Novel Cage Compounds from Inter-intra-molecular Diels–Alder Reactions of 1,2,4-Triazines with Cyclo-octa-1,5-diene

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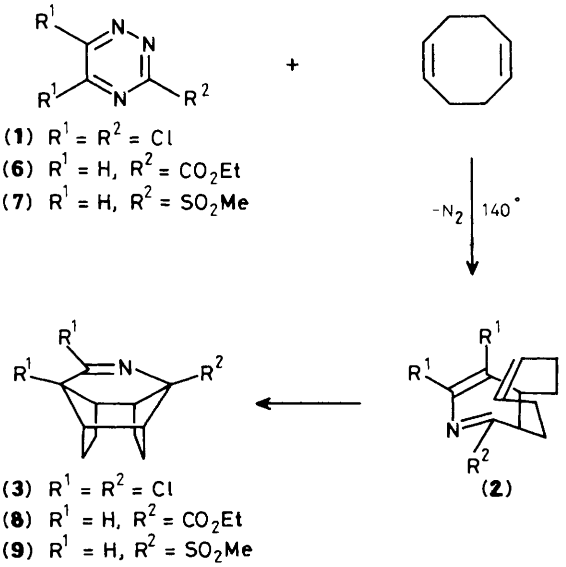
1,2,4-Triazines with electron-withdrawing substituents at the three position react with cyclo-octa-1,5-diene by intermolecular Diels–Alder addition followed by elimination of nitrogen; the 2-azadiene so formed then undergoes an intramolecular Diels–Alder reaction producing novel cage compounds.

1,2,4-Triazines have proved to be attractive sources of 2-aza-1,3-diene fragments for hetero Diels–Alder reactions.[1–4] 3,5,6-Trichlorotriazine[5] has been reported[6] to react with *cis*-alkenes by addition across C_3/C_6 followed by extrusion of nitrogen. The resulting 3,4-dihydropyridine can either aromatise *via* a 1,5-sigmatropic proton shift followed by elimination of hydrogen chloride (as in reaction with cyclopentene)[6] or, in particular cases Diels–Alder addition of a second mole of alkene occurs (as in reaction with bicyclo[2.2.1]hept-2-ene).[6,7]

In the course of another project, we were investigating the reaction of 3,5,6-trichloro-1,2,4-triazine (**1**) with a wide variety of alkenes. With certain reactive, electron-rich alkenes addition of a second mole of the alkene occurred to the exclusion of the aromatisation process. Since intramolecular cycloadditions are often more facile than their intermolecular counterparts it occurred to us that a judiciously chosen diene might undergo sequential intermolecular and intramolecular Diels–Alder reactions (separated only by the nitrogen extrusion process) leading to interesting cage compounds. We therefore heated trichloro-1,2,4-triazine with 10 equiv. of cyclo-octa-1,5-diene (COD)† in anhydrous xylene at 140 °C for 3 h obtaining one major product. After removal of solvent and excess COD, crystallisation from hexane at −10 °C (Scheme 1) gave the product in 65% yield. Analytical



(**1**) $R^1 = R^2 = Cl$
(**6**) $R^1 = H$, $R^2 = CO_2Et$
(**7**) $R^1 = H$, $R^2 = SO_2Me$

(**2**)

(**3**) $R^1 = R^2 = Cl$
(**8**) $R^1 = H$, $R^2 = CO_2Et$
(**9**) $R^1 = H$, $R^2 = SO_2Me$

Scheme 1

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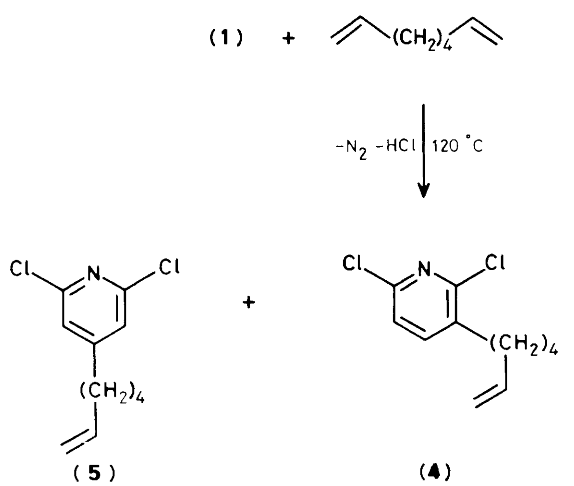
† A ten molar excess of dienophile was found to be necessary for the initial intermolecular Diels–Alder reaction to occur at a reasonable rate.



Scheme 2

and spectral data‡ showed that this was the novel imidoyl chloride cage compound (**3**), 7-aza-6,8,9-trichloro-tetracyclo-$[7.3.0.0^{2,6}.0^{5,10}]$dodec-7-ene. The formation of this compound can be rationalised by considering the intermediate (**2**) formed after the initial Diels–Alder reaction and loss of N_2. The cyclic system containing the remaining double bond from COD can be placed over the 2-aza-1,3-diene in juxtaposition for ring closure *via* an intramolecular Diels–Alder reaction. Indeed, the intramolecular reaction must occur at a much faster rate than the intermolecular addition of a second molecule of dienophile as the COD is present in large excess.

The need for the double bond to be favourably disposed for the intramolecular cycloaddition process is demonstrated by the reactivity of octa-1,7-diene which reacted with (**1**) to give equal amounts of 2,6-dichloro(hex-5-enyl) pyridines (**4**) and (**5**) in 48% total yield (Scheme 2).

Other triazines have been found to react similarly provided that they are sufficiently reactive to undergo the initial intermolecular Diels–Alder reaction. Thus 3-ethoxycarbonyl-1,2,4-triazine (**6**) and 3-methysulphonyl-1,2,4-triazine (**7**) both reacted with excess COD at temperatures above 90 °C to gave the cage compounds (**8**) and (**9**) in 66 and 44% yields respectively (Scheme 1). However, 3-methyl-1,2,4-triazine and 3-methylthio-1,2,4-triazine failed to react.

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‡ The compositions of the novel cage compounds (**3**), (**8**), and (**9**) were determined by C,H,N analysis and high-resolution mass spectroscopy. The structures were also supported by ^1H and ^{13}C n.m.r. and i.r. spectroscopy.