[6 + 3⁻] Cycloadditions of 1,1- and 1,3-Diphenyl-2-aza-allyl-lithium to Cycloheptatriene

By **David J. Bower** and **Merlin E. H. Howden**,* School of Chemistry, Macquarie University, Sydney, Australia

Reactions between cycloheptatriene and 1,1-diphenyl- (1) and 1,3-diphenyl-2-aza-allyl-lithium gave [6 + 3⁻] cycloadducts exclusively. The products were identified as 7,7-diphenyl-8-azabicyclo[4.3.1]deca-2,4-diene (2), and *trans*- (5) and *cis*-7,9-diphenyl-8-azabicyclo[4.3.1]deca-2,4-diene (6). [6 + 3⁻] Cycloadditions, the anionic analogues of [6 + 4] cycloreactions, have not been reported previously. Evidence is presented which is consistent with a concerted mechanism for these reactions.

CYCLOADDITIONS of allyl-type anions to ' anionophiles ' containing one or two double bonds are well known.[1-5] Many reactions of this kind are apparently similar to the Diels–Alder reaction, in that they are stereospecific [2,3] and regioselective [4] in those cases where these features were investigated. However, reaction mechanisms in which cycloaddition is not concerted have also been postulated.[4,5] Few examples [5,6] have been published of the extension of the field of thermal 1,3-anionic cycloaddition reactions to those of higher homologues which are theoretically allowed by the Woodward–Hoffmann rules.[7] These include [6 + 3⁻] cycloadditions, which have not yet been described in the literature. This paper reports the reactions of two diphenyl-2-aza-allyl-lithium compounds with cycloheptatriene as examples of [6 + 3⁻] cycloadditions.

RESULTS AND DISCUSSION

Reaction between equimolar amounts of cyclo-heptatriene and 1,1-diphenyl-2-aza-allyl-lithium (1) in ethereal solution at −45 °C, followed by hydrolysis,

(1)

(2)

(3)

(4)
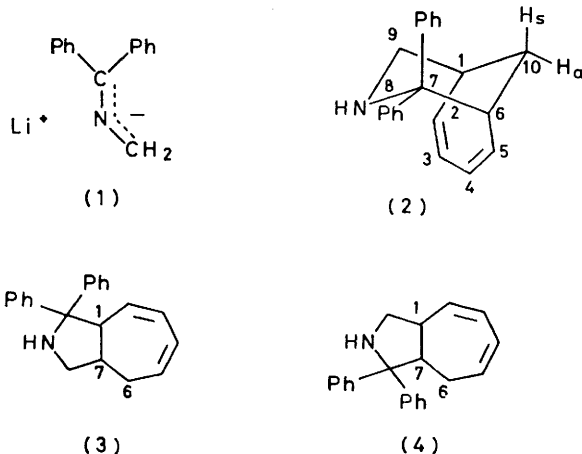
afforded a single product, the structure of which was determined by elemental analysis, ¹H and ¹H-coupled ¹³C n.m.r., and by mass spectra. The analysis and spectra indicated that the product was a bicyclic second-ary amine containing two methylene and two methine groups. Inspection of the spectra of the product narrowed the choice of its structure to three possibilities, (2)—(4).

An important feature of the ¹H-coupled ¹³C n.m.r.

spectrum of the product is a triplet at δ 24.5. Based on the reported chemical shifts of the methylene carbon atoms in cyclohepta-1,3-diene,[8] this triplet resonance was assigned to C-10 of structure (2). In the ¹H n.m.r. spectrum, when the resonance at δ 3.99 assigned to the proton at C-6 was decoupled, the double triplets centred at δ 1.65 and 2.46 (attributed to the protons on C-10) became double doublets. Such an effect is only likely for structures (2) and (4), since only they have methylene groups flanking a methine group, which would have a low-field resonance at δ 3.99. However structure (4) is otherwise inconsistent with the ¹H chemical-shift values of the product.[9] Further evidence for the assignment of structure (2), 7,7-diphenyl-8-azabicyclo[4.3.1]deca-2,4-diene, to the product was the spin–spin coupling pattern for the C-10 methylene protons which was similar to that for a closely related ring structure.[10] The mass spectrum of the adduct gave a base peak at m/e 194, which was attributed to the product of a cycloreversion-type degradation analogous to that reported for a known [6 + 4] cycloadduct.[11]

The reaction at −35 °C of an anion solution, prepared by hydrogen–lithium exchange of N-benzylidenebenzyl-amine, PhCH=NCH₂Ph, (in which both EE- and EZ-isomers of the anion may be present [2,4]), with cyclo-heptatriene, followed by hydrolysis, afforded only two main products. A small yield of a dimer, which from its ¹H n.m.r. and mass spectra is thought to be tetra-phenylpyrazine, was also obtained. It was found [12] that this dimer was produced in the absence of cyclo-heptatriene and of light. It is therefore not the oxidised derivative of the product of a concerted [3⁻ + 3⁻] cyclo-addition pathway, which is allowed by the Woodward–Hoffmann rules.[7]

The mass spectra of the two main products exhibited parent peaks at m/e 287 and the elemental analyses of both conformed to $C_{21}H_{21}N$. One product gave a ¹H n.m.r. spectrum which revealed a much lower degree of symmetry in the aliphatic region than that of the other product.

The ¹H-coupled ¹³C n.m.r. spectra of both products indicated that only one methylene and four aliphatic methine carbon atoms were present. A methylene triplet at δ 25 (the peaks at highest field) and four separate methine resonances occurred in the ¹³C spec-trum of the product of lower symmetry. As for adduct (2), a triplet at δ 25 could only be due to the [6 + 3⁻]

adducts (5) or (6). However (6) can be excluded from consideration because it would be expected to give only two methine resonances, since it has a plane of symmetry. Compound (5) presumably arises by reaction of cycloheptatriene with the EZ-conformer of the anion. The other adduct showed only two methine resonances in its ^{1}H n.m.r. spectrum. On this basis it must have structure (6). Compound (6) would have been formed by reaction of the EE-conformer of the anion.

Hoffmann and Woodward [13] have predicted that in a concerted [6 + 4] thermal cycloaddition reaction the *exo*-adduct would be formed. This prediction has been confirmed in practice.[7,14] Although the conformation

(5)

(6 a) - *exo*

(6 b) - *endo*
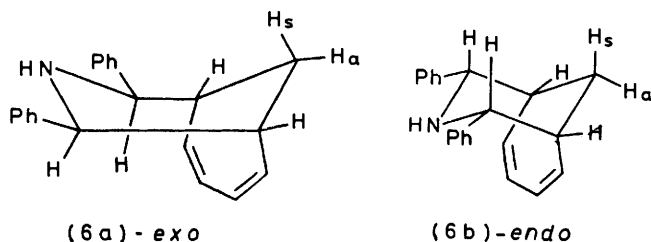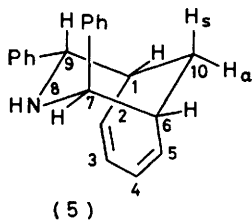
of the piperidine ring in adduct (6) was not determined directly, we suspect that it is in the boat form [as in (6a), the *exo*-adduct] on the basis of the following evidence: (a) adduct (5) showed a singlet for the resonance assigned to H-9 in its ^{1}H n.m.r. spectrum, indicating little or no spin–spin coupling with H-1; a similar result would be expected for the *endo*-adduct (6b); however, compound (6) exhibits a doublet (J 3.8 Hz) for H-9; (b) the methylene proton, H_a, in (6) is deshielded by 0.2—0.3 p.p.m. relative to the similarly disposed protons in adducts (2) and (5); this is consistent with a different (*i.e.* boat) conformation for the piperidine ring in (6) compared to the chair form assigned to both (2) and (5); the possibility that the proximity of phenyl groups has caused this effect cannot be ruled out, but seems unlikely since inspection of models reveals that the positions of the phenyl groups should lead to relative shielding rather than deshielding; (c) in the ^{13}C n.m.r. spectrum of (6), C-10 is deshielded by 5 p.p.m. relative to the corresponding carbon atoms in (2) and (5), again pointing to a different conformation for the piperidine ring in (6); and (d) compound (6) is unstable in air, whereas (2) and (5) are stable; the product of exposure of (6) to air showed a peak in its mass spectrum at m/e 303 which may indicate that oxidation has occurred. Furthermore, study of models indicates that in the conformation of

exo-(6) in which the piperidine ring is in the chair form considerable steric interference between the phenyl groups is likely to occur.

We conclude that the cycloaddition reactions between cycloheptatriene and 1,1- and 1,3-diphenyl-2-aza-allyl-lithium, respectively, gave [6 + 3$^-$] adducts exclusively, and that the reaction with 1,3-diphenyl-2-aza-allyl-lithium was stereospecific in that only one of the two possible stereoisomeric cycloadducts [probably (6a)] was obtained. These observations are consistent with a concerted cycloaddition reaction mechanism. Ford and Luteri [2] have similarly indicated the likelihood of concertedness in certain [3$^-$ + 2] cycloreactions based on the observed stereospecificity. The 8-azabicyclo-[4.3.1]deca-2,4-diene ring system in (2), (5), and (6) has been synthesized previously by a different route.[15]

EXPERIMENTAL

Microanalyses were performed by the Australian Microanalytical Service, Melbourne. N.m.r. spectra were determined for solutions in deuteriochloroform with tetramethylsilane as internal reference by the National NMR Centre, Canberra, at 270 MHz for ^{1}H and at 67.89 MHz for ^{13}C resonances. Mass spectra were obtained on an AEI MS12 instrument at an ionizing potential corresponding to 11.2 × 10^{-18} J. I.r. spectra were recorded on a Perkin-Elmer 197 spectrophotometer using potassium bromide discs. T.l.c. was carried out on Merck silica gel 60 u.v.-fluorescent plates. All the reactions took place in a three-necked 250-cm³ round-bottomed flask fitted with a combined gas inlet thermometer tube, mercury-sealed stirrer, and a reflux condenser, dropping funnel, or stopper as required. All reaction mixtures were blanketed by a slow stream of dry oxygen-free nitrogen. All solvents were dried and purified by standard procedures.

7,7-*Diphenyl*-8-*azabicyclo*[4.3.1]*deca*-2,4-*diene* (2).—The desired quantity of lithium di-isopropylamide was prepared from butyl-lithium [16] in diethyl ether by adding an equimolar amount of di-isopropylamine in diethyl ether and allowing the temperature to rise to ambient to destroy any excess of butyl-lithium. The mixture was then filtered through glass wool into a flask flushed by nitrogen. The solutions used were approximately 1M in amide. A solution of lithium di-isopropylamide (12 mmol) in diethyl ether (10 cm³) was added to tetrahydrofuran (70 cm³) at −45 °C. A solution of N-(diphenylmethylene)methylamine [17] (11 mmol) in tetrahydrofuran (10 cm³) was added slowly and a deep orange-red colour immediately appeared. A solution of cycloheptatriene (11 mmol) in tetrahydrofuran (5 cm³) was then added slowly. The temperature of the mixture was raised to −20 °C for 2 h and then to 0 °C for a further 2.5 h. At this stage examination of a hydrolysed aliquot of the reaction mixture by t.l.c. [development with hexane–chloroform–acetone (7 : 2 : 1)] showed that no imine remained. The mixture was then hydrolysed by addition of water (15 cm³), evaporated *in vacuo*, and the residue was taken up in chloroform (100 cm³). The chloroform solution was passed through a short column of alumina (30 g) and the eluate was evaporated. The residue was crystallised twice from methanol or light petroleum and gave adduct (2) (1.50 g, 47%), m.p. 142.5—143 °C; δ 1.65 (1 H, dt, J 11.6 and 2.3 Hz, H_a-10), 1.74 (1 H, s, exchanged in D$_2$O, H-8). 2.40 (1 H, m, H-1), 2.40—2.46 (1 H, m, H_s-10), 2.86 (1 H,

dt, J 13.7 and 1.8 Hz, H-9), 2.94 (1 H, dt, J 13.7 and 4.2 Hz, H-9), 3.99 (1 H, m, H-6), 5.4—5.9 (4 H, m, H-2, -3, -4, and -5), and 7.3—7.7 (10 H, m, Ph); ^{1}H-coupled ^{13}C (aliphatic region) δ 24.5 (t), 34.8 (d), 40.4 (d), 47.9 (t), and 66.7 (s); $v_{max.}$ 3 025, 2 940, 1 601, 1 495, 1 453, 1 220, 945, 795, 730, and 710 cm^{-1}; m/e 287 (M^+), 195, 194 (base peak), 165, and 91 (Found: C, 87.8; H, 7.3; N, 4.6. $C_{21}H_{21}N$ requires C, 87.8; H, 7.4; N, 4.9%).

trans- (5) and cis-7,9-Diphenyl-8-azabicyclo[4.3.1]deca-2,4-diene (6).—N-Benzylidenebenzylamine, PhCH=NCH$_2$-Ph, was prepared by heating equimolar amounts of benzylamine and benzaldehyde at 110 °C for 10 min. A solution of lithium di-isopropylamide (0.05 mol) in diethyl ether (90 cm^3) was cooled to −45 °C. Tetrahydrofuran (45 cm^3) was added, followed by a solution of N-benzylidenebenzylamine (0.044 mol) in tetrahydrofuran (20 cm^3). The mixture immediately turned deep purple-red. It was refluxed for 1 h, cooled to −35 °C and a solution of an excess of cycloheptatriene (0.09 mol) in tetrahydrofuran (20 cm^3) was added. The mixture was kept at room temperature for 2 d. It was then hydrolysed by addition of water (50 cm^3). T.l.c. analysis [development with chloroform–light petroleum (b.p. 40—70 °C) (2 : 3)] showed that the resulting mixture contained two major products and a small amount of a fluorescent substance, but no imine. The mixture was evaporated in vacuo. The residue was dissolved in chloroform, the chloroform solution was washed with water (2 × 20 cm^3), and the solvent was evaporated in vacuo, to afford an oil (11.9 g) which set to a semi-crystalline solid. The solid (300 mg) was chromatographed on a column of Merck silica gel 60 (100 g, 70—230 mesh) with chloroform as eluant. The fluorescent compound (7.5 mg) was eluted first, followed by adduct (5) (95 mg), and then compound (6) (69 mg). Adduct (6) was closely followed by an orange-red band, which is thought to contain decomposition or oxidation products of (6). The fluorescent compound crystallised from light petroleum and afforded fine white needles, ascribed to tetraphenylpyrazine, m.p. 241—242 °C (lit.,[18] 246—247 °C); δ 7.34 (12 H, m) and 7.65 (8 H, m); m/e 384 (M^+, base peak) and 178.

Adduct (5) crystallised from light petroleum at 2 °C and yielded colourless crystals (31 mg), m.p. 118—119 °C; δ 1.7 (1 H, d, J 13.7 Hz, H$_a$-10), 1.74 (1 H, s, exchanged with D$_2$O, H-8), 2.26 (1 H, dt, J 13.7 and 4.8 Hz, H$_s$-10), 2.89 (1 H, m, H-1), 3.38 (1 H, m, H-6), 4.1 (1 H, d, J 3.6 Hz, H-9), 4.25 (1 H, s, H-7), 5.4—6.1 (4 H, m, H-2, -3, -4, and -5), and 7.2—7.7 (10 H, m, Ph); ^{1}H-coupled ^{13}C (aliphatic region) δ 25 (t), 36 (d), 41 (d), 58 (d), and 61 (d);

m/e 287 (M^+), 195 (base peak), 194, and 91; $v_{max.}$ 3 025, 2 900, 1 601, 1 499, 1 465, 1 450, 1 220, 930, 890, 763, 745, 730, 725, and 700 cm^{-1} (Found: C, 87.6; H, 7.35; N, 4.75. $C_{21}H_{21}N$ requires C, 87.8; H, 7.4; N, 4.9%). Compound (6) crystallised from light petroleum at −20 °C and yielded colourless crystals (15 mg), m.p. 97—100 °C, which turned pale brown in air after several days; δ 1.73 (1 H, s, exchanged with D$_2$O, H-8), 1.95 (1 H, dt, J 13.2 and 2.2 Hz, H$_a$-10), 2.44 (1 H, dt, J 13.2 and 4.4 Hz, H$_s$-10), 3.0 (2 H, m, H-1,6), 4.3 (2 H, d, J 3.8 Hz, H-7,9), 5.4—5.9 (4 H, m, H-2, -3, -4, and -5), and 7.2—7.3 (10 H, m, Ph); ^{1}H-coupled ^{13}C (aliphatic region) δ 30 (t), 41 (d), and 68 (d); m/e 287 (M^+), 195 (base peak), 194, and 91; $v_{max.}$ 3 025, 2 890, 1 601, 1 499, 1 455, 1 430, 1 283, 1 235, 1 030, 885, 775, 750, and 710 cm^{-1} (Found: C, 87.8; H, 7.4; N, 4.8. $C_{21}H_{21}N$ requires C, 87.8; H, 7.4; N, 4.9%).

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