Pergamon

Tetrahedron Letters, Vol. 35, No. 19, pp. 3059-3062, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0465-A

A Synthetic Pathway to Macrocyclic and Optically Active Pentamethinium Salts

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Abstract: The design of new types of azodyes with optical activity and macrocyclic structure was achieved by the generalization of the reaction of stabilized carboxonium ions with various primary and secondary amino compounds.

The conjugated organic polymethine salts (azodyes), and in particular the pentamethinium salts are widely used industrially. Numerous applications in chemistry (dyes, photochemical sensitizers for photographic emulsions...) and physics (in optical devices, non linear optics and erasable laser disks) have been developed and more than 500 papers including patents were published on these subjects in 1992 (Chem. Abs. Source).

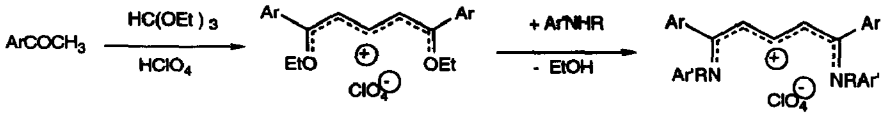
However the design of new structures including macrocycles and the synthesis of chiral systems leading to new physical (*i.e.* nematic phases) or chemical properties (chiral, anionic and molecular recognition) is currently limited by the need to improve methods to incorporate these building blocks in structures designed to provide new properties in bioorganic or material fields.

We recently discovered a new method[1] for the synthesis of pentamethinium salts starting from pyrylium salts and tricoordinated *tris*dialkylaminoarsanes and stibanes. The method is very useful to obtain symetrically aminated and highly substituted pentamethinium salts on the pentacarbonic chain. Somes limitations in this method have been identified: the accessibility of the *tris*(dialkylamino)arsanes or stibanes and the obtention of symmetrical products only.

We presents here the first results of a new competitive synthetic pathway avoiding these problems.

A classic method of synthesis of 2,6 symmetrically disubstituted pyrylium salts is based on the reaction of arylmethylketones with triethylorthoformiate in acidic medium.[2] Mezheritskii and coll.[3] described the isolation of a carboxonium ion intermediate[4] during this synthesis leading to crowded polycyclic pyridines.

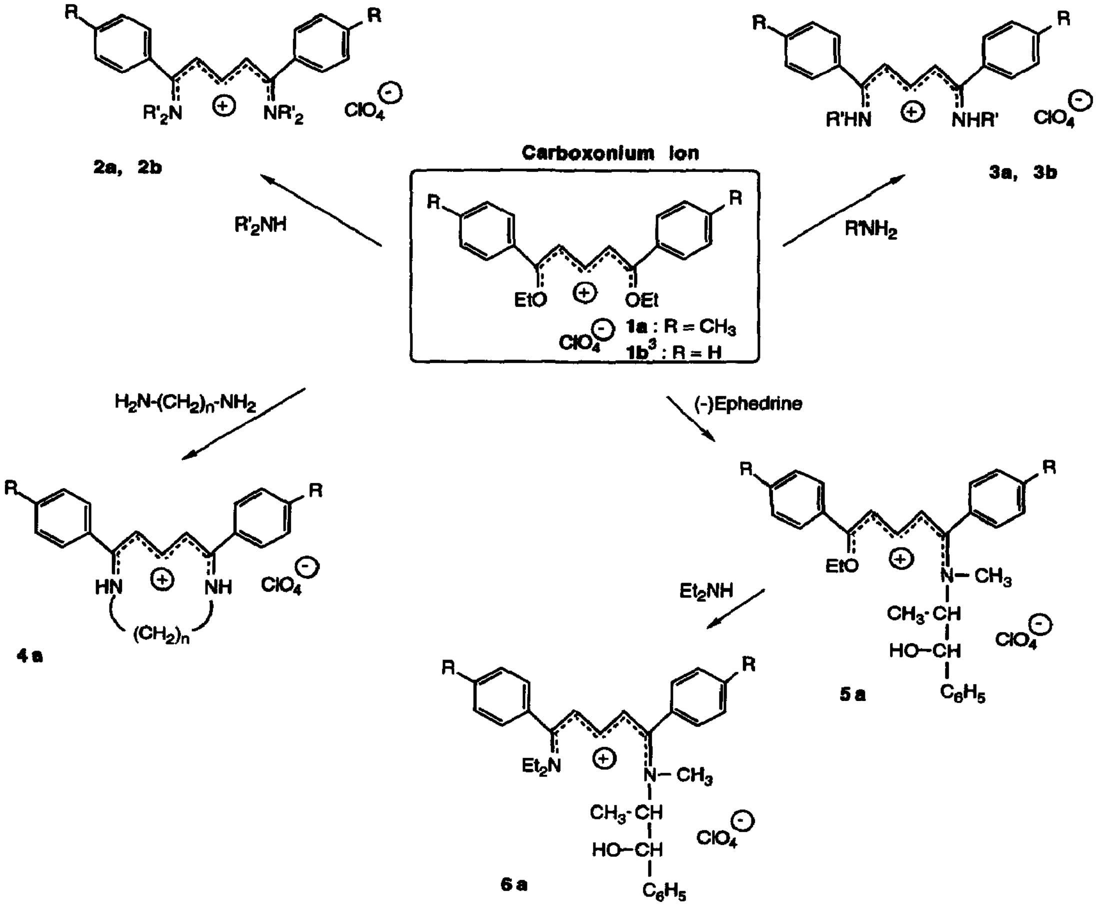
Mezheritskii achieved the characterization of the intermediate by the reaction of secondary aromatic amines to obtain the pentamethinium derivative.



They claimed that the reaction was limited to aromatic amines and that it was not possible to stop the reaction at the formation of the monoimmonium salt.

However, as our synthetic objectives were to obtain either dissymetric (for non linear optic) or macrocyclic (for anionic recognition) salts, we decided to re-examine the synthesis and the reactivity of various carboxonium perchlorates like **1a** and **1b**.

The general reaction scheme is summarized below :



As shown the reaction of various aliphatic amines leads to new dyes. In particular the use of diamines should be noted as macrocyclic pentamethinium salts like **4a** as well as polymeric ones can be obtained.

Another interesting feature is the reaction of ephedrine, optically active aminoalcohol, which lead to the monoimmonium compounds **5a**. The reactivity of the second ethoxy group is lowered either by steric hindrance or by internal coordination. Compound **5a** presents a high rotatory power (+124°) as compared with the starting ephedrine (-42°) indicating a special intra or supramolecular organisation. In a second step it reacts with another amine to give dissymmetric compound with a largely enhanced rotatory power (+321°). Same results are obtained with (+)ephedrine (**5a'**, **6a'**).

Thus the reactivity of the carboxonium ions may be adjusted to the design of the desired dissymmetric, optically active, or macrocyclic products and this work is currently beeing extended to other nucleophile reactive species.

Typical reaction processes together with analytical and spectrochemical data are gathered in notes.[5]

References and notes

1. Madaule, Y.; Ramarohetra, M.; Wolf, J.G.; Declercq, J.P.; Dubourg, A.; *Angewandte Chem.*, **1991**, *103*, 1044-1046; *Angewandte Chem. Int. Ed. Eng.*, **1991**, *30*, 994-996
Madaule, Y.; Ramarohetra, M.; Wolf; *Tetrahedron Lett.*, **1992**, *33*, 1741-42
2. Balaban, A.T.; *Org.Synth.Mod.Trends Proc.IUPAC Symp.6th* , **1986**, (pub 1987), 263-274 and references therein.
3. Pikus, A.L.; Feigel'man,V.M.; Mezheritskii,V.V.; *Zh.Org.Khim.*, **1989**, *25*, 2603-08
4. A new stabilized carboxonium ion was recently described in this review:
Lüning, U.; Baumstark, R.; *Tetrahedron Lett.*, **1993**, *34*, 5059-62

5. General experimental procedure and physical results

All synthesis were carried out under an argon atmosphere at room temperature. Pentamethinium salts were obtained by addition of the amine in CH_3CN solution on the carboxonium intermediate. After 1 hour stirring, the solvant is evaporated. After several washes in pentane, the residue is crystallised in ethanol. The amines used are diethylamine (**2a, 2b**), methoxyethylamine (**3a, 3b**), (-)ephedrin (**5a**), (-)ephedrin and diethylamine (**6a**), (+)ephedrin (**5a'**), (+)ephedrin and diethylamine (**6a'**);

Very dangerous explosions were recently reported with perchlorates salts handling. However in our case owing to the fact that experiments are performed in limited scale we never observed any problem. Nevertheless we are currently trying to avoid the use of ClO_4^- by replacement with BF_4^- or $CF_3SO_3^-$. Following previously published works, no changes in reactivity or structure are expected in these cases.

1a: 1,5-diethoxy-1,5-bis(paramethylphenyl) pentadienylium perchlorate

Greenish crystals. Yield: 83% . m.p. = 180-190 °C (dec.). ^1H NMR (200 MHz, CD_3CN): δ ppm, J Hz 1.49 (t, 6H, $\underline{CH}_3$-CH_2); 2.38 (s, 6H, $\underline{CH}_3C_6H_4$); 4.55 (q, 4H, $\underline{CH}_3$-CH_2); 7.33 and 7.52 (4H, AA'BB', $J_{AB} = J_{A'B'} = 8$); 6.86 and 8.03 (3H, A_2X, $J_{AX} = 13$). ^{13}C NMR (50.32 MHz, CD_3CN): δ ppm 14.49 ($\underline{C}H_3$-CH_2); 21.83 ($\underline{C}H_3$-C_6H_4); 71.54 (CH_3-$\underline{C}H_2$); 112.08 (C_2-C_4); 130.6-146.78 (C_6H_5); 175.50 (C_3); 190.36 (C_1-C_5). IR (KBr): ν cm^{-1} 1085 (Cl-O)

2a: 1,5-bis(diethylamino)-1,5-bis(paramethylphenyl)pentadienylium perchlorate

Orange crystals. Yield: 60%. m.p. = 276°C. ^1H NMR (200 MHz, CD_3CN): δ ppm, J Hz 1.01 (t, 6H, $\underline{CH}_3$-CH_2); 1.32 (t, 6H, $\underline{CH}_3$-CH_2) 2.34 (s, 6H,$\underline{CH}_3CH_4$); 3.15 (q, 4H, CH_3-$\underline{CH}_2$); 3.63 (q, 4H, CH_3-$\underline{CH}_2$); 5.98-6.12 (3H, A_2B, $J_{AB} = 13$); 6.85 and 7.11 (AA'XX', $J_{A'X'} = J_{AX} = 8$). ^{13}C NMR (50.32 MHz, CD_3CN): δ ppm 12.66 ($\underline{C}H_3$-CH_2); 14.29 ($\underline{C}H_3$-CH_2); 21.46 ($\underline{C}H_3$); 45.70 ($\underline{C}H_2$-CH_3); 48.95 (CH_3-$\underline{C}H_2$); 106.1 (C_2-C_4); 129.06-140.71 (C_6H_5); 162.93 (C_3); 170.38 (C_1-C_5). IR (KBr): ν cm^{-1} 1087 (Cl-O). M.S. (DCI, NH_3): 389 M^+. Anal. Calcd. for: $C_{27}H_{27}N_2ClO_4$; C 66.31; H 7.63; N 5.73; O 13.09 Found: C, 66.00; H, 7.58; N, 5.60; O, 13.25. UV (CH_2Cl_2): $\lambda_{max} = 443$ nm; $\varepsilon_{max} = 107400$

2b: 1,5-bis(diethylamino)-1,5-bis(phenyl)pentadienylium perchlorate

Yellow crystals; Yield: 60%; m.p. = 276°C ^1H NMR (200 MHz, CD_3CN): δ ppm, J Hz 1.00 (t, 6H, $\underline{CH}_3$-CH_2); 1.30 (t, 6H, $\underline{CH}_3$-CH_2); 3.10 (q, 4H, CH_3-$\underline{CH}_2$); 3.60 (q, 4H, CH_3-$\underline{CH}_2$); 5.97-6.17 (3H, A_2B $J_{AB} = 13$); 6.99 (m, 4H, C_6H_5); 7.30 (m, 6H, C_6H_5). ^{13}C NMR (50.32 MHz, CD_3CN): δ ppm 12.68 ($\underline{C}H_3$-CH_2); 14.25 ($\underline{C}H_3$-CH_2); 45.77 ($\underline{C}H_2$-CH_3); 49.01 (CH_3-$\underline{C}H_2$); 106.25 (C_2-C_4); 129.06-133.93 (C_6H_5); 162.93 (C_3); 170.38 (C_1-C_5). IR (KBr): ν cm^{-1} 1094 (Cl-O). M.S. (DCI, NH_3): 361 M^+. Anal. Calcd. for : $C_{25}H_{33}N_2ClO_4$: C 65.14; H 7.22; N6.08; O 13.88 Found: C, 64.90; H, 7.17; N, 5.96; O, 14.31.
UV (CH_2Cl_2): $\lambda_{max} = 444$ nm; $\varepsilon_{max} = 111600$

3a:1,5-bis(methoxyethylamino)-1,5-bis(paramethylphenyl)pentadienylium perchlorate

Yellow crystals. Yield: 70%. m.p. = 137°C. ^1H NMR (200 MHz, CD_3CN): δ ppm, J Hz 2.35 (s, 6H, $\underline{CH}_3$-C_6H_4); 3.33 (s, 6H, $\underline{CH}_3O$); 3.63 (s, 8H,CH_2); 6.18 (d, 2H, A_2X, $J_{AX} = 14$); 7.00-7;30 (m, 10 H, C_6H_4 + A_2X). ^{13}C NMR (50.32 MHz, CD_3CN): δ ppm 21.44 ($\underline{C}H_3$-C_6H_4); 45.51 (CH_2N); 59.10 ($\underline{C}H_3O$); 70.24 ($\underline{C}H_2O$); 103.93 (C_2-C_4); 130.26-131.94-142.93 (C_6H_4); 163.32 (C_3); 170.91 (C_1-C_5). IR (KBr): ν cm^{-1}

3293 (N-H); 1107 (Cl-O). M.S. (DCI, NH_3): 393 M^+. Anal. Calcd. for: $C_{25}H_{33}N_2ClO_6$: C 60.91; H 6.75; N 5.68. Found : C, 61.06; H, 6.86; N, 5.64. UV (CH_2Cl_2): λ_{max} = 439 nm; ε_{max} = 73207

3b: 1,5-bis(methoxyethylamino)-1,5-bis(phenyl)pentadienylium perchlorate

Yellow crystals. Yield: 75% . m.p. = 146°C. ^1H NMR (200 MHz, CD_3CN): δ ppm, J Hz 3.34 (s, 6H, $\underline{CH}_3$); 3.64 (s, 8H, $\underline{CH}_2$) 6.22 and 7.09 (m, , 3H, A_2X, J_{AX} = 14); 7.21-7.55 (m, 12 H, C_6H_5). ^{13}C NMR (50.32 MHz, CD_3CN): δ ppm 45.57 (CH_2N); 59.11 ($\underline{C}H_3O$); 70.21 ($\underline{C}H_2O$); 104.18 (C_2-C_4); 129.63-134.75 (C_6H_5); 163.32 (C_3); 170.93 (C_1-C_5). IR (KBr): ν cm^{-1} 3240 (N-H); 1073 ($\nu_{Cl\text{-}O}$). M.S. (DCI, NH_3): 365 M^+. Anal. Calcd. for: $C_{23}H_{29}N_2ClO_6$; C, 59.42; H 6.29; N 6.03; O 20.65.Found : C, 59.38; H, 6.28; N, 5.89; O,20.82. UV (CH_2Cl_2): λ_{max} = 435 nm; ε_{max} = 77545

4a: N,N'-octamethylen-1,5-diamino-1,5-bis(paramethylphenyl)pentadienylium perchlorate

Yellow crystals. Yield: 72%. m.p. = 191°C (dec.). ^1H NMR (200 MHz , DMSO-d_6): δ ppm, 1.37 (m, 8H, $(CH_2)_4$); 1.68 (m, 4H, $\underline{CH}_2$-$(CH_2)_4$); 2.33 (s, 6H, $\underline{CH}_3C_6H_4$) ;3.41 (m, 4H, $\underline{CH}_2$-NH-); 6.17 (m, 1H, A_2X); 6.80-7.44 (m, 10H,arom+methine A_2X); 9.17 (2H, NH). ^{13}C NMR (50.32 MHz, DMSO-d_6): δ ppm 20.74 ($\underline{CH}_3$-C_6H_4); 26.30; 27.87 and 28.52 ($(CH_2)_6$); 44.07 ($\underline{CH}_2$-NH); 102.18 (C_2-C_4); 128.87-140.64 (C_6H_5); 160.15 (C_3); 168.15 (C_1-C_5). IR(KBr): ν cm^{-1} 3288 (N-H); 1097 (Cl-O). S.M.(DCI, NH_3): 387 M^+ and evidences of oligomeric species. Anal. Calcd. for: $C_{27}H_{35}N_2O_4Cl$: C, 66.59; H, 7.24; N, 5.75; O, 13.14. Found : C, 65.89; H, 7.24; N, 7.24; O, 12.82. UV (CH_2Cl_2): λ_{max} = 436 nm; ε_{max} = 49756

5a: 1-ethoxy-5-amino([1R,2S]-N-(2-hydroxy-1-methyl-2phenyl)-Nmethyl)-1,5-bis(paramethylphenyl) pentadienylium perchlorate

Orange crystals. Yield: 68%. m.p. = 192°C. ^1H NMR (80 MHz, CD_3CN): δ ppm, J Hz 1.35 (d, 3H, ^3J = 6.8, $\underline{CH}_3$-CH); 1.39 (t, 3H, ^3J = 7, $\underline{CH}_3$-CH_2); 2.32 (s, 3H, $\underline{CH}_3$-C_6H_4); 2.38 (s, 3H, $\underline{CH}_3$-C_6H_4); 3.52 (s, 3H, N-CH_3); 3.75-4.11 (m, 2H, CH); 4.19 (q, 2H, ^3J = 7, CH_3-$C\underline{H}_2$); 4.85 (m, 1H, OH); 6.09-6.78 (A_2B, 3H); 6.91-7.4 (m, 13H, C_6H_5). ^{13}C NMR (50.32 MHz, CD_3CN): δ ppm 13.42 ($\underline{C}H_3$-CH_2); 14.57 ($\underline{C}H_3$-CH); 21.47 ($\underline{CH}_3C_6H_4$); 37.07 (N-CH_3); 67.48 (CH_3-$\underline{C}H$); 67.61 (CH_3-$\underline{C}H_2$); 75.05 (CH-OH); 104.7 (C_4); 117.05 (C_3); 127.01-142.6 (C_6H_5); 176.45 (C_5); 177.66 (C_1). IR(KBr): ν cm^{-1} 3432 (O-H); 1116 (Cl-O). M.S.(DCI, NH_3): 454 M^+. $[\alpha]^{20}$ = + 124° (c = 0.053, CH_3CN, Hg lamp 578 nm). Anal. Calcd. for: $C_{31}H_{36}NO_6Cl$: C, 67.20; H, 6.52; N, 2.53. Found: C, 67.20; H, 6.55; N, 2.32.UV (CH_2Cl_2): λ_{max} = 422 nm; ε_{max} = 44398

5a': 1-ethoxy-5-amino([1S,2R]-N-(2-hydroxy-1-methyl-2phenyl)-Nmethyl)-1,5-bis(paramethylphenyl) pentadienylium perchlorate

$[\alpha]^{20}$ = - 121° (c = 0.056, CH_3CN, Hg lamp 578 nm)

6a: 1-diethylamino([1R,2S]-N-(2-hydroxy-1-methyl-2phenyl)-Nmethyl)-1,5-bis(paramethylphenyl) pentadienylium perchlorate

Orange powder. Yield: 65%. m.p. = 90°. ^1H NMR (200 MHZ , CD_3CN): δ ppm, J Hz 1.00 (t, 3H, $\underline{CH}_3$-CH_2); 1.30 (t, 3H, $\underline{CH}_3$-CH_2); 1.24 (d, 2H,^3J = 7, CH_3-CH); 2.32 (s, 3H, $\underline{CH}_3C_6H_4$); 2.34 (s, 3H, $\underline{CH}_3C_6H_4$); 3.15 (s, 3H, N-CH_3); 3.15 (q, 2H, CH_3-$C\underline{H}_2$); 3.65 (q, 2H, CH_3-$C\underline{H}_2$); 4.66 (q, 1H, OH); 5.79-6.19 (A_2B, 3H); 6.70-7.49 (m, 13H, C_6H_5, C_6H_4). ^{13}C NMR (50.32 MHz, CD_3CN): δ ppm 12.73 ($\underline{C}H_3$-CH_2); 14.21 ($\underline{C}H_3$-CH_2); 14.35 ($\underline{C}H_3$-CH); 21.44 ($\underline{CH}_3C_6H_4$); 34.74 (N-CH_3); 45.89 (CH_3-$\underline{C}H_2$); 49.24 (CH_3-$\underline{C}H_2$); 64.48 (CH_3-$\underline{C}H$); 75.62 (CH-OH); 105.82 (C_2); 107.21 (C_4); 127.20-142.96 (C_6H_5); 163.24 (C_3); 171.06 and 171.26 (C_1-C_5). IR(KBr): $\nu_{cm^{-1}}$ (Cl-O)1094. M.S (DCI, NH_3): 481 M. $[\alpha]^{20}$ = + 321° (c = 0.0526, CH_3CN, Hg lamp 578 nm). Anal. Calcd. for: $C_{31}H_{36}NO_6Cl$: C, 67.57; H, 7.21; N, 4.7. Found : C, 68.20; H, 7.15; N, 64.82. UV (CH_2Cl_2): λ_{max} = 422 nm; ε_{max} = 49077

6a': 1-diethylamino([1S,2R]-N-(2-hydroxy-1-methyl-2phenyl)-Nmethyl)-1,5-bis(paramethylphenyl) pentadienylium perchlorate

$[\alpha]^{20}$ = - 323° (c = 0.053, CH_3CN, Hg lamp 578 nm)

(*Received in France* 26 *January* 1994; *accepted* 2 *March* 1994)