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Orientation of azide addition to homoconjugated dienes

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The 1,3-dipolarcycloaddition of phenyl azide to bicyclic dienes **8–10** proceeds readily at the angle strained double bond to give both 1,2,3-Δ^2-triazoline isomers which would result from the two possible orientations of addition. The major triazoline isomer in each case is that resulting from stabilization of the dipolar transition state by the neighboring unreactive double bond. The structures of the triazolines were deduced from their nuclear magnetic resonance spectra in CCl_4, $CDCl_3$, and C_6H_6.

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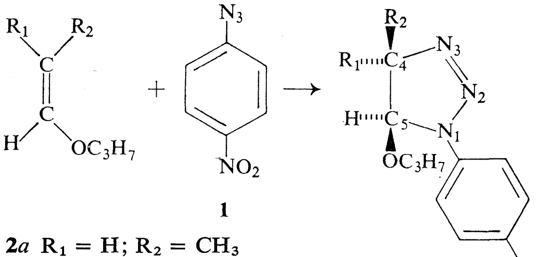
The 1,3-dipolarcycloaddition of organic azides to alkenes to give 1,2,3-Δ^2-triazolines has been the object of continued interest for nearly four decades. The investigations of Huisgen and coworkers have established the stereospecifically *cis* nature of the addition as well as the principle electronic factors influencing the direction of addition (1). Thus, *p*-nitrophenyl azide (**1**) reacts stereospecifically with the *cis* and *trans* enol ethers, **2***a* and **2***b*, to give the corresponding *cis* and *trans* 4,5-disubstituted triazolines, **3***a* and **3***b* respectively (2). Addition of phenyl azide to styrene occurs in only one direction giving **4** in high yield (3). Likewise 1,3-cyclohexadiene and 1-hexene are reported to yield **5** and **6** respectively upon reaction with *p*-bromophenyl azide (4).



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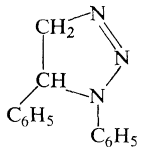
2*a* $R_1 = H; R_2 = CH_3$
b $R_1 = CH_3; R_2 = H$

3*a* $R_1 = H; R_2 = CH_3$
b $R_1 = CH_3; R_2 = H$



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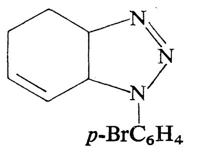

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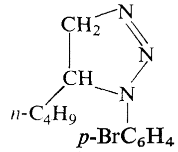

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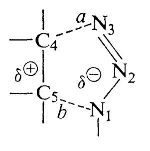
Although the 1,3-dipolarcycloaddition of azides to alkenes is formally classified as a concerted addition, the distinct preference for the orientation of addition noted above has been interpreted in terms of a transition state in which there is charge imbalance. Thus, the formation of bond *a* is considered to proceed more rapidly than bond *b* in the cycloaddition. Substituents on C_5 which stabilize the incipient positive charge at this position should not only facilitate addition but cause the particular orientation of azide addition noted above to be favored (transition state **7**). Except in cases where overriding steric effects operate, azide addition to alkenes has always been observed to take place in a Markownikoff fashion initiated by electrophilic attack by the terminal azide nitrogen on the alkene (2, 4). The dipolar nature of the addition process is also reflected by the observed substituent effect ($\rho = +0.84$) for the addition of substituted phenyl azides to norbornene (5).



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The electronic effects of the alkene substituents on the orientation of azide addition in all cases reported to date has been quite pronounced. In order to gain an insight into the effect of more remote alkene substituents on the orientation of azide addition we have determined the orientation

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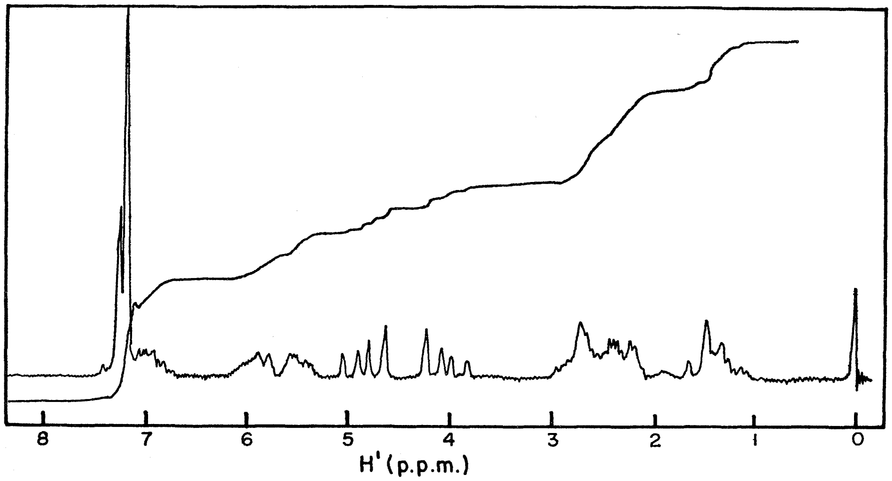
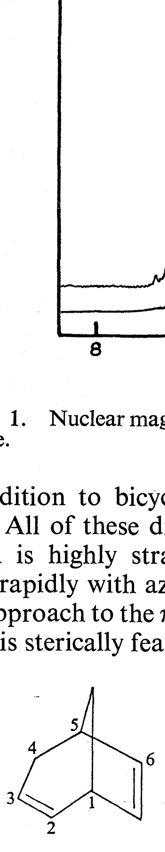


FIG. 1. Nuclear magnetic resonance spectrum of product **11** from reaction of phenyl azide and bicyclo(3.2.1)octa-2, 6-diene.

of addition to bicyclic homoconjugated dienes **8**–**10**. All of these dienes have one alkene bond which is highly strained and therefore should react rapidly with azide (1, 6). In each case only *exo* approach to the π cloud of the reactive alkene bond is sterically feasible (7). Furthermore, there are no steric interactions which would favor either of the two possible orientations for addition of an azide to the *exo* side of the reactive double bonds of these dienes. Any preference for one orientation of *exo* addition of azide would therefore be a measure of the extent to which the distant, unreactive double bond of each diene provided stabilization to the dipolar transition state, **7**.



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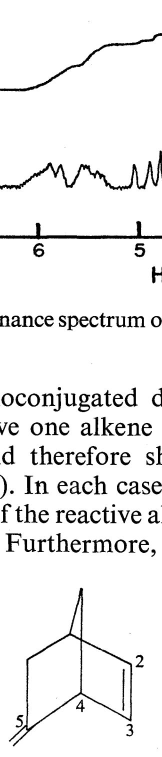

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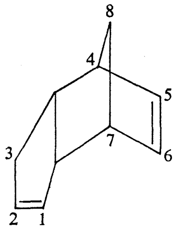

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The reaction of excess phenyl azide with bicyclo(3.2.1)octa-2,6-diene (**8**) in inert solvent, at room temperature, leads to the formation of a monoaddition product, **11**. The nuclear magnetic resonance (n.m.r.) spectrum of **11** is reproduced in Fig. 1. The signals appearing in the δ 3.6–5.1 region are due to the hydrogens attached to the carbons bearing the nitrogens of the triazoline ring and definitely indicate the presence of more than one isomer. The presence of absorptions due to two olefinic hydrogens in the n.m.r. spectrum of **11** can, *a priori*, have two interpretations. First, **11** could be a mixture of triazoline adducts resulting from addition of azide to *both* the Δ^2 and Δ^6 double bonds of **8**. On the other hand, addition could have occurred *only* to the more strained Δ^6 double bond, but in two orientations. Since under the conditions of this reaction phenyl azide addition to bicyclo(3.2.1)oct-2-ene does not occur (8) but addition to bicyclo(2.2.1)hept-2-ene is facile, azide reaction with the Δ^6 and not the Δ^2 double bond of **8** is the correct interpretation. The mixture of isomers obtained is thus **11***a* and **11***b*.

Assignment of n.m.r. signals to H_2 and H_6 in **11***a* and **11***b* was made by comparison of the position of these signals with those due to similar hydrogens in **12** (9) and other triazolines (4). Huisgen *et al.* (9) report that signals due to H_2 and H_6 in **12** and its aryl-substituted derivatives are doublets (9.2–9.5 Hz) appearing at δ 3.64–3.68 and δ 4.51–4.58 respectively. Scheiner reports (4) hydrogens attached to C_5 of monocyclic triazo-

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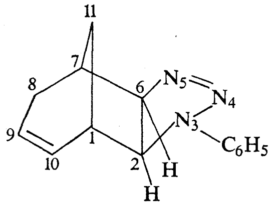
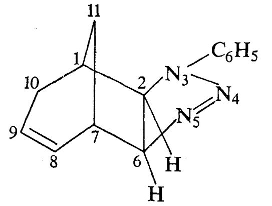
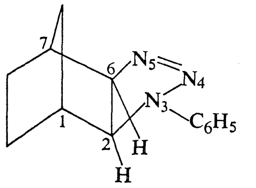


11*a*



11*b*



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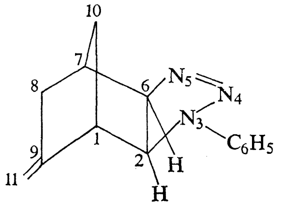
lines give n.m.r. signals between δ 3.6 and 4.0 whereas C_4 hydrogens resonate between δ 4.1 and 4.7. The two pairs of doublets (9.2 Hz) centered at δ 3.91 and 4.17 in the n.m.r. spectrum of **11** were thus assigned to H_2 of the isomers. Since H_2 of **11***a* is sterically situated in the shielding portion of the π-cloud of the Δ^9 double bond, the n.m.r. signal due to this hydrogen would be expected at higher field than H_2 of **11***b*. Thus the doublet centered at δ 3.91 is assigned to H_2 in **11***a* and the δ 4.17 doublet to H_2 in **11***b*. In a similar manner the doublets (9.2 Hz) centered at δ 4.74 and 4.98 were assigned to H_6 of **11***b* and **11***a* respectively. The above assignment is substantiated by the appearance of the doublets at δ 4.17 and 4.74 (**11***b*) which show strong perturbations causing the inside signal of each doublet to be significantly more intense than the outside signal. These perturbations are much less pronounced in the δ 3.91 and 4.98 doublets (**11***a*) as they should be. Integration also shows the pairs of doublets assigned to **11***a* and **11***b* to be correctly assigned. Integration of the AB quartets assigned to H_2 and H_6 of **11***a* and **11***b* showed **11***a*:**11***b* was 1.3:1.

Using benzene as an n.m.r. solvent had the effect of causing all hydrogens to resonate at higher field (10). That the effect is not uniform is evident from Table 1. The shielding experienced by H_2 of both **11***a* and **11***b* is considerably more (0.30–0.40 p.p.m.) than that experienced by H_6 (0.18–0.23 p.p.m.) in these isomers. We consider this to be due to unsymmetrical complexation of the benzene with **11***a* and with **11***b*.

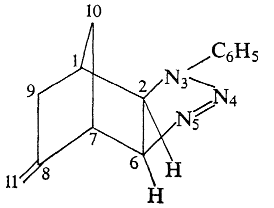
Ledaal (10) has summarized evidence for the formation of collision complexes between benzene and many different solutes. The model he proposed was one in which the dipole axis of the solute molecule coincided with the 6-fold symmetry axis of the benzene nucleus with the positive end of the dipole nearest to the benzene. For solutes with a dipole the solvent shift of different hydrogens of the solute increased as their proximity to the positive end of the dipole increased (i.e. the hydrogen lying in the diamagnetic shielding cone of the benzene nucleus was solvent-shifted the greatest amount). The larger the dipole moment, the larger the solvent shift for solutes of similar type.

Using the above model and the observed changes in chemical shift in **11***a* and **11***b* it is possible to designate the form of the **11***a*–benzene and **11***b*–benzene collision complexes. In both cases the benzene nucleus appears to lie below the solute molecule and to the side near the phenyl substituted nitrogen. The possibility that the benzene nucleus is situated at the end of the phenyl substituent of **11** as well as its location above the bicyclic ring system may be discounted because of the shifts observed *vide infra* (11).

The addition of phenyl azide to **9** gave a mixture of triazolines **13***a* and **13***b*. That addition occurred to only the highly strained Δ^2 double bond was evident from the appearance of signals due to the C_{11} methylene hydrogens at δ 4.75 and 5.05. The hydrogens at C_2 and C_6 of **13***a* and **13***b* have an orientation with respect to the methylene bond similar to that of H_2 and H_6 in **11***a* and **11***b* with respect to the nuclear double bond in those triazolines. Thus, although in CCl_4, H_2 and H_6 in **13***a* and **13***b* were exhibited as a single AB quartet for both isomers, in benzene the two sets of AB quartets were sufficiently resolved to allow the assignment specified in Table 1. The **13***a*:**13***b* ratio was calculated in this case from integration of H_1 and H_7 signals in the benzene spectrum of these isomers to be 1.3:1. The bridgehead signal



13*a*



13*b*

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TABLE 1
Chemical shifts of H_1, H_7, H_2, and H_6 of triazoline adducts

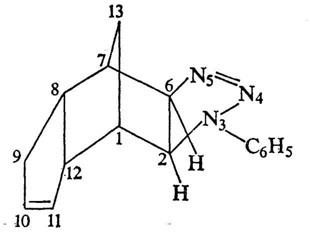
		Isomer *a*					Isomer *b*				
Sample	Solvent	H_1	H_7	H_2	H_6	$J_{2,6}$(Hz)	H_1	H_7	H_2	H_6	$J_{2,6}$(Hz)
12	CCl_4	2.63	2.76	3.66	4.53	9.2	—	—	—	—	—
	C_6H_6	2.23	2.50	3.12	4.17	9.2	—	—	—	—	—
	$\delta_{CCl} - \delta_{C_6H_6}$	0.40	0.26	0.54	0.36	—	—	—	—	—	—
11	$CDCl_3$	—	—	3.91	4.98	9.2	—	—	4.17	4.74	9.2
	C_6H_6	—	—	3.51	4.80	9.2	—	—	3.87	4.51	9.2
	$\delta_{CDCl_3} - \delta_{C_6H_6}$	—	—	0.40	0.18	—	—	—	0.30	0.23	—
p-NO_2**11**	C_5H_5N	—	—	4.00	5.15	9.0	—	—	4.25	4.99	9.0
13	CCl_4	2.98	2.79	3.64	4.51	9.0	2.69	3.10	3.64	4.51	9.0
	C_6H_6	2.80	2.59	3.29	4.41	9.0	2.36	3.01	3.41	4.29	9.0
	$\delta_{CCl_4} - \delta_{C_6H_6}$	0.18	0.20	0.35	0.10	—	0.33	0.9	0.23	0.22	—
	C_6F_6	2.97	2.71	3.59	4.46	9.0	2.71	2.97	3.59	4.46	9.0
	$\delta_{CCl_4} - \delta_{C_6F_6}$	0.01	0.08	0.05	0.05	—	−0.02	0.13	0.05	0.05	—
14	CCl_4	—	—	3.56	4.37	9.0	—	—	3.56	4.43	9.0
	C_6H_6	—	—	3.27	4.27	9.0	—	—	3.27	4.26	9.0
	$\delta_{CCl_4} - \delta_{C_6H_6}$	—	—	0.19	0.10	—	—	—	0.29	0.16	—
	$CDCl_3$	—	—	3.65	4.48	9.5	—	—	3.65	4.53	9.5
	$\delta_{CCl_4} - \delta_{CDCl_3}$	—	—	−0.09	−0.11	—	—	—	−0.09	−0.10	—

occurring at highest field in the benzene spectrum of the isomer mixture was assigned to H_1 of **13***b* because of its similarity in chemical shift to H_1 of **12**. Likewise, the signal at δ 2.79 was assigned to H_7 of **13***a*. Since the lowest field bridgehead hydrogen (δ 3.10) should be H_7 of **13***b*, the signal at δ 2.98 is deduced to be due to H_1 of **13***a*.

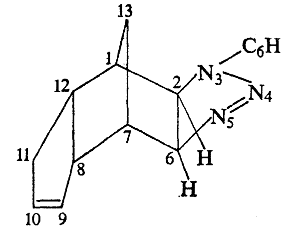
Addition of phenyl azide to *endo*-dicyclopentadiene has been reported several times (12, 13) but no evidence as to the homogeneity of the product has been available. Indeed the rather sharp melting range of the product could be construed as evidence for formation of a single triazoline adduct (14).

The n.m.r. spectrum of the addition product, **14**, revealed the presence of two olefinic hydrogens. Since phenyl azide addition proceeds readily with *exo*-1,2-dihydro-**10** (13, 15) but not with *exo*-5,6-dihydro-**10** (15) addition in the present case must have occurred to the Δ^5-double bond of **10**. Inspection of the δ 3.5–4.5 region of the n.m.r. spectrum of **14** revealed the presence of two isomeric triazolines. The AB quartet patterns of H_2 and H_6 in **14** were assigned to **14***a* and **14***b* as given in Table 1. Integration of the AB quartets due to H_2 and H_6 in **14***a* and **14***b* showed **14***a*:**14***b* to be 1.3:1.

The observation that there is a higher proportion of the "*a*" isomers than the "*b*" isomers in **11**, **13**, and **14** is interpreted in terms of stabilization of the positive charge generated at C_2 in the transition state leading to the "*a*" isomers. In each case (**8**–**10**) studied the π-cloud of the unreacting double bond is favorably situated for such homoconjugative stabilization. It is noteworthy that the addition of formic acid to **8** gives over 90% **15**, the result of homoconjugative participation by the Δ^2 double bond (16). Likewise **9** is reported to give a high proportion of **16** with formic acid (17). The orientation effect of the unreacting double bond in the dienes studied is significantly less in the azide reaction than in the formic acid addition. The



14*a*



14*b*

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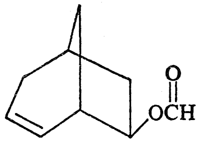

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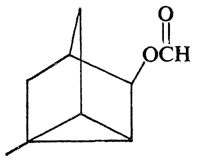

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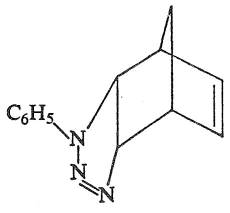
origin of this difference presumably lies in the amount of electron deficiency generated at C_2 in each type of reaction. The greater the electron deficiency the greater the orientation effect. Pursuing this reasoning one might expect (5) that substitution of an electron-withdrawing group (e.g. *p*-NO_2) on the aryl azide would introduce greater dipolar character into the transition state (7) for addition and thereby produce a greater orientational preference. The addition of *p*-nitrophenyl azide to **8** gave a mixture of *p*-nitrophenyl substituted **11***a* and **11***b*. The ratio of "isomer *a*" to "isomer *b*" was 1.5:1.

Calculation of the isomer ratio resulting from the *p*-nitrophenyl azide addition to **9** and **10** was unsuccessful because of the insolubility of the adducts in solvents in which the necessary signals could be resolved.

NOTE ADDED IN PROOF — Since the submission of this paper a report of *exo* and *endo* addition of phenyl azide to bicyclo(2.2.1)-2,5-heptadiene (**17**) has appeared (20). The ratio of *exo* to *endo* addition for monoaddition was 11:1. These workers observed a coupling of 3.5–4.5 Hz between the bridgehead hydrogens and the *exo* hydrogens attached to the *endo* triazoline adduct (**18**). Since the degree of steric hindrance on the *endo* side of **17** is less than in either **8**, **9**, or **10** one would expect an even higher proportion of *exo* addition in the present cases. The fact that no coupling of hydrogens attached to the triazoline rings in any of the adducts revealed any appreciable coupling with adjacent bridgehead hydrogens indicates all of the adducts presently investigated were *exo*.



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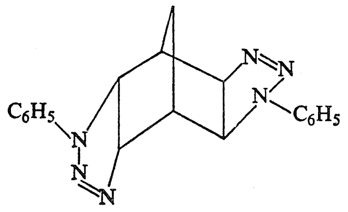

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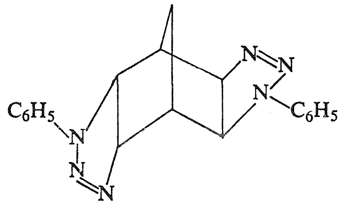

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Finally, in agreement with the above discussion, the addition of phenyl azide to **18** gave a mixture of **19** and **20** in which **19** predominated (**19**:**20** was 1:5).

Experimental

Melting points were determined using a Fisher–Johns melting point apparatus and are uncorrected.

Nuclear magnetic resonance spectra were recorded on a Varian Model A56/60 spectrometer using tetramethylsilane as an internal standard.

Mass spectra were recorded on a Hitachi Perkin–Elmer RU-6 mass spectrometer.

Preparation of 3-Phenyl-3,4,5-triazotricyclo(5.2.1.$0^{2,6}$)dec-4-ene (12)

The phenyl azide adduct of bicyclo(2.2.1)hept-2-ene was prepared in the usual manner (18) and had m.p. 99–100 °C (lit. (5) m.p. 101–102 °C). The n.m.r. spectra (18) confirmed the structure and purity of the adduct (Table 1).

Preparation of 3-Phenyl-3,4,5-triazotricyclo(5.3.1.$0^{2,6}$)undec-4,8(9)-dienes (11)

A solution of 0.5 g of phenyl azide and 0.5 g of bicyclo-(3.2.1)octa-2,6-diene (19) in 25 ml of petroleum ether (b.p. 60–110°) was allowed to stand for several days. The excess phenyl azide was removed under vacuum and the crystalline sample was analyzed by n.m.r. Recrystallization from $CHCl_3$ – petroleum ether (b.p. 30–60°) gave a white solid in 85% yield, m.p. 67.5–69 °C. The n.m.r. analysis of the recrystallized product (Fig. 1) revealed no detectable change in **11***a*:**11***b* had occurred during the recrystallization.

Anal. Calcd. for $C_{14}H_{15}N_3$: $(M)^+$ 225. Found (mass spectrometry): $(M)^+$ 225; $(M\text{-}28)^+$ 197.

The *p*-nitrophenyl derivative of **11** had m.p. 168–90°; n.m.r. (pyridine) δ 1–2 (m, 4H), 2–3 (m, 8H), 4.0–5.2 (m, 2H Table 1) and 5.35–6.3 (m, 2H).

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Preparation of 3-Phenyl-8(9)-methylene-3,4,5-triazotricyclo(5.2.1.0^{2,6})dec-4-enes (13)

The phenyl azide adduct of 5-methylene-2-norbornene (K and K Laboratories, Inc.) was prepared in the usual manner by reaction at room temperature for several days. The crude product showed the same **13***a*:**13***b* as that (70%) recrystallized from $CHCl_3$ – petroleum ether (b.p. 30–60°) m.p. 60.5–62°.

Anal. Calcd. for $C_{14}H_{15}N_3$: $(M)^+$ 225. Found (mass spectrometry): $(M)^+$ 225; $(M\text{-}28)^+$ 197.

The *p*-nitrophenyl derivative of **13** had m.p. 159–160 °C (decomposition) n.m.r. (pyridine) δ 1.14 (AB, J = 11Hz, $2H_{10}$), 1.83–2.35 (b, $2H_{8(9)}$), 2.42–2.92 (m, $2H_{BH}$), 3.12 (m, $1H_2$), 3.82 (d, J = 9Hz, $1H_6$), 4.80, and 5.08 ($H_2C{=}C\langle$). The AB quartets due to H_2 and H_6 of isomers *a* and *b* were also uncompletely resolved in benzene, chloroform.

Preparation of 14

The phenyl azide adduct of *endo*-dicyclopentadiene (Aldrich Chemical Co.) was prepared by reaction at room temperature for several days. Recrystallization of the crude product gave 75% **14**, m.p. 117–118° (lit. (13) 127–128 °C (MeOH); for n.m.r. see Table 1.

Anal. Calcd. for $C_{13}H_{17}N_3$: $(M)^+$ 251. Found (mass spectrometry): $(M)^+$ 251; $(M\text{-}28)^+$ 223.

The *p*-nitrophenyl derivative of **14** had m.p. 183–184 °C (decomposition); n.m.r. ($CHCl_3$) δ 1.28 (AB, J = 11Hz, $2H_{13}$), 2.2–2.8 (m, 4H), 2.8–3.5 (m, $2H_{BH}$), 3.72 (d, J = 9.2 Hz, $1H_2$), 4.62 (d, J = 9.2 Hz, H_{6b}), 4.67 (d, J = 9.2 Hz, H_{6a}), and 5.72 (s, 2H).

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