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CYCLOADDITION REACTIONS OF 1,3-OXAZEPINE AND 1,2-DIAZEPINES TO 2,5-DIMETHYL-3,4-DIPHENYLCYCLOPENTADIENONE[1]

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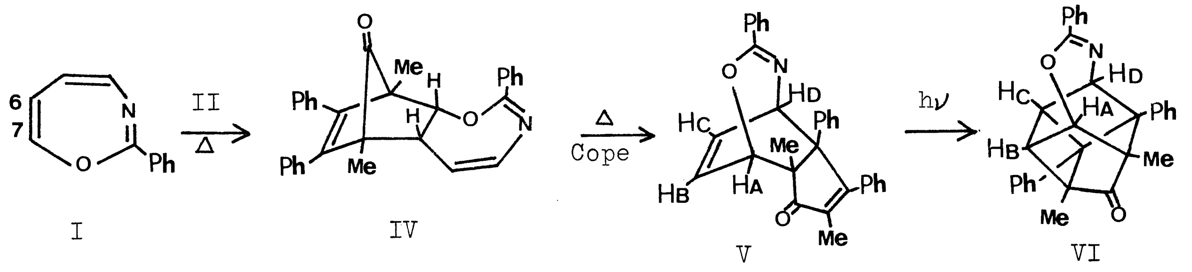
This report describes the first example of a cycloaddition reaction of 1,3-oxazepine derivatives. 2-Phenyl-1,3-oxazepine (I) added thermally to 2,5-dimethyl-3,4-diphenylcyclopentadienone (II) to give [4+2] adducts IV and V. Irradiation of V afforded VI, a novel type of the cage compound containing oxygen and nitrogen atoms. For comparison, the cycloaddition reactions of N-substituted 1H-1,2-diazepines (IIIa and IIIb) and 1H-azepine (XII) were examined.

In connection with their double bond characters, the cycloaddition reactions of oxepines,[2] 1H-azepines,[3] and 1H-1,2-diazepines[4] have been extensively studied. However, there are no reports on 1,3-oxazepines. We found that, although 2-phenyl-1,3-oxazepine (I)[5] did not add to maleic anhydride, N-phenylmaleimide or dimethyl acetylenedicarboxylate, it reacted with 2,5-dimethyl-3,4-diphenylcyclopentadienone (II) affording a [4+2] adduct IV, which was subsequently transformed to another [4+2] adduct V by a Cope rearrangement. For comparison, the cycloaddition of N-substituted-1H-1,2-diazepine (III) to II was studied, and [4+2] adducts IX and X were also obtained, although the reaction site in the cycloaddition of III to II differed from that in the case of I. These adducts, V and X, upon irradiation, provided novel cage molecules containing two hetero atoms such as VI and XI.

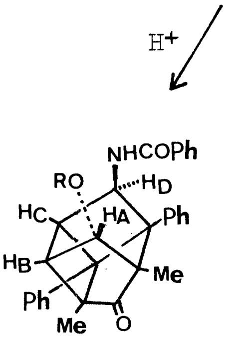
When a mixture of I and II (1.0 : 1.4 equiv) was heated at 120°C in tetrachloroethylene for 10 hr, V (mp 191°C, 72%) was obtained.[6] On the other hand, when a benzene solution of the same mixture was heated at 70-75°C for 24 hr, IV (10 %) was obtained, II (80 %) being recovered unchanged. When IV was then heated to 120°C, it suffered a Cope rearrangement, producing V (100 %). Irradiation of compound V (350 nm, in methanol) underwent the intramolecular [2+2] addition to provide VI (mp 181°C, 100%), which upon hydrolysis with dil hydrochloric acid gave a hydroxybenzamide compound VII (mp 217°C, 100%); O-acetate VIII (mp 132°C). The structural assignment of these products was mainly based on their spectral data: the arrangement of $H_A \sim H_D$ was established by decoupling and NOE experiments in their nmr spectra.[6] While the formation of VI verified the endo forms of IV and V, further work was required to discriminate between the position isomers V and V'. In the nmr spectra of VII and VIII (in DMSO-d_6),[6] the acetylation caused the shift of the H_A signal (δ 4.03) to lower field by 1.2 ppm, in addition to loss of the coupling between the H_A and OH (δ 7.80), implying that H_A is located at the carbon atom bearing the OH group. Furthermore, in VII, double irradiation of the methyl signal (δ 1.06) resulted in both sharpening and enhancement (13 %) of the H_A signal, whereas saturation on phenyl protons (δ 7.05) brought about enhancement (11 %) of the H_D signal (δ 5.53). Thus, the structure of VII was unequivocally established, and in turn the gross structures of IV, V, and VI could be assigned.

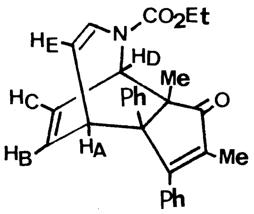
For comparison, the cycloaddition of 1H-1,2-diazepines (III) to II was examined. When a mixture of IIIa and II was heated in benzene at 70-80°C for 24 hr, two adducts, IXa (mp 137°C, 10%) and Xa (mp 186°C, 30%), were formed with IIIa being recovered unchanged (40 %). Heating of compound IXa at 120°C resulted in the Cope rearrangement to form Xa (100 %). The adduct Xa was also obtained in high yield (91 %) by heating IIIa with II at 120°C for 15 hr. An NOE study of Xa clearly established the proximity of the bridgehead Me (δ 0.99) to both H_A and H_E (δ 2.84 and 6.11) as well as the proximity of the bridgehead phenyl (δ 7.32) to H_D (δ 5.54). Photolysis of Xa gave a corresponding cage product, XIa (mp 194°C, 100%). Based on this evidence as well as spectral properties,[6] the structures of IXa, Xa, and XIa were established. In the same manner, Xb (mp 184°C, 93%) and XIb (mp 244°C, 100%) were obtained from IIIb and II.

The results cited above prompted us to re-examine the cycloaddition of N-ethoxycarbonylazepine (XII) to II, which had been studied by Paquette and his coworkers.[3a] We also obtained two products (mp 141°C, 35% and mp 152°C, 20%), and the lower melting compound was identified with XIII, structure of which has been assigned by previous authors. However, we proposed a new structure XIV for the higher melting adduct, which was already suggested to be XIV',[3a] on the following evidence. The Cope rearrangement of XIII afforded XIV (100 %), which, on irradiation, gave the

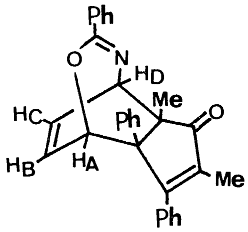


I IV V VI





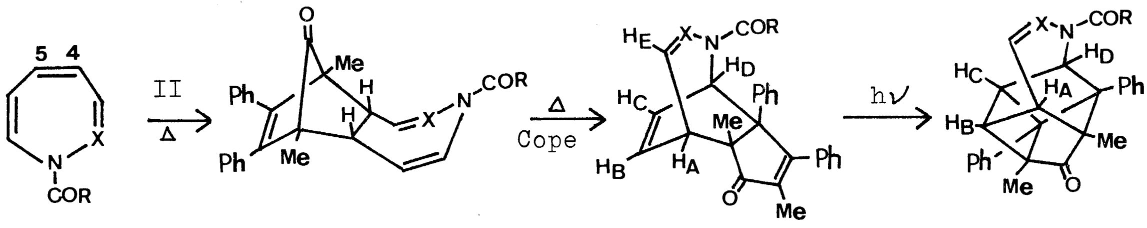
XIV'



V'

VII : R=H

VIII : R=Ac



IIIa : X=N ;R=OEt	IXa : X=N ;R=OEt	Xa : X=N ;R=OEt	XIa : X=N ; R=OEt
IIIb : X=N ;R=Ph		Xb : X=N ;R=Ph	XIb : X=N ; R=Ph
XII : X=CH;R=OEt	XIII: X=CH;R=OEt	XIV: X=CH;R=OEt	XV : X=CH; R=OEt

cage compound XV (mp 208°C, 100%). An NOE study confirmed the proximity of the methyl group (δ 1.11) to H_A (δ 2.21) and H_B (δ 3.15) in XV.

In summary, it became clear that heteroepines, I, III, and XII, underwent the cycloaddition to II with a high degree of stereospecificity and regioselectivity to give the endo [4+2] adducts, IV, IX, and XIII, which all were converted to the isomeric adducts, V, X, and XIV, by the Cope rearrangement. The stereospecificity, that is the formation of the endo adducts, is explained by the concept of β-orbital overlapping.[7] The selectivity that the cycloaddition occurred at the C_4-C_5, the remotest C-C double bond from the N_1 atom in III and XII, whereas at the C_6-C_7 bond in I, is still puzzling. However, such selectivity would be interpreted in term of the perturbation theory; the HOMO and LUMO interaction between the heteroepines and the diene.[8] The selectivity of the cycloaddition of I to II seems similar to that of cycloheptatriene to II, in which case, however, the reaction was so complicated that even [6+4] adduct was included.[9]

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REFERENCES

1. Organic Thermal Reaction XXXIII. For paper XXXII, see R. Miyamoto, T. Tezuka, and T. Mukai, Tetrahedron Lett., 891 (1975).
2. E. Vogel and H. Günther, Angew. Chem. Internat. Edit., 6, 385 (1967).
3. (a) L.A. Paquette, D.E. Kuhla, J.H. Barrett, and L.M. Leichter, J. Org. Chem., 34, 2888 (1969). The authors thank Professor L.A. Paquette for identification of XIII and XIV with his samples; (b) L.A. Paquette, J.H. Barrett, and D.E. Kuhla, J. Amer. Chem. Soc., 91, 3616 (1969); (c) H. Prinzbach, D. Stusche, and R. Kitzing, Angew. Chem., 82, 393 (1970).
4. (a) T. Sasaki, K. Kanematsu, A. Kakehi, I. Ichikawa, and K. Hayakawa, J. Org. Chem., 35, 426 (1970); (b) J. Streith and J.M. Cassal, Angew. Chem., 80, 117 (1968); (c) V. Sniechus, Chem. Commun., 831 (1969); (d) J.P. Luttringer and J. Streith, Tetrahedron Lett., 4163 (1973); (e) B. Willig and J. Streith, ibid., 4167 (1973).
5. T. Mukai and H. Sukawa, ibid., 1835 (1973).
6. Satisfactory elemental analyses were obtained for all new compounds reported in this paper. The spectral properties will be described in detail elsewhere.
7. R.B. Woodward and R. Hoffmann, " The Conservation of Orbital Symmetry ", Academic Press Inc., New York (1970), p. 145.
8. (a) R. Sustmann, Tetrahedron Lett., 2717 (1971); (b) K.N. Houk, J. Amer. Chem. Soc., 94, 8953 (1972).
9. K.N. Houk and R.B. Woodward, J. Amer. Chem. Soc., 92, 4143 (1970).

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