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THE ADDITION OF BENZYNE TO AZULENE

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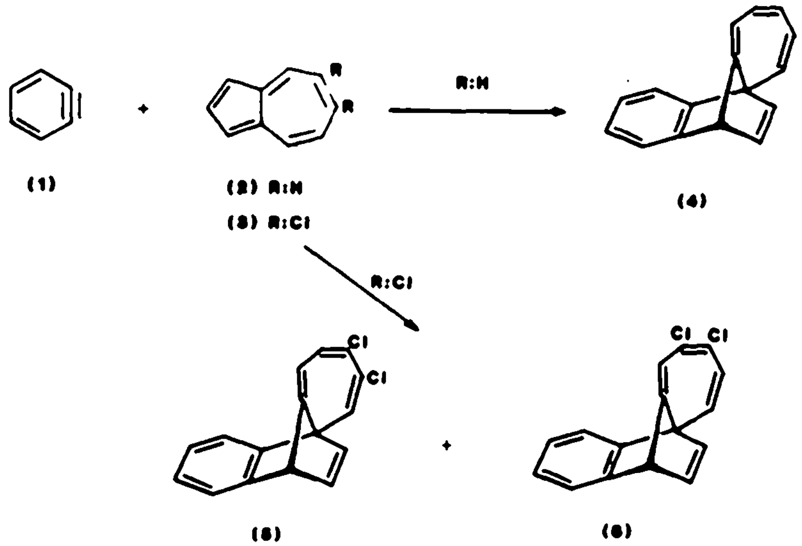
Abstract - The title reaction afforded the Diels-Alder adduct 4b,10-ethenobenz[*a*]azulene (4), while an analogous reaction involving 5,6-dichloroazulene gave the 6,7- and 7,8-dichloro-derivatives of (4). Treatment of (4) with 3,6-di(pyridin-2-yl)-*s*-tetrazine yielded benz[*a*]azulene.

The addition of benzyne (1) to unsaturated and aromatic substrates can give rise to a variety of interesting products.[1,2] In a continuation of our work on the use of benzyne and substituted benzynes for the synthesis of novel ring systems,[3-10] we have investigated the reaction of (1) with azulene.



SCHEME 1

When benzyne was generated by the oxidation of 1-aminobenzotriazole with lead tetraacetate[11] in the presence of azulene, the adduct (4) was obtained in 33% yield. Lower yields of (4) (10% and 16%) were obtained when benzenediazonium-2-carboxylate[12] or the corresponding hydrochloride were used as benzyne precursor, due to the competing formation of a dark red-brown polar by-product, apparently resulting from azo coupling between the benzyne precursor and azulene.[13] The structure of (4) is apparent from its spectroscopic properties. The ^1H n.m.r. spectrum (Figure 1 and Table)

FIGURE 1 ^1H n.m.r. spectrum of (4) (300 MHz, $CDCl_3$)

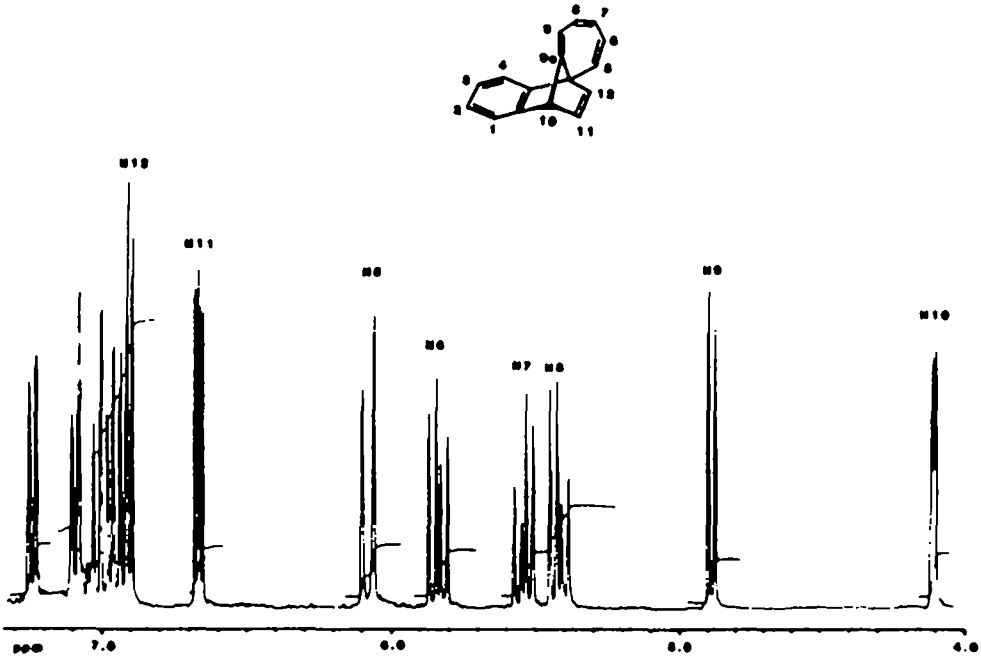
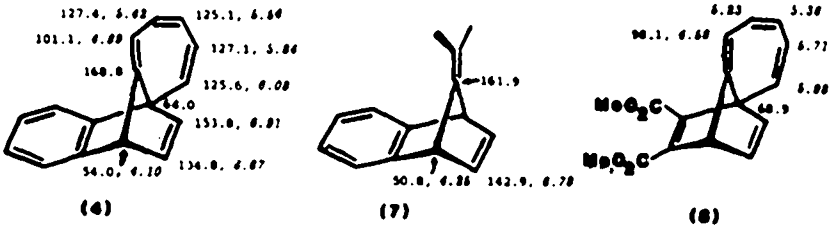


TABLE ^1H n.m.r. spectral data for the adducts in $CDCl_3$
(Chemical shift, multiplicity, coupling constants)

Proton	Compound (4)[a]	(5)[b]	(6)[b]
H1-H4	6.94-7.26,m	7.0-7.4,m	7.0-7.4,m
H5	6.08,dd,$J_{5,6}$12.0,$J_{5,7}$0.8	6.64,s	6.11,s[c]
H6	5.84,ddd,$J_{6,5}$12.0,$J_{6,7}$7.5,$J_{6,8}$ 1.0	-	6.11,s[c]
H7	5.54,dddd,$J_{7,8}$11.9,$J_{7,6}$7.5, $J_{7,5}$1.0,$J_{7,9}$1.0	-	-
H8	5.42,ddt[d],$J_{8,7}$11.9,$J_{8,9}$7.2, $J_{8,6}$1.0	6.03,d,$J_{8,9}$8.6	-
H9	4.89,dd,$J_{9,8}$7.2,$J_{9,7}$1.0	4.80,d,$J_{9,8}$8.6	5.17,s
H10	4.10,dd,$J_{10,11}$3.3,$J_{10,12}$1.0	4.16,d,$J_{10,11}$3.4	4.14,dd,$J_{10,11}$3.4,$J_{10,12}$1.0
H11	6.67,dd,$J_{11,12}$5.6,$J_{11,10}$3.3	6.73,dd,$J_{11,12}$5.7,$J_{11,10}$3.4	6.70,dd,$J_{11,12}$5.6,$J_{11,10}$3.2
H12	6.91,dd,$J_{12,11}$5.6,$J_{12,10}$1.0	6.87,dd,$J_{12,11}$5.7,$J_{12,10}$1.0	6.86,dd,$J_{12,11}$5.6,$J_{12,10}$1.0

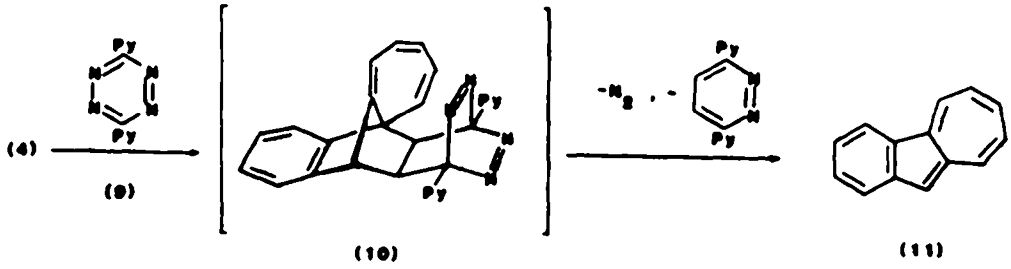
a 300 MHz; b 80 MHz; c isochronous; d virtual coupling to H5 in conjunction with spin decoupling experiments showed the presence of three isolated spin systems due to the aromatic protons, the benzonorbornadiene-type protons H10, H11, H12, and the cycloheptatrienyl protons H5, H6, H7, H8 & H9 respectively. It was possible to correlate the nonaromatic proton and carbon resonances with the aid of a ^{1}H-^{13}C hetero-COSY spectrum, and this established that the cycloheptatrienyl proton H9 (δ4.89) and the corresponding carbon atom C9 (δ100.1) resonated at unusually high field. Such a situation is characteristic of a 7-alkylidenenorbornadiene or 7-alkylidenebenzonorboradiene structural moiety[14,15] and provides strong evidence for the structure of (4). The chemical shifts of the relevant nuclei of some model compounds are shown in Scheme 2. Compound (8) was recently isolated from the reaction of azulene with dimethyl acetylenedicarboxylate under high pressure[16] and the chemical shifts of the cycloheptatrienyl nuclei of (8) and (4) are very similar.



SCHEME 2 ^{13}C and ^{1}H chemical shifts

The reaction of benzyne (from benzenediazonium-2-carboxylate) with 5,6-dichloroazulene (3) afforded adducts (5) and (6) in 9% and 3% yield respectively. These compounds showed the expected changes in the cycloheptatrienyl regions of their ^{1}H n.m.r. spectra when compared with (4) (Table), although surprisingly for (6) H5 and H6 were found to be isochronous at 80 MHz.

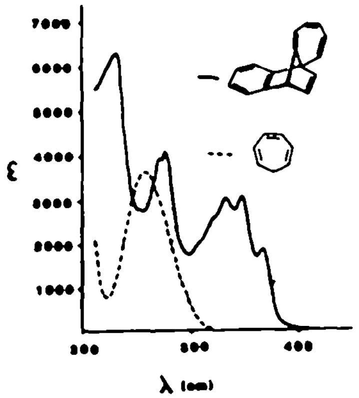
Chemical proof for the structure of (4) was obtained as shown in Scheme 3. Brief treatment of (4) with the electron-deficient dienophile 3,6-di(pyridin-2-yl)-s-tetrazine (9) afforded benz[a]-azulene (11) in high yield. This reaction involves addition of (9) to the strained, electron-rich benzonorbornadiene double bond of (4), and subsequent retro-Diels-Alder loss of nitrogen and 3,6-di(pyridin-2-yl)dipyridazine from the adduct (10).[17,18]

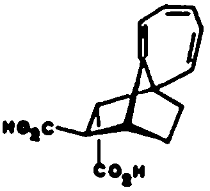


SCHEME 3

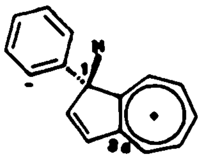
Ermer and co-workers have recently determined the crystal structure of the diacid (12) obtained by hydrolysis of the tetrahydro derivative of (8).[19] The cycloheptatriene ring of (12) was found to be essentially planar and a manifestation of this was observed in the electronic spectrum of (12), in which the broad absorption of the cycloheptatrienyl chromophore usually located at 260 nm was seen to be shifted to considerably longer wavelength and the absorption peak exhibited some fine structure.[19] The electronic spectrum of adduct (4) (Figure 2) is very similar in shape and intensity in the 300-400 nm region to that of (12), indicating that in (4) the cycloheptatriene ring is also forced into a planar conformation as a consequence of its fusion to the benzonorbornadiene ring system.

FIGURE 2 Electronic spectrum of (4) and cycloheptatriene in EtOH





(12)



(13)

Compound (4) is a Diels-Alder adduct of benzyne and azulene (2) and represents, after (8), only the second example of the cycloadduct in which (2) has served as the diene component.[20] However, the formation of (4) need not necessarily proceed through a concerted $\Pi^4_s+\Pi^2_s$ cycloaddition. Benzyne is known to be an electrophilic species[1],[2] and azulene is prone to electrophilic attack at C1.[21],[22] It is therefore possible to postulate zwitterion (13) as an intermediate in the reaction. Bonding of the phenyl ring to C3a (azulene numbering) would then afford (4). Alternatively, if a concerted pathway operates, the transition state is likely to possess significant polar character, with bond making to C1 of azulene being well advanced over bond making to C3a.

In summary, this work has shown that azulene will behave as a diene towards the highly reactive dienophile benzyne. The conversion of adduct (4) into benz[a]azulene (11) provides further variety to the existing routes to (11) and its derivatives.[20,23-27]

EXPERIMENTAL

M.ps were determined on a Kofler block and are uncorrected. Rapid silica gel chromatography was carried out by elution (under water aspirator vacuum) through a pad of Fluka Kieselgel G packed in a 6x6 cm cylindrical glass funnel, using the stated solvents. Fractions (50 ml) were collected and monitored by t.l.c. Radial chromatography was performed on 2 mm silica gel plates using a Chromatotron Model 7924 system. The following instruments were used for spectroscopic measurements - N.m.r. spectra: Bruker WP 80 (^{1}H 80 MHz, ^{13}C 20.1 MHz), Bruker AM 300 (^{1}H 300 MHz, ^{13}C 75.5 MHz); electronic spectra: Hewlett-Packard 8450 A; mass spectra: MS 30, MS 902. The following compounds were prepared by literature procedures: azulene,[28] 5,6-dichloroazulene,[29,30] 1-aminobenzotriazole,[11] and 3,6-di(pyridin-2-yl)-*s*-tetrazine.[31]

Addition of benzyne to azulene

(a) Solutions of 1-aminobenzotriazole (1.10 g, 8.2 mmol) in CH_2Cl_2 (12 ml) and $Pb(OAc)_4$ (3.60 g, 8.2 mmol) in CH_2Cl_2 (12 ml) were added dropwise over 10 min from separate addition funnels to an ice-cold stirred solution of azulene (1.0 g, 7.8 mmol) in CH_2Cl_2(10 ml). The mixture was stirred for 30 min, filtered through Celite, evaporated, and then subjected to rapid silica gel chromatography. Elution with 10% CH_2Cl_2-light petroleum gave a blue band, shown to consist of azulene and biphenylene (t.l.c. and n.m.r. analysis) (660 mg). Subsequent fractions afforded 4b,10-etheno-benz[a]azulene (4) (524 mg, 33%) as an oil, which crystallised as colourless prisms, m.p. 64-6° (MeOH) (Found: M^+ 204.0952. $C_{16}H_{12}$ requires 204.0937). Mass spectrum m/z 204(78%), 203(100), 178(92), 101(23), 89(23), 88(16), 76(26). ^{13}C n.m.r. (75.5 MHz, $CDCl_3$) δ : 54.0,d,C10; 64.0,s,C4b; 100.1,d,C9; 120.9,d,aryl; 121.9,d,aryl; 124.8,d,aryl; 125.0,d,aryl, 125.1,d,C7; 125.6,d,C5; 127.1,d,C6; 127.4,d,C8; 130.4,s,aryl; 134.8,d,C11; 153.8,d,C12; 156.7,s,aryl;

168.6,s,C9a. Electronic spectrum (EtOH) λ_{max} (log ε) 236(3.77), 275(3.56), 280(3.58), 336(3.45), 351(3.46), 370(3.24) nm (Figure 2). ^{1}H n.m.r. spectrum: see Figure 1 and Table.

(b) A slurry of benzenediazonium-2-carboxylate (prepared from 1.4 g anthranilic acid)[12] in 1,2-dichloroethane (10 ml) was added portionwise over 15 min to a solution of azulene (1.0 g, 7.8 mmol) in refluxing 1,2-chloroethane (50 ml). The solution was refluxed for 10 min, the solvent was evaporated, and the residue adsorbed onto silica gel and submitted to rapid chromatography. Elution with light petroleum and 10% CH_2Cl_2-light petroleum gave blue fractions consisting of azulene and adduct (4) (t.l.c. analysis). Most of the azulene (395 mg) was removed by sublimation (60°/0.1 mm) and the residue was submitted to radial chromatography using 10% CH_2Cl_2-light petroleum to give the adduct (4) (161 mg, 10%) as a colourless solid, spectroscopically identical with material prepared in (a). Elution of the original silica gel adsorbent with 5% MeOH-CH_2Cl_2 afforded a dark red-brown solid (780 mg) (presumably azo dye), which was not further investigated.

(c) Anthranilic acid (1.4 g, 10 mmol) was converted into the derived diazonium chloride using the general method of Hart and Oku.[32] This material was added as a slurry in 1,2-dichloroethane (10 ml) over 10 min to a refluxing solution of azulene (1.0 g, 7.8 mmol) in 1,2-dichloroethane (50 ml) containing propylene oxide (5 ml). Work up as in (b) afforded unchanged azulene (405 mg), adduct (4) (245 mg, 16%) and an azo dye fraction (510 mg).

Addition of benzyne to 5,6-dichloroazulene

A slurry of benzenediazonium-2-carboxylate prepared from anthranilic acid (1.6 g, 12 mmole) was heated under reflux with a solution of 5,6-dichloroazulene (2.8 g, 14 mmol) in 1,2-dichloroethane (50 ml) until gas evolution ceased (30 min). The mixture was filtered through a pad of alumina, and the solvent was evaporated. The residue was subjected to repeated radial chromatography, using 10% CH_2Cl_2-light petroleum to afford (in order of elution) 5,6-dichloroazulene (1.52 g), 6,7-dichloro-4b,10-ethenobenz[a]azulene (5) (368 mg, 9%) and 7,8-dichloro-4b,10-ethenobenz[a]azulene (6) (129 mg, 3%). Adduct (5) was obtained as colourless prisms, m.p. 93-4° (MeOH). (Found: M^+ 272.0173. $C_{16}H_{10}{}^{35}Cl_2$ requires 272.0159). Mass spectrum m/z 274(16%), 272(23), 248(34), 246(52), 239(16), 238(16), 237(51), 236(21), 203(18), 202(100), 201(16), 200(19), 176(25), 101(21), 100(28), 99(13), 93(11), 88(28), 87(15). ^{13}C n.m.r. (20.1 MHz, $CDCl_3$) δ : 53.7,d; 62.1, s; 97.0,d; 121.1,d; 122.4,d; 124.7,d; 125.7,2xd; 127.4,d; 128.5,s; 131.2,s; 135.6,d; 143.3,s; 152.5,d; 155.1,s; 168.1,s. Adduct (6) was obtained as colourless prisms, m.p. 114-6° (MeOH). (Found: M^+ 272.0153. $C_{16}H_{10}{}^{35}Cl_2$ requires M 272.0159). Mass spectrum m/z 274(19%), 272(30), 248(44), 246(77), 239(15), 238(15), 237(48), 236(28), 201(23), 200(100), 199(22), 198(24), 176(35), 101(14), 100(28), 88(25), 87(15). ^{13}C n.m.r. (20.1 MHz, $CDCl_3$) δ : 54.1,d; 61.4,s; 102.4,d; 120.9,d; 122.4,d; 124.7,d; 125.7,2xd; 127.0,s; 129.2,d; 129.8,s; 135.8,d; 143.5, s; 152.1,d; 154.9,s; 165.1,s.

Conversion of 4b,10-ethenobenz[a]azulene (4) into benz[a]azulene (11)

A solution of adduct (4) (100 mg, 0.49 mmol) and 3,6-di(pyridin-2-yl)-s-tetrazine (123 mg, 0.52 mmol) in $CHCl_3$ (5 ml) was refluxed for 30 min. The mixture was adsorbed onto silica gel (5 g), and placed onto a small funnel packed with that adsorbent. Elution with 10% CH_2Cl_2-light petroleum gave a blue-green solution, which was evaporated to afford benz[a]azulene (11) as lustrous green plates (82 mg, 94%), m.p. 192-3° (lit.[33] 189-90°), spectroscopically identical with material prepared previously.[26]

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