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ON THE SYNTHESIS AND VALENCE ISOMERIZATION OF SUBSTITUTED 5H-1,2-DIAZEPINES[1]

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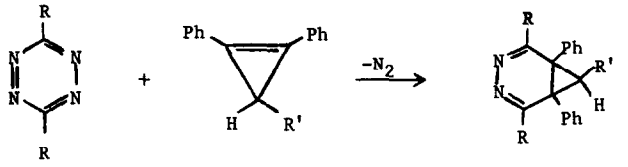
Previous studies in our laboratory have illustrated the utility of cyclopropene derivatives in the synthesis of substituted cycloheptatrienes.[2] As a logical extension of this work we have examined the reaction of several cyclopropenes with heterocyclic dienes in the hope of obtaining convenient synthetic routes to some of the more elusive heterocyclic unsaturated seven-membered ring systems. We now report a simple and convenient diene synthesis of substituted 5H-1,2-diazepines (3,4-diazacyclohepta-1,3,5-trienes)[3] and, in addition, describe a novel valence isomerization and thermal fragmentation in this series. These findings are reported in preliminary form as they have a direct bearing on some similar results recently communicated by Sauer and Heinrichs.[4] The structural conclusions of these authors are somewhat at variance to those suggested by our data reported here.

Refluxing an initially dark purple benzene solution of the colored diphenyl-*s*-tetrazine (Ia) with an approximately equimolar amount of triphenylcyclopropene (IIa) resulted in the evolution of gas and a gradual fading in color of the reaction solution.[5] Partial removal of solvent afforded an 80% yield of IVa as a crystalline yellow solid, $C_{35}H_{26}N_2$(m/e 474), m.p. 237-239° (rapid heating). In a similar reaction with Ia, methyl 2,3-diphenylcyclopropenecarboxylate (IIb) required 14 days refluxing in benzene to give a 32% yield of ester IVb as yellow needles, $C_{31}H_{24}N_2O_2$, m.p. 240-241°. The sluggishness of olefin IIb in Diels-Alder reactions with electron-poor dienes has previously been noted.[6] The reaction of IIa with the more reactive diene component, *bis*(perfluoroethyl)-*s*-tetrazine (Ib)[7], proceeded rapidly in refluxing benzene to give a 72% yield of the yellow crystalline solid IVc, $C_{27}H_{16}N_2F_{10}$ (m/e 558), m.p. 201-202°. The infrared spectra of these adducts supported the assigned diazepine structures showing typical medium intensity absorption for a *cis*-azo linkage[8] at *ca.* 1550 $cm.^{-1}$ No -NH absorption could be detected by infrared or n.m.r. means.

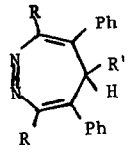


Ia; R = Ph IIa; R' = Ph IIIa; R = R' = Ph

b; R = C_2F_5 b; R' = CO_2CH_3 b; R = Ph

R' = CO_2CH_3

c; R = C_2F_5; R' = Ph



IVa; R = R' = Ph

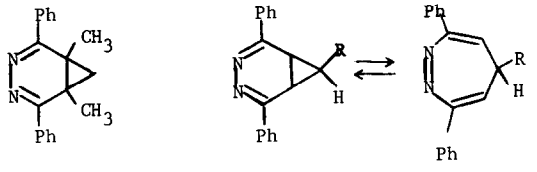
b; R = Ph; R' = CO_2CH_3

c; R = C_2F_5; R' = Ph

The ultraviolet spectra of adducts IVa-c are likewise in accord with the diazepine structure, showing broad absorption maxima in methanol at 313, 306, and 287 mμ respectively. The small hypsochromic shift produced by replacing the C-7 phenyl of IVa by a carbomethoxy group is similar to that observed in the polyphenylcycloheptatriene series.[9] In acid solution the long wavelength maxima of IVa and IVb are shifted bathochromically by ca. 20 mμ, as would be anticipated for a conjugated azo chromophore. The spectrum of the perfluoroethyl compound IVc was unaffected by dilute acid, apparently reflecting the low basicity of the ring nitrogens in this derivative.

Although the infrared and ultraviolet data are consistent with the 1,2-diazepine structure for these adducts, they do not eliminate from consideration the valence tautomeric structures IIIa-c which are almost certainly formed in the adductions, if only as intermediates. There is, in fact, considerable precedent for the latter structures. Thus Maier has prepared the 2,5-diphenyl-3,4-diazanorcaradiene derivatives V, VIa and VIb in several steps from appropriate cyclopropane precursors,[10] and 2,5,7-triphenyl-3,4-diazanorcaradiene(VIc) has been isolated as an intermediate in the N-halosuccinimide promoted ring contraction of the corresponding dihydro-diazepine.[11] We have prepared the norcaradiene derivative VIa, m.p. 197-198°,

λ_{max}^{MeOH} 315(log ϵ 4.26), 249(3.92) mμ, by the Diels-Alder reaction of Ia and cyclopropene.[12] The n.m.r. spectrum is in agreement with that reported by Maier and rules out any contribution of diazacycloheptatriene VIIa at room temperature. However, high temperature n.m.r. studies (> 110°), have permitted us to observe the reversible conversion of VIa into VIIa. At 180° this equilibrium is displaced almost entirely towards the cycloheptatriene form VIIa.[13]



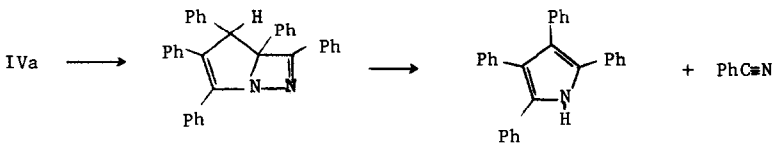
V VI VII

a, R = H; b, R = CH_3; c, R = Ph

The cyclopropene-tetrazine adducts having phenyl groups at the C-1 and C-6 positions are assigned 1,2-diazepine structures IVa-c on the basis of their n.m.r. spectra which show a lone, low field allylic proton signal in the τ 5.0-5.5 region. For comparison heptaphenylcycloheptatriene and hexaphenylcycloheptatriene-7-carboxylic acid show corresponding allylic proton absorption at τ 4.6 and 5.1 respectively.[14] For a norcaradiene structure of type IIIa or IIIc one would anticipate benzylic cyclopropyl proton absorption at ca. τ 7-8 as was found for several related adducts of triphenylcyclopropene with cyclic and acyclic dienes.[6] Furthermore, the triphenyldiazanorcaradiene VIc, a more closely analogous compound, exhibits its benzylic cyclopropyl proton at τ 8.14.[11]

Examination of the curious melting behavior of pentaphenyldiazepine IVa revealed a facile thermal isomerization of this derivative at temperatures above 100°. Thus in refluxing xylene IVa was converted quantitatively after 17 hours to a nearly colorless isomer, m.p. 242-243°, showing no -NH and only weak -C=N- absorption in the infrared. Further heating of this isomer at 235-245° for 15 minutes resulted in the formation of tetraphenylpyrole and benzonitrile in ca. 50% yield. In striking agreement with the thermal fragmentation result, the most intense peak in the mass spectrum of IVa (m/e 371) corresponded to the loss of a benzonitrile fragment. The expected metastable peak for this fragmentation was found at m/e 290.5. The related fragmentation involving loss of nitrogen from IVa is relatively unimportant as evidenced by

the low intensity of the m/e 446 ion. The thermal fragmentation products and the mass spectral results, together with the ultraviolet and n.m.r. data (λ_{max}^{MeOH} 305(sh), 257 (4.40)mμ; τ4.10(singlet, area 1), 2.30-3.04(multiplet, area 25)) strongly suggest a diazabicyclo-[3.2.0]heptadiene structure VIII for the colorless isomer. Further work is underway to establish this point.[15]



In their communication Sauer and Heinrichs proposed norcaradiene structure IIIa for the yellow adduct of triphenylcyclopropene with diphenyl-s-tetrazine, basing their assignment largely on the similarity of its ultraviolet spectrum to that of VIa. Unfortunately this agreement is fortuitous, for as noted by Maier,[10] substituents at the C-1 and C-6 positions have a marked effect on the ultraviolet spectra of VIa and its derivatives. The long wavelength maximum of 1,6-dimethyl-2,5-diphenyl-3,4-diazanorcaradiene(V),[10] for example, is shifted hypsochromically to 290 mμ (4.07), most probably the result of steric interaction of the methyl and phenyl groups which prevents coplanarity of the phenyl rings with the azine chromophore. A similar, if not larger, effect would be expected of 1,6-phenyl groups. Therefore structures IIIa and IIIc, and by analogy, IIIb, are incompatible with the ultraviolet data as well as the n.m.r. spectra. The additional assignment by the German authors of the 1,2-diazepine structure IVa to the colorless thermal isomerization product VIII is likewise untenable in light of the above arguments.

It is striking that, at room temperature, V is a stable norcaradiene derivative while IVa exists in the open triene form. In all probability this can be ascribed to the extra conjugation provided by the 1,6-phenyl substituents of IV which should more than offset the diphenylazine conjugation in norcaradiene tautomers III. This would not be true of the cycloheptatriene tautomers of V, VIa, VIb and VIc.

REFERENCES

1. Presented in part at the Fourth Carribean Chemical Symposium, Kingston, Jamaica, January 3-7, 1967. Support of this work by National Science Foundation Grants GP-254 and GP-3352 is gratefully acknowledged.

2. M. A. Battiste, Chem. Ind. (London), 550(1961); J. Am. Chem. Soc., 85, 2175(1963).

3. For convenience, the numbering of the diazepine ring system in the present paper will be the same as that for cycloheptatriene. This allows a direct correspondence with the numbering used in the related diazanorcaradiene valence tautomers.

4. J. Sauer and G. Heinrichs, Tetrahedron Letters, 4979(1966).

5. R. A. Carboni and R. V. Lindsey (J. Am. Chem. Soc., 81, 4342(1959)) were apparently the first to recognize the remarkable Diels-Alder reactivity of s-tetrazines with olefins and acetylenes to give pyridazine derivatives.

6. M. A. Battiste, Tetrahedron Letters, 3795(1964).

7. H. J. Gisler, Jr., Masters Thesis, University of Florida, August, 1965.

8. C. G. Overberger, J. P. Anselme, and J. R. Hall, J. Am. Chem. Soc., 85, 2752(1963), and references cited therein.

9. The absorption maxima for heptaphenylcycloheptatriene and methyl hexaphenylcycloheptatriene-7-carboxylate are found at 266 and 260 mμ respectively.

10. G. Maier, Ber., 98, 2438, 2446(1965).

11. R. G. Amiet, R. B. Johns, and K. R. Markham, Chem. Comm., 128(1965).

12. The cyclopropene used in this reaction was generated by the convenient procedure of G. L. Closs and K. R. Krantz, J. Org. Chem., 31, 638(1966).

13. The results of this n.m.r. study will be reported separately.

14. M. A. Battiste and T. J. Barton, unpublished results.

15. The isomerization of IVa to VIII is, to our knowledge, the first reported example of the thermal conversion of a cycloheptatriene derivative to its bicyclo[3.2.0]heptadiene valence tautomer. The prohibitiveness of this process in the carbocyclic series is explained by the stereoelectronic requirements of a 4n(n=1) electrocyclic reaction.[16] Incorporation of a nitrogen atom at an unsaturated position in the seven-membered ring might be expected to remove the unfavorable steric requirements for the intramolecular cyclization.

16. R. B. Woodward and R. Hoffman, J. Am. Chem. Soc., 87, 395(1965).