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Easy Separation of the Cis-syn-Cis and Cis-anti-Cis Isomers of Dicyclohexyl-18-crown-6

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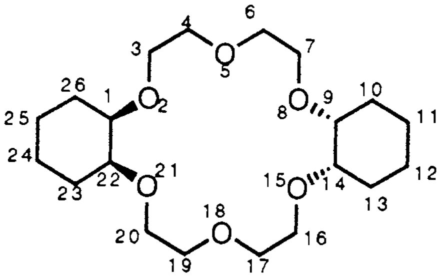
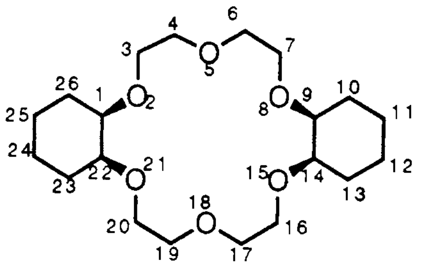
The separation of the cis-anti-cis and the cis-syn-cis isomers of DCH18C6 from a mixture of cis isomers of commercial DCH18C6 is achieved by selective crystallization of the uranyl nitrate/DCH18C6 cis-anti-cis complex.

Dicyclohexyl-18-crown-6 (DCH18C6) has proven to be of special interest due to the extractant properties of this macrocycle.1) The use of DCH18C6 in various conditions has allowed selective extraction of Sr^{2+},2) Pu^{4+},3) in high yields and selectivities. Selectivity of extraction with such macrocycles was sufficiently high in some cases to observe the isotopic separation of Uranium and Cerium.4) The DCH18C6 is prepared by catalytic hydrogenation of dibenzo-18-crown-67) and then the commercially available DCH18C6 is predominantly, a mixture of cis-syn-cis and cis-anti-cis isomers. It has been shown that these two isomers exhibited very different formation constants for several cations.5) Owing to these interesting properties, separation methods of the two isomers were proposed in the literature. Partial separation and/or low yields of the two isomers can be obtained using liquid chromatography6) and selective crystallization of complexes of an isomer with NaOAc7) or BaSCN.8) The only method which permits the complete separation in good yields of these two isomers was published by R.M. Bradshaw et al.,$^{9)}$ who used the selective crystallization of lead perchlorate/cis-anti-cis isomer and displaced, after separation, the lead salt by dihydrogen sulfide. Although the Bradshaw method is highly efficient, it cannot be used on a large scale because the heavy metal perchlorate required during the separation is incompatible with an industrial process. Here we describe a new method, based on the same methodology (selective crystallization of heavy metal salt complex) but which avoids the use of explosive and/or dangerous reagents.



DCH18C6 cis-anti-cis



DCH18C6 cis-syn-cis

Among the heavy metal salt easily available, uranyl nitrate was chosen for his high atomic weight. Wen Ji Wang has shown a constant extraction of the uranyl ion, 150 times higher with the cis-syn-cis isomer than with the cis-anti-cis isomer of DCH18C6.$^{10)}$ On the contrary, we have found that uranyl nitrate complex crystallizes more easily with the cis-anti-cis than with the cis-syn-cis isomer. It was then possible to crystallize selectively, in heptane solution, the overall cis-anti-cis from a syn/anti mixture. The cis-syn-cis isomer is recovered in pure form in the organic phase. The uranyl complex of cis-anti-cis isomer is filtrated and can be easily displaced by using chloroform/water reextraction. Then the pure anti isomer is obtained by evaporation of the chloroform phase and the uranyl nitrate can be reused for another separation. To optimize the separation, the ratio of the two isomers was estimated by ^{13}C NMR; carbons 4,6,17,19 are chemically identical and exhibit chemical shift at 71.2 ppm for the syn isomer and at 70.6 ppm for the anti in $CDCl_3$. Ratio of the peak size furnished a broad evaluation of the isomers ratio. This method was correlated with GC by using DB 1701 capillary column (Shimadzu). Uranyl nitrate (3.5 mol per mol of the anti isomer) in 25% aqueous solution was found to be the optimal amount to precipitate selectively the overall anti complex. A concentration in heptane of 25 g l^{-1} in DCH18C6 was found to be more efficient condition at room temperature to obtain rapid and complete separation. Microanalyses were compatible with the uranyl complex formula [DCH18C6 cis-anti-cis $UO_2(NO_3)_2.2H_2O$]. This method was applied with success on 100 g scale.

General procedure is as follows: 24.6 g of DCH18C6 (Janssen Chemicals) containing 63% of the cis-syn-cis isomer and 37% of the cis-anti-cis isomer evaluated by using ^{13}C NMR are crystallized in 74 ml of heptane. Cis anti cis (3.4 g) is isolated in pure form. The organic solution is evaporated leading to 21.2 g of an oil containing 73% of the cis-syn-cis isomer. This oil is dissolved in 850ml of heptane and added to 108 ml of water containing 0.5 mol l^{-1} of $UO_2(NO_3)_2$. The suspension is maintained under stirring during 24 hours at room temperature to permit the complete crystallization of DCH18C6 cis-anti-cis,$UO_2(NO_3)_2.2H_2O$ complex. The precipitate is filtrated and dried in oven (12g), dissolved in 300 ml of $CHCl_3$ and then washed two times by 150 ml of water. The organic layers are dried and evaporated, and 5.6 g of pure cis-anti-cis isomer are obtained. Distillation of the heptane solution gives rise to 15.4 g of cis-syn-cis isomer. Thus 9 g of pure cis-anti-cis11) and 15.4 g of pure cis-syn-cis12) isomers are recovered by our method, corresponding to 99% of the starting commercial mixture.

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11) DCH18C6 cis-anti-cis, mp 83°C. NMR ^{1}H 200 MHz, $CDCl_3$: 3.64 m (20H), 1.79 m (4H), 1.45 m (12H). ^{13}C 50.32 MHz, $CDCl_3$: 77.3 (C 1,9,14,22); 70.6 (C 4,6,17,19); 68 (C 3,7,16,20); 27.7 (C 10,13,23,26); 22.1 (C 11,12,24,25).

12) DCH18C6 cis-syn-cis, mp 62°C. NMR ^{1}H 200 MHz, $CDCl_3$: 3.64 m (20H), 1.8 m (4H), 1.45 m (12H). ^{13}C 50.32 MHz, $CDCl_3$: 77.5 (C 1,9,14,22); 71.2 (C 4,6,17,19); 68 (C 3,7,17,19); 27.56 (C 10,13,23,26); 22.05 (C 11,12,24,25).

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