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INTERCEPTION OF AN INTERMEDIATE IN THE ALKALINE DEGRADATION OF 4-HALO-2-PYRAZOLIN-5-ONES.

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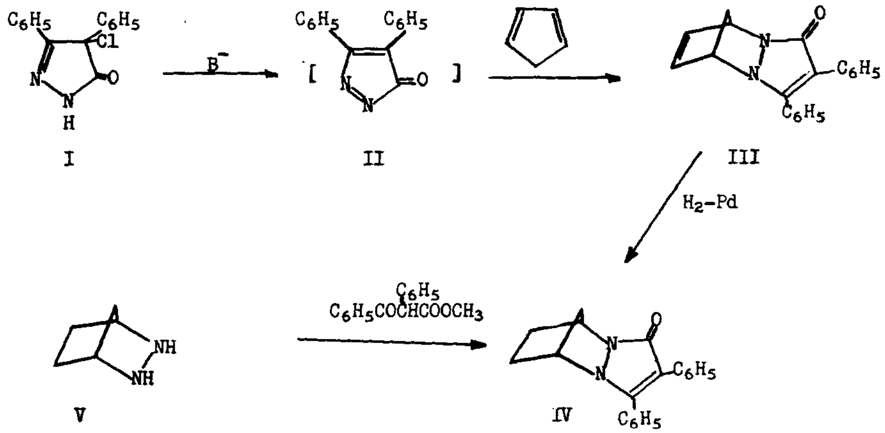
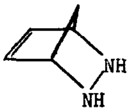
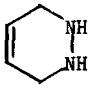
A recently developed convenient synthetic route to α,β-acetylenic and α,β-olefinic acids involves treatment of 4,4-dihalo- and 4-halo-4-substituted -2-pyrazolin-5-ones with aqueous alkali[1]. For example the 3,4-diphenyl derivative (I) with aqueous sodium hydroxide yields a mixture of cis- and trans-α-phenylcinnamic acids. No evidence has heretofore been available on the mechanism of this novel reaction although it has been postulated[2] to proceed by dehydrohalogenation of I to a diazacyclopentadienone[3] intermediate (II) followed by subsequent ring opening, loss of nitrogen and appropriate proton transfers. Evidence for the transient formation of the postulated diazacyclopentadienone (II) has now been obtained by treatment of I with triethylamine in ether for 1 - 2 days in the presence of cyclopentadiene. The Diels-Alder adduct (III)[7], m.p. 151-154° dec., was obtained in 70-90% yield. That the adduct has the antipyrine-type structure (III) is indicated by the n.m.r. spectrum which exhibits six sets of complex multiplets centered at δ 2.15(2H), 4.63(1H), 5.27(1H), 5.68(1H), 6.44(1H) and 7.30(10 H).



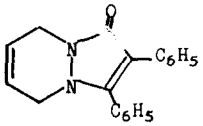
These resonances can be ascribed to the methylene protons, the two different bridgehead protons, the two different vinyl protons and the aromatic hydrogens respectively. Catalytic hydrogenation of III over palladium-carbon gave in 90% yield a dihydro derivative (IV), m.p. 229.5-232°. The indicated selectivity in the reduction of III follows from the n.m.r. spectrum of IV which in contrast to that of III shows no absorption in the vinyl region. In addition to the peaks centered at δ 7.40(10 H) due to the aromatic protons there is present a complex multiplet due to the methylene protons between about 1.2 - 2.5(6 H) and two broad peaks at 4.33(1 H) and 4.83(1 H) ascribed to the two bridgehead protons. The structure of IV and thereby that of the original Diels-Alder adduct (III) was established unequivocally by an alternate synthesis. Heating together a mixture of 2,3-diazabicyclo [2.2.1] heptane (V)[8] or the corresponding hydrochloride with methyl α-phenyl-α-benzoylacetate[9] gave IV, identified by its infrared spectrum, in 26% yield. This method could not be adapted to the synthesis of the Diels-Alder adduct (III) itself because of the instability of the requisite intermediate (VI) which has been shown by previous workers[10,11] to suffer a reverse Diels-Alder reaction under relatively mild conditions. The corresponding tetrahydropyridazine (VII) derived from butadiene is not subject to such a reverse Diels-Alder reaction and can be easily isolated and handled[12]. Condensation of VII with methyl α-phenyl-α-benzoylacetate by warming at 145° for 1 - 2 hours gave a pyrazolinone (VIII), m.p. 187-189°, which was identical with that obtained by generating the diazacyclopentadienone (II)[13] in the presence of butadiene.



VI



VII



VIII

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