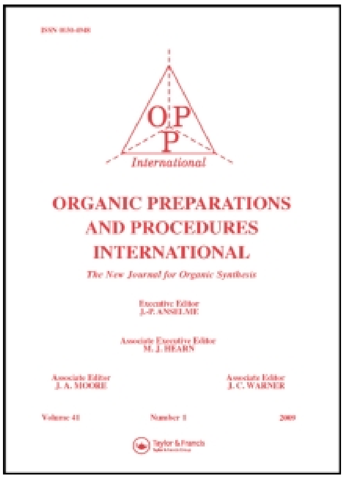

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PREPARATION OF 4,4-BIS(DIFLUORAMINO)CYCLOHEXANONE AND 5,5-BIS(DIFLUORAMINO)-2-AZACYCLOHEPTANONE[1]

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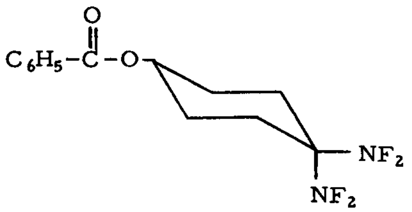
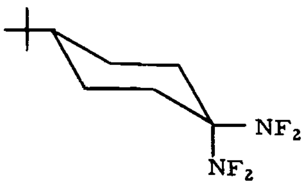
As part of our synthetic studies on poly(difluoramino) compounds[2], we prepared 4,4-bis(difluoramino)cyclohexanone (4) and converted it to 5,5-bis(difluoramino)-2-azacycloheptanone (7) as outlined in Scheme I. The ketoester 1 was prepared by the reported method[3], and the details of the other steps are outlined in the Experimental Section.

The F^{19} NMR spectrum of 2 deserves further comment; two broad peaks, one at -1024, -1008 and -992 Hz (from CCl_3F, 40 m Hz) and the other at -924, -908 and -892 Hz, were observed at ambient temperature in CCl_4 solution. The same type of spectrum was exhibited by 4,4-bis-(difluoramino)-t-butylcyclohexane (8). Here, peaks at -1152, -1136, -1120 and -724, -708 and -692 Hz were evident. Assuming these spectra are not deceptively simple, an interpretation is that the $-NF_2$ groups are not equivalent[4], but the fluorine atoms on each NF_2 group are equivalent. Thus, a 16 Hz F-F coupling is observed in both 2 and 8.



2

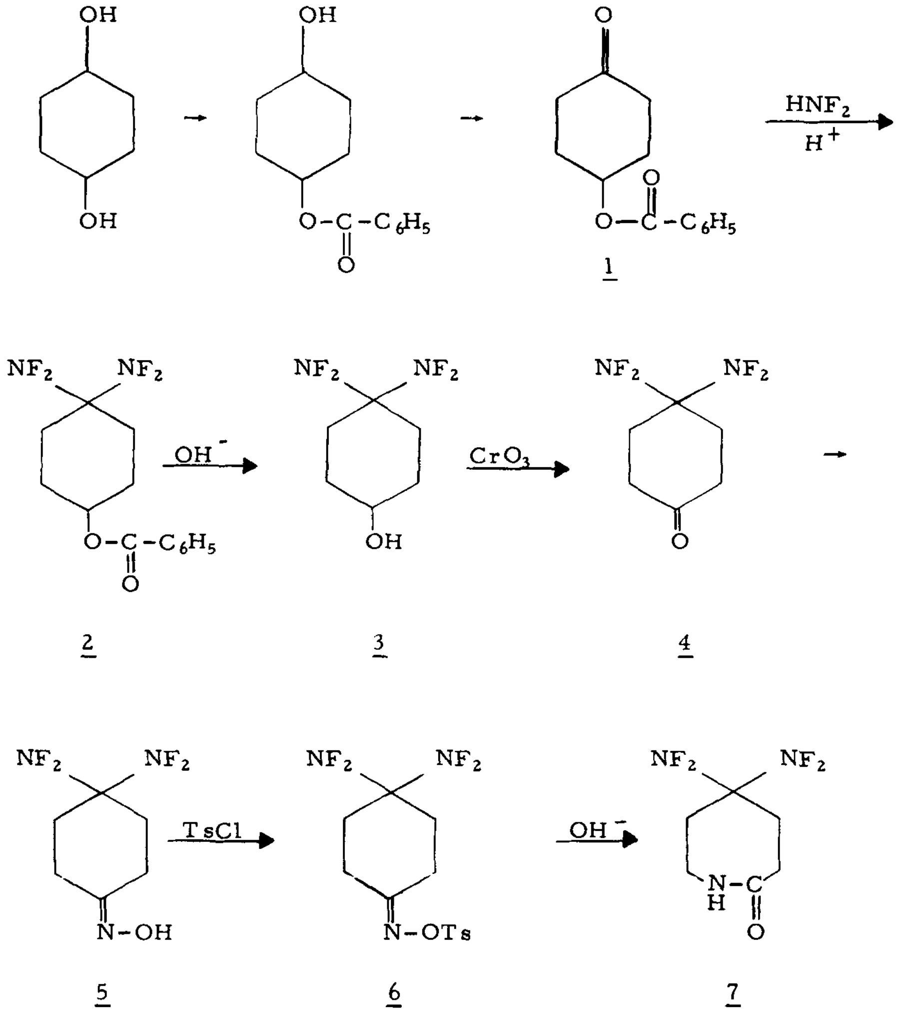


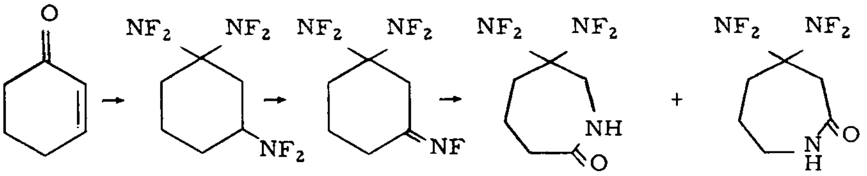
8

Attempts to convert 5 to 7 with acidic catalysts (PCl_5, HSO_3F) gave only low yields of 7; the basic procedure outlined was far superior.

Another potential route to geminal bis(difluoramino)lactams involving fewer steps is outlined below. Beckmann rearrangement of

Scheme I





9 **10**

2,2-bis(difluoramino)cyclohexylfluorimine and related N-fluorimines has been examined in detail.[2d] No difficulty was encountered in converting 2-cyclohexenone to 1,1,3-tris(difluoramino)cyclohexane (**9**)[2c], but the dehydrofluorination step necessary to prepare **10** was not successful. In contrast to the 1,1,2-tris(difluoramino)alkanes that dehydrofluorinate readily upon contact with methanolic sodium methoxide at 0°, **9** was resistant to such treatment. At 20°, complete loss of fluorine from the organic molecule was observed. Apparently, **10** is rapidly destroyed by the dehydrofluorination reaction conditions.

Experimental

Difluoramine and organic difluoramino compounds are hazardous materials. Adequate precautions[2] must be observed when handling these materials.

Preparation of 4,4-Bis(difluoramino)-Benzoyloxycyclohexane. - A solution of 8.72 g of 4-benzoyloxycyclohexanone[3] in 40 ml of methylene chloride was added to a mixture of 10 ml of methylene chloride, 10 ml of 96% H_2SO_4, 10 ml of 30% fuming H_2SO_4 and 125 mmoles of difluoramine maintained at 4°. As soon as the addition was complete the HNF_2 was vented and the residue was dumped over crushed ice. The methylene chloride layer was washed with water and aqueous sodium bicarbonate. Evaporation of the methylene chloride left a solid that was recrystallized from ethanol. The 4,4-bis(difluoramino)benzoyloxycyclohexane, 8.2 g, (67%) melted at 77-79°.

Anal.

Calc'd. for $C_{13}H_{14}N_2F_4O_2$: C, 50.98; H, 4.61; N, 9.15; F, 24.8.

Found: C, 50.44; H, 4.66; N, 8.98; F, 24.1.

Preparation of 4,4-Bis(difluoramino)cyclohexanol. - A solution of 3.10 g of 4,4-bis(difluoramino)-benzoyloxycyclohexane in 40 ml of methanol-10 ml of water was treated with 20 ml of 1.30 N sodium methoxide in methanol. The mixture was warmed to 40° and then set aside for one hour. It was poured into H_2O and the organic product was extracted into methylene chloride. Evaporation of the methylene chloride and recrystallization of a portion of the residue from hexane gave 4,4-bis(difluoramino)cyclohexanol, mp 77-79°. The ^{19}F NMR spectrum had a broad peak at ϕ -23.7.[5]

Anal.

Calc'd. for $C_6H_{10}N_2F_4O$: C, 35.65; H, 4.99; N, 13.86.
Found: C, 35.05; H, 4.86; N, 13.55.

Preparation of 4,4-Bis(difluoramino)cyclohexanone. - The product from saponification of 3.1 g of 4,4-bis(difluoramino)benzoylcycloxycyclohexane in 15 ml of acetic acid was stirred at 20° while 14 ml of a solution of chromic acid in acetic acid (3.25 g CrO_3, 20 ml H_2O, 75 ml acetic acid) was added slowly. After 4 hours the mixture was poured into H_2O and the organic product was extracted into methylene chloride. Evaporation of the methylene chloride left crude 4,4-bis(difluoramino)cyclohexanone. A portion was chromatographed on silica gel. Elution of the column with pentane-methylene chloride (1:1) gave 4,4-bis(difluoramino)cyclohexanone, a white solid, mp 45-46° (hexane). The ^{19}F NMR spectrum had a single peak at ϕ -26.8.

Anal.

Calc'd. for $C_6H_8N_2F_4O$: C, 36.00; H, 4.03; N, 14.00.
Found: C, 35.88; H, 4.21; N, 13.52.

Preparation of 4,4-Bis(difluoramino)cyclohexanone Oxime. - The crude 4,4-bis(difluoramino)cyclohexanone (1.8 g) was converted directly to the oxime in ethanolic sodium hydroxide (steam bath, 10 minutes). The 4,4-bis(difluoramino)cyclohexanone oxime, 1.3 g (60% yield based on **2**) mp 107-108° (ethanol) was isolated in the usual way. The ^{19}F NMR spectrum had a single peak at ϕ -25.6.

Anal.

Calc'd. for $C_6H_9N_3F_4O$: C, 33.49; H, 4.22; N, 19.53.

Found: C, 33.66; H, 4.51; N, 19.48.

The oxime tosylate was prepared by stirring a mixture of the oxime (1.0 g), and tosyl chloride (1.0 g) in 20 ml of acetone at 0° while 2.5 ml of 2 N sodium hydroxide solution was added dropwise. Then, after 2 hr at 25°, the mixture was poured into water and the tosylate was isolated by filtration. The tosylate, 1.6 g, 92%, from chloroform-hexane, melted at 124-126°; the ^{19}F NMR spectrum had a single peak at ϕ-26.1.

Anal.

Calc'd. for $C_{13}H_{15}N_3O_3SF_4$: C, 42.27; H, 4.09; N, 11.38.

Found: C, 41.93; H, 4.21; N, 10.82.

5,5-Bis(difluoramino)-2-Azacycloheptanone. - A mixture of 0.72 g of the p-toluenesulfonate of 4,4-bis(difluoramino)cyclohexanone oxime, 4 ml of ethanol, 4 ml of water and 1 ml of 2 N aqueous sodium hydroxide was warmed on the steam bath for one hour. The mixture was cooled, poured into water, and the organic material was extracted into methylene chloride. The residue obtained upon evaporation of the methylene chloride was recrystallized from pentane-methylene chloride and gave 5,5-bis(difluoramino)-2-azacycloheptanone, 0.25 g (58%), mp 100-102°.

Anal.

Calc'd. for $C_6H_9N_2F_4O$: C, 33.49; H, 4.22; N, 19.53.

Found: C, 33.59; H, 4.08; N, 19.09.

Preparation of 4,4-Bis(difluoramino)-t-butylcyclohexane. - A solution of 0.31 g of 4-t-butylcyclohexanone in 2 ml of methylene chloride was added to a mixture of 2 ml of 100% sulfuric acid, 2 ml of methylene chloride and 5 mmoles of difluoramine. After ninety minutes at ice-bath temperature, excess difluoramine was removed at reduced pressure and the residue was quenched over crushed ice. The organic product was isolated via extraction into methylene chloride. Chromatography on silica gel gave, in the pentane-methylene chloride (99:1) eluate, 4,4-bis(difluoramino)-t-butylcyclohexane, 0.40 g, 83%, as a clear liquid.

Anal.

Calc'd. for $C_{10}H_8N_2F_4$: C, 49.57; H, 7.49; N, 11.56; F, 31.4.

Found: C, 49.45; H, 8.05; N, 10.98; F, 31.1.

References

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2. (a) R. C. Petry and J. P. Freeman, J. Org. Chem., 32, 4304 (1967); (b) W. H. Graham and J. P. Freeman, ibid., 34, (1969); (c) J. P. Freeman, R. C. Petry and T. E. Stevens, J. Am. Chem. Soc., 91, 4778 (1969); and (d) T. E. Stevens, J. Org. Chem., 34, 2451 (1969).

3. E. R. H. Jones and F. Sondheimer, J. Chem. Soc., 616 (1949).

4. An NF_2 group on a asymmetric carbon usually leads to an AB spectrum, F. A. Johnson, C. Haney, and T. E. Stevens, J. Org. Chem., 32, 466 (1967).

5. ϕ Values are parts per million from internal CCl_3F.

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