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[15] Crystal structure analyses of **4** – **6** were performed on STOE IPDS diffractometers with $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å) for **5** and $Ag_{K\alpha}$ radiation ($\lambda = 0.56087$ Å) for **4** and **6**. The structures were solved by direct methods with the program SHELXS-97,[19a] and full-matrix least-squares refinement on F^2 in SHELXL-97[19b] was performed with anisotropic displacements for non-hydrogen atoms. Hydrogen atoms were located in idealized positions and refined isotropically according to the riding model. **4**·0.5 CH_2Cl_2: $C_{10.5}H_{16}Cl_2CuFeP_5$, $M_r = 487.37$, crystal dimensions $0.20 \times 0.14 \times 0.04$ mm^3, monoclinic, space group $C2/c$ (No. 15), $a = 20.184(4)$, $b = 16.885(3)$, $c = 13.860(3)$ Å, $\beta = 129.33(3)^\circ$, $T = 203(2)$ K, $Z = 8$, $V = 3653.7(13)$ Å^3, $\rho_{calcd} = 1.772$ Mg m^{-3}, $\mu = 1.382$ mm^{-1}, 3831 independent reflexes ($R_{int} = 0.0365$, $2\theta_{max} = 42^\circ$), 3128 observed with $F_o = 4\sigma(F_o)$, 190 parameters, $R_1 = 0.0370$, $wR_2 = 0.0974$. **5**: $C_{10}H_{15}BrCuFeP_5$, $M = 489.37$, crystal dimensions $0.20 \times 0.20 \times 0.01$ mm^3, tetragonal, space group $P\bar{4}2_1c$ (No. 114), $a = b = 12.147(2)$, $c = 21.859(4)$ Å, $T = 200(1)$ K, $Z = 8$, $V = 3225.2(9)$ Å^3, $\rho_{calcd} = 2.016$ Mg m^{-3}, $\mu = 5.170$ mm^{-1}, 3152 independent reflexes ($R_{int} = 0.0777$, $2\theta_{max} = 52^\circ$), 2681 observed with $F_o = 4\sigma(F_o)$, 168 parameters, $R_1 = 0.0345$, $wR_2 = 0.0809$. **6**: $C_{10}H_{15}CuFeIP_5$, $M_r = 536.36$, crystal dimensions $0.10 \times 0.10 \times 0.10$ mm^3, tetragonal, space group $P\bar{4}2_1m$ (No. 113); $a = b = 12.372(2)$, $c = 11.241(2)$ Å, $T = 203(1)$ K, $Z = 4$, $V = 1720.6(5)$ Å^3, $\rho_{calcd} = 2.071$ Mg m^{-3}, $\mu = 2.258$ mm^{-1}, 8297 independent reflexes ($R_{int} = 0.1663$, $2\theta_{max} = 40^\circ$), 1475 observed with $F_o = 4\sigma(F_o)$; 94 parameters, $R_1 = 0.0496$, $wR_2 = 0.1312$. CCDC 175139 – 175141 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Center, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

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Structure and Synthesis of the Natural Heptachloro-1′-methyl-1,2′-bipyrrole (Q1)

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A number of anthropogenic organohalogen compounds such as polychlorinated biphenyls (PCBs), polychlorinated dibenzo-*p*-dioxins (PCDDs), and chlorinated pesticides (DDT, toxaphene, lindane, and others) are recognized as persistent, bioaccumulative, and toxic chemicals.[1] The majority of these substance classes are ubiquitously distributed in the environment, and long-term exposure is one of the major threats to humans and wildlife from these substances.[2] The scientific interest in anthropogenic halogenated compounds is reflected in the fate of these contaminants and related compounds in the environment, which was reported on in more than 1000 publications in the past 40 years.

More than 3600 naturally occurring organohalogens have been identified to date.[3] The total amount of these compounds is not known, but is probably higher than currently known.[4] It was thought that these natural products are neither persistent nor lipophilic, and thus do not accumulate in the lipids of higher organisms. This hypothesis is currently under reconsideration, as recent work has resulted in the detection of a series of unknown halogenated compounds that

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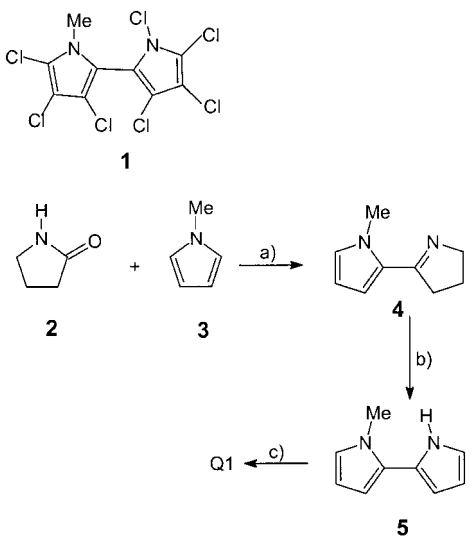
  1433-7851/02/4110-1740 $ 20.00+.50/0

can reach significant levels in organisms. Some of these compounds were supposed to be natural compounds because of the lack of a plausible anthropogenic source.[5–8]

One of these potential natural organohalogens is the heptachloro compound Q1, which was previously detected in over 100 environmental samples from virtually all over the world and in matrices, such as Antarctic air, human milk, eggs of seabirds, and the blubber of marine mammals.[7, 9, 10] The highest concentrations of Q1 found in wildlife reported to date exceed 9 mg kg^{-1} lipid content.[7] GC, in combination with high resolution MS, revealed that the molecular formula of Q1 is $C_9H_3Cl_7N_2$.[6] No stable compound with this chemical composition has been synthesized to date.[6] Furthermore, GC–MS analysis suggested that Q1 is a heptachlorobipyrrole derivative.[9] Synthesis of Q1 was attempted independently in two laboratories, and the results are reported together herein.

The naturally occurring 3,3′,4,4′,5,5′-hexabromo-2,2′-bipyrrole as well as 3,3′,4,4′-tetrabromo-5,5′-dichloro-1,1′-dimethyl-2,2′-bipyrrole and analogues have been identified in marine bacteria and seabird eggs.[5, 11, 12] This occurrence suggested that the structure of Q1 may be heptachloro-1-methyl-2,2′-bipyrrole (**1**; Scheme 1). The presence of such a structural variant would be surprising in view of the proposed N–Cl bond, but on the basis of the structurally similar 2,2′-bipyrrole derivatives mentioned above, **1** could not be generally ruled out.

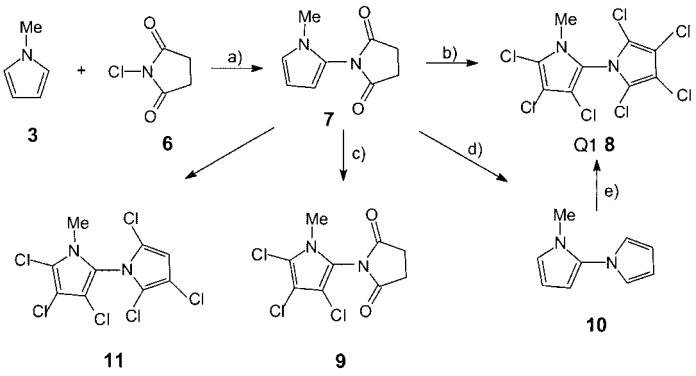


Scheme 1. Reagents and conditions: a) $POCl_3$, Et_2O, RT, 2 h (43 %); b) Ar, Pd/C 10 %, xylene, 138 °C, 4 h (51 %); c) SO_2Cl_2, RT, 6 h (< 0.1 %).

Preparation of the precursor 1-methyl-2-(pyrrol-2-yl)pyrrole (**5**) (also known as 1-methyl-2,2′-bipyrrole) was synthesized by dehydrogenation of 1-methyl-2-(4,5-dihydropyrrol-2-yl)pyrrole (**4**) over Pd/C; compound **4** was prepared from pyrrolidin-2-one and 1-methylpyrrole.[13, 14] Reaction of **5** with sulfuryl chloride (in a molar ratio of 1:10) should produce Q1. However, none of the major products was as nonpolar as expected for Q1 ($\log K_{OW} \approx 6$[9]), so the analytical method we employed for the analysis of the environmental samples[10] (extraction into *n*-hexane, followed by chromatography on 8 g activated silica, 16 h, 130 °C) was applied to the reaction solution. This method allowed us to obtain μg amounts of pure Q1 for ^{13}C NMR spectroscopic investigation. Compound **5** is susceptible to oxidation and polymerization in acid solution.

The ^{13}C NMR spectrum of Q1 shows only six singlets arising from pyrrole carbon atoms, two of which have an intensity that is double that of the others. This is contrary to the proposed structure **1**, which should have eight individual signals of bipyrrole carbons in the ^{13}C NMR spectrum. Rearrangement of the basic 2,2′-bipyrrole framework to a 1,2′-bipyrrole framework during the chlorination of **5** is a possibility; this is supported by the identification of several pyrrole derivatives as cleavage products of the bipyrrole. Thus, synthesis of the heptachloro-1′-methyl-1,2′-bipyrrole **8** was attempted.

The Dartmouth group synthesized the known compound *N*-(1-methyl-1*H*-pyrrol-2-yl)succinimide (**7**) from 1-methylpyrrole and *N*-chlorosuccinimide[15] in 51 % yield, according to the procedure of Rosa et al. Reduction of **7** with triethoxysilane and titanium tetraisopropoxide[16] gave 1′-methyl-1,2′-bipyrrole (**10**) in 30 % yield. Chlorination of **10** with sulfuryl chloride gave Q1 (**8**) in 16 % yield (Scheme 2).



Scheme 2. Reagents and conditions: a) $NaHCO_3$, CH_2Cl_2, reaction in the dark, RT, 4 h (49 %); b) $PCl_5/POCl_3$, 100 °C, 6 h (7.2 %); c) PCl_5, $CHCl_3$, 55 °C, 3 h (61 %); d) $HSi(OEt)_3$, $Ti(OiPr)_4$, THF, 65 °C, 12 h (30 %); e) SO_2Cl_2, Et_2O, RT, 3 h (16 %).

The Jena group also produced **7** according to the method of Rosa et al.;[15] this was then directly chlorinated. Treatment of **7** with phosphorus pentachloride at 55 °C gave *N*-(3,4,5-trichloro-1-methyl-1*H*-pyrrol-2-yl)succinimide (**9**; Scheme 2). Treatment of **7** with a mixture of phosphorus pentachloride and phosphorus oxychloride at 100 °C provided Q1 in a yield of 7 %, while the use of sulfuryl chloride in the chlorination of **7** gave less Q1.

Spectroscopic investigation confirmed that both groups had synthesized the heptachloro-1′-methyl-1,2′-bipyrrole (**8**; Figure 1). Solutions of **8** and the Q1 isolated from the environmental samples had matching retention times on three GC capillary columns of different polarity. Furthermore, the mass-spectral fragmentation patterns and the relative abundances of the molecular ion and fragment ions also agreed. The synthetic compound and the Q1 isolated from marine creatures also showed the same chromatographic behavior. Therefore, it is clear that Q1 is identical to **8**.

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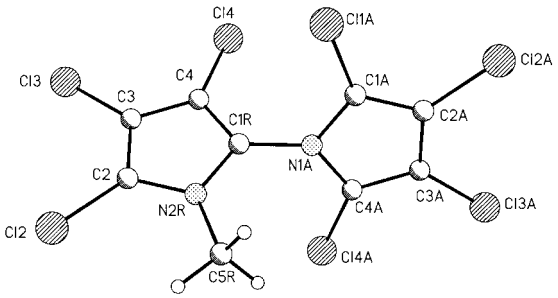

Figure 1. Molecular structure of Q1 (**8**). Selected bond lengths [Å] and bond angles [°]: C1R-N1A 1.409(4), C1R-N2R 1.376(3), N2R-C5R 1.501(4), N2R-C2 1.367(3), C2-C3 1.396(3), C2-Cl2 1.695(2), C3-C4 1.384(3), C3-Cl3 1.702(2), C4-C1R 1.380(3), C4-Cl4 1.688(2), N1A-C4A 1.380(3), N1A-C1A 1.376(3), C1A-Cl1A 1.676(4); C1R-N1A-C1A 127.1(2), C1R-N1A-C4A 124.1(2), C1R-N2R-C5R 124.3(2), N1A-C1A-Cl1A 124.3(2). Torsional angle N2R-C1R-N1A-C4A 71.5. Symmetry transformations used to generate equivalent atoms: A $-X+2$, Y, $-Z+3/2$.

Furthermore, a hexachloro congener of **8** was obtained as a by-product. According to the ^{1}H NMR spectroscopic data, the additional proton is in the β position as it gives rise to a resonance signal with the expected chemical shift of $\delta =$ 6.2 ppm (while α protons give signals at $\delta = 6.8$ ppm[13]). Because of the fast formation of **9**, the β proton is probably attached to the nonmethylated ring, which results in the chiral compound **11**. In the case of hindered rotation about the C–N bond, stable atropisomers may be separated by GC with a chiral stationary phase.

Halogenated 1,2′-bipyrroles have not been reported and, because of the cumbersome synthesis (yield $< 3.5\%$), we can exclude the possibility of an anthropogenic source of Q1, which is found in high concentrations in marine samples from all over the world. However, natural halogen-free 1,2′-bipyrroles have also not been discussed by natural-product chemists, which makes the source of Q1 a phenomenon. It will thus be highly interesting to elucidate the biochemical pathway/system that produces this molecule with 64% chlorine by weight, in which every third atom is a halogen.

Figure 2 shows the GC/NCI-MS (NCI = negative chemical ionization) chromatogram of the blubber extract of an Australian melon-headed whale (*Peponocephala electra*). Compound Q1 accounted for $> 50\%$ of all halogenated compounds present in this sample. This example illustrates that Q1 is of environmental concern, even though its toxic potential has not been established. The present synthesis of the compound may thus open up various possibilities for determination of the environmental impact of this natural halogenated compound.

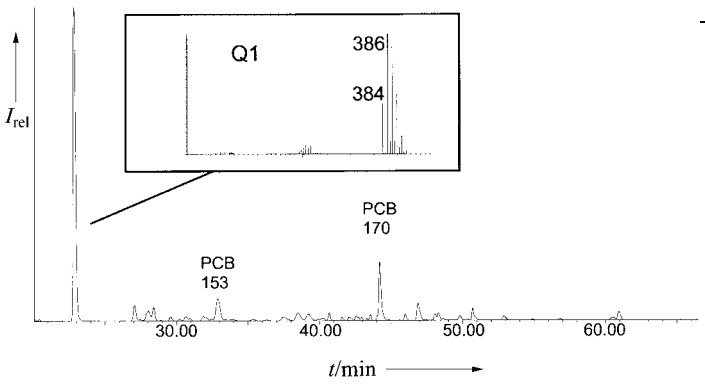

Figure 2. GC-MS-CNI chromatogram of a blubber extract of an Australian melon-headed whale (*Peponocephala electra*).

Experimental Section

9: m.p. 137–139 °C; ^{1}H NMR (250 MHz, $CDCl_3$): $\delta =$ 3.40 (3H, s, NCH_3), 3.01 ppm (4H, s, $COCH_2CH_2CO$); GC-MS (EI 70 eV): m/z (%) 280 (88), 217 (100).

8: m.p. 154–155.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.33$ ppm (3H, s, NCH_3); ^{13}C NMR (250 MHz, $CDCl_3$): $\delta = 116.6$, 115.6, 115.1, 111.2, 111.1, 108.3, 31.3 ppm; GC-MS (NCI, 70 eV): m/z 384 ($[M^-]$); GC-MS (EI, 70 eV): m/z 314 ($[M^+ - 2\,Cl]$, 349 $[M^+ - Cl]$, 384 $[M^+]$.

Crystal Structure Determination: The intensity data for Q1 were collected on a Nonius Kappa CCD diffractometer, with graphite-monochromated $Mo_{K\alpha}$ radiation. Data were corrected for Lorentz and polarization effects, but not for absorption.[17, 18] The structure was solved by direct methods (SHELXS[19]) and refined by full-matrix least-squares techniques against F_o^2. Compound Q1 crystallized in the centro-symmetric space group *Pbcn* on a special position with a two-fold axis passing through the atoms C1R and N1A. Therefore, the atoms C1R, N2R, and C5R are superimposed on the atoms N1A, C1A, and Cl1A, respectively. The superposition was solved by refining the pairs C1R/N1A and N2R/C1A at the same positions and with identical thermal parameters. Only the C5R atom of the methyl group and the chloride atom Cl1A were refined without such restraints (SHELXL-97[20]). The hydrogen atoms of the C5R methyl group were included at geometrically idealized positions with fixed thermal parameters (1.5-fold isotropic temperature factor). The non-hydrogen atoms (except for the methyl group C5R) were refined anisotropically.[20] XP (SIEMENS Analytical X-ray Instruments, Inc.) was used for structure representations.

Crystal data:[21] $C_9H_3Cl_7N_2$, $M_r = 387.28$ g mol^{-1}, colorless prism, size $0.10 \times 0.10 \times 0.08$ mm^3, orthorhombic, space group *Pbcn*, $a = 12.1617(6)$, $b = 8.7043(3)$, $c = 12.9576(4)$ Å, $V = 1371.68(9)$ Å^3, $T = -90$ °C, $Z = 4$, $\rho_{calcd} = 1.875$ g cm^{-3}, $\mu(Mo_{K\alpha}) = 14.26$ cm^{-1}, $F(000) = 760$, 9217 reflections in $h(-10/15)$, $k(-10/11)$, $l(-16/16)$, measured in the range $2.88° \le \Theta \le 27.46°$, completeness $\Theta_{max} = 99.2\%$, 1562 independent reflections, $R_{int} = 0.029$, 1410 reflections with $F_o > 4\sigma(F_o)$, 86 parameters, no restraints, $R1_{obs} = 0.0367$, $wR2_{obs} = 0.105$, $R1_{all} = 0.040$, $wR2_{all} = 0.1086$, GOF = 1.053, largest difference peak and hole: 0.394/ −0.480 e Å^{-3}.

Sample origin and preparation: The blubber sample of melon-headed whale came from a creature that was found dead in Queensland (Australia). The sample preparation was described elsewhere.[7] The GC-MS (NCI) spectrum was recorded in full scan mode (m/z 50–550) after a solvent delay of 20 min, all the other parameters have been published in detail.[6]

Received: November 13, 2001 [Z18211]

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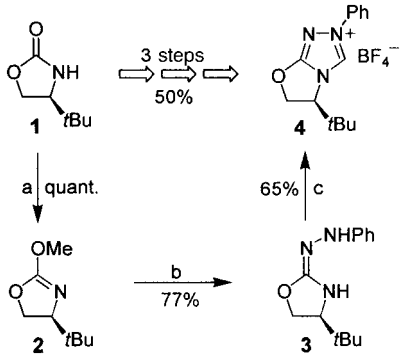
An Efficient Nucleophilic Carbene Catalyst for the Asymmetric Benzoin Condensation**

Dieter Enders* and Ulrike Kallfass

Since the early work of Ugai et al.[1] and Breslow et al.[2] it is known that thiazolium salts, such as 3-ethylthiazolium bromide or the naturally occurring thiamine (vitamin B_1), catalyze the condensation of benzaldehyde to benzoin under basic conditions. In 1966 Sheehan et al.[3–4] reported the first investigations into an asymmetric variant of the benzoin condensation by using (*S*)-4-methyl-3-(1-naphthyl)-ethylthiazolium bromide[4] as a precatalyst; the 52% *ee* obtained was remarkable for that time. In the following years, a great number of differently substituted chiral thiazolium salts were synthesized and tested in the asymmetric benzoin condensation.[5–10] However, the enantiomeric excesses hardly increased (1 – 57%).

A true breakthrough in which 1,2,4-triazolium salts[11–12] were employed was described in 1995 by our group in cooperation with Teles et al. (BASF)[13]. We reported the first efficient chiral system of this class of compounds, (4*S*,5*S*)-4-(2,2-dimethyl-4-phenyl-1,3-dioxan-5-yl)-1-phenyl-4*H*-1,2,4-triazol-1-ium perchlorate, in 1996[11] (yield of benzoin 66%, 75% *ee*, 1.25 mol% cat.). These results allowed the enantioselective benzoin condensation to be extended for the first time to a variety of aromatic aldehydes (yields 22 – 72%, 20 – 86% *ee*). Later, comparable enantioselectivities were found with chiral bicyclic triazolium salts developed by Knight and Leeper (20 – 82.5% *ee*).[12]

We report herein the synthesis of a novel enantiopure bicyclic triazolium salt **4** and its application as an efficient chiral catalyst in the form of the corresponding Wanzlick carbene in the asymmetric variant of the benzoin condensation. We used a modification of the Knight and Leeper synthesis[12] for the three-step conversion of the oxazolidin-2-one **1**[14] into the triazolium salt **4**, which was isolated as a crystalline solid (Scheme 1). Methylation of **1** with Meerwein's reagent yielded iminoether **2**, which was transformed into phenylhydrazone **3**. Final cyclization with trimethylorthoformate gave **4** (50% yield over three steps). The structure of the salt **4** was confirmed by X-ray crystallographic analysis.



Scheme 1. Synthesis of triazolium salt **4**. a) Me_3OBF_4 (1.2 equiv), CH_2Cl_2, room temperature, 15 h; b) $PhNHNH_2$ (1 equiv), NEt_3 (1 equiv), THF, 80 °C, 7 d; c) HBF_4 (1 equiv) in diethyl ether, CH_2Cl_2, room temperature; $HC(OMe)_3$ (20 equiv), MeOH, 80 °C, 12 h.

Bicyclic chiral triazolium salt **4** (10 mol%) was used as a precatalyst in the asymmetric benzoin condensation; benzoin was obtained in very good yields (83%) and with the highest enantioselectivities ever reported (90% *ee*). The condensation of different substituted aromatic aldehydes **5** led to the corresponding α-hydroxyketones **6** in moderate to good yields and with excellent enantiomeric excesses of up to 95% (Scheme 2). The active catalyst is actually the corresponding nucleophilic Wanzlick carbene **4′**, which is formed in situ by deprotonation of **4** with KO*t*Bu in the presence of the aldehyde **5**. This nucleophilic carbene **4′** then enters the catalytic cycle of the thiazolium-catalyzed acyloin condensation, which was first proposed by Breslow more than 40 years ago.[2, 13]

After aqueous work-up and column chromatography, the acyloins **6a – j** were isolated in 6 – 100% yield and with enantiomeric excesses of 53 – 95% (Tables 1 and 2). As shown in Table 2, an increase in the amount of catalyst led to higher yields. The higher concentration of base or triazol-5-ylidene

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[**] This work was supported by the Fonds der Chemischen Industrie. We are grateful to Degussa AG, BASF AG, and Bayer AG for donations of chemicals.