Diels–Alder reactions of trichloro-1,2,4-triazine: intramolecular additions with 1,5 and 1,6 dienes[1]

Michael G. Barlow,* Lakhdar Sibous, Nadia N. E. Suliman and Anthony E. Tipping

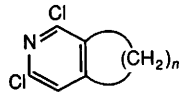
Chemistry Department, The University of Manchester Institute of Science and Technology, Manchester M60 1QD, UK

Trichloro-1,2,4-triazine reacts with cycloheptene and cyclododecene to give the 2,6-dichloropyridine derivatives 6 and 7 *via* an intermediate dihydropyridine formed by Diels–Alder addition and loss of N_2, and with cyclopenta-1,3-diene and indene by addition of a second molecule of alkene to the intermediate dihydropyridine. Bicyclo[2.2.1]hepta-2,5-diene and quadricyclane give mainly 2,3,6-trichloropyridine by loss of cyclopentadiene from the intermediate dihydropyridine. With hexa-1,5-diene, the dihydropyridine is trapped by an intramolecular Diels–Alder reaction, forming tricyclic compounds 17 and 18. With diallyl ether, the dihydropyridine partly undergoes intramolecular cycloaddition to give 23 and partly [1,5]-sigmatropic shift of hydrogen before intramolecular cycloaddition to give 25. With cyclododeca-1,5,9-triene formation of pyridine derivatives is incomplete and the immediate precursor can be trapped with water.

Trichloro-1,2,4-triazine **1** acts as an electron-deficient diene in the Diels–Alder reaction,[2,3] undergoing reactions with olefins such as ethene, (*Z*)-but-2-ene, cyclopentene and cyclooctene to give largely 3,4-substituted 2,6-dichloropyridines. For example, with cyclopentene, the dichloropyridine derivative **2** is the main product (77%). It was suggested that this pyridine was formed by initial Diels–Alder reaction and loss of nitrogen to give the dihydropyridine **3**, which largely aromatised by [1,5]-sigmatropic shift of hydrogen to give **4** and loss of hydrogen chloride, while Diels–Alder addition of a second mole of cyclopentene, giving **5**, occurred only to a limited extent (3%) (see Scheme 1). Only with bicyclo[2.2.1]hept-2-ene was the second Diels–Alder reaction the favoured process.[2,4]

The reluctance to form di-adducts was also shown by the cycloalkenes, cycloheptene and cyclododecene. Cycloheptene (5.5 mol equiv.) reacted with the triazine **1** at 70 °C during 7 days to give the pyridine **6** (73%). Cyclododecene [2.6 mol equiv.; (*Z*):(*E*)-isomer ratio 2:5] gave the pyridine **7** (61%) after 4 days at 70 °C. The (*Z*):(*E*)-ratio (2:3) in the recovered olefin indicated that it was largely the (*E*) isomer that had reacted.

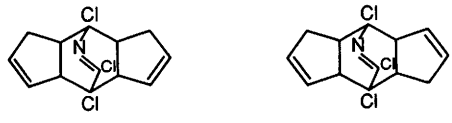
We reasoned that the probability of the second Diels–Alder reaction would be increased if (i) the reactivity of the olefin was enhanced, or (ii) the sigmatopic hydrogen shift was hindered, or (iii) a diene was used where the second double bond was suitably placed for intramolecular addition. In the addition to bicyclo[2.2.1]hept-2-ene, the sigmatropic hydrogen shift is hindered since it results in a double bond *exo* to a strained ring.



6 *n* = 5

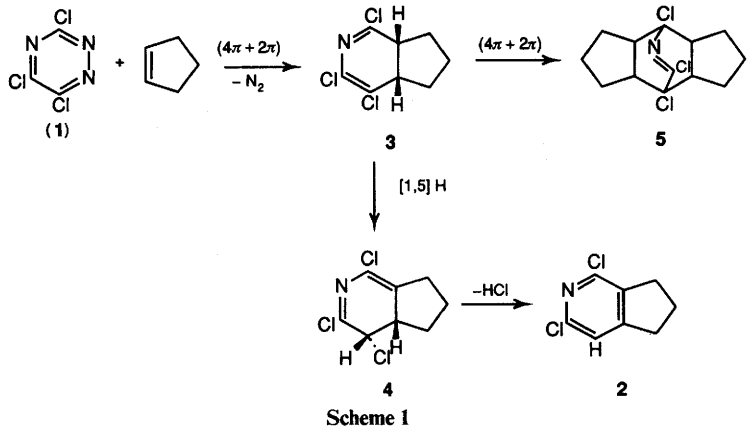
7 *n* = 10

1,3-Dienes showed enhanced reactivity. Cyclopenta-1,3-diene (10 mol equiv.) reacted at 70 °C during 2 days to give a 2:1 mixture of adducts **8** and **9** in 58% yield. Indene (7 mol equiv.) reacted analogously to give the adduct **10**, as shown by X-ray crystallography.[5] The adduct **10** results from *endo*-addition of indene to the intermediate azadiene **11** from the less crowded side (see Scheme 2). We are unable to account for the regioselectivity shown.

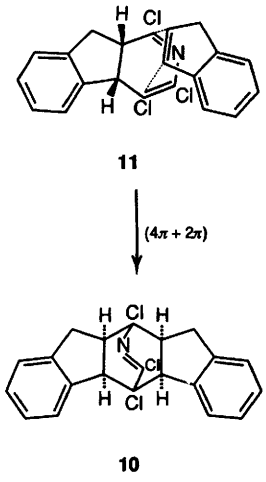


8 **9**

The imidoyl chloride **10** was surprisingly resistant to hydrolysis by basic media, being unaffected by sodium



Scheme 1

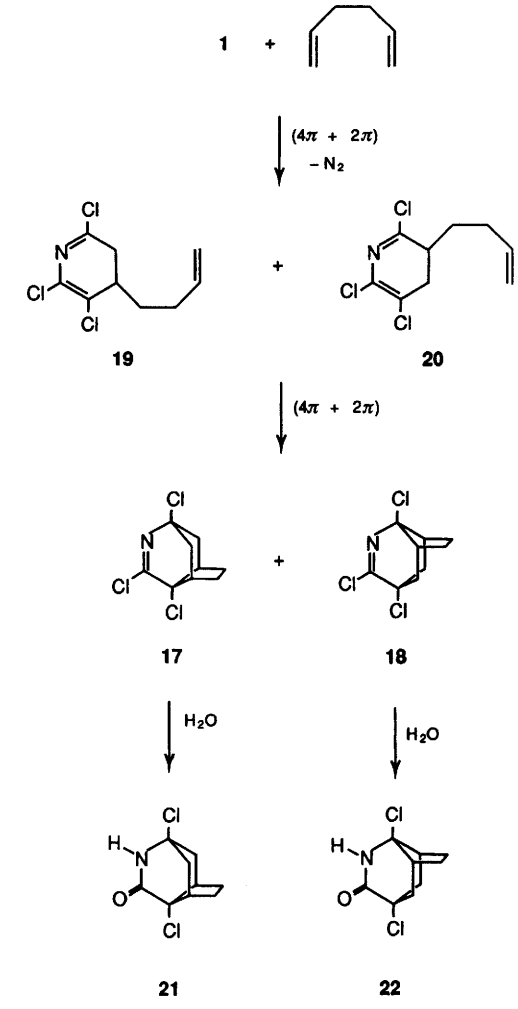


Scheme 2

hydroxide in refluxing tetrahydrofuran for 2 h. The molecule adopts a gull-wing shape,[5] where the imidoyl chloride group is shielded. The cyclopentadiene adducts **8** and **9** were similarly resistant to basic hydrolysis.

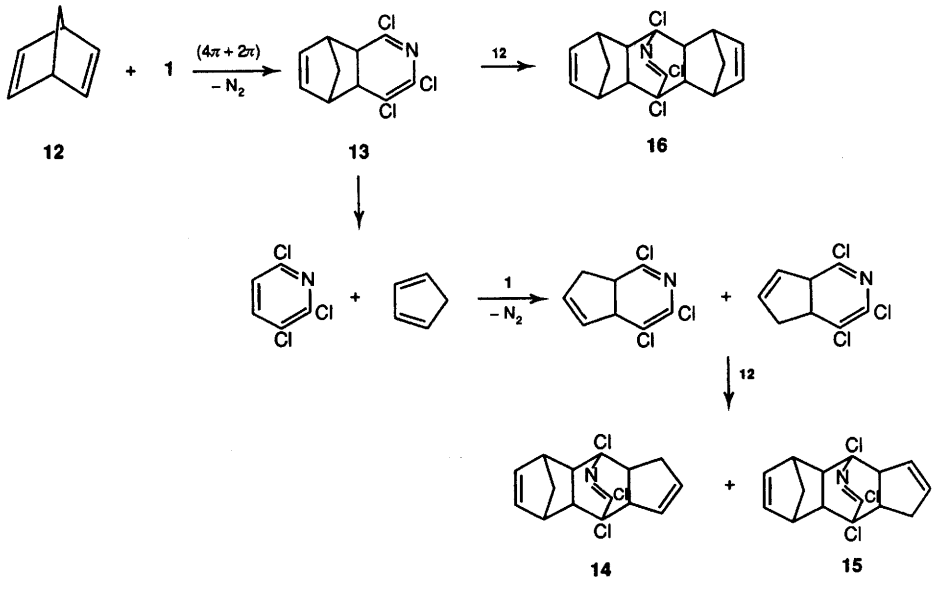
Bicyclo[2.2.1]hepta-2,5-diene **12** (7 mol equiv.) reacted with the triazine **1** at 70 °C during 2 days to give 2,3,6-trichloropyridine (70%), formed by retro-Diels–Alder cleavage of cyclopenta-1,3-diene from the initially formed dihydropyridine **13** (see Scheme 3). Also formed was a mixture of two mixed adducts, **14** and **15**, involving both **12** and cyclopentadiene (15%), containing (by mass spectrometry) a trace of the diadduct **16** of **12**. The suggested pathway assumes that cyclopenta-1,3-diene reacts more readily than bicyclo[2.2.1]-hepta-2,5-diene, which is always present in large excess. Formation of the adducts **14** and **15** from **13** seems less likely since this would require **13** to react highly selectively with cyclopentadiene. Trifluoro-1,2,4-triazine gave analogous trifluoro-adducts, **14** and **15**.[2] In these reactions, bicyclo[2.2.1]-hepta-2,5-diene acts as an acetylene equivalent.[6] Quadricyclane (1 mol equiv.) appears to be considerably more reactive than bicyclo[2.2.1]hepta-2,5-diene, giving 2,3,6-trichloropyridine (83%) in 2 days at 70 °C; no cyclopentadiene-containing adducts were obtained. In this case, formation of the precursor to dihydropyridine **13** formally involves a forbidden $[_{\pi}2_s + _{\pi}2_s + _{\sigma}2_s + _{\sigma}2_s]$ process, so a non-concerted pathway seems probable.

Hexa-1,5-diene (8 mol equiv.) reacted with the triazine **1** at 70 °C during 9 days to give a 9:1 mixture (78%) of the two symmetrical adducts **17** and **18**, formed by intramolecular Diels–Alder addition in the intermediate dihydropyridines **19** and **20** (see Scheme 4). The adducts **17** and **18** were easily



Scheme 4

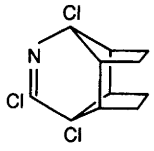
hydrolysed to the corresponding amides **21** and **22** by water or upon attempted flash chromatography on silica gel. The structure of **21** was established by X-ray crystallography.[7] The regioselectivity favouring **19** is also shown by simple alkenes.



Scheme 3

Hex-1-ene gives a 2:1 mixture of 4- and 3-butyl-2,6-dichloropyridine (83%).

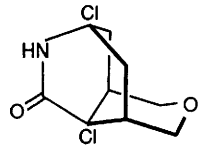
Analogous reactions of cycloocta-1,5-diene with trichloro-, 3-ethoxycarbonyl- and 3-methylsulfonyl-1,2,4-triazine have been described by Lantos, Sheldrake and Wells.[8] For example, trichlorotriazine gave the cage compound **23** (65%) after 3 h in



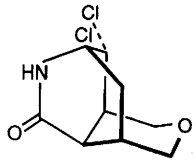
23

refluxing xylene. We obtained an 85% yield of **23** after 7 days at 70 °C in the absence of solvent. With cyclooctadiene and with the more flexible hexa-1,5-diene, no aromatisation to give pyridine derivatives was observed, the intramolecular Diels–Alder reaction intercepting the dihydropyridine effectively. We explored the effect of increasing chain-length, where the intramolecular trapping might be less effective, by examining the reaction with diallyl ether.

Diallyl ether (7 mol equiv.) and the triazine **1**, heated at 70 °C for 4 days, gave a very moisture-sensitive product, from which, after treatment with water and/or flash chromatography on silica gel, the two dichloro lactams **24** (46%) and **25** (34%) were



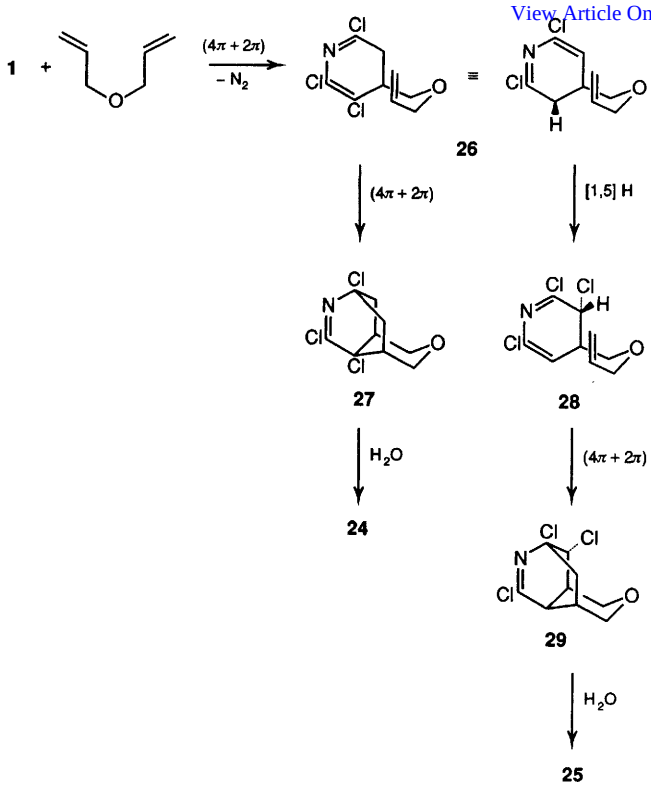
24



25

obtained. The structure of **24** was established by X-ray crystallography,[9] while that of **25** rests upon analysis of the ^{1}H and ^{13}C NMR spectra, including H,H-COSY, DEPT and HETCOR spectra. The dihydropyridine **26** is formed regioselectively, with the substituted alkyl group containing the alkene moiety in the 4-position. The longer chain length compared with that in the hexa-1,5-diene reaction allows competing intramolecular Diels–Alder reaction, to give **27**, and [1,5]-sigmatropic hydrogen shift to give **28**, which still contains the 2-aza-1,3-diene fragment, and another intramolecular Diels–Alder reaction gives **29** (see Scheme 5). The hydrogen which migrates is the one *cis* to the $CH_2OCH_2CH{=}CH_2$ group.

In the diallyl ether reaction, competition between intramolecular cycloaddition and sigmatropic hydrogen shift is delicately poised. (1*E*,5*E*,9*Z*)-Cyclododeca-1,5,9-triene possesses the hexa-1,5-diene moiety, which can give rise to successful intramolecular cycloaddition, but the ring system is rather rigid, which would tend to hinder such reaction. Indeed, (1*E*,5*E*,9*Z*)-cyclododeca-1,5,9-triene (3.5 mol equiv.) and **1**, heated at 70 °C for 4 days, gave a 2:1 mixture of the pyridine derivative **30** and its (*Z*,*E*)-isomer (42%) and from the moisture-sensitive product, after flash chromatography on silica gel, a 4:1 mixture (22%) of the (*E*,*Z*)-amide **31** and the corresponding (*Z*,*E*)-isomer (see Scheme 6). The structure of **31** was established by X-ray crystallography,[10] and a staggered conformation is adopted about the CHCl–CH bond shown. Presumably, a similar conformation is adopted in the precursor **32**. Adoption of an *anti*-coplanar conformation for HCl elimination is impossible, and the relative rigidity of the 12-membered ring hinders adoption of a *syn*-coplanar conformation, so aromatisation to give **30** is much slower than is, for example, observed with cyclododecene where addition to a C=C bond with the (*E*)-



Scheme 5

configuration appears favoured, like the case with cyclododecatriene, but where the absence of further double bonds makes the ring much more flexible. The configuration found for **31** is as expected for suprafacial addition to cyclododecatriene and a suprafacial [1,5]-hydrogen shift.

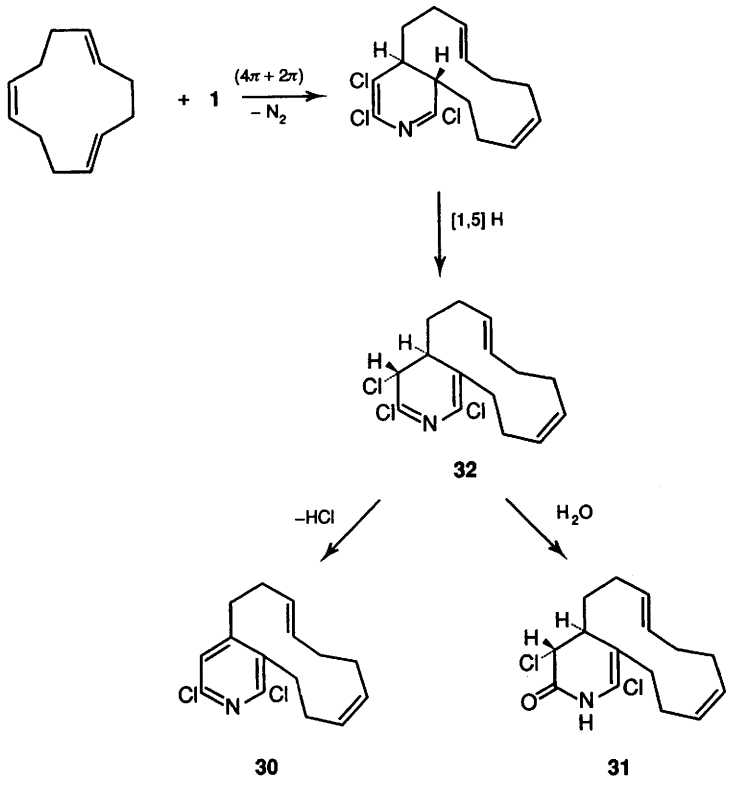
The present results provide clear cut support for the proposal that reaction of olefins with trichloro-1,2,4-triazine is initiated by Diels–Alder addition, with inverse electron demand, and loss of nitrogen to give a dihydropyridine followed by [1,5]-sigmatropic hydrogen shift and HCl elimination to give a pyridine. With conjugated olefins like cyclopenta-1,3-diene and indene, the dihydropyridine ready undergoes a second Diels–Alder addition, and a suitably positioned olefin moiety can result in intramolecular Diels–Alder reaction. With diallyl ether, the product of [1,5]-hydrogen shift is intercepted by intramolecular Diels–Alder reaction, and with cyclododeca-1,5,9-triene aromatisation by loss of HCl is incomplete.

Experimental

The compounds hex-1-ene, cycloheptene, cyclodecene, hexa-1,5-diene, diallyl ether, cycloocta-1,5-diene, norbornadiene, quadricyclane, (1*E*,5*E*,9*Z*)-cyclododeca-1,5,9-triene and indene were commercial samples, and cyclopenta-1,3-diene was made by cracking dicyclopentadiene at 200 °C. Trichloro-1,2,4-triazine was prepared by the method of Loving *et al.*[11]

Reactions of substrates with trichlorotriazine were carried out using neat reactants in sealed Rotaflo-tapped Pyrex ampoules (50 cm^3). Crude reaction product mixtures were examined by TLC and individual components were separated by dry column 'flash' chromatography (DCFC) (SiO_2, Merck-Kieselgel 60 H) and further purification, where necessary, was achieved by TLC or repeated DCFC. Eluents for chromatography are indicated in the text; light petroleum refers to the fraction bp 40–60 °C.

Products were examined by IR (Perkin-Elmer DE 783 spectrometer), ^{1}H NMR [Bruker AC300 instrument operating at 300 MHz with tetramethylsilane (TMS) as external reference] and ^{13}C NMR [Bruker AC 300 instrument



Scheme 6

operating at 75.0 MHz with broad band proton decoupling, D_2O as the deuterium lock and TMS as external reference; DEPT 135° spectra were also recorded] spectroscopy and mass [Kratos MS 25 or 45 instruments with electron beam energy of 70 eV using electron impact (EI) or chemical ionisation (CI, NH_3 gas) conditions] spectrometry. NMR samples were run as solutions in $CDCl_3$ and chemical shifts to low field of the reference are designated positive, *J* values in Hz.

Single crystal X-ray structure determinations were carried out on either a Rigata AFC65 or CAD4 diffractometer.

Bps were determined by distillation and mps are uncorrected.

Reactions of trichloro-1,2,4-triazine 1

(a) With hex-1-ene. Hex-1-ene (5.68 g, 67.6 mmol) and the triazine **1** (2.0 g, 10.8 mmol) were heated at 70 °C for 4 days. Volatile material was removed *in vacuo* and identified (IR) as hex-1-ene (4.90 g, 58.3 mmol, 86% recovery) and hydrogen chloride (0.33 g, 9.0 mmol, 85%). The dark brown residue (2.16 g) was extracted with diethyl ether (2 × 10 cm^3) and the solvent removed under reduced pressure to give an oil (1.90 g), which was purified by DCFC [eluent, pentane–dichloromethane (1 : 1, v/v)] to give a mixture of 3- and 4-butyl-2,6-dichloropyridine (1.82 g, 8.9 mmol, 83%) (Found: C, 53.0; H, 5.6; Cl, 35.1; N, 6.8%; M^+, 203. Calc. for $C_9H_{11}Cl_2N$: C, 53.0; H, 5.4; Cl, 34.8; N, 6.8%; *M*, 203) in the ratio 1 : 2 (by ^1H NMR spectroscopy), as a yellow oil, bp 187–200 °C; *m/z* 203 (M^+ 18.9%) and 161 ($C_6H_5NCl_2^+$, 100%).

(b) With cycloheptene. Cycloheptene (5.68 g, 59.2 mmol) and the triazine **1** (2.0 g, 10.8 mmol) were heated at 70 °C for 7 days. Volatile material was removed *in vacuo* and identified (IR) as cycloheptene (4.91 g, 51.1 mmol, 86% recovery) and hydrogen chloride (0.28 g, 7.7 mmol, 72%). The residual pale brown oil (2.25 g) was extracted with diethyl ether to give, after removal of the solvent on a rotary evaporator, a brown oil which rapidly solidified. This oil was shown by TLC [eluent, pentane–dichloromethane (1 : 1, v/v)] to contain one component and was purified by DCFC (same eluent) to give 1,3-dichloro-6,7,8,9-tetrahydro-5*H*-cyclohepta[*c*]pyridine **6** (11.70 g, 7.9 mmol, 73%) as a white powder, mp 58 °C (Found: C, 55.3; H, 5.2; Cl, 33.4; N, 6.4. $C_{10}H_{11}Cl_2N$ requires C, 55.5; H, 5.1; Cl, 32.9; N, 6.5%); *m/z* 215 (M^+, 62.0%) and 180 [$(M - Cl)^+$, 100%].

(c) With cyclododecene. Cyclododecene (4.70 g, 28.3 mmol), as a mixture of (*Z*)- and (*E*)-isomers in the ratio 2 : 5, and the triazine **1** (2.0 g, 10.8 mmol) were heated at 70 °C for 4 days. Hydrogen chloride (0.24 g, 6.6 mmol, 62%) was removed *in vacuo* and the residue was washed out with diethyl ether to give, after removal of the solvent under reduced pressure, a brown oil (5.60 g), separated by DCFC [eluent, pentane–dichloromethane (1 : 1, v/v)] to give unchanged cyclodecene [3.50 g, 21.1 mmol, 75%, (*Z*)/(*E*) ratio 2 : 3 by ^{13}C NMR and GLC] and a solid (2.03 g), purified by DCFC to give 1,3-dichloro-5,6,7,8,9,10,11,12,13,14-decahydrocyclodeca[*c*]pyridine **7** (1.90 g, 6.6 mmol, 61%) as a white powder, mp 82–84 °C (Found: C, 62.6; H, 7.5; Cl, 25.2; N, 4.8. $C_{15}H_{21}Cl_2N$ requires C, 62.9; H, 7.3; Cl, 24.8; N, 4.9%); *m/z* 285 (M^+, 100%) and 250 [$(M - Cl)^+$, 90.4%].

(d) With cyclopenta-1,3-diene. Cyclopentadiene (7.13 g, 108 mmol) and the triazine **1** (2.0 g, 10.8 mmol) were heated at 70 °C for 2 days. Unchanged cyclopentadiene (5.63 g, 85.3 mmol, 79% recovery) was then removed *in vacuo* and the residue was washed out with diethyl ether to give, after removal of the solvent under reduced pressure, a brown oily solid (3.32 g). This was washed with pentane (3 × 20 cm^3) and purified by DCFC [eluent, pentane–dichloromethane (1 : 2, v/v)] followed by sublimation at 120–130 °C *in vacuo* to give a 2 : 1 mixture (by ^{13}C NMR spectroscopy) of 1,7,13-trichloro-14-azatetracyclo[5.5.2.$0^{2,6}$.$0^{8,12}$]tetradeca-3,10,13-triene **8** and the corresponding 3,9,13-triene **9** (1.82 g, 6.3 mmol, 58%) as a white powder, mp 152–156 °C (Found: C, 54.4; H, 4.4; Cl, 36.3; N, 4.8. Calc. for $C_{13}H_{12}Cl_3N$: C, 54.1; H, 4.2; Cl, 36.9; N, 4.9%); *m/z* 287 (M^+, 45.2%), 252 [$(M - Cl)^+$, 96.8%], 222 ($C_8H_7NCl_3^+$, 96.8%), 186 ($C_8H_6NCl_2^+$, 76.8%) and 66 ($C_5H_6^+$, 100%).

A mixture of the trienes **8** and **9** (0.50 g) was recovered unchanged (98%) after refluxing for 6 h with a mixture of sodium hydroxide (0.42 g), water (5 cm^3) and dichloromethane (5 cm^3).

(e) With indene. Indene (6.12 g, 52.7 mmol) and the triazine **1**

(1.40 g, 7.6 mmol) were heated at 70 °C for 2 days. Nitrogen was released and the contents were washed out with dichloromethane to give, after removal of the solvent on a rotary evaporator, an oily solid. Unchanged indene (5.44 g, 46.9 mmol) was removed with cold diethyl ether (3 × 20 cm^3) and the residue was recrystallised from chloroform to give 5,11,13-trichloro-4a,5,5a,10,10a,11,11a,12-octahydro-5,11-methanonitrilobenzo-[4,5-*a*';1,2-*a*]diindene **10** (2.06 g, 5.3 mmol, 70%) as white crystals, mp 250–254 °C (Found: C, 64.6; H, 4.0; Cl, 27.7; N, 3.6. $C_{21}H_{10}Cl_3N$ requires C, 64.9; H, 4.1; Cl, 27.4; N, 3.6%), identified by X-ray crystallography;[5] *m/z* 387 (M^+, 8.0%), 352 [$(M - Cl)^+$, 9.2%] and 116 ($C_5H_7NCl^+$, 100%).

The adduct **10** (0.50 g) was recovered unchanged (86%) when refluxed for 2 h with a solution of sodium hydroxide (0.45 g) in water (5 cm^3) and tetrahydrofuran (5 cm^3).

(f) With bicyclo[2.2.1]hepta-2,5-diene. Bicyclo[2.2.1]hepta-2,5-diene (6.98 g, 75.9 mmol) and the triazine **1** (2.0 g, 10.8 mmol) were heated at 70 °C for 2 days. Unchanged bicycloheptadiene (5.94 g, 64.5 mmol, 85% recovery) was then removed *in vacuo* leaving a brown residue, which was extracted with diethyl ether (3 × 20 cm^3). Evaporation of the extract under reduced pressure, gave oily brown crystals, fractional sublimation of which gave 2,3,6-trichloropyridine (1.39 g, 7.6 mmol, 70%), mp 60–63 °C (lit,[12] 62–64 °C) (Found: C, 32.9; H, 1.0; Cl, 58.8; N, 7.6. Calc. for $C_5H_2Cl_3N$: C, 32.9; H, 1.1; Cl, 58.3; N, 7.7%), which sublimed at 20–50 °C/2–3 mmHg, and a mixture (by ^{13}C NMR) of 1,8,15-trichloro-14-azapentacyclo-[6.5.2.1^{3,6}.0^{2,7}.0^{8,13}]hexadeca-4,10,14-triene **14** and -4,11,14-triene **15** (0.51 g, 1.6 mmol, 15%) as a white powder, mp 90–94 °C (Found: C, 56.9; H, 4.6; Cl, 33.4; N, 4.5; Calc. for $C_{15}H_{14}Cl_3N$: C, 57.2; H, 4.5; Cl, 33.8; N, 4.5%), which sublimes at 130 °C/< 1 mmHg; *m/z* 313 (M^+, 1.0%), 212 ($C_{10}H_8NCl_2^+$, 12.9%) and 66 ($C_5H_6^+$, 100%). DCFC [eluent, pentane–dichloromethane (1 : 1, v/v)] failed to separate these trienes and mass spectrometry indicated the presence of traces (< 10%) of a compound containing two bicycloheptadiene residues [*m/z* 339 ($C_{17}H_{16}NCl_3^+$)].

The mixture of adducts **14** and **15** (0.20 g) was recovered unchanged (85%) after reflux with a mixture of sodium hydroxide (0.46 g) in water (5 cm^3) and dichloromethane (5 cm^3) for 6 h.

(g) With cycloocta-1,5-diene. Cycloocta-1,5-diene (8.82 g, 81.6 mmol) and the triazine **1** (2.10 g, 11.4 mmol), heated at 70 °C for 7 days, gave unchanged cycloocta-1,5-diene (82% recovery), nitrogen (0.27 g, 9.4 mmol, 82%) and a pale brown oil, which was extracted with diethyl ether. The extract was evaporated under reduced pressure, and the resultant solid purified by DCFC [eluent, pentane–dichloromethane (1 : 1, v/v)] and sublimation at 100–120 °C *in vacuo* to give 9,10,12-trichloro-11-azatetracyclo[6.4.0.0^{4,12}.0^{5,9}]dodec-10-ene **23** (2.56 g, 9.7 mmol, 85%) (Found: C, 50.2; H, 4.9; Cl, 39.7; N, 5.0%; M^+, 263. Calc. for $C_{11}H_{12}Cl_3N$: C, 49.9; H, 4.6; Cl, 40.2; N, 5.3%; *M*, 263) as colourless crystals [from light petroleum ether (bp 60–80 °C)], mp 118 °C (lit.,[8] mp 120 °C).

To adduct **23** (1.0 g, 3.8 mmol) in dichloromethane (10 cm^3) was added water (10 cm^3) dropwise. The mixture was then stirred at room temperature for 24 h, after which the organic layer was separated, dried ($MgSO_4$) and evaporated under reduced pressure to give 9,10-dichloro-11-azatetracyclo-[6.4.0^{4,12}.0^{5,9}]dodecan-10-one (0.92 g, 3.7 mmol, 99%) (Found: C, 53.3; H, 5.3; Cl, 29.2%; N, 5.5; M^+, 245. Calc. for $C_{11}H_{13}Cl_2NO$: C, 53.6; H, 5.3; Cl, 28.9; N, 5.7%; *M*, 245) a white solid, mp 245 °C (lit.,[8] mp 215 °C).

(h) With hexa-1,5-diene. Hexa-1,5-diene (7.12 g, 86.8 mmol) and the triazine **1** (2.0 g, 10.8 mmol), heated at 70 °C for 9 days, gave unchanged hexa-1,5-diene (6.13 g, 74.6 mmol, 86% recovery), which was removed under reduced pressure, and a residue, which was washed out with diethyl ether to give brown oily crystals. These were washed with dry pentane (3 × 10 cm^3) and sublimed at 70–85 °C *in vacuo* to give a 9:1 mixture (by ^{13}C NMR spectroscopy) of 1,7,8-trichloro-9-azatricyclo-[4.3.1.0^{3,7}]dec-8-ene **17** and 1,7,9-trichloro-8-azatricyclo-[4.3.1.0^{3,7}]dec-8-ene **18** (2.0 g, 8.4 mmol, 78%) (Found: C, 45.6; H, 4.4; Cl, 44.2; N, 5.9%; M^+, 237. Calc. for $C_9H_{10}Cl_3N$: C, 45.3; H, 4.2; Cl, 44.6; N, 5.9%; *M*, 237), as a white powder, mp 70–76 °C.

The mixture of adducts **17** and **18** (0.50 g, 2.1 mmol) in dichloromethane (5 cm^3) was stirred with water (10 cm^3) for 6 h at room temperature. The organic layer was then separated, dried ($MgSO_4$) and evaporated under reduced pressure to give an 8 : 1 mixture of 1,7-dichloro-9-azatricyclo[4.3.1.0^{3,7}]-decan-8-one **21** and 1,7-dichloro-8-azatricyclo[4.3.1.0^{3,7}]-decan-9-one **22** (0.44 g, 2.0 mmol, 96%) (Found: C, 49.1; H, 5.3; Cl, 32.7; N, 6.4%; M^+, 219. Calc. for $C_9H_{11}Cl_2NO$. C, 49.1; H, 5.0; Cl, 32.3; N, 6.4%; *M*, 219), as a white powder, mp 170–178 °C. This solid was dissolved in chloroform (4 cm^3) and the solvent allowed to evaporate slowly over several days until crystallisation resulted; recrystallisation from acetone then gave the major *isomer* **21** (0.16 g, 1.2 mmol, 57%) (Found: C, 48.8; H, 5.1; Cl, 32.4; N, 6.1%; M^+, 219), mp 192 °C, identified by X-ray crystallography.[6]

(i) With diallyl ether. Diallyl ether (7.01 g, 71.5 mmol) and the triazine **1** (2.0 g, 10.8 mmol), heated *in vacuo* at 70 °C for 4 days, gave unchanged diallyl ether (6.24 g, 63.7 mmol, 89% recovery), which was removed *in vacuo*, and a residue (2.45 g). The residue was extracted with diethyl ether (3 × 10 cm^3). Evaporation of the extract gave a solute (2.26 g), shown by TLC [eluent CH_2Cl_2–EtOAc (10 : 3, v/v)] to comprise two components (R_F 0.82 and 0.79).

The components were separated by DCFC (same eluent) to give 1,8-*dichloro*-5-*oxa*-10-*azatricyclo*[5.3.1.0^{3,5}]*undecan*-9-*one* **24** (R_F 0.82) (1.18 g, 5.0 mmol, 46%) (Found: C, 45.9; H, 4.7; Cl, 30.1; N, 5.8. $C_9H_{11}Cl_2NO_2$ requires C, 45.7; H, 4.6; Cl, 30.0; N, 5.9%), mp 228 °C, identified by X-ray crystallography,[8] *m/z* 235 (M^+, 40.6%), 200 ($C_9H_{11}NO_2Cl^+$, 100.0%) and 1,2-*dichloro*-5-*oxa*-10-*azatricyclo*[5.3.1.0^{3,8}]*undecan*-9-*one* **25** (R_F 0.79) (0.87 g, 3.70 mmol, 34%) (Found: C, 45.9; H, 4.8; Cl, 30.1; N, 6.1%), mp 235–239 °C, *m/z* 235 (M^+, 46.3%) and 200 ($C_9H_{11}NO_2Cl^+$, 100.0%).

A similar reaction where the diethyl ether solution was kept overnight gave a brown solution and a pale brown precipitate. The moisture-sensitive precipitate was washed with diethyl ether and was shown by ^1H NMR spectroscopy to contain the lactams **24** and **25**; hydrolysis was completed by stirring with water and dichloromethane for 3 h (0.67 g, 2.8 mmol, 26%). The diethyl ether solution and precipitate washings were combined, dried ($MgSO_4$) and evaporated to give a brown oil (1.63 g), which was separated by DCFC [eluent, CH_2Cl_2–hexane (2 : 1, v/v)] to give 2,6-dichloro-3-chloromethylpyridine (R_F 0.72) (0.66 g, 3.3 mmol, 31%) (Found: C, 36.9; H, 1.9; Cl, 53.5; N, 7.1%; M^+, 195. Calc. for $C_6H_4Cl_3N$: C, 36.9; H, 2.0; Cl, 53.8; N, 7.1%; *M*, 195), mp 80–82 °C (lit.,[13] mp 82 °C) and an oil (R_F 0.54) (0.34 g), which ^1H NMR spectroscopy indicated to be a complex mixture containing aromatic hydrogens, and several $OCH_2CH{=}CH_2$, CH_2O, OCH_2O, OCH_2CH and CH_2CH groupings. DCFC [eluent, CH_2Cl_2–hexane (1 : 2 v/v)] failed to yield any pure components.

(j) With (1*E*,5*E*,9*Z*)-cyclododeca-1,5,9-triene. The cyclododecatriene (6.15 g, 38.0 mmol) and the triazine **1** (2.0 g, 10.8 mmol), heated *in vacuo* at 70 °C for 4 days, gave hydrogen chloride (0.11 g, 3.0 mmol) and nitrogen (0.21 g, 7.6 mmol), which were removed *in vacuo*, and a residue which was removed by dissolution in dichloromethane. Removal of the dichloromethane on a rotary evaporator afforded a brown oil, which was extracted with diethyl ether (3 × 20 cm^3). The extract was evaporated under reduced pressure, and the resulting reddish oil (7.22 g) subjected to DCFC [eluent, CH_2Cl_2–pentane (1 : 1, v/v)] to give the fractions: (i) recovered cyclododecatriene (4.75 g, 29.3 mmol, 77% recovery); (ii) a viscous yellow oil (R_F 0.63)

(0.91 g), which ^{1}H and ^{13}C NMR spectroscopy revealed to be largely a 2:1 *mixture of* (7*E*,11*Z*)-1,3-dichloro-5,6,9,10,13,14-hexahydrocyclododeca[*c*]pyridine **30** and its (7*Z*,11*E*)-isomer (Found: C, 62.9; H, 6.4; Cl, 25.2; N, 5.5%; M$^+$, 281. Calc. for $C_{15}H_{17}Cl_2N$: C, 63.8; H, 6.0; Cl, 25.2; N, 5.0%; *M*, 281); and (iii) a solid (1.22 g), which was sublimed *in vacuo* at 60 °C to give recovered trichlorotriazine **1** (0.59 g, 3.2 mmol, 30% recovery) and a solid residue, involatile at 120 °C. ^{1}H and ^{13}C NMR spectroscopy indicated this to be a 4:1 mixture of (4*E*,8*Z*,12*E*)-13,16-dichloro-14-azabicyclo[10.4.0]hexadeca-4,8,12-trien-15-one **31** and its (4*Z*,8*E*)-isomer (0.51 g, 1.7 mmol, 22%) (Found: C, 59.8; H, 6.4; Cl, 23.7; N, 4.6%; M$^+$, 299. Calc. for $C_{15}H_{19}Cl_2NO$: C, 60.0; H, 6.4; Cl, 23.6; N, 4.7%; *M*, 299). A sample of this mixture was dissolved in chloroform and the solution allowed to evaporate slowly to yield crystals of the major component **31**, identified by X-ray crystallography.[9] Attempts to separate the mixture by DCFC and HPLC were unsuccessful.

(k) With quadricyclane. Quadricyclane (1.00 g, 10.9 mmol) and the triazine **1** (2.00 g, 10.8 mmol), heated *in vacuo* at 70 °C for 2 days, gave volatile material (0.28 g), presumed to be nitrogen, and a brown residue, which was extracted with diethyl ether (3 × 20 cm^3). The extract was evaporated under reduced pressure, and the solute sublimed at 20–50 °C *in vacuo* to give 2,3,6-trichloropyridine (1.62 g, 8.95 mmol, 83%), mp 62 °C (lit.,[12] mp 62–64 °C). No further volatile material was obtained on attempted sublimation up to 130 °C.

NMR spectral data

Compound **6**. δ_H 6.95 (4-H), 2.92, 2.70, 1.80 (3 × CH_2), 1.60 [$(CH_2)_2$]; δ_C 158.2 (C-4a), 148.8 (C-1), 146.8 (C-3), 135.9 (C-9a), 123.2 (C-4), 35.9, 31.8, 30.1, 26.8. and 26.1 (5 × CH_2).

Compound **7**. δ_H 7.04 (4-H), 2.70, 2.57 (2 × CH_2) and 1.65–1.35 [$(CH_2)_8$]; δ_C 156.2 (C-4a), 151.0 (C-1), 146.8 (C-3), 133.8 (C-14a), 123.6 (C-4), 30.1, 28.4, 26.9, 26.5, 26.4 (2), 26.1, 25.0, 22.9 and 21.7 (all CH_2).

Compound **8**. δ_C 160.8 (CCl=N), 135.3, 127.4 (C=C), 92.5 (CCl–N), 75.9 (CCl–C=), 59.5, 49.7 (CH) and 37.5 (CH_2).

Compound **9**. δ_C 159.0 (CCl=N), 135.2, 133.1, 128.5, 127.6 (C=), 91.2 (CCl–N), 76.4 (CCl–C=), 60.4, 59.9, 48.6 (CH), 37.5 and 37.0 (CH + 2CH_2, masked by **8**).

Compound **10**. δ_H 7.80 (d, 1 H, ArH), 7.21 (m, 3 H, ArH), 4.04 (d, ^3J = 9, CCl–CHAr), 3.47–3.28 (m, 3 H, CH_2, CH); δ_C 161.3 (CCl=N), 143.3, 138.6. (C-4,5), 128.6, 127.8, 126.2, 124.6 (4sp^2-CH), 92.8 (CCl–N), 76.3 (CCl–C=) 58.1, 51.5 (CH) and 36.0 (CH_2).

Compounds **14** and **15** (mixture). δ_C 161.3, 159.4 (CCl=N), 91.5, 90.2 (CCl–N), 75.3, 74.3 (CCl–C) plus 9 bands in the 140.5–127.0 (sp^2-C) and 92.5–30.0 (sp^3-C) regions.

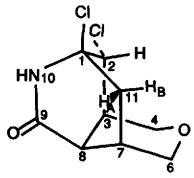
Compound **16**. δ_C 160.2 (CCl=N), 83.1 (CCl–N), 71.5 (CCl–C), 47.5, 45.0 and 29.8 (2CH_2, CH).

Compound **17**. δ_C 161.5 (CCl=N), 84.4 (CCl–N), 72.2 (CCl–C), 50.2, 44.4 and 30.8 (2CH_2, CH).

Compound **21**. δ_C 169.8 (C=O), 77.4 (CCl–N), 72.2 (CCl–C), 50.9, 45.1 and 31.5 (2CH_2, CH).

Compound **22**. δ_C 171.2 (C=O), 85.0 (CCl–N), 63.9 (CCl–C), 46.3, 45.1 and 29.3 (2CH_2, CH).

Compound **24**. δ_H 7.86 (s, 1 H, NH), 4.02 (d, 2 H, CHO, ^2J = 11.5), 3.62 (d, 2 H, CH–O), 2.48 (d, 4 H, CH_2, ^3J = 7) and 2.15 (t, 2 H, CH); δ_C 168.9 (C=O), 73.0 (CCl–N), 69.3 (CCl–C), 66.6 (CH_2–O), 44.3 (CH_2) and 37.7 (CH).



25

Compound **25**. δ_H 7.58 (s, NH, $^4J_{10\text{-}8}$ = 1), 4.28 (d, 2-H, $^3J_{2\text{-}3}$ = 2.5), 4.01 (br dd, 4e-H, $^2J_{4\text{-}4}$ = 11.6, $^3J_{4e\text{-}3}$ = 2.0, $^4J_{4\text{-}6e}$ < 1), 3.75 (br dd, 6e-H, $^2J_{6\text{-}6}$ = 11.5, $^3J_{6e\text{-}7}$ = 1.5, $^4J_{4e\text{-}6e}$ < 1), 3.46 (dd, 4ax-H, $^2J_{4\text{-}4}$ = 11.6, $^3J_{4ax\text{-}3}$ = 1.7), 3.45 (dd, 6ax-H, $^2J_{6\text{-}6}$ = 11.5, $^3J_{6ax\text{-}7}$ = 1.4), 2.56 (dd, 11A-H, $^2J_{11\text{-}11}$ = 14.0, $^3J_{11A\text{-}7}$ = 12.4), 2.54 (br td, 8-H, $^3J_{8\text{-}3}$, $^3J_{8\text{-}7}$ ≈ 2, $^4J_{8\text{-}10}$ ≈ 1), 2.38 (m, 3-H), 2.22 (br d, 11B-H, $^2J_{11\text{-}11}$ ≈ 14), 2.21 (br d, 7-H, $^3J_{7\text{-}11A}$ ≈ 12); δ_C 172.8 (C-9), 77.2 (C-1), 69.5 (C-6), 67.9 (C-4), 66.1 (C-2), 43.0 (C-3), 42.6 (C-8), 41.1 (C-11) and 29.3 (C-7).

Assignments are based upon H,H- and H,C-COSY and DEPT-135° spectra and selective ^{1}H decoupling. Noteworthy is the large $|^3J_{7\text{-}11A}|$, corresponding to a near zero dihedral angle, while $|^3J_{2\text{-}3}|$, where the dihedral angle is ~60°, is much smaller (2.5 Hz). Four-bond couplings are apparent between 8-H and 10-H and 4-H and 6-H occupying the equational position in the pyranose ring, where the W pathway operates.

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References

1 Reported in part in a preliminary communication: M. G. Barlow, L. Sibous and A. E. Tipping, *Tetrahedron Lett.*, 1992, **33**, 4653.
2 M. G. Barlow, R. N. Haszeldine and D. J. Simpkin, *J. Chem. Soc., Perkin Trans. 1*, 1982, 1245.
3 Diels–Alder reaction of 1,2,4-triazines have been reviewed: D. L. Boger, *Chem. Rev.*, 1986, **86**, 718; D. L. Boger and S. N. Weinreb, *Diels–Alder Methodology in Organic Synthesis*. Academic Press, New York, 1987, pp 323–335.
4 W. Dittmar, J. Sauer and A. Steigel, *Tetrahedron Lett.*, 1969, 5171.
5 M. G. Barlow, R. G. Pritchard, L. Sibous and A. E. Tipping, *Acta Crystallogr., Sect. C*, 1994, **50**, 552.
6 K. MacKenzie, *J. Chem. Soc.*, 1960, 473.
7 M. G. Barlow, R. G. Pritchard, L. Sibous and A. E. Tipping, *Acta Crystallogr., Sect. C*, 1994, **50**, 550.
8 T. Lantos, P. W. Sheldrake and A. S. Wells, *J. Chem. Soc., Perkin Trans. 1*, 1990, 1887.
9 M. G. Barlow, R. G. Pritchard, L. Sibous and A. E. Tipping, *Acta Crystallogr., Sect. C*, 1992, **48**, 1908.
10 M. G. Barlow, R. G. Pritchard, L. Sibous and A. E. Tipping, *Acta Crystallogr. Sect C*, 1993, **49**, 103.
11 B. A. Loving, C. E. Snyder, G. L. Whittier and K. R. Fountain, *J. Heterocycl. Chem.*, 1971, **8**, 1095.
12 U. Horm, F. Mutterer and C. D. Weis, *Helv. Chim. Acta*, 1976, **59**, 190.
13 V. H. Fritz, C. D. Weis and T. Winkler, *Helv. Chim. Acta*, 1976, **59**, 179.

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