

MESOMERIC BETAINIUM SALTS. SYNTHESIS, X-RAY ANALYSIS, AND ESIMS STUDIES OF TRIPOLAR PYRIMIDIN-4-OLATES AND PYRIMIDIN-4-AMINIDES

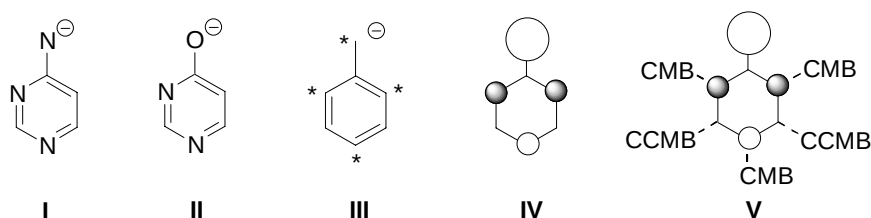
Andreas Schmidt^{*a} and Martin Nieger^b

) Technische Universität Clausthal, Institut für Organische Chemie, Leibnizstrasse 6, D-38678 Clausthal-Zellerfeld, Germany

b) Rheinische Friedrich-Wilhelms-Universität Bonn, Institut für Anorganische Chemie, Gerhard-Domagk-Strasse 1, D-53121 Bonn, Germany

Abstract - Reaction of tetrachloropyrimidine (**1**) with pyridine in acetone in the presence of sodium iodide yielded the pyrimidin-4-olate (**3**). Applying analogous reaction conditions to 4-amino substituted 2,5,6-trichloropyrimidine (**4a,b**) resulted in the formation of bispyridinium salts (**5a,b**) which yield aminides (**6a,b**) on deprotonation. As evidenced by means of UV spectroscopy and electron spray MS spectrometry, the title compounds (**3**) and (**6a,b**) form π -sandwich complexes in solution.

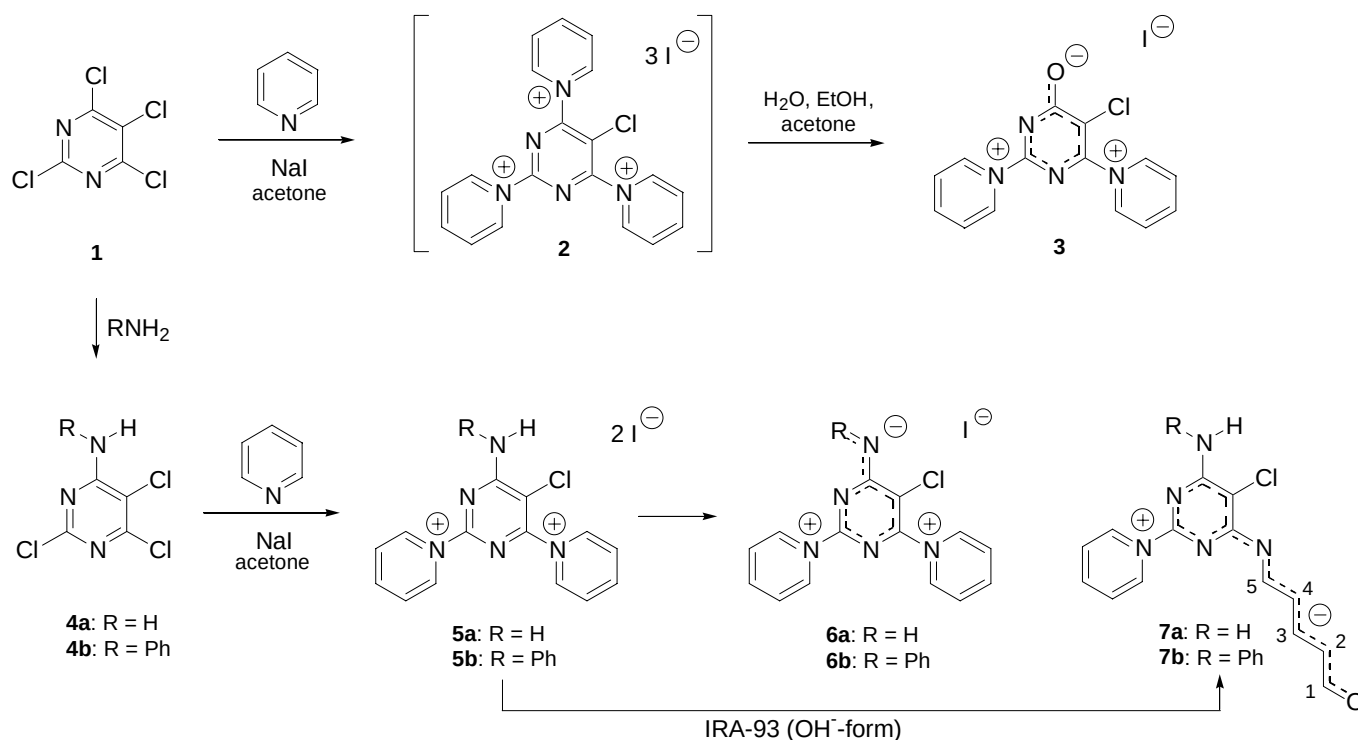
In contrast to the pyrimidin-4-aminide (**I**), the corresponding 4-olate moiety (**II**) is a well-known structure element of mesomeric betaines (MB).¹ Depending on the *union*² of positive partial structures to the isoconjugated benzyl anion (**III**), the design of distinct types of betaines is possible. Union to an electronically inactive atom, *i.e.* an unstarred atom in **III** and a nodal position of the HOMO **IV** results in cross-conjugated mesomeric betaines (CCMB), whereas union to an active position forms conjugated systems (CMB).³ Molecules with an odd number of positive and negative structure elements are hybrids between MB and heteroaromatic salts. In continuation of our interest in betaines⁴ we report here the synthesis, X-Ray analysis, and ESIMS studies of cationic tripolar representatives of these systems, *i.e.* mesomeric betainium salts.



Scheme 1

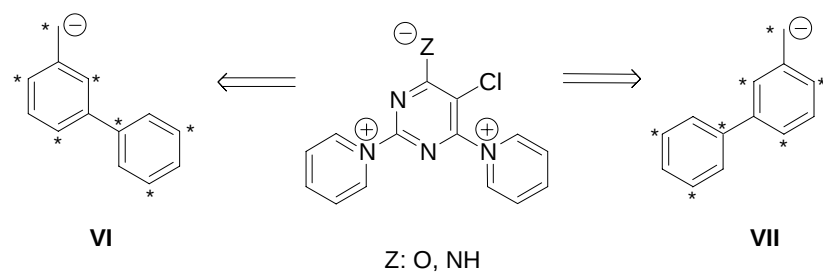
Treatment of tetrachloropyrimidine (**1**) with sodium iodide in anhydrous acetone resulted in the formation of a brown solution which is due to the partial or complete nucleophilic exchange of the 2,4,6-chlorine atoms to iodine.⁵ Addition of pyridine to the solution formed a yellow-orange precipitate which presumably consisted of the highly electrophilic tricationic species (**2**) which is not isolable.⁶ Heating at

reflux temperature for 1 h and subsequent quenching of the suspension with aqueous ethanol/acetone resulted in the formation of the heteroaromatic tripole 2,6-dipyridiniopyrimidin-4-olate iodide (**3**) (79%) in one single step.⁷ In contrast to that, applying analogous reaction conditions to the 4-amino substituted 2,5,6-trichloro-pyrimidines (**4a,b**) - readily available from **1** on treatment with ammonia and aniline, respectively⁸ - yielded 1,1'-(4-amino-5-chloropyrimidine-2,6-diyl)dipyridinium diiodides (**5a**) and 1,1'-(4-anilino-5-chloropyrimidin-2,6-diyl)dipyridinium diiodide (**5b**) in 74 and 62% yields, respectively. Attempts to deprotonate **5a,b** in aqueous ethanol to the tripoles (**6a,b**) using Amberlite® IRA-93 in its hydroxy form resulted in the pericyclic ring-cleavage to the purple colored *N*-(6-anilino-5-chloro-2-pyridiniopyrimidin-4-yl)-5-iminopenta-1,3-dienolate (**7b**) in 44% yield, whereas **7a** proved to be unstable and decomposed rapidly on the anion exchange resin.⁹ As evidenced by the coupling constants $J_{2,3} = 15.0$ and $J_{4,5} = 13.2$ Hz, **7b** adopts the *all-E* configuration in the pentadienolate side chain.¹⁰ Whereas **5a** could not be transformed to the tripole (**6a**), deprotonation of the phenylamino derivative (**5b**) to 2,6-dipyridiniopyrimidin-4-phenylaminide iodide (**6b**) was accomplished by potassium carbonate in anhydrous DMSO at room temperature in 82% yield. This observation is in accord to *Kröhnke's* rule which predicts increasing stability of ylides with increasing number of atoms involved in the delocalisation of the negative charge.¹¹ However, tripole (**6a**) unambiguously forms during ESIMS spectrometry. The novel heteroaromatic tripoles (**3**) and (**6a,b**) form π -sandwich complexes with iodide in solution (*vide infra*).



Scheme 2

The compounds (**7a,b**) – possessing an even number of positive and negative charges - are cross-conjugated mesomeric betaines CCMB. However, two positive and one negative charges are delocalized in separated parts of the common π -electron system in **3** and **6**, forming monocationic systems plus one external anion, respectively. The tripoles (**3**) and (**6**), mesomeric betainium salts, contain two *overlapped* partial structures of CCMB that are isoconjugated to the odd alternant hydrocarbon anions (**VI**) and (**VII**). Per definition,¹ they do not belong to the class of mesomeric betaines as they are charged.



Scheme 3

We performed a X-Ray single crystal structure analysis to unambiguously elucidate the structure of the mesomeric betainium salt **3**.¹² The ORTEP-plots and the elemental cell are presented in Figures 1, 2 and 3, respectively. Monoclinic single crystals were obtained by slow evaporation of a concentrated solution of **3** in water.

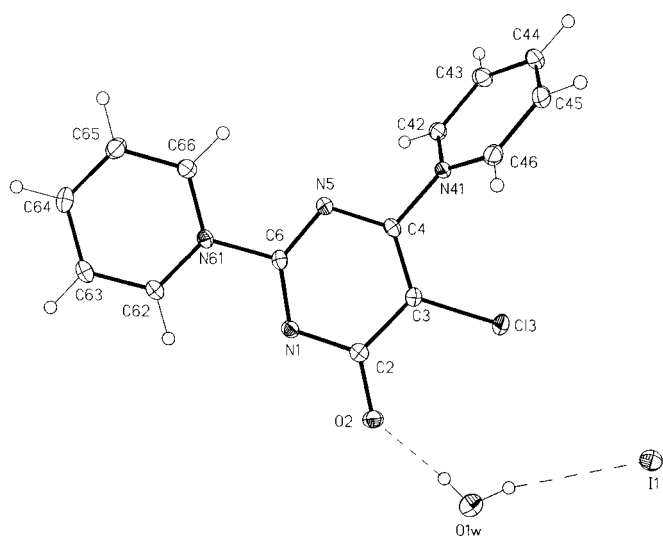


Figure 1

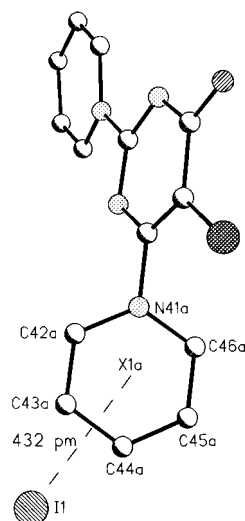


Figure 2

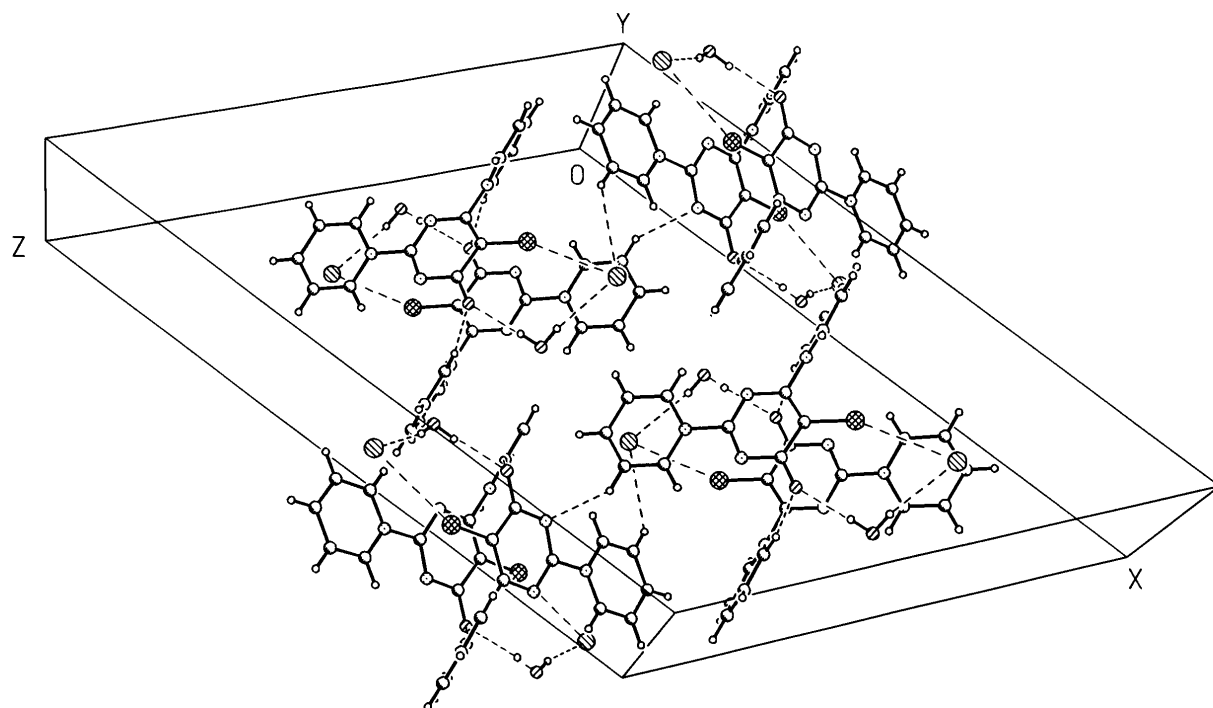


Figure 3

In the elemental cell, the tripole adopts a nonplanar conformation with the pyridinium substituents twisted by 9.96° and -57.0(2)° from the pyrimidin-4-olate plane. One molecule of water of crystallization is found per molecule of **3**. The larger torsion angle of the C(6)-bound pyridinium ring (crystallographic numbering in Figure 1: C4) is obviously due to steric hindrance to the C(5)-Cl atom (crystallographic numbering: Cl3). Thus, the charge-separation within the π -electron system is due to cross-conjugation as well as reduced *p*-overlap between the positively and negatively charged partial structures. As presented in Figure 2, the iodine anion is located in a distance of 432 pm from the center of the C(6)-bound pyridinium, so that in the solid state no π -interactions between anion and heteroaromatic π -electron sextet can be observed. Some selected bond lengths, bond angles, and torsion angles are given in Tables 1 and 2.

Table 1. Atom Nos. / Selected bond lengths [pm], bond angles [°], and torsion angles [°] of (**3**).

N(1)-C(6)	131.2(2)	C(4)-C(3)-C(2)	117.97(14)	C(6)-N(1)-C(2)-O(2)	-179.51(15)
N(1)-C(2)	137.1(2)	C(4)-C(3)-Cl(3)	124.41(12)	C(6)-N(1)-C(2)-C(3)	-0.4(2)
C(2)-O(2)	124.75(19)	N(5)-C(4)-C(3)	124.94(14)	O(2)-C(2)-C(3)-Cl(3)	0.5(2)
C(2)-C(3)	145.3(2)	N(5)-C(4)-N(41)	113.77(13)	N(1)-C(2)-C(3)-Cl(3)	-178.63(11)
C(3)-C(4)	136.1(2)	C(3)-C(4)-N(41)	121.30(14)	N(5)-C(4)-N(41)-C(42)	-56.99(18)
C(4)-N(5)	134.5(2)	N(1)-C(6)-N(61)	114.65(13)	C(3)-C(4)-N(41)-C(42)	122.99(17)
C(4)-N(41)	145.4(2)	N(5)-C(6)-N(61)	114.57(13)	N(1)-C(6)-N(61)-C(66)	167.36(14)
C(6)-N(61)	146.1(2)	C(42)-N(41)-C(4)	118.60(13)	N(5)-C(6)-N(61)-C(62)	70.04(14)
C(3)-Cl(3)	172.02(16)	C(66)-N(61)-C(6)	119.70(13)	N(1)-C(6)-N(61)-C(62)	-10.0(2)

Table 2. Hydrogen bonds of (**3**): Distances [pm] and angles [°].

D-H $\cdots$ A	d(D-H)	d(H $\cdots$ A)	d(D $\cdots$ A)	<(DHA)
O(1W)-H(1W1) $\cdots$ O(2)	83.2(17)	206.2(17)	289.06(17)	174(3)
O(1W)-H(1W2) $\cdots$ I(1)	82.6(17)	279.6(18)	360.58(14)	167(2)

However, in UV spectroscopy, with increasing solvent polarity the absorption maxima of **3** shift to shorter wavelengths ($\Delta\lambda_{\text{max}}(\text{CH}_2\text{Cl}_2/\text{MeOH}) = 30.2 \text{ nm}$). This effect of negative solvatochromism is indicative of a charge-separation in the ground-state of a molecule.¹⁵ In **3**, two effects can be differentiated. First, on electronic excitation electrons are shifted from the HOMO which is located in the pyrimidin-4-olate moiety, to the LUMO which is essentially located in the pyridinium substituent bound at C-6 of the central pyrimidine ring¹⁶ (Figure 4). As a consequence, the permanent dipole moment of the molecule decreases on electronic excitation. Second, it is known that iodide forms *charge-transfer* complexes with pyridinium rings.¹⁸ On electronic excitation, electron density is shifted from the iodide to the pyridinium rings. To investigate these two possibilities, we performed *electron spray ionization* MS spectrometry (ESIMS) in the positive mode on **3** as well as on **5a,b** in anhydrous acetonitrile at fragmentor voltages between 0 and 150 V. As a matter of fact, the monocationic associate (**8**) between two molecules of **3** and one iodide anion was unambiguously identified between fragmentor voltages of 0 and 90 V as a peak at $m/z = 697.0$. The base peak was found at 285.0 which corresponds to the tripole (**3**) without anion (Figure 5). As the ESI method exclusively allows the measurement of charged systems,¹⁹

we added 0.1 parts of 1% formic acid to the acetonitrile. However, **3** remained unprotonated, so that 1:1- π -interactions of the cation and the anion in **3** – which result in a neutral species - could not be detected. At higher fragmentor voltages, **3** decomposes under loss of the pyridinium rings as presented in the Scheme 4. The ESIMS spectra performed at fragmentor voltages of 0 and 120 V, respectively, are given in Figures 5 and 6.

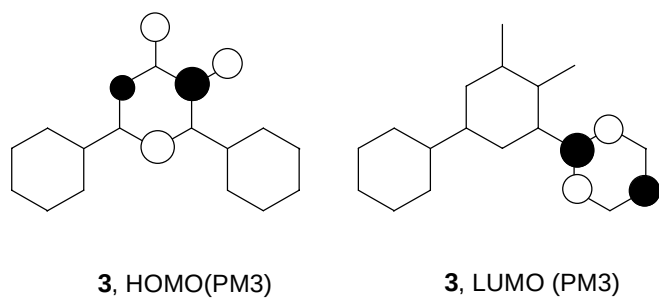


Figure 4

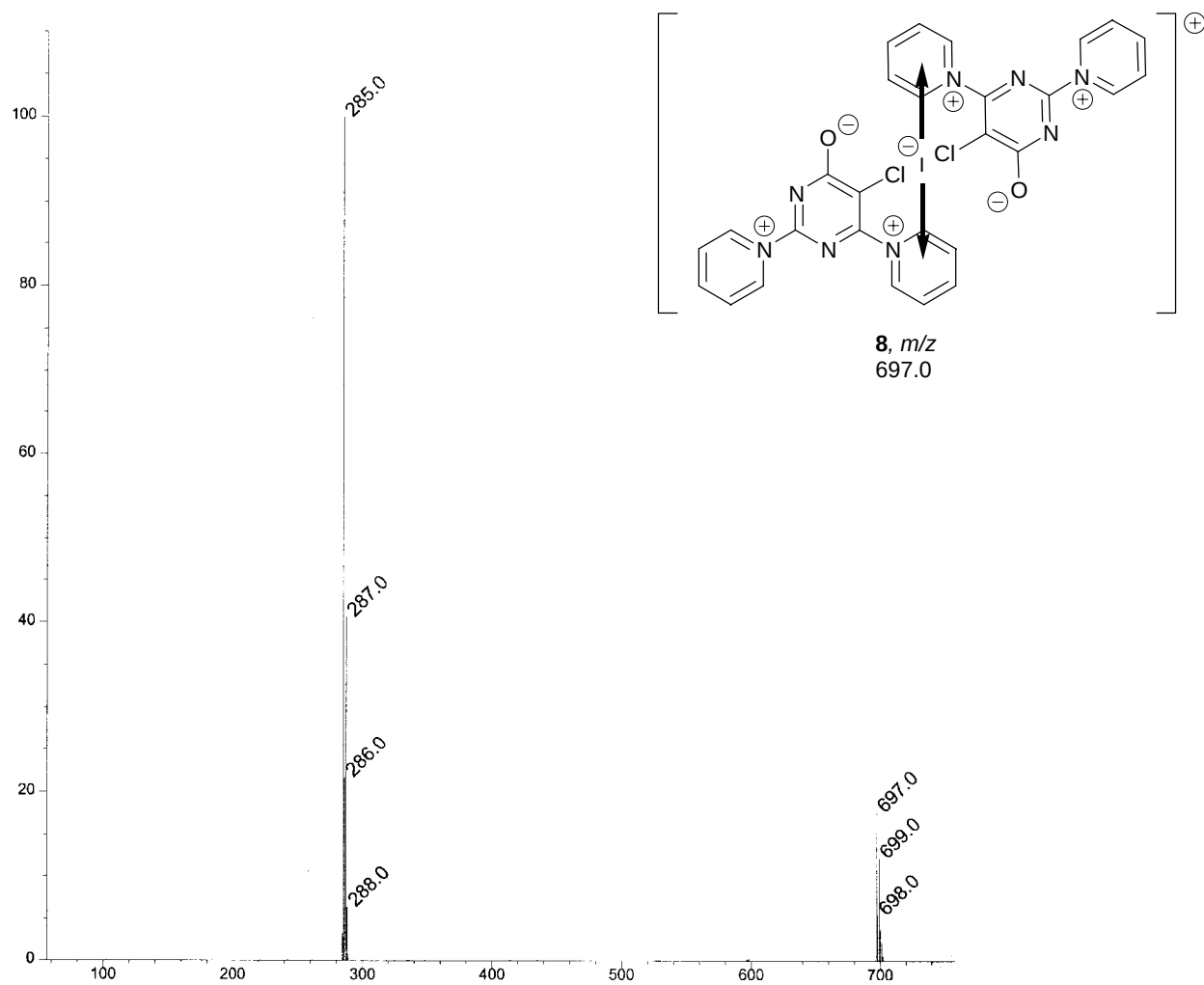


Figure 5

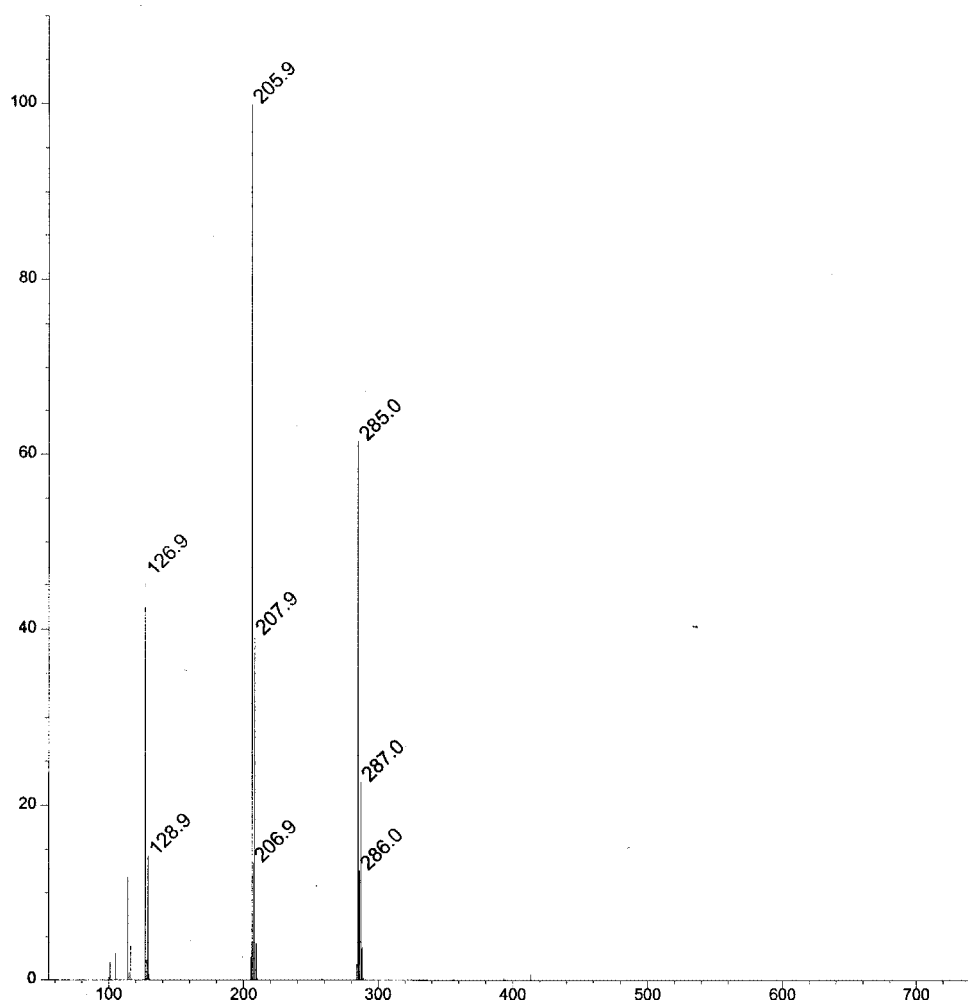
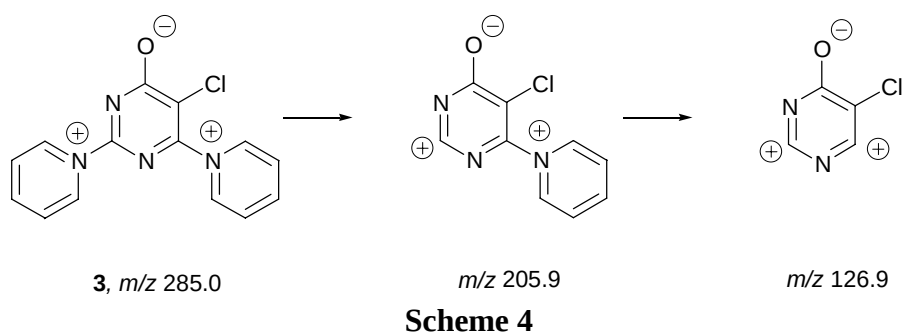
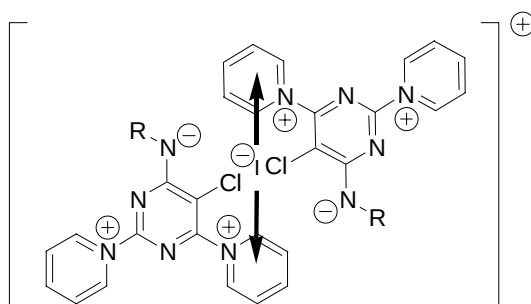


Figure 6

The dicationic 4-amino derivatives (**5a,b**), however, display a distinct behavior. At fragmentor voltages between 10 V and 40 V, the dicationic species (**5a,b**) are detectable at $M^{2+}/2 = 142.6$ and 180.6, respectively. At voltages between 80 and 200 V, the molecular peak of the tripoles (**6a,b**) increase gradually and reach a maximum at 150 V, whereas the peak of **5a,b** disappears. Parallely, the peak of the π -complexes (**9a,b**) at $m/z = 695.2$ and 847.2 develop. Obviously, the formation of π -complexes is dependent on the tripole concentration and on the fragmentor voltage. These results gain insights into the interesting supramolecular properties of the novel class of mesomeric betainium salts.



9a: R = H, m/z 695.2
9b: R = Ph, m/z 847.2

Scheme 5

ACKNOWLEDGEMENTS

Prof. Dr. E. Niecke, Prof. Dr. K. H. Dötz, and Prof. Dr. F. Vögtle, university of Bonn, are gratefully acknowledged for providing the X-ray crystallography facilities. The Deutsche Forschungsgemeinschaft (DFG) and the Fonds der Chemischen Industrie (FCI) is gratefully acknowledged for financial support.

REFERENCES AND NOTES

- W. D. Ollis, S. P. Stanforth, and C. A. Ramsden, *Tetrahedron*, 1985, **41**, 2239.
- M. J. S. Dewar, *The Molecular Orbital Theory of Organic Chemistry*, McGraw-Hill, New York, 1969; M. J. S. Dewar and R. C. Dougherty, *The PMO Theory of Organic Chemistry*, Plenum Press, New York, 1975; W. D. Ollis and C. A. Ramsden, *Adv. Het. Chem.*, 1976, **19**, 1.
- K. T. Potts, P. M. Murphy, and W. R. Kuehnling, *J. Org. Chem.*, 1988, **53**, 2889.
- M. Mäkinen, A. Schmidt, and P. Vainiotalo, *Eur. J. Mass Spectrom.*, 2000, **6**, 259; A. Schmidt, M. K. Kindermann, and M. Nieger, *Heterocycles*, 1999, **51**, 237; A. Schmidt and M. Nieger, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1325; A. Schmidt, M. K. Kindermann, P. Vainiotalo, and M. Nieger, *J. Org. Chem.*, 1999, **64**, 9499; A. Schmidt and M. K. Kindermann, *J. Org. Chem.*, 1998, **63**, 4636; A. Schmidt and M. K. Kindermann, *J. Org. Chem.*, 1997, **62**, 3910; A. Schmidt, A. Hetzheim, and D. Albrecht, *Heterocycles*, 1996, **43**, 2153.
- D. J. Brown, in *Comprehensive Heterocyclic Chemistry*, ed. by A. R. Katritzky and C. W. Rees, Pergamon Press, New York, 1984, Vol. 3, pp. 57 – 155.
- C-5-Unsubstituted 2,4,6-tris(hetarenium)pyrimidines, however, are stable at room temperature: A. Schmidt and A. Hetzheim, *Tetrahedron*, 1997, **53**, 1295.
- Selected spectroscopic data (all NMR in DMSO- d_6): **3**, mp > 165°C (decomp), ^1H NMR: δ = 8.29 (t, J = 6.9 Hz, 2H), 8.47 (t, J = 6.9 Hz, 2H), 8.87 (dd, J = 6.9 and 7.5 Hz, 1H), 8.97 (t, J = 6.9 Hz, 1H), 9.53 (dd, J = 6.9 and 1.2 Hz, 2H), 9.93 (dd, J = 6.9 and 1.2 Hz, 2H); UV: $\lambda_{\text{max}}(\text{CH}_2\text{Cl}_2)$ = 358.90 nm; $\lambda_{\text{max}}(\text{MeCN})$ = 343.00 nm; $\lambda_{\text{max}}(\text{MeOH})$ = 328.70 nm. **5b**, mp > 300°C (decomp), ^1H NMR: δ = 11.00 (s, 1H), 9.84 (d, J = 6.8 Hz, 2H), 9.64 (d, J = 6.8 Hz, 2H), 9.10 (t, J = 7.9 Hz, 1H), 8.95 (t, J = 7.8 Hz, 1H), 8.59 (m, 2H), 8.36 (m, 2H), 7.73 (m, 2H), 7.55 (m, 2H), 7.40 (t, J = 7.3 Hz, 1H). **6b**, mp > 300°C, ^1H NMR: δ = 9.68 (d, J = 5.9 Hz, 2H), 9.55 (d, J = 5.7 Hz, 2H), 8.97 (t, J = 7.9 Hz, 1H), 8.84 (t, J = 7.6 Hz, 1H), 8.48 (m, 2H), 8.28 (m, 2H), 7.33 (m, 2H), 7.24 (m, 1H), 7.02 (m, 2H). **7b**, mp > 300°C, ^1H NMR: δ = 10.56 (s, 1H), 9.90 (dd, J = 6.9 and 1.2 Hz, 2H), 9.48 (d, J = 8.1 Hz, 1H, 1-H), 8.88 (tt, J = 9.0 and 1.2 Hz, 1H), 8.33 (m, 3H, 5-H and H_{ar}), 7.61 (d, J = 7.5 Hz, 2H), 7.45 (t, J = 7.5 Hz, 2H), 7.34 (m, 1H, 3-H), 7.23 (t, J = 7.5 Hz, 1H), 6.58 (dd, J = 13.2 and 11.7 Hz, 1H, 4-H), 6.11 (dd, J = 15.0 and 8.1 Hz, 1H, 2-H).
- H. Ackermann and P. Dussy, *Helv. Chim. Acta*, 1962, **155**, 1683.
- 7a** is detectable by ^1H NMR spectroscopy together with decomposition products.

10. K. E. Wilzbach and D. J. Rausch, *J. Amer. Chem. Soc.*, 1970, **92**, 2178.
11. I. Zugravesku and M. Petrovanu, *N-Ylid Chemistry*, McGraw Hill, New York, 1966.
12. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-158542. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk). Some crystal data of **3**: C₁₄H₁₂N₄O₂Cl · I; M = 430.63; space group C2/c (no. 15); dimensions 0.50 x 0.30 x 0.25 mm³, a = 25.0374(6), b = 8.0499(2), c = 19.6881(5) Å; β = 128.975(2) °; V = 3081.75(13) Å³, D_c = 1.856 MG m⁻³, Z = 8, μ(MoK_α) = 2.264 mm⁻¹; T = 123(2) K; F(000) = 1680, 22269 reflections were collected in a Nonius KappaCCD diffractometer (2Θ_{max.} = 56.4 °, -32 ≤ h ≤ 33, -10 ≤ k ≤ 10, -26 ≤ l ≤ 26), 3795 symmetry independent reflections (R_{int} = 0.0344) were used for the structure solution (direct methods)¹³ and refinement (full-matrix least-squares on F²,¹⁴ 208 parameters, 2 restraints), non-hydrogen atoms were refined anisotropically, H atoms localized by difference electron density, aromatic hydrogen atoms were refined using a riding model, other free; wR2 (all data) = 0.046 [R1 = 0.018 for 3570 I>2σ(I)].
13. G. M. Sheldrick, SHELXS-97, *Acta Cryst.*, 1990, A46, 467.
14. G. M. Sheldrick, SHELXL-97, University of Göttingen, 1997.
15. C. Reichardt and E. Harbusch-Görnert, *Liebigs Ann. Chem.*, 1983, 721.
16. Results of PM3 calculations using MOPAC 6.0¹⁷ on a CONVEX 3440.
17. J. J. P. Stewart, *QCPE*, No 455, Department of Chemistry, Bloomington, IN, 1989.
18. E. M. Kosower, *J. Am. Chem. Soc.*, 1958, **80**, 3253.
19. J. B. Fenn, M. Mann, C. K. Meng, S. F. Wong, and C. M. Whitehouse, *Science*, 1989, **246**, 64.