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DIELS-ALDER REACTIONS OF 1,3-DIENES WITH 4-NITROBENZENEDIAZONIUM SALT AS A DIENOPHILE

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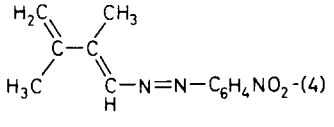
Summary *Further examples of the title reaction, discovered by Carlson, Sheppard, and Webster, reveal scope and regiochemistry of the formation of 1,6-dihydropyridazines; all the evidence points to a concerted primary addition.*

It was in 1919 that K.H. Meyer [1], in a bold generalization, asserted that phenyl ethers and aliphatic 1,3-dienes are capable of *azo coupling* with aromatic diazonium ions; *e.g.*, formula 1 was assigned to the yellow needles obtained from 4-nitrobenzenediazonium chloride and 2,3-dimethylbutadiene. What had become accepted textbook knowledge, required revision more than fifty years later. Carlson, Sheppard and Webster [2] demonstrated the *dienophilic* activity of arenediazonium nitrogen and established structure 3 for the above-mentioned product. As a benzene substituent, $-N_2^+$ commands the highest electron attraction known. According to the MO perturbation theory,[3] 1,3-dienes with high HOMO energy, *i.e.*, electron-rich dienes, should be especially reactive in concerted Diels-Alder additions which are LU(diazonium ion) - HO(diene) controlled. We have varied the 1,3-diene beyond 2,3-dimethylbutadiene and *trans*-piperylene [2] to learn about scope and regiochemistry.



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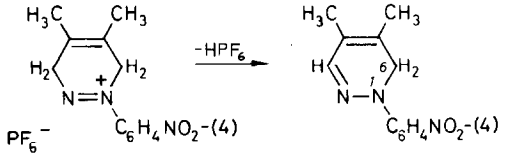
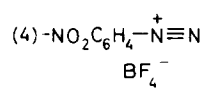


2 3 (79%)

The suspension of the 4-nitrobenzenediazonium fluoborate (4) in acetonitrile at 0°C was stirred with 2 equiv. of the diene; the rate of dissolution corresponded to the reactivity of the 1,3-diene. Either the crystalline product precipitated or the mixture was worked up with dichloromethane/water. One mol of HBF_4 is generated which can polymerize some diene; addition of triethylamine was not

advantageous, however. Occasionally, the sensitivity of the 1,6-dihydropyridazine derivatives posed problems.



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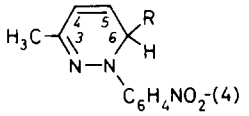
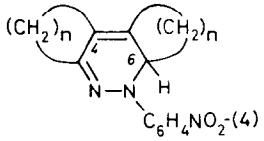
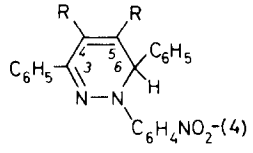


5 R = H (68%)
6 R = CH_3 (58%)

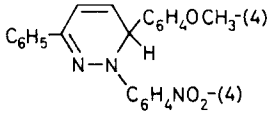


7 n = 3 (67%)
8 n = 4 (65%)

Butadiene did not combine with 4. The unstable product from isoprene and 2,4-dinitrobenzenediazonium fluoborate (59%, dec.p. 108°C; lit.:[1] 98°C) revealed in the ^{1}H-NMR spectrum the methyl signals of both regioisomers, accompanied by those of decomposition products. *trans,trans*-2,4-Hexadiene, 1,1'-dicyclopentenyl, 1,1'-dicyclohexenyl furnished the orange-yellow crystals of 6 (mp 93-94.5°C), 7 (mp 37.5-139.5°C), and 8 (mp 157-158°C).[4] The λ_{max} values (CH_2Cl_2) of these cyclic hydrazones occur at 421, 431 and 442 nm (log ε 4.4), respectively, *i.e.*, at longer waves than crotonaldehyde-*N*-methyl-4-nitrophenylhydrazone (402 nm, log ε 4.6). In the ^{1}H-NMR spectrum of 6, the s(3-CH_3) at δ 2.10 corresponds to s(3-CH_3) in 5 (δ 2.03) and appears at lower field than the 4-CH_3 of 3 (δ 1.77); the 6-CH_3 of 6 absorbs at δ 1.19 and the 6-H as a quintuplet at 4.83 with J = 6.5 Hz. The 6-H of 7 and 8 display homoallylic couplings to 4-CH_2.



9 R = H (69%)
10 R = CH_3 (74%)



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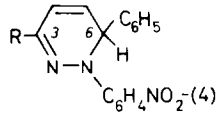


12 R = CH_3 (39%)
13 R = C_2H_5 (30%)

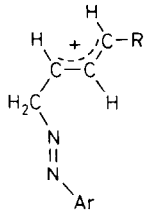
In the formation of 6 - 8, the salt 4 dissolved in 30 min at 0°C. The addition to *trans,trans*-1,4-diphenylbutadiene was slower and required 12 hr. The ABC spectrum of the ring protons of 9 (mp 165-166°C) was simulated by LAME:[5] 4-H δ 6.50, 5-H 6.35, 6-H 5.80. The reaction of 4 with 2,3-dimethyl-*trans,trans*-1,4-diphenylbutadiene, despite its steric encumbrance, was complete after 30 min and afforded 10 (mp 202-203°C). The introduction of one *p*-methoxy group into *trans-trans*-1,4-diphenylbutadiene reduced the reaction time to 1 hr whereas one *p*-nitro

group thwarts the interaction with 4.

The 1:1 reaction of 1-*p*-methoxyphenyl-4-phenylbutadiene provided the amorphous 11; its ^{1}H-NMR spectrum revealed no other admixture than <5% of the starting diene. The singlet of the non-conjugated 6-C_6H_5 of 9 has disappeared in 11, and the 6-H absorbs in 11 at higher field (δ 5.64) than in 9 (5.80), due to the electron release by OCH_3. In the ^{13}C-NMR spectra ($CDCl_3$) of 9 and 11, the singlet of the C-3 shows virtually the same δ_C (142.8 and 142.7) while the d(C-6) of 9 at 57.1 is shifted to 55.1 for 11.

The reactions of 4 with *trans,trans*-1-phenyl-1,3-pentadiene and -hexadiene were run at -30°C to avoid polymerization of the diene. Adduct 12 (mp 140-141°C) displayed in the ^{1}H-NMR spectrum the methyl singlet at δ 2.07, the 6-H at 5.64, and the singlet of 6-C_6H_5 at 7.20. The quadruplet of the CH_2 group at δ 2.47 leaves no doubt that in product 13 (mp 83-84.5°C) the alkyl group is likewise located in position 3; the singlets for 6-H at δ 5.71 and for 6-C_6H_5 at 7.20 corroborate structure 13.

We confirm formula 5 for the piperylene product;[2] the American authors emphasized that the addition direction is opposite to that which one would expect for the best carbonium intermediate in the framework of a two-step cycloaddition, the first step being the electrophilic attack by the aromatic diazonium ion. However, structures 11 - 13 are consistent with either a one-step or a two-step cycloaddition. Both mechanisms furnish the 3,6-dihydropyridazinium salts of type 2 which are deprotonated. The fact that the adducts of benzene- and halobenzenediazonium salts suffer dehydrogenation to aromatic pyridazinium salts,[2] is in agreement with the type 2 intermediate.



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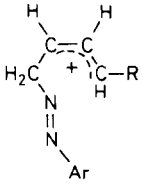

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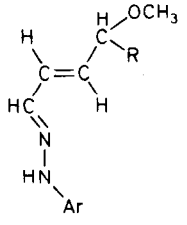

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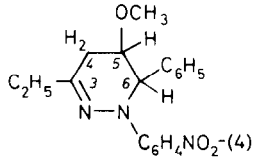

17

Butadienes usually favor the *s-trans* to the *s-cis* conformation; the equilibrium depends on the substituents. The *s-cis* arrangement is *a conditio sine qua non* for the concerted Diels-Alder reaction. On the other hand, in the terminal azo coupling the *s-trans* conformation should be preferred because *exo,exo*-disubstituted allyl cations like 14 are better than the *exo,endo*-disubstituted 15. The cyclization of 14 to the 3,6-dihydropyridazinium ion would require a rotation within the allylic system; such a rotation costs 24 kcal mol^{-1} for the *exo,endo* → *exo,exo*-

dimethylallyl cation in SbF_5/SO_2ClF at 35°C.[6] The cyclization of 15 is free of this disadvantage. It is anticipated that the *exo,exo*-disubstituted cation 14 should be captured by a nucleophilic solvent, *e.g.*, giving 16 with methanol. On carrying out the reactions of 4 with various 1,3-dienes *in methanol*, we obtained the same 1,6-dihydropyridazines described above, although in somewhat diminished yields.

From the reaction of 4 with 1-phenylhexa-1,3-diene in methanol we isolated the yellow methanol adduct 17 (mp 125-126°C) in 28% yield besides 13. The λ_{max} = 395 nm (CH_2Cl_2) indicates a non-conjugated 4-nitrophenylhydrazone system and the ^{1}H-NMR spectrum is void of olefinic H signals. Besides the t and q of 3-C_2H_5, the 4-H_2 gives rise to a multiplet at δ 2.16 and the 5-H to q at 3.90. The ^{13}C-data are consistent with 17; some MS peaks: 339 (M^+, 100%), 226 (C_6H_5-CH=N-$C_6H_4NO_2^+$, 97%), 134 (CH_3O-CH=CH-$C_6H_5^+$, 20%). 17 is not the result of trapping, but of a *subsequent* addition of methanol. The dihydropyridazine 13 was converted to 17 (60%) in methanol in the presence of sulfuric acid.

Thus, all the findings point to a concerted cycloaddition of 1,3-dienes to the diazonium nitrogens giving the 3,6-dihydropyridazines. This reaction needs not necessarily be an exothermic one. It is conceivable that a slightly *endothermic* Diels-Alder addition is followed by an exothermic step, either the deprotonation affording the 1,6-dihydropyridazines or the dehydrogenation which furnishes the pyridazinium ions.

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