 4.45 (1 H, s, -NH), 7.06 (1 H, q, J = 6 Hz, -CH-); minor isomer 1.14 (9 H, s, three CH_3), 1.65 (3 H, d, J = 6 Hz, CH_3), 4.45 (1 H, s, -NH), 6.68 (1 H, q, J = 6 Hz, -CH-).

To a solution of 0.316 g (2 mmol) of anhydrous *p*-toluenesulfonic acid in 15 mL of dry ether (from Na ribbon) was added 0.113 g (1 mmol) of **12**. The ether was evaporated, and the residue was recrystallized from ether/THF to yield 0.25 g (90%) of **acetaldehyde *tert*-butylhydrazonium *p*-toluenesulfonate (4)** as a white solid: mp 95–100 °C dec; NMR (CD_3CD_2OD) δ 1.40 (9 H, s, three CH_3), 2.02 (3 H, d, J 6 Hz, CH_3), 2.39 (3 H, s, CH_3), 7.30 (2 H, d, J = 8 Hz, Ar H), 7.85 (2 H, d, J = 8 Hz, Ar H), 8.48 (1 H, q, J = 6 Hz, C-H). Anal. ($C_{13}H_{20}O_3N_2S$): C, H.

A sample of (20 mg) of perchlorate **3** in 0.5 mL of CH_2Cl_2 under N_2 in a sealed Pyrex tube was heated at 75 °C for 5 h. Removal of the solvent under high vacuum left acetaldehyde *tert*-butylhydrazonium perchlorate (**4**) as a colorless viscous liquid that did not crystallize; NMR (CD_2Cl_2) δ 1.50 (9 H, s, three CH_3), 2.15 (3 H, d, J = 6 Hz, CH_3), 8.35 (1 H, q, J = 6 Hz, C-H).

***trans*-1,1-Dimethylazoethane (10).** A mixture of 3.5 g (31 mmol of hydrazone **12** and 0.6 g (150 mmol) of $LiAlH_4$ in 15 mL of anhydrous ether under an N_2 atmosphere was stirred and refluxed for 3 h. Under an N_2 blanket, the reaction was quenched with 10 mL of H_2O, the solution was extracted two times with 10-mL portions of ether, and the combined extracts were dried with anhydrous K_2CO_3. The ether was removed by evaporation, and the concentrate was distilled from BaO at 38–40 °C (30 mm) to yield 2.0 g (56%) of **1-*tert*-butyl-2-ethylhydrazine**; NMR ($CDCl_3$) δ 1.10 (9 H, s, three CH_3), 1.12 (3 H, t, J = 7 Hz, CH_3), 2.78 (2 H, q, J = 7 Hz, $-CH_2-$).

To 10 mL of pentane was added 1.0 g (8.7 mmol) of the above hydrazine, 1.9 g (8.7 mmol) of yellow HgO, and an NaOH pellet. This mixture was stirred at room temperature for 2 h, the solids were removed by filtration, and the filtrate was distilled from BaO at atmospheric pressure to give ***trans*-1,1-dimethylazoethane (10)**. The product **10** was further purified by preparative GC on column B: UV ($CHCl_3$) **359** nm (ϵ 22); NMR ($CDCl_3$) δ 1.20 (9 H, s, three CH_3), 1.26 (3 H, t, J = 7 Hz, CH_3), 3.80 (2 H, q, J = 7 Hz, $-CH_2-$). Anal. ($C_6H_{14}N_2$): C, H. Azo compound **10** was assigned the trans configuration on the basis of the synthetic method and the fact that the UV λ_{max} and ϵ values are exactly in the range found for acyclic *trans*-azoalkanes.[31]

Thermolysis of 3 in CD_2Cl_2 or $CDCl_3$. In a typical experiment, 20 mg (0.074 mmol) of perchlorate **3** dissolved in 0.5 mL of CD_2Cl_2 was placed in a 5-mm NMR tube, flushed with N_2, and sealed under an N_2 atmosphere. This NMR tube was placed in a constant-temperature bath at 55.0 °C, and the tube was removed at appropriate times (over the range 10–90% reaction), cooled in an ice bath for observation of the NMR spectrum, and then returned after each spectral measurement to the bath. The progress of thermolysis was determined at each time interval by integrating the δ 1.80 signals of **3** against Me_4Si internal standard. The rate constant value obtained from these data is listed in Table I.

Product formation was carefully examined at each NMR spectral observation for the thermolysis of **3** in $CDCl_3$ at 75 °C. From the onset of reaction, **5**, with NMR signals δ 1.75 (6 H, m) and 4.70 (2 H, m), and **4**, with NMR signals δ 1.50 (9 H, s), 2.15 (3 H, d, J = 6 Hz), and 8.35 (1 H, q, J = 6 Hz), were observed to form in a 1:1 ratio; final yields were >95%. Both products were identified by comparison with authentic specimens. Unidentified product(s) in trace amounts (<5%) appeared with NMR peaks partially underlaying the *tert*-butyl and methyl resonances of **4**. In addition, at each spectral examination, the spectrum was scrutinized in the δ 3.9 region for the presence of azo compound **10**. No peak was ever discernible.

Thermolysis Control Experiments Concerning the Relative Reactivity of 3:10. A solution of 11 mg (0.04 mmol) of **3** and 1.6 mg (0.016 mmol) of **10** in 0.4 mL of $CDCl_3$ was reacted at 75 °C, and the rate of disappearance of **10** was monitored by NMR (δ 3.9 ($-CH_2-$) and 1.22 (t-C_4H_9) signals) as described above for **3**. After a short induction period, the reactivity ratio for **3**:**10** was found to be ca. 0.9:1. In a separate control experiment, it was shown that **10** in $CHCl_3$ rearranges to **4** in the presence of acid (HOTs). As an additional check on the reactivity of **10** under thermolysis conditions, a mixture of 14 mg (0.05 mmol) of **4** *p*-toluenesulfonate and 2.5 mg (0.022 mmol) of **10** in 0.4 mL of $CDCl_3$ was heated at 75 °C, and the rate of **10** disappearance was followed by the NMR method. The reactivity comparison for **3**:**10** was ca. 0.8:1.

Ethanolysis of 3 in $CDCl_3$. A representative experiment consisted of preparing a solution of 10 mg (0.037 mmol) of diazenium perchlorates **3** in 0.4 mL of a mixture of $CD_3CD_2OD/CDCl_3$ (2:1 v/v) and sealing this under N_2 in an NMR tube. Kinetic measurements were carried out by ^1H NMR spectroscopy as described for thermolysis. Rate constant values at various temperatures are given in Table I.

The reaction mixture from the kinetic measurements was used for product identification and yield determination. After completion of ethanolysis (ca. 10 half-lives), the NMR signals at δ 4.80 (2 H, m, vinyl H) of **5** and δ 1.20 (9 H, s, t-C_4H_9) of **6** were free of interference from other peaks. Integration showed yields of **5** and **6** to be 29% and 68%, respectively. The NMR tube was opened, and the volatile material was transferred under vacuum into a dry ice–acetone cooled trap. GC analysis of the volatile fraction with column C established the presence of **6** on the basis of retention-time comparison with an authentic sample and showed a 25–31% yield of **6**. Another GC analysis with column E showed **7** to be present in 24% yield. Products **6** and **7** were separated and isolated by preparative GC with columns A and B, respectively. Their identifications were confirmed by NMR spectral comparisons with authentic specimens. Control experiments with the above GC analyses indicated that diethyl ether (**9**) is not a product of ethanolysis. The NMR spectrum ($CDCl_3$) of the nonvolatile residue remaining from the vacuum transfer treatment showed the presence of **4** and **8** in yields of 76% and 24%, respectively. Structures of these products were assigned on the basis of spectral identities found by comparison with authentic compounds. During the above NMR kinetic study, each spectrum was examined carefully in the δ 3.9 region for the presence of azo compound **10**. No signal was ever discernible. In addition, the δ 4.9 region of each spectrum was monitored carefully for evidence of H–D exchange in the $-CH_2-$ moiety of **3**. There were no changes in integration ratios or signal shape.

Ethanolysis Control Experiments Concerning the Relative Reactivity of 3:10. A solution consisting of 25 mg (0.092 mmol) of **3** and 3 mg (0.026 mmol) of **10** in 0.4 mL of a mixture of $CD_3CD_2OD/CDCl_3$ (2:1 v/v) was reacted at 75 °C, and the rate of disappearance of **10** was followed by NMR as described above for thermolysis. The overall reactivity ratio of **3**:10 was found to be ca. 1:0.4. As a check on the nature of the reaction of **10** under the ethanolysis conditions, a solution of 11 mg (0.01 mmol) of **10** and 28 mg (0.16 mmol) of anhydrous HOTs in

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0.5 mL of anhydrous CH_3CH_2OH containing $CHCl_3$ was heated at 75 °C for 7 min. The tube was cooled and opened, and the volatile material was transferred under vacuum to a dry ice–acetone cooled trap. GC analysis of the volatile part with column D showed the complete absence of **10**. NMR analysis of the nonvolatile residue showed a quantitative formation (100%) of **4** *p*-toluenesulfonate. This was repeated with **10**:HOTs in a 1.00:0.12 mol ratio. In this case, the final ratio of **10**:**4** was found to be 0.88:0.12.

Ethanolysis H–D Exchange with 4 Perchlorate. A solution of 16 mg (0.075 mmol) of **4** perchlorate in 0.3 mL of CD_3CD_2OD under N_2 in a sealed NMR tube was heated at 75 °C. The ensuing reaction was tracked by NMR at selected time intervals as described above. The signals at δ 1.45 (t-C_4H_9, s), 2.20 (CH_3, d), and 8.35 (methine C–H, q) for **4** decreased as signals for **7** (δ 1.30 (CH_3, d) 4.80 (methine C–H, q) and **8** (δ 1.38 (t-C_4H_9, s)) appeared. In addition, the δ 2.20 and 8.35 signals of **4** decreased in intensity relative to the δ 1.45 peak with time as both signals gradually broadened and lost resolution. Also, the two signals decreased in relative intensity at different rates, indicating that the two sites undergo H–D exchange at different rates. The δ 4.80 signal of **7** was observed as a multiplet instead of a quartet.

Equilibration between 4, CD_3CD_2OD, 7, and 8. A mixture of 40 mg (0.34 mmol) of **7** and 60 mg (0.32 mmol) of **8** in 0.35 mL of $CD_3CD_2OD/CDCl_3$ mixed solvent (2:1 v/v) was heated at 75 °C. Appearance of **4**, decreases of **7** and **8**, and H–D exchanges were followed by NMR. Changes in concentrations of **4**, **7**, and **8** appeared to cease after ca. 6 h.

Ethanolysis of 3 with Added Lutidine Base in $CDCl_3$. A solution consisting of 21 mg (0.078 mmol) of **3** and 37 mg (0.35 mmol) of 2,6-lutidine in 0.74 mL of $CD_3CD_2OD/CDCl_3$ mixed solvent (2:1 v/v) was sealed under N_2 in an NMR tube and heated in a constant-temperature bath. Kinetic measurements were made by the above-described ^1H NMR method. Rate constant values at various temperatures are listed in Table I.

After completion of ethanolysis (ca. 10 half-lives), NMR samples were used for product identification and yield determination. The NMR signals at δ 4.70 (2 H, m, vinyl H) of **5**, δ 3.85 (2 H, q, $-CH_2-$) of *trans*-**10**, and δ 1.30 (18 H, s, t-C_4H_9) of **11** were free of interference from other peaks. Integration of these signals showed yields of **5**, **10**, and **11** to be 13%, 55%, and 45%, respectively. The NMR tube was opened, and the volatile part was transferred under vacuum into a dry ice–acetone cooled trap. When a sample of the volatile material was shaken with 70% aqueous $HClO_4$, **10** with δ 1.20 (9 H, s, t-C_4H_9) was converted to **4** with δ 1.45 (9 H, s, t-C_4H_9). Integration of the remaining δ 1.20 (9 H, s, t-C_4H_9) signal belonging to **6** and the δ 1.45 signal of **4** corresponded to 40% and 55% yields of **6** and **10**, respectively. Preparative GC with column B afforded **6** and *trans*-**10** and with column A gave **7**. The structures were confirmed by GC retention times and NMR spectral comparisons with authentic samples. GC analyses with columns C and E showed a 38–43% yield of **6** and a 25–35% yield of **7**, respectively. Control experiments with the above GC analyses indicated that diethyl ether (**9**) is not a reaction product. The NMR spectrum ($CDCl_3$) of the nonvolatile residue remaining from vacuum transfer showed the presence of lutidinium perchlorate and one other salt with δ 1.35 (18 H, s, t-C_4H_9), which appeared to be **11** perchlorate. Shaking the $CDCl_3$ salt solution with 40% KOH caused the *tert*-butyl singlet to shift to δ 1.05, which is the same chemical shift as authentic, 1,2-*tert*-butylhydrazine. The freed hydrazine solution was allowed to stand in air (O_2) for several days. After this treatment, the *tert*-butyl singlet had shifted to δ 1.20, which is the exact chemical shift of authentic 2,2′-azobis(isobutane) (300-MHz NMR). The GC retention times of the product from **11** perchlorate and known 2,2′-azobis(isobutane) were identical.

During the above NMR kinetic study, each spectrum was monitored carefully in the δ 4.9 region for evidence of H–D exchange in the $-CH_2-$ moiety of **3**. No changes in integration ratios or signal shape were observed.

Stability of Products 7 and 11 in Ethanol/Lutidine ($CDCl_3$). A solution of 10.0 mg (0.032 mmol) of **11** *p*-toluenesulfonate, 4.0 mg (0.033 mmol) of **7**, 11 mg (0.01 mmol) of lutidine, and Me_4Si in 0.4 mL of $CD_3CD_2OD/CDCl_3$ (2:1 v/v) was sealed under N_2 in an NMR tube and heated at 75 °C for 4 h (ca. 10 ethanolysis half-lives of **3**). The various ^1H NMR signals for **7** and **11** had the correct initial integration values, and there were no change in these values or the spectrum during the time period.

A Search for Iminium Cation 14. During the NMR kinetic studies of the thermolysis, ethanolysis, and ethanolysis with lutidine reactions of **3**, the NMR spectra were scrutinized for the appearance of **14**. No signals were ever observed that could be taken as evidence for **14**.

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Registry No. **3**, 82571-40-2; **4** *p*-toluenesulfonate, 82571-42-4; **10**, 65444-37-3; **12**, isomer 1, 82571-43-5; **12**, isomer 2, 82571-45-7; 1-*tert*-butyl-2-ethylhydrazine, 82571-44-6.

Analysis of the Atomic Environment of Quaternary Ammonium Groups in Crystal Structures, Using Computerized Data Retrieval and Interactive Graphics: Modeling Acetylcholine–Receptor Interactions

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Abstract: The atomic environment of the trimethylammonium methyl cationic group (**1**) has been reexamined in 34 reported crystal structures containing simple halides (Cl, Br, I) as counterions and in nine structures containing oxyanionic groups (carboxylate, picrate, phosphate, perchlorate). For the halides (X), three-dimensional scatter plots of N···X vectors <5.65 Å about a reference $RCH_2NMe_3^+$ group clearly show clustering in the N···X approach directions. Clustering occurs close to the centers of the three sterically unhindered faces of the tetrahedron formed by the carbon atoms of the quaternary ammonium group, allowing minimization of d(N···X). For the oxyanion structures, a similar scatter plot of intra- and intermolecular N···O vectors <5.0 Å shows a much more even distribution over **1**'s entire surface. Some oxyanions coordinate to **1** via two or three oxygen atoms. The preferences observed for the N···X directions suggest that the binding of acetylcholine to its receptor may involve a preferred orientation between the quaternary ammonium group and anionic groups in the receptor. This work is an example of computer-assisted retrieval, visualization, and analysis of data in the Cambridge Crystallographic Data Files, performed on a PDP 11/40 minicomputer equipped with a Vector General series 3 graphics display.

The trimethylammonium methyl cationic group (**1**, Figure 1) is an important biochemical fragment, occurring in choline, acetylcholine, choline phospholipids, and related compounds. Unlike most other organic cations, it cannot form N–H···R hy-

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