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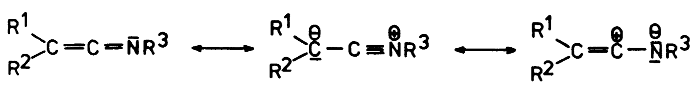
SYNTHESIS AND CONFIGURATIONAL STABILITY OF 3,8-DIBENZYL-1-AZACYCLOOCTA-1,2-DIENE: THE FIRST EIGHT-MEMBERED CYCLIC KETENIMINE

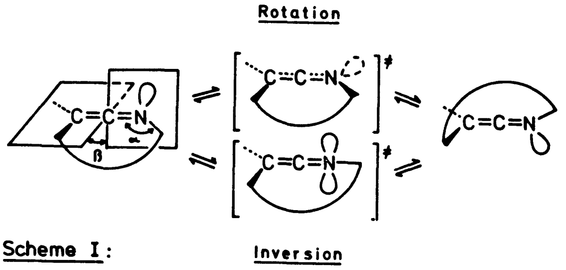
Joachim FIRL, Karl SCHINK, and Wolfgang KOSBAHN
Organisch-Chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching, Germany

The preparation of the eight-membered cyclic ketenimine 4 is reported. 4 is a mixture of two diastereomers which interconvert through configuration inversion of the C=C=N-moiety with $\Delta G^{\neq} > 19$ kcal/mol. The fact that 4 shows a far higher barrier than structurally similar open chain derivatives or larger ring analogues of 4 proves that ketenimines stereoisomerize through nitrogen inversion.

X-ray analysis$^{1)}$ as well as DNMR investigations$^{2,3,4)}$ have proven that the C=C=N-moiety of most ketenimines shows local C_s symmetry. Therefore, ketenimines with unequal substituents at the terminal carbon are chiral molecules. However, their inherent configurational instability ($\Delta G^{\neq} < 15$ kcal/mol$^{2,3,4)}$) has prevented the isolation of enantiomers until now. Configuration inversion of the C=C=N-moiety can proceed by either of two mechanisms: nitrogen inversion or rotation around either of the formal double bonds. Especially for the C=C-bond which is weakened by enamine like resonance,$^{5)}$ a low barrier of rotation can be expected. Though substituent effects seem to be in better agreement with nitrogen inversion,$^{3,4)}$ they do not exclude a bond rotation mechanism definitely. An unequivocal distinction between the two mechanisms, however, should be possible by examination of cyclic ketenimines. The incorporation of a linear three atom unit into a less than ten-membered ring generates appreciable strain.$^{6)}$ This strain will increase further if the bond angle α (see Scheme I) is enlarged to reach the linear transition state of nitrogen inversion. On the other hand, the strain should de-



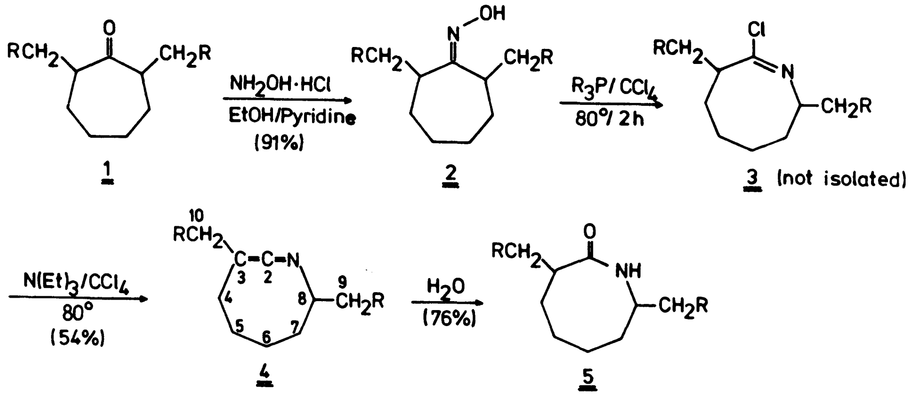
crease if the dihedral angle β is reduced. This occurs on the way to the planar transition state of bond rotation. Therefore, if the mechanism follows nitrogen inversion, cyclic ketenimines with a less than ten-membered ring should racemize more slowly than their open chain analogues. Furthermore, their configurational stability should increase with decreasing ring size. For a bond rotation mechanism, on the other hand, the contrary has to be expected.



Scheme I:

Therefore, we have started an investigation of cyclic ketenimines which obviously have attracted little attention until now. We wish to report here on the preparation and properties of 3,8-dibenzyl-1-azacycloocta-1,2-diene (4) which represents the first eight-membered cyclic ketenimine. This molecule is remarkable in so far as cumulenes of the same ring size, e. g. 1,3-diazacycloocta-1,2-diene[7] or even cycloocta-1,2-diene,[8] are known only as elusive intermediates.[9]

The ketenimine 4 was prepared as depicted in Scheme II. Starting from the



Scheme II: Synthesis of 4; R = C_6H_5

known 2,7-dibenzylcyclooctanone (1)[10] the oxime 2 was obtained. On treatment with triphenylphosphine/carbon tetrachloride[11] 2 rearranged to the cyclic imidochloride 3, which without isolation was transformed into 4 on adding excessive triethylamine to the reaction mixture and heating until the ν-C=C=N-vibration at 2015 cm^{-1} reached maximum intensity. After evaporation of the solvent under reduced pressure, 4 was extracted from the residue with pentane. Cooling the extract to -25°C removed most of the impurities and byproducts. Ultimately, 4 was isolated as a yellow oil which, because of its thermal instability especially at high concentrations, its low tendency to crystallize, and its sensitivity against moisture, could not be obtained with analytical purity until now.

Like other ketenimines 4 adds water under formation of the lactame 5 (76% from crude 4) which was fully characterized by elemental analysis and spectral data. The ketenimine structure is further substantiated by the 2015 cm^{-1} absorption in the IR spectrum as well as the ^{13}C chemical shifts of the quarternary carbons C^{2} and C^{3} (see Table) which are most characteristic for ketenimines.5) Moreover, the number of signals, their chemical shifts, and their splittings in the SFORD spectrum prove the cyclic structure.

Since 4 contains two chirality elements, there are two possible diastereomers which are interconvertible through configuration inversion of the C=C=N-moiety. This process proceeds with other ketenimines at room temperature already fast on the NMR time scale.2,3,4) The ^{13}C NMR spectrum of 4, however, shows at ambient temperature two lines for every carbon with the integral intensity of 2.7 : 1 indicating the presence of two diatereomers 4a and 4m, respectively, which obviuosly still interconvert slowly. Even on heating to 360 K, which was the highest temperature studied because of beginning decomposition, only slight exchange broadening is observed. By line shape simulation of the signals of C^{2} ($\Delta\nu$ = 30 Hz), C^{3} ($\Delta\nu$ = 212 Hz), and C^{8} ($\Delta\nu$ = 187 Hz)13) using Binsch's DNMR program14) the rate of interconversion at 360 K could be determined. With the equilibrium constant K = [4a]/[4m] = 2.3 13) we obtained $\bar{k}$ = 9 sec^{-1} for the transformation of the more stable isomer 4a into 4m and $\bar{k}$ = 21 sec^{-1} for the reverse reaction. With these rate constants and the Eyring equation free energy barriers $\Delta G^{\neq}$ = 19.0 kcal/mol and $\Delta G^{\neq}$ = 19.6 kcal/mol, respectively, are calculated.

Table. ^{13}C chemical shifts of the diastereomers 4a and 4m12)

4a (abundant): 196.54 (s,C^{2}), 69,09 (d,C^{8}), 62.46 (s,C^{3}), 43.05 (t,C^{9}), 38.89 (t,C^{10}), 34.80 (t,C^{7}), 32.60 (t,C^{4}), 26.95, 26.75 (t,t,C^{6},C^{5})

4m (minor) : 197.19 (s,C^{2}), 66.94 (s,C^{3}), 65.13 (d,C^{8}), 41.03, 40.84 (t,t,C^{10},C^{9}), 35.05, 33.31 (t,t,C^{7},C^{4}), 28.43, 27.92 (t,t,C^{6},C^{5})

These results reveal that 4 is the configurational most stable ketenimine which is known until now.[2,3,4] Its stereoisomerisation barrier turns out to be more than 5 kcal/mol higher than that of the most similar open chain derivative: ethyl-benzyl-ketene-N-2-(1-phenylbutyl)imine (6) ($\Delta G^{\neq}$(6a → 6m) = 14.1 kcal/mol).[15] Moreover, its barrier exceeds that of its cyclic homologue 3,9-dibenzylcyclonona-1,2-diene (7) ($\Delta G^{\neq}$(7a → 7m) = 15.9 kcal/mol)[15] by more than 3 kcal/mol. Since the entropy of activation for bond rotation or configuration inversion processes usually is close to zero,[16] structural effects normally can be discussed on the basis of $\Delta G^{\neq}$. On the likely assumption that this is valid also in the present case our results prove, for the reasons given above, that the ketenimines stereoisomerize through nitrogen inversion.

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