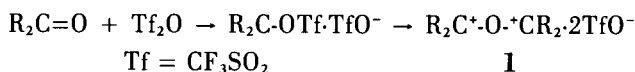Gerhard Maas*, Ralf Brückmann und Bernhard Feith

Fachbereich Chemie der Universität Kaiserslautern, Postfach 3049,
D-6750 Kaiserslautern, West Germany
Received September 20, 1984

The bicyclic bisureas **2** react with triflic anhydride to give the dication ether salts **4**. Further transformation of the remaining carbonyl groups of **4** into bis-carbenium ether linkages was not possible. The monocyclic bisurea **8** yields the dicationic heterocycle **9** in an intramolecular fashion. The structure of **9**, which is the first dication ether salt with an endocyclic ether linkage, was established by independent synthesis from **10** as well as by its hydrolysis to give the hemi-protonated bisurea **11**.

Strongly polarized carbonyl compounds like cyclopropenones, tropone, ureas or pyridones react with trifluoromethanesulfonic acid anhydride (triflic anhydride, Tf_2O) in a two-step reaction to give trifloxycarbenium salts and then dication ether salts **1** [2].

$$R_2C=O + Tf_2O \rightarrow R_2C\text{-}OTf\cdot TfO^- \rightarrow R_2C^+\text{-}O\text{-}^+CR_2\cdot 2TfO^-$$
$$Tf = CF_3SO_2 \qquad\qquad \mathbf{1}$$

In most cases, the second reaction step, *i.e.* nucleophilic displacement of a triflate anion from the trifloxycarbenium ion by still available carbonyl compound, is faster than the first one, and trifloxycarbenium salts cannot be isolated, even if a 1:1 stoichiometry is applied.

Considering the aptitude of simple ureas for dication ether formation (**1**, $R_2C^+ = (R_2'N)_2C^+$) [2,3], we were interested in the behavior of molecules containing two urea units in the same molecule. A priori, formation of a bis(trifloxy-formamidinium) salt could be expected and hence, formation of a tetracation with two ether linkages, or even higher oligomers thereof. For our investigation, we chose molecules with two urea moieties incorporated in a monocyclic or bicyclic system, as well as a system in which these functionalities were parts of two isolated rings.

Reaction of triflic anhydride with the bicyclic bisureas **2a** or **2b** in a 2:1 ratio led to dication ether salts **4a,b** in yields of 59 and 46%, respectively. The trifloxy-substituted monocations **3** must be intermediates in these reactions, but they could neither be isolated nor detected spectroscopically under the reaction conditions. Furthermore, the dication ether salts **4**, and not the bis(trifloxy) salts **5** were formed when **2a** or **2b** were slowly added to a solution of two molar amounts of triflic anhydride in chloroform. This seems remarkable, as the twofold *O*-alkylation of **2a** with triethyloxonium tetrafluoroborate has been reported [4]. Also, twofold protonation of **2a,b** with triflic acid to give the salts **6a,b** as viscous gum-like compounds is possible.

All attempts to convert the free carbonyl groups of **4** into (trifloxy)carbenium functions with an excess of triflic anhydride proved unsuccessful. Heating a suspension of **4a** in chloroform, or a homogeneous solution of **4a** in
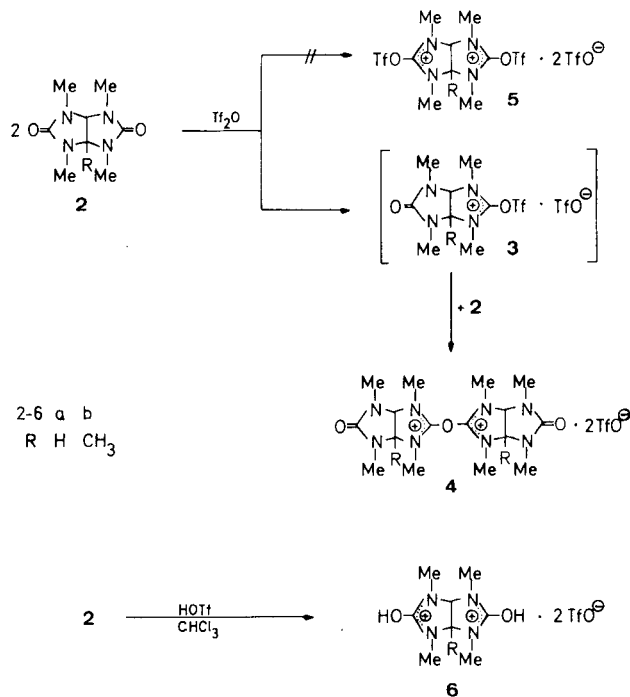

nitromethane, with triflic anhydride left the dication ether salt unchanged. The -I effect of the formamidinium function in **4**, which reduces the carboxamide resonance and hence the nucleophilicity of the carbonyl oxygen in the same bicyclic ring, is considered to be the reason for the failure of *O*-sulfonylation of **4**. An indication of the reduced carboxamide resonance, *i.e.* higher double bond character of the C=O group in the dication ether salts **4**, is the shift of ν (CO) in the ir spectrum (**4a**, 1735 cm^{-1}; **4b**, 1733/1725 cm^{-1}) to higher wave numbers than in the neutral bicyclic bisureas (**2a**, 1710 cm^{-1}; **2b**, 1695 cm^{-1}).

On the other hand, protonation of the C=O groups in **4** with triflic acid to give the tetracationic species **7** is possible: When triflic acid was added dropwise to a solution of **4a** in d$_3$-acetonitrile, a continuous shift to lower field of all signals was observed in the ^{1}H nmr spectrum, until δ-values of 3.25, 3.36 and 6.15 ppm were reached at a six to eightfold excess of triflic acid. This corresponds to down-

field shifts of 0.27 (urea-NMe), 0.13 (formamidinium-NMe) and 0.43 ppm (CH$_2$) for the three signals of the dication ether salt **4a**. Upon dilution with deuterioacetonitrile the nmr signals moved back upfield, as the acid/base equilibrium **4a** + 2H$^+$ ⇌ **7** was shifted to the left side. Acetonitrile was chosen as a solvent because of the low solubility of **4a** in less polar solvents. Protonation of acetonitrile by triflic acid may occur, but it should be a fast reversible process with a low concentration of the protonated form [5]. Therefore this process cannot account for the observed changes in the nmr spectrum of **4a**. Compound **7** could not be isolated from the solution. Upon addition of ether to the solution of **7** in acetonitrile, the dication ether salt **4a** was precipitated quantitatively.
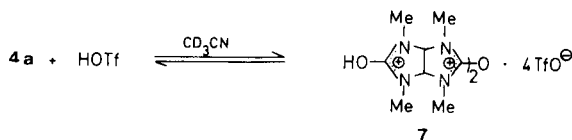
Reaction of the monocyclic bisurea **8** with triflic anhydride did not result in a dication ether salt built up from two urea molecules like **4**, instead, the dicationic salt **9** is formed in an intramolecular reaction. Compound **9** is the first dication ether salt with an endocyclic ether function. Its structure is confirmed by independent synthesis from the open-chain bisurea **10** and triflic anhydride, as well as by an X-ray structure analysis [6] of **11**, the product of its careful hydrolysis; **11** was also prepared independently from **10** and triflic acid. Breaking of the ether linkage and transformation into two carbonyl functions is a well known reaction mode of dication ether salts. The mode of formation of **9** from **8** is not clear yet; triflic anhydride initiated cleavage of one of the aminal-type functions in **8** to give **10** as the precursor to **9** appears as a possibility. In fact, the highest yield of **9** (66%) was obtained when a 1:2 ratio of **8**:triflic anhydride was applied, although the composition of **9** would require only an equimolar amount of triflic anhydride. Ring-opening of **8** by triflic anhydride would be analogous to the acid-induced reaction: Triflic acid in acetonitrile cleaves **8** quantitatively to the salt **11**, the protonated form of urea **10**.
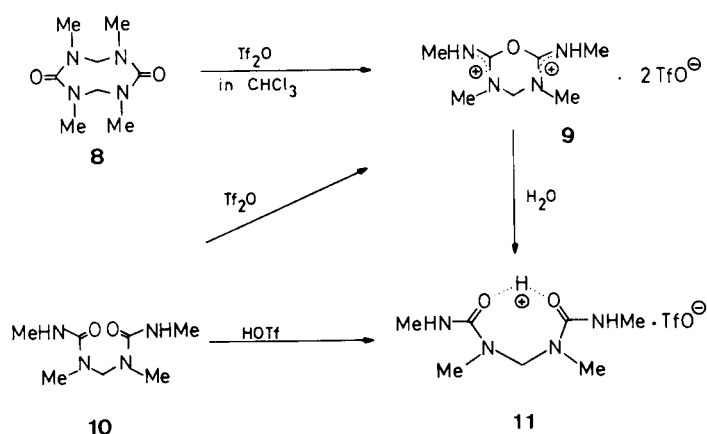

No dication ether structure, but only the very unstable bis(trifloxyimidazolium) salt **13** was accessible by reaction of **12** with triflic anhydride. This behavior resembles completely the reactivity of 1,3-diphenyl-4-imidazolin-2-one [2]. It seems that the nucleophilicity of imidazolinones in general is not sufficient to bring about a nucleophilic displacement of a triflate anion from the corresponding trifloxy salts. Compound **13** is an extremely moisture-sensitive salt; its hydrolysis with equimolar amounts of water leads to the doubly protonated bis-imidazolinone **14** which was prepared independently from **12** and triflic acid in dichloromethane. In aqueous solution, extensive dissociation of **14** occurs.

All dication ether salts, protonated ureas as well as the trifloxycarbenium salt **13** are only stable in the absence of all moisture. Like other dication ether salts [2,7,8,9,10] and trifloxycarbenium salts [9], **4**, **9** and **13** should display high reactivity in nucleophilic displacement reactions. A simple illustration is given by the cleavage of **4a** with N-methylaniline, leading the the bicyclic guanidinium derivative **15** and urea **2a**.
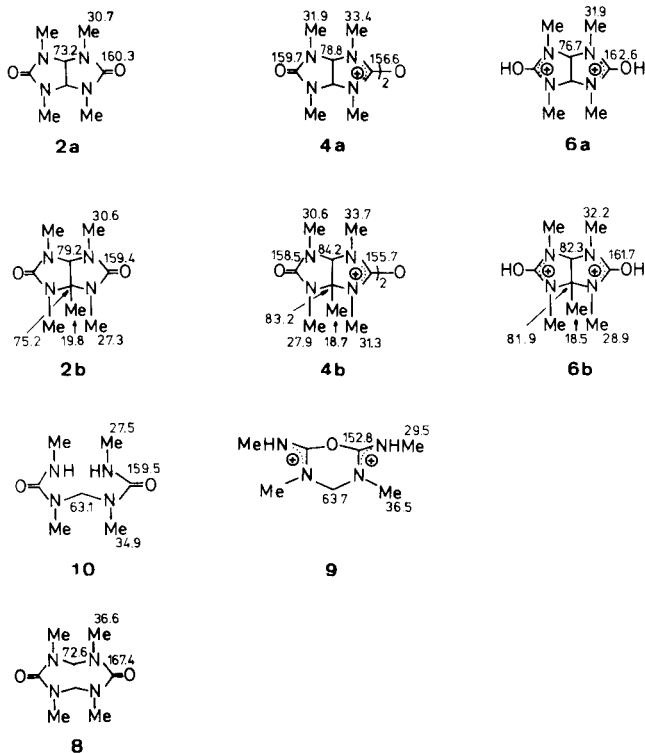
^{13}C NMR Spectra.

^{13}C nmr data for dication ether salts **4** and **9**, diprotonated ureas **6** and the corresponding neutral ureas are as-

15
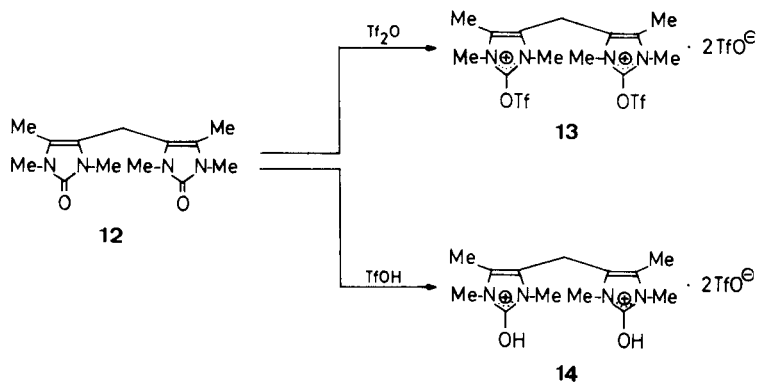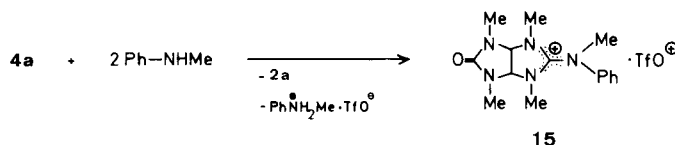
sembled in Chart 1. Assignments of magnetically different methyl signals in the series **2b, 4b, 6b**, were made by comparison with the corresponding compounds **2a, 4a, 6a**. Generation of a formamidinium system, either by dication ether formation or by *O*-protonation, results in a paramagnetic shift of all C-atoms adjacent to that group, relative to the neutral urea. Notwithstanding the higher positive charge density, however, the central carbon in the formamidinium part of all dication ethers suffers a high-field shift. This has already been observed in simple *O*-alkylated or *O*-arylated uronium salts [11] as well as in other dication ether salts [1,2,7]. In contrast, *O*-protonation of the carbonyl group leads to the expected low-field shift of this carbon atom. The same behavior is displayed for example by tetramethylurea in the presence of not more than one equivalent of trifluoroacetic acid [12].

Chart 1

^{13}C NMR Spectra of Dication Ethers, Neutral and Protonated Ureas [a]

2a   **4a**   **6a**

2b   **4b**   **6b**

10   **9**

8

[a] All spectra were taken in d_3-acetonitrile, except **8** in deuteriochloroform. Given are δ- values relative to TMS as internal standard.

EXPERIMENTAL

The ^{1}H nmr spectra (TMS as internal standard) were measured on a Varian EM 390 (90 MHz) Spectrometer. The ^{13}C nmr spectra were taken on a Bruker WP 200 (50.19 MHz) Spectrometer. The ir spectra were recorded on a Perkin-Elmer 397 Spectrometer. Elemental analyses were carried out with the Perkin-Elmer Elemental Analyzer 240. All mps are uncorrected. All preparations (except for the preparations of **11** and **15**) were carried out in an argon atmosphere. All solvents were dried.

Bis(7-oxo-2,4,6,8-tetramethyl-2,4,6,8-tetraazabicyclo[3.3.0]octane-3-ylium) Ether Bis(trifluoromethanesulfonate) (**4a**).

A solution of 1.26 ml (7.5 mmoles) of triflic anhydride [13] in 5 ml of chloroform was added dropwise to a solution of 2.97 g (15 mmoles) of 2,4,6,8-tetramethyl-2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-dione (**2a**) [14] in chloroform (30 ml). The mixture was then heated to reflux for 1 hour, allowed to assume room temperature, and the precipitate was filtered off. After washing with chloroform and ether, one obtained 2.98 g (59%) **4a** as a white powder, mp 150-155° dec; ir (nujol): 1735, 1685-1668, 1590, 1556, 1418, 1270, 1255, 1225, 1165, 1152, 1044, 1031 cm⁻¹; ^{1}H nmr (d_3-acetonitrile): δ 2.98 (NMe), 3.23 (N⁺Me), 5.72 (CH).

Anal. Calcd. for $C_{18}H_{28}F_6N_8O_9S_2$ (678.6): C, 31.8; H, 4.15; N, 16.5. Found: C, 31.4; H, 4.10; N, 16.3.

Bis(7-oxo-2,4,5,6,8-pentamethyl-2,4,6,8-tetraazabicyclo[3.3.0]octane-3-ylium) Ether Bis(trifluoromethanesulfonate) (**4b**).

A solution of 0.42 ml (2.5 mmoles) of triflic anhydride [13] in dichloromethane (5 ml) was added dropwise to 1.06 g (5 mmoles) of 2,4,5,6,8-pentamethyl-2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-dione (**2b**) [15] in dichloromethane (5 ml) at 0°. After stirring for 3 hours at 0°, the precipitate was filtered off, dissolved in acetonitrile and reprecipitated with ether. After washing with cold dichloromethane, 0.82 g (46%) of a pale-pink powder was obtained, mp 124-127° dec; ir (nujol): 1735, 1725, 1684, 1660, 1588, 1549, 1417, 1305, 1275/1267 (v br), 1223, 1160, 1032 cm⁻¹; ^{1}H nmr (d_3-acetonitrile): δ 1.88 (C4-methyl), 2.90, 2.99 (both NMe), 3.18, 3.27 (both N⁺-Me), 5.51 (CH).

Anal. Calcd. for $C_{20}H_{32}F_6N_8O_9S_2$ (706.6): C, 33.9; H, 4.56; N, 15.8. Found: C, 33.7; H, 4.47; N, 15.8.

3,7-Dihydroxy-2,4,6,8-tetramethyl-2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-diylium Bis(trifluoromethanesulfonate) (**6a**).

To a solution of 0.99 g (5 mmoles) of **2a** [14] in chloroform (15 ml) was added dropwise 0.88 ml (10 mmoles) of triflic acid in chloroform (5 ml). The mixture was heated to 70° for 1 hour, whereupon a brownish oil separated. The solvent was evaporated at 25°/0.01 Torr to leave a brown hygroscopic gum (2.41 g, 97%) of **6a** which could not be purified further and thus gave poor analyses due to the hygroscopic nature of **6a**. The ^{1}H nmr (d_3-acetonitrile): δ 3.14 (NMe), 5.51 (CH), 12.84 (OH).

Anal. Calcd. for $C_{10}H_{16}F_6N_4O_8S_2$ (498.4): C, 24.1; H, 3.23; N, 11.2. Found: C, 23.1; H, 3.33; N, 11.1.

3,7-Dihydroxy-2,4,5,6,8-pentamethyl-2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-diylium Bis(trifluoromethanesulfonate) (**6b**).

To a solution of 1.06 g (5 mmoles) of **2b** [15] in 15 ml of dichloromethane, 0.88 ml (10 mmoles) of triflic acid in 5 ml of dichloromethane was added dropwise at 0°. After stirring for 30 minutes at room temperature, the volatile material was evaporated at 25°/0.01 Torr to leave 2.34 g (91%) of **6b** as a pale brown hygroscopic gum, which could not be purified further and thus gave poor analyses due to the hygroscopic nature of **6b**. The ^{1}H nmr (d_3-acetonitrile): δ 1.79 (C4-methyl), 3.02 and 3.13 (NMe),

5.35 (OH), 13.40 (OH).

Anal. Calcd. for $C_{11}H_{18}F_6N_4O_8S_2$ (512.4): C, 25.7; H, 3.54; N, 10.9. Found: C, 24.8; H, 3.46; N, 10.3.

2,6-Bis(methylamino)tetrahydro-1,3,5-oxadiazine-2,6-diylium Bis(trifluoromethanesulfonate) (9). a) From 8.

Triflic anhydride (1.68 ml, 10 mmoles) in chloroform (5 ml) was added dropwise at 0° to a solution of 1 g (5 mmoles) of 1,3,5,7-tetramethyloctahydro-1,3,5,7-tetraazocine-2,5-dione (8) [16] in chloroform (30 ml). The mixture was brought to room temperature and stirred for 30 minutes. The precipitate was filtered off, dissolved in acetonitrile and reprecipitated with ether. This afforded 1.56 g (66%) of 9 as colorless crystals, mp 176°; ir (nujol): 3140 (NH), 1760, 1704, 1528, 1403, 1345, 1309/1294 (br), 1240/1225 (br), 1170 (br), 1030 cm⁻¹; ¹H nmr (d₃-acetonitrile): δ 3.13 (d, NH*Me*), 3.23 (s, NMe), 4.89 (CH₂), 8.77 (m, NH).

Anal. Calcd. for $C_9H_{16}F_6N_4O_7S_2$ (470.4): C, 23.0; H, 3.42; N, 11.9. Found: C, 22.9; H, 3.36; N, 12.0.

b) From 10.

Triflic anhydride (1.68 ml, 10 mmoles) in chloroform (5 ml) was added dropwise at 0° to a solution of 1.88 g (10 mmoles) of methylenebis(*N,N'*-dimethylurea) (10) [17] in chloroform (40 ml). The further procedure was as above, yielding 4.44 g (94%) of 9 as colorless crystals, mp 177°. This compound proved identical in all spectroscopic data with that obtained under a).

Anal. Calcd. for $C_9H_{16}F_6N_4O_7S_2$ (470.2): C, 23.0; H, 3.42; N, 11.9. Found: C, 23.1; H, 3.43; N, 11.9.

Methylenebis(*N,N'*-dimethylurea) Hydrogen Trifluoromethanesulfonate) (11). a) By Hydrolysis of 9.

Aqueous ammonia (*ca.* 0.3%, 1 ml) was added to a solution of 0.70 g (1.5 mmoles) of 9 in acetonitrile (20 ml). After stirring for 16 hours, the solvent was taken off, and the residue was stirred with ether (30 ml); 0.31 g (61%) of 11 remained undissolved, which was recrystallized from acetonitrile/ether, mp 161°; ir (potassium bromide): 3350 (NH), 1658 (m), 1595 (CO), 1453, 1382, 1338, 1274, 1246, 1228, 1153, 1092, 1036, 991 cm⁻¹; ¹H nmr (d₃-acetonitrile): δ 2.72 (s, broadened), 2.99 (s), 4.68 (s, CH₂), 6.35 (very broad, NH), *ca.* 10.0 (very broad, OH).

Anal. Calcd. for $C_8H_{17}F_3N_4O_5S$ (338.3): C, 28.4; H, 5.06; N, 16.56. Found: C, 28.2; H, 4.95; N, 16.5.

b) From 10 and Triflic Acid.

Triflic acid (0.66 ml, 7.5 mmoles) in chloroform (5 ml) was added at 0° to a solution of 1.41 g (7.5 mmoles) in chloroform (30 ml). After stirring for 15 minutes, the preciptate was filtered off and washed with ether. This afforded 2.33 g (93%) of 11 as a white powder, mp 162°; ir and nmr spectra agree with those obtained under a).

Anal. Calcd. for $C_8H_{17}F_3N_4O_5S$ (338.3): C, 28.4; H, 5.06; N, 16.56. Found: C, 28.1; H, 4.90; N, 16.3.

4,4'-Methylenebis(1,3,5-trimethyl-2-trifloxyimidazolium) Bis(trifluoromethanesulfonate) (13).

Triflic anhydride (0.41 ml, 2.44 mmoles) [13] in dichloromethane (5 ml) was added dropwise to the solution of 4,4'-methylenebis(1,3,5-trimethyl-4-imidazolin-2-one 12 [18] (324 mg, 1.22 mmoles) in 15 ml of dichloromethane. The solution turned violet immediately and a violet oil started to separate. Ether (10 ml) was then added and the solvent mixture was decanted. This process was repeated with dichloromethane (5 ml). When the oil was kept at 25°/0.01 Torr, it turned into a violet solid of 13 (760 mg, 75%), which decomposed after a short time even under argon atmosphere; ¹H nmr (d₃-acetonitrile): δ 2.29 (C5-methyl), 3.67 and 3.73 (NMe), 4.29 (CH₂).

Anal. Calcd. for $C_{17}H_{20}F_{12}N_4O_{12}S_4$ (828.6): C, 24.6; H, 2.43; N, 6.7. Found: C, 24.9; H, 2.36; N, 6.7.

4,4'-Methylenebis(2-hydroxy-1,3,5-trimethylimidazolium) Bis(trifluoromethanesulfonate) (14).

Triflic acid (0.35 ml, 4 mmoles) in dichloromethane (10 ml) was added dropwise to a solution of 12 [18] (527 mg, 2 mmoles) in 15 ml of dichloromethane. After stirring for 30 minutes, the precipitate was filtered off and washed with dichloromethane. This afforded 870 mg (77%) of 14 as a pink powder, mp 132°; ir (potassium bromide): *ca.* 3200-2200 (v br, OH), 1645, 1569, 1440, 1306, 1245-1150 (v br), 1100, 1025 cm⁻¹; ¹H nmr (d₃-acetonitrile): δ 2.12 (C5-methyl), 3.36 and 3.48 (NMe), 3.91 (CH₂), 12.12 (OH).

Anal. Calcd. for $C_{15}H_{22}F_6N_4O_8S_2$ (564.5): C, 31.9; H, 3.93; N, 9.9. Found: C, 31.6; H, 3.81; N, 10.0.

(7-Oxo-2,4,6,8-tetramethyl-2,4,6,8-tetraazabicyclo[3.3.0]octane)-2-(*N*-methyl-*N*-phenyliminium) Trifluoromethanesulfonate (15).

N-Methylaniline (0.33 ml, 3.12 mmoles) in 2.5 ml of acetonitrile was added to a solution of 4a (1.06 g, 1.56 mmoles) in acetonitrile (25 ml). After stirring for 1 hour, the solvent was evaporated at 25°/0.01 Torr. A small amount of ether was added and crystallization was induced by grating. The solid was dissolved in dichloromethane, reprecipitated with ether and triturated with ethyl acetate. After drying, 15 (0.21 g, 62%) remained as a colorless powder, mp 181°; ir (potassium bromide): 1730/1710, 1616, 1567, 1505, 1416, 1368, 1272, 1154, 1037 cm⁻¹; ¹H nmr (d₃-acetonitrile): δ 2.90 and 2.98 (CH₃-ring), 3.50 (CH₃-aniline), 5.39 (s, CH), 7.2-7.6 (m, 5H-aromatic).

Anal. Calcd. for $C_{16}H_{22}F_3N_5O_4S$ (437.4): C, 43.9; H, 5.07; N, 16.0. Found: C, 43.5; H, 5.09; N, 16.2.

REFERENCES AND NOTES

[1] Part 6: G. Maas and B. Singer, *Z. Naturforsch.*, **40B**, 90 (1985).
[2] P. J. Stang, G. Maas, D. L. Smith and J. A. McCloskey, *J. Am. Chem. Soc.*, **103**, 4837 (1981).
[3] T. Gramstad, S. Husebye and J. Saebø, *Tetrahedron Letters*, 3919 (1983).
[4] L. I. Suvorova, L. V. Epishina, O. V. Lebedev, L. I. Khmel'nitskii and S. S. Novikov, *Izv. Akad. Nauk. SSSR, Ser. Khim.*, 2282 (1979).
[5] The protonated form of acetonitrile was not observed in neat FSO₃H even at − 78°, but only in the stronger acid system FSO₃H/SbF₅/-SO₂: G. A. Olah and T. E. Kiovsky, *J. Am. Chem. Soc.*, **90**, 4666 (1968). These findings indicate fast exchange in the weaker acidic medium.
[6] G. Maas, *Acta Cryst.*, Section C, submitted. Further data concerning the X-ray analysis of 11 are also available on request from Fachinformationszentrum Energie-Physik-Mathematik, D-7514 Eggenstein-Leopoldshafen 2, West Germany by reference to the deposition number CSD 51039, the authors and the citation of this paper.
[7] G. Maas and B. Singer, *Chem. Ber.*, **116**, 3659 (1983).
[8] G. Maas and B. Feith, *Synth. Commun.*, **14**, 1073 (1984).
[9] B. Singer and G. Maas, *Z. Naturforsch., Part B*, **39B**, 1399 (1984).
[10] S. Araki, J. Mizuya and Y. Butsugan, *Chem. Letters*, 1045 (1984).
[11] H.-O. Kalinowski and H. Kessler, *Org. Magn. Reson.*, **7**, 128 (1975).
[12] H.-O. Kalinowski and H. Kessler, *Org. Magn. Reson.*, **6**, 305 (1974).
[13] P. J. Stang and T. E. Dueber, *Org. Synth.*, **54**, 79 (1974).
[14] I. Nematollahi and R. Ketcham, *J. Org. Chem.*, **28**, 2378 (1963).
[15] L. I. Suvorova, V. A. Eves'ko, L. V. Epishina, O. V. Lebedev, L. I. Khmel'nitskii, S. S. Novikov, M. B. Povstyanoi, V. D. Krylov, G. V. Korothova, L. V. Lapshina and A. F. Kulik, *Izv. Akad. Nauk SSR, Ser. Khim.*, 1306 (1979).
[16] H. Petersen, *Synthesis*, 243 (1973).
[17] A. Einhorn, *Ann. Chem.*, **361**, 113 (1908).
[18] A. R. Butler and I. Hussain, *J. Chem. Soc., Perkin Trans. II*, 310 (1982).