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"THE SYNTHESIS OF HOMOAZEPINE DERIVATIVES"

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We wish to report the synthesis of two homo-derivatives (1) of N-carbethoxyazepine, 1 (2).

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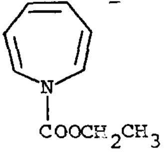

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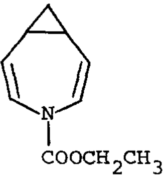

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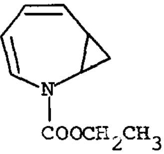
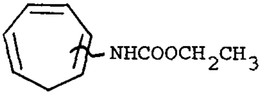


The reaction of cycloheptatriene with ethyl azidoformate (8% solution) at 125°C (2c , 2d) for 3.5 hours produced a 56-71% yield of a mixture of cycloheptatriene/N-COOCH$_2$CH$_3$ adducts. Of this mixture,[*] ~70% consisted of 4-carbethoxy-4-azabicyclo[5.1.0]octa-2,5-diene (2, referred to as the symmetrical homoazepine) and 2-carbethoxy-2-azabicyclo[5.1.0]octa-3,5-diene (3, referred to as the asymmetrical homoazepine) in a ratio of *ca.* 1:2.7 (4) and ~30% of cycloheptatrienylurethane, 4.

4



The reaction of N-p-nitrobenzenesulfonoxyurethane, triethylamine and cycloheptatriene in dichloromethane, Lwowski's method (3), at room temperature for 10 hours also produced 2 and 3, but in a ratio of *ca.* 5:1 (4) and in low yield (10% after purification). The homoazepines, 2 and 3, were separated by preparative vapor phase chromatography (SE-30 on

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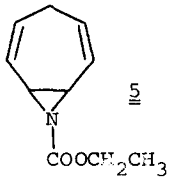
[*] At least three minor components were also detected.

chromosorb W, 165°, 50 ml helium/minute). Isomer 3 could also be obtained pure and in larger amounts by fractional crystallization (pentane, -78°C) from a mixture enriched in 3 by careful distillation.

The symmetrical isomer 2 was obtained as a faintly yellow liquid, b.p. 69-71°/0.1 mm[±] and the asymmetrical isomer 3 as a colorless crystalline solid, m.p. 45.5-46.0°C and b.p. 59-61°/0.1 mm[±]. Spectral data are consistent with the assigned structures. The n.m.r. spectra of 2 and 3 are presented in the Table. Isomer 2 exhibits $\lambda_{max}^{n\text{-}hexane}$ 232 mμ (ε 13,000) and ν_{max}^{film} 1725(s)cm^{-1} (C=O) and 1665(s)cm^{-1} (C=C); isomer 3 exhibits $\lambda_{max}^{n\text{-}hexane}$ 265 mμ (ε 10,200) and ν_{max}^{film} 1718(s)cm^{-1} (C=O), 1645 (m) and 1619(s)cm^{-1} (C=C).

The material 4 which accounted for ~30% of the products (b.p. 87-99°/0.2 mm, a pale yellow, air-sensitive oil) from the azidoformate reaction is assigned the isomeric cycloheptatrienylurethane structure because it readily absorbed 2.8 molar equivalents of hydrogen (5% rhodium on carbon, ethanol) to produce a compound identical (ir, nmr, vpc) with authentic cycloheptylurethane.* The spectral data are also consistent with the assigned structure 4: its ir spectrum shows ν_{max}^{film} 3310(s)cm^{-1}(N-H), 1705(s)cm^{-1} (C=O), and 1625(s)cm^{-1} (C=C); its nmr spectrum is summarized in the Table. The cycloheptatrienylurethane 4 is apparently a mixture of isomers which we have not yet been able to separate.

The homoazepines 2 and 3 are probably formed by valence isomerization (4b, 5) of the initially produced aziridines 5 and 6 respectively. We are currently attempting to synthesize 5 and 6 by generating $NCOOCH_2CH_3$ in the presence of cycloheptatriene at lower temperatures.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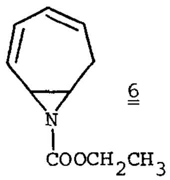
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Acknowledgements

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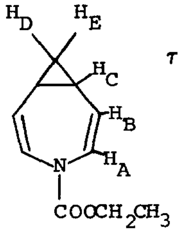
[±] A satisfactory microanalysis and molecular weight by mass spectrometry were obtained.

*Prepared by reaction of ethylchloroformate with cycloheptylamine.

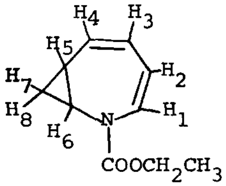
TABLE

NMR Data[±] (CCl_4, 60MHz) on 2, 3, and 4



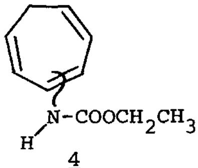
2

τ 3.35(2H_A, doublet, $J \approx 9.8$ Hz)
4.88(2H_B, broad doublet, $J \simeq 9.8$ Hz)
5.75($-CH_2-$, quartet, $J \approx 7.3$ Hz)
8.3-8.9(CH_3, triplet centered at τ8.67, $J \approx 7.4$ Hz, overlapped by 2H_C and H_D or H_E)
9.7-10.0(Multiplet, H_E or H_D)



3

τ 3.33(H_1, doublet, $J \simeq 9.6$ Hz)
3.86(H_4, double-doublet, $J \approx 11.1, 3.1$ Hz)
4.35(H_3, double-doublet, $J \approx 11.1, 6.7$ Hz)
4.96(H_2, double-doublet, $J \approx 9.6, 6.7$ Hz)
5.81($-CH_2-$, quartet, $J \approx 7.2$ Hz)
6.95(H_6, multiplet)
8.4-8.9(CH_3-, triplet centered at τ8.70, $J \simeq 7.4$ Hz, overlapped by H_5 and H_7 or H_8)
9.6-9.9(H_8 or H_7, multiplet)



4

τ2.9(N-H, broad peak)
3.1-4.1 and 4.4-5.0 (5 vinylic protons, multiplet)
5.92($-CH_2-$, quartet, $J \approx 7.2$ Hz)
7.5-7.9(2 allylic protons, multiplet)*
8.82(CH_3-, triplet, $J \approx 7.2$ Hz)

[±] The resonances showed the appropriate relative intensities for the structures assigned.

*The allylic protons integrated for 2 protons and consisted of a doublet ($J \simeq 7.3$ Hz, τ7.52) and a triplet ($J \approx 7.1$ Hz, τ7.86) in a ratio of *ca.* 3:1. This suggests that 4 is mainly 1-cycloheptatrienylurethane.

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