Easy Access to Medium Rings by Entropy/Strain Reduction, Part 3 [1]. Competition between Dihydroazepine and Enamine Formation in Reaction of Tetrahalosubstituted Dibromides with Primary Amines

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The reaction of *Z,Z*-2,3,4,5-tetrahalo-2,4-dien-1,6-dibromides (**3**, R^1 - R^4 = Cl, Br) with primary amines in the presence of potassium carbonate leads to both the dihydroazepines **4** and secondary enamines **5**. The formation of enamine is suppressed with toluene sulfonamide as nitrogen source. (2*Z*,4*Z*)-2,3,4,5-Tetrabromohexa-2,4-diene-1,6-diol (**2**, R^1 - R^4 = Br) is atropisomeric in solution.

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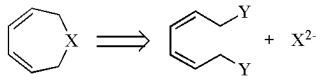
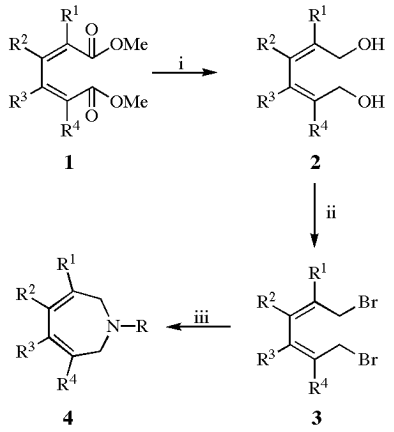
The synthesis of medium and large rings has always been a challenging problem [3]. We have previously communicated [1,4] an entropy/strain reduction strategy to overcome the low yields inherent in cycloaddition routes to medium rings. This is based on the use of a *cis,cis*-2,4-hexadiene [5] unit as one of the components in the cycloaddition which has the effect of (i) reducing the degrees of freedom in the chain; (ii) bringing the ends of the chain within reacting distance in certain conformations and (iii) reducing or eliminating eclipsing and transannular steric interactions in the product. Thus, for example, a seven-membered ring is readily constructed based on a [6+1] disconnection:



This strategy is crucially dependent on the ready availability of a precursor 1,6-biselectrophile which has the correct *cis,cis* stereochemistry of the double bonds. We have recently reported [6] the details of lead tetraacetate oxidative ring-opening of catechols which is an effective source of just such stereochemistry furnishing substituted *Z,Z*-2,4-dien-1,6-dioates **1** in high yields and free of any of the other alkene isomers. We have also reported [1] the conversion of these esters, *via* the derived diols **2**, to the required dibromides **3** and the use [1] of the latter for the construction of substituted 2,7-dihydroazepines **4** using primary amines as nucleophiles, Scheme 1. This synthetic sequence provided ready access for the first time to the *cis,cis*-stereochemistry of 2,4-diene-1,6-diols and dibromides and the first general route to 2,7-dihydro-1*H*-azepines.

We now report the extension of this methodology to the tetrahalo-substituted cases (R^1 - R^4 = Cl, Br) which gives, as well as the dihydroazepines, halo-substituted conjugated enamines whose formation can be suppressed by the correct choice of amine precursor.

Scheme 1



i: DIBAL-H, hexane/toluene or heptane/benzene, r.temp., 12-24 h; ii: PBr_3, Et_2O, 0 °C, 12-24 h; iii: RNH_2, K_2CO_3, THF, t. temp., 1-2 days

Results and Discussion.

Z,Z-2,3,4,5-Tetrahalohexa-2,4-diene-1,6-dibromides (**3**, R^1 - R^4 = Cl, Br).

These were synthesised by hydride reduction and bromination with phosphorus tribromide according to Scheme 1 by our previously published methods [1] in overall yields of greater than 70%, for both cases. It is noteworthy that the attempted conversion of the tetrachlorodiol (**2**, R^1 - R^4 = Cl) to the corresponding hexachloride using the triphenylphosphine-carbon tetrachloride system [7] yielded only starting material. Characterisation of **2** and **3** by elemental analysis and spectroscopy was satisfactory and mostly unremarkable. The exceptions were the ^{1}H nmr spectrum of the tetrabromodiol (see below) and the mass spectra which gave the predicted complex and distinctive isotope clusters and fragmentation patterns. Thus the hexabromide (**3**, R^1 - R^4 = Br) shows clearly the sequential loss of each of the bromines while the dibromotetrachlo-

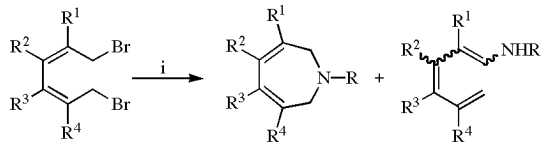
ride (**3**, R^1 - R^4 = Cl) shows the loss of the two bromines individually before the sequential loss of the chlorines. It was not possible, due to the substitution patterns, to discern in the ^{1}H nmr spectra any coupling constants for proof of stereochemistry. We rely on our own previous work which established the *cis,cis*-stereochemistry of the diols derived from a series of other diesters **1**. Also Rosner and Kobrich [8] reported data for the (*E,E*)-isomer of 2,3,4,5-tetrabromohexa-1,6-diol and cited a melting point of 100-101 °C whereas the tetrabromodiol reported here melts at 134-136 °C.

The ^{1}H nmr spectrum in dilute d^6-acetone of (2*Z*,4*Z*)-2,3,4,5-tetrabromohexa-2,4-diene-1,6-diol (**2**, R^1 - R^4 = Br) showed it to be atropisomeric in solution as judged by the non-equivalence of the methylene hydrogens (AB quartet resonating at 4.3 ppm). A similar phenomenon was reported for the corresponding (*E,E*)-isomer by Rosner and Kobrich [8] who attributed it to restricted rotation about the central single bond of the diene. It is noteworthy that the corresponding hexabromide (**3** R^1 - R^4 = Br) does not show this effect. It must be surmised that the chemical shift difference between the two-methylene hydrogens is so small that the effect is not detected.

Reaction of Tetrahalodibromides (**3,** R^1 - R^4 = Cl, Br) with Primary Amines and Sulfonamide.

For this reaction we had previously [1] utilised conditions developed by other workers [9] for different but related reactions. The procedure calls for the addition of a tetrahydrofuran solution of the amino compound to a stirred solution of various alkyl-substituted dibromides (**3**, R^1 - R^4 = H, ^{t}Bu) in the presence of solid potassium carbonate. This resulted in reasonable yields of the corresponding dihydroazepines (**4**, R = Bu, Bn, $(MeO)_2CHCH_2$, tosyl) and, in all cases bar the sulfonamide, there was at least one other reaction product which was too unstable to isolate. We now report one possible identity of this side-product because application of the Gleiter protocol to the tetrahalodibromides (**3**, R^1 - R^4 = Cl, Br) produces, again in all cases bar the sulfonamide, two isolable products. One is the expected dihydroazepine **4** and the second is the isomeric secondary enamine **5** produced by elimination, Scheme 2 and Table.

Scheme 2



3 **4** **5**

i: RNH_2, K_2CO_3, THF, r. temp, 1-2 days

Table

Yields of Dihydroazepines **4** and Enamines **5** Obtained from Dibromides **3** According to Scheme 2 [a]

Entry	R^1 - R^4	R	Yield of 4 [b]	Yield of 5 [b]
1	Br	benzyl	45 [c]	41
2	Br	$(MeO)_2CHCH_2$	39	29
3	Br	butyl	60	34
4	Cl	butyl	51	42
5	Cl	tosyl	48 [d]	0

[a] Reaction in the presence of K_2CO_3 in THF at 25 °C for 1-2 days, for procedures: see experimental section; [b] Liquid, yield after chromatography, unless stated otherwise; [c] Solid; [d] solid, yield after recrystallisation, starting material recovered.

For each entry in the Table the compounds were separated by chromatography. Spectroscopic data and elemental analyses were in agreement with the dihydroazepine structures **4** and correlated well with our previously published cases [1]. Thus in the fairly sparse nmr spectra the allylic methylene unit showed the expected shifts from the precursors: upfield for the hydrogens (from about 4.2-4.3 to 3.6-3.7 ppm) and downfield for the carbons (from 32-34 to 60-61 ppm).

The identity of the enamine was firmly established from the *N*-benzyl case (entry 1) which gave consistent elemental analysis. The other cases (entries 2-4) were then identified by spectral comparison. In the *N*-benzyl case, an isomeric 1:1 adduct was clearly indicated by elemental analysis and mass spectrometry data. We considered a large number of possible isomers including aminohexadienes, dihydropyrroles and butenylaziridines which are all possible products of the reaction but these were all excluded by ^{1}H nmr spectroscopy which was consistent only with the secondary enamine structure **5**. This is further supported by the presence of an N-H signal at 3120 cm^{-1} in the ir spectrum although we found no corresponding signal in the ^{1}H nmr spectrum. In the latter the allylic methylene signals are replaced by a pair of mutually coupled doublets and a singlet in the alkene region while the benzylic signal is significantly shifted downfield to approximately 5.1 ppm consistent with literature examples of similar *N*-benzyl substituted secondary enamines [10]. Unfortunately, because of their substitution pattern, the stereochemistry of compounds **5** remains undetermined. If elimination was by loss of bromide from the initially formed open chain bromo-amine, then steric considerations would suggest that the products should be the 1*Z*,3*E*-isomers. On the other hand if elimination was from the ring-closed ammonium precursors of the azepines the products would have to be the 1*Z*,3*Z*-isomers.

Secondary enamines are considered to be thermodynamically unstable with respect to the tautomeric imines [11] but in fact they are quite stable so long as the double bond

is conjugated [11,12]. In addition the position of equilibrium can be affected by the presence of various substituents at the positions α or β to the nitrogen, with the β-substituents having the greatest effect, electron accepting substituents strongly favouring enamine [11,13-15].

We note that in the case of toluenesulfonamide as nitrogen source in this reaction (Table, entry 5) no side-product is produced. This is consistent with our previous work [1] where we speculated that it was due to its reduced basicity precluding elimination reaction. Obviously then the nitrogen is most satisfactorily introduced with sulfonyl protection. Finally, although we have identified the secondary enamines as the side products in the cases reported here, we would be reluctant to assign definitively the same structures to the side products in our previous work [1]. This is because we have some evidence that the latter had characteristics of either dihydropyrroles or butenylaziridines [16].

Acknowledgement.

We acknowledge financial support from the Irish Department of Education (JGW), St. Patricks College, Maynooth (JGW) and the Federation of Irish Chemical Industries (JGW). We thank Dr. Patrick Furlong for the improved synthesis of the tetrabromodiol (**2**, R^1 - R^4 = Br).

EXPERIMENTAL

Elemental analyses were carried out commercially by the Microanalysis Department at University College Cork. IR spectra were obtained as potassium bromide discs or as a thin film between sodium chloride plates on a Perkin-Elmer 783 spectrophotometer. Mass spectra were obtained in the EI mode on an A.E.I. 30 instrument and on a Kratos Profile machine. Mp's were determined using a Reichart hot-stage apparatus and are uncorrected. Unless otherwise stated ^{1}H and ^{13}C NMRs were obtained in deuteriochloroform and were recorded using the Fourier transform mode at 80 Mz and 20 Mz respectively on a Brucker AC80 spectrometer using tetramethylsilane (TMS) as internal standard (*J* values are given in Hz). Analytical TLC was performed on commercial silica-coated aluminium sheets with a fluorescent indicator (Merck-Art.5554) or on neutral aluminium oxide-coated aluminium sheets with fluorescent indicator (Merck-Art.5550). Realisation was by ultraviolet irradiation. Preparative chromatography was performed on Flash grade silica gel supplied by Aldrich Fine Chemicals (cat. no. 22,719-6,230-400 mesh) and neutral aluminium oxide (Aldrich cat. no. 19,997-4). The columns were pressurised using a fish pump, which was found to be adequate for all diameters up to and including 4 cm. Solvents were dried using recognised procedures [17]. Oxygen-free nitrogen (Irish Industrial Gases) was dried by passage through concentrated sulfuric acid and then sodium hydroxide pellets. The starting substituted 2,4-hexadiene-1,6-diesters **1** were prepared by oxidation of the appropriate catechol or *o*-benzoquinone with lead tetraacetate according to our published procedures [6]. All other chemicals used were purchased from Aldrich.

(2*Z*,4*Z*)-2,3,4,5-Tetrachlorohexa-2,4-diene-1,6-diol (**2**, R^1 - R^4 = Cl).

Dimethyl (2*Z*,4*Z*)-2,3,4,5-tetrachloro hexa-2,4-diene-1,6-dioate (**1**, R^1 - R^4 = Cl) [6] (1.35 g, 4.4 mmol) was dissolved in dry benzene (70 ml). To this stirred solution was added DIBAL-H in heptane (17.5 ml of a 1.0 *M* solution, 10 mmol) slowly by syringe under nitrogen. After 24 h stirring a small amount of methanol (*ca.* 2-4 ml) was carefully added until the mixture became paste-like with precipitated aluminium salts. Then a large volume of methanol was added (100 ml) and vigorous stirring undertaken to break up the paste-like salts which were removed by filtration. The filtrate was dried over anhydrous sodium sulfate and evaporated to give a yellow oil, which solidified to a yellow tinged solid. This was purified by column chromatography (alumina, diethyl ether/hexane (1:1)) to give an off-white solid which was recrystallised from diethyl ether (0.88 g, 80%) mp 123-125 °C (lit: 74-75 °C [18]); IR: ν_{max}/cm^{-1} 3280, 2940, 2920, 1590, 1450, 1420, 970, 850, 770, 680, 620, 550; ^{1}H NMR (CD_3COCD_3): δ_H 3.00 (s, br, 2H, OH), 4.31 (s, 4H, -CH_2-); ^{13}C NMR (CD_3COCD_3): δ_C 64.3 (-CH_2-), 126.5, 141.1 (-CH=CH-); MS: m/z 215 (100%, M^+-Cl), 200 (12), 198 (30), 196 (31, M^+-H_2O-HCl), 184 (15), 182 (17), 180 (14, M^+-2xCl), 178 (23, M^+-2xH_2O-HCl), 147 (15), 145 (25, M^+-3xCl), 134 (25), 132 (42).

Anal. Calcd. for $C_6H_6O_2Cl_4$: C, 28.60; H, 2.40; Cl, 56.29. Found: C, 28.75; H, 2.48; Cl, 56.00.

(2*Z*,4*Z*)-2,3,4,5-Tetrabromohexa-2,4-diene-1,6-diol (**2**, R^1 - R^4 = Br).

Dimethyl (2*Z*,4*Z*)-2,3,4,5-tetrabromohexa-2,4-diene-1,6-dioate (**1**, R^1 - R^4 = Br) [6] (8.0 g, 16.5 mmol) was dissolved in dry toluene (250 ml) under an atmosphere of nitrogen and cooled to 0 °C. To this stirred solution was added DIBAL-H in hexane (44 ml of a 1.5 *M* solution, 66 mmol) slowly over 30 minutes by syringe under nitrogen. The solution was then allowed to warm to room temperature and left to stir overnight. A small amount of methanol (*ca.* 2-4 ml) was carefully added until the mixture became paste-like with precipitated aluminium salts. Then a large volume of methanol was added (100 ml) and vigorous stirring undertaken to break up the paste-like salts. The salt suspension was filtered, the filtrate set aside, and the solids ground in a mortar and resuspended in methanol to be filtered again. The combined filtrate was dried over anhydrous sodium sulfate and evaporated to give the crude diol, which was purified using column chromatography (alumina, diethyl ether/hexane (1:3)). The resulting crude oil solidified on standing and was recrystallised from diethyl ether to give a beige solid (6.1 g, 86%) mp 136-138 °C (lit. for (*E*,*E*)-isomer: 100-101 °C [8]); IR: ν_{max}/cm^{-1} 3200, 2940, 1580, 1450, 960, 700, 620, 540, 500; ^{1}H NMR (CD_3COCD_3 very dilute solution): δ_H 4.3 (AB quartet of doublets, 4H, -CH_2-, ^{3}J = 5.3 Hz), 5.1 (t, 2H, OH, ^{3}J = 5.3 Hz); (CD_3COCD_3/D_2O, very dilute solution): δ_H 4.3 (AB quartet, -CH_2-, J_{AB}= 16.2 Hz, δ_A-δ_B = 4.9 Hz); ^{13}C NMR (CD_3COCD_3): δ_C 65.8 (-CH_2-), 122.7, 136.4 (-CH=CH-); MS: m/z 351 (2), 349 (6), 347 (8), 345 (2, M^+-1-HBr), 334 (6), 332 (18), 330 (18), 328 (6, M^+-HBr-H_2O), 270 (8), 268 (16), 266 (9, M^+-2xHBr), 253 (15), 251 (32), 249 (18, M^+-2xHBr-OH), 172 (10), 170 (11, M^+-2xBr-HBr-H_2O), 81 (97), 79 (100, Br).

Anal. Calcd. for $C_6H_6O_2Br_4$: C, 16.77; H, 1.41; Br, 74.38. Found: C, 16.58; H, 1.48; Br, 74.71.

(2*Z*,4*Z*)-1,6-dibromo-3,4,5,6-tetrachlorohexa-2,4-diene (**3**, R^1 - R^4 = Cl).

(2*Z*,4*Z*)-2,3,4,5-Tetrachlorohexa-2,4-diene-1,6-diol (**2**, R^1 - R^4 = Cl) (0.5 g, 2.0 mmol) was dissolved in dry diethyl ether (20 ml) and cooled to 0 °C with stirring. To this was added slowly phosphorus tribromide (0.42 g, 0.15 ml, 1.55 mmol) in diethyl ether (10 ml). After overnight stirring the solvent was evaporated to leave an orange liquid which on column chromatography (silica, dichloromethane/hexane (1:2)) gave a white solid (0.71 g, 95%) mp 57-59 °C; IR: ν_{max}/cm^{-1} 1580, 1420, 925, 910, 665, 645, 570, 535, 505; ^{1}H NMR: δ_H 4.21 (s, -CH_2-); ^{13}C NMR: δ_C 31.4 (-CH_2-), 126.6, 136.3, (-CH=CH-); MS: m/z 381 (3%), 379 (8), 377 (14), 375 (11), 373 (3, M^+-1), 300 (9), 298 (38), 296 (30), 295 (14, M^+-Br), 216 (14, M^+-2xBr), 215 (14, M^+-HBr-Br), 181 (78, M^+-2xBr-Cl), 180 (47, M^+-Br-HBr-Cl), 179 (82, M^+-2xHBr-Cl), 145 (28, M^+-2xBr-2xCl), 108 (29, M^+-2xBr-3xCl), 75 (100).

Anal. Calcd. for $C_6H_4Cl_4Br_2$: C, 19.08; H, 1.07. Found: C, 19.07; H, 1.11.

Attempted Preparation of (2*Z*,4*Z*)-1,2,3,4,5,6-Hexachlorohexa-2,4-diene using Appels Reagent.

(2*Z*,4*Z*)-2,3,4,5-Tetrachlorohexa-2,4-diene-1,6-diol (**2**, R^1 - R^4 = Cl) (0.25 g, 1 mmol), dissolved in dry diethyl ether (10 ml), was added under dry nitrogen and at room temperature to a stirred mixture of triphenylphosphine (0.7 g, 2.6 mmol) and dry carbon tetrachloride (0.44 ml) in dry diethyl ether (30 ml) and left stirring for 24 h. Evaporation of the solvents yielded a white solid mass, which was analysed by TLC to reveal two main products that were separated by column chromatography (silica, diethyl ether/hexane (1:1)) and identified as the two starting materials.

(2*Z*,4*Z*)-1,2,3,4,5,6-hexabromohexa-2,4-diene (**3**, R^1 - R^4 = Br).

(2*Z*,4*Z*)-2,3,4,5-Tetrabromohexa-2,4-diene 1,6-diol (**2**, R^1-R^4 = Br) (0.75 g, 1.74 mmol) was dissolved in dry diethyl ether (30 ml). To this stirred cooled solution, phosphorus tribromide (0.40 g, 0.14 ml, 1.5 mmol) in diethyl ether (10 ml) was added slowly. After 24 h work-up yielded an orange liquid, which was purified by column chromatography (silica, DCM/hexane(1:1)) to an off-white solid and recrystallised from dichloromethane (0.78 g, 80%) mp 134-136 °C; IR: ν_{max}/cm^{-1} 1565, 1420, 900, 780, 630, 555, 535, 520; ^{1}H NMR: δ_H 4.32 (s, -CH_2-); ^{13}C NMR: δ_C 34.0 (-CH_2-), 122.7, 130.7 (-CH=CH-); MS: m/z 559 (5%), 557 (10), 555 (17), 553 (13), 551 (5), 549 (not detected, M^+-1), 478 (7), 476 (16), 474 (16), 472 (8), 470 (not detected, M^+-HBr), 397 (17), 395 (25), 393 (23, M^+-HBr-Br), 318 (23), 316 (60), 315 (31), 314 (60), 313 (25, M^+-2xHBr-Br), 312 (24, M^+-HBr-2xBr), 237 (25), 235 (62), 233 (28, M^+-HBr-3xBr), 75 (100, M^+-6xBr).

Anal. Calc. for $C_6H_4Br_6$: C, 12.97; H, 0.73; Br, 86.30. Found: C, 13.23; H, 0.82; Br, 85.95.

Reactions of (2*Z*,4*Z*)-1,2,3,4,5,6-Hexabromohexa-2,4-diene (**3**, R^1 - R^4 = Br) with Amines.

With Benzylamine.

The hexabromide (0.57 g, 1.0 mmol) was stirred in dry THF (20 ml) with potassium carbonate (0.28 g, 2.1 mmol). To this mixture was added benzyl amine (0.11 g, 1.0 mmol) in dry THF (10 ml). The resultant mixture was stirred at room temperature for 48 h during which time the mixture became cloudy white in color. Filtration of the inorganic salts and evaporation of the filtrate generated a viscous yellow/brown liquid that according to TLC and NMR analysis showed the presence of two major products. These were isolated by column chromatography on silica using petroleum ether (40-60) followed by dichloromethane/petroleum ether (40-60) (2:3) as eluants.

Material of higher Rf, a brown liquid, identified as ((1*Z*,3*Z*)-2,3,4,5-tetrabromohexa-1,3,5-trienyl)benzylamine (**5**, R = Bn, R^1 - R^4 = Br) (0.21 g, 41%); IR: ν_{max}/cm^{-1} 3120, 3020, 2940, 1630, 1510, 1500, 1470, 1440, 1430, 980, 910, 750, 730, 700, 670; ^{1}H NMR: δ_H 5.08 (s, 2H), 5.88 (d, 1H, J = 1.5 Hz), 6.03 (d, 1H, J = 1.5 Hz), 6.63 (s, 1H), 7.05-7.34 (m, 5H, -Ar); ^{13}C NMR: δ_C 52.9 (-NCH_2-), 99.5, 101.4, 117.2(x2), 122.7, 128.0, 128.8, 129.5, 136.7, 142.2; MS: m/z 423 (1%), 421 (3), 419 (4), 417 (1, M^+-HBr), 342 (9), 340 (17), 338 (9, M^+-HBr-Br), 106 (9, $NHCH_2C_6H_5$), 91 (100, -$CH_2C_6H_5$),.

Anal. Calcd. for $C_{13}H_{11}NBr_4$: C, 31.17; H, 2.21; N, 2.80; Br, 63.82. Found C, 31.45; H, 2.49; N, 3.01; Br, 63.50.

Material of lower Rf, a white solid, identified as 1-benzyl-3,4,5,6-tetrabromo-2,7-dihydro-1*H*-azepine (**4**, R = Bn, R^1 - R^4 = Br) (0.23 g, 45%) mp 98-100°C; IR: ν_{max}/cm^{-1} 3040, 2960, 2920, 2820, 2800, 1580, 1560, 1460, 1440, 960, 870, 830, 760, 710, 700, 660, 620; ^{1}H NMR: δ_H 3.58 (s, 4H, -NCH_2-), 3.82 (s, 2H, -CH_2N-), 7.23-7.33 (m, 5H, -Ar); ^{13}C NMR: δ_C 60.4 (-NCH_2-), 60.6 (-CH_2N-), 126.0, 128.3 (-CH=CH-), 128.4, 129.2, 129.5, 138.2 (-Ar); MS: m/z 505 (1%), 503 (5), 501 (7), 499 (4), 497 (1, M^+), 424 (3), 422 (8), 420 (8), 418 (3, M^+-Br), 414 (2), 412 (7), 410 (11), 408 (7), 406 (2, M^+-Bz) 343 (4), 341 (8), 339 (4, M^+-2xBr), 252 (4), 250 (10), 248 (4, M^+-2xr-Bz), 91 (100, $CH_2C_6H_5$).

Anal. Calcd. for $C_{13}H_{11}NBr_4$: C, 31.17; H, 2.21; N, 2.80; Br, 63.82. Found: C, 31.49; H, 2.33; N, 2.98; Br, 63.41.

With Aminoacetaldehyde Dimethyl Acetal.

The hexabromide (0.5 g, 0.9 mmol), potassium carbonate (0.15 g, 1.1 mmol) and aminoacetaldehyde dimethyl acetal (0.1 g, 9.5x10^{-4} mole) were used in a manner similar to the previous experiment, over 4 days. Work-up and column chromatography (silica, chloroform/cyclohexane (1:1)) gave two clear brown liquids

Material of higher Rf, a brown liquid, identified as ((1*Z*,3*Z*)-2,3,4,5-tetrabromohexa-1,3,5-trienyl)(2,2-dimethoxyethyl)amine (**5**, R = $(MeO)_2CHCH_2$, R^1 - R^4 = Br) (0.12 g, 29%); IR: ν_{max}/cm^{-1} 3120, 2960, 2940, 2840, 1720, 1630, 1510, 1480, 1440, 970, 920, 760, 710; ^{1}H NMR: δ_H 3.38 (s, 6H, -OCH_3), 4.01 (d, 2H, -NCH_2-, J = 5.1 Hz), 4.48 (t, 1H, -CH-, J = 5.1 Hz), 6.02 (d, 1H, J = 1.5 Hz), 6.14 (d, 1H, J = 1.5 Hz), 6.82 (s, 1H); ^{13}C NMR: δ_C 51.1 (-NCH_2-), 55.7 (-OCH_3), 99.3, 101.3, 104.0 (-CH-), 117.4, 123.7, 128.9, 130.1; MS: m/z 470 (28%), 469 (44), 468 (24), 467 (100), 465 (52), 463 (11, M^+-HOMe), 426 (51), 424 (79), 422 (56), 420 (22, M^+-$CH(OMe)_2$), 390 (8), 388 (26), 386 (26), 384 (8, M^+-Br-$HOCH_3$), 347 (8), 345 (33), 343 (32), 341 (12, M+-Br-$CH(OCH_3)_2$).

Material of lower Rf, a brown liquid, identified as 3,4,5,6-tetrabromo-2,7-dihydro-1-(2,2-dimethoxyethyl)-1*H*-azepine (**4**, R = $(MeO)_2CHCH_2$, R^1 - R^4 = Br) (0.16 g, 39%); IR: ν_{max}/cm^{-1} 2960, 2930, 2840, 1560, 1450, 970, 920, 850, 720, 670, 620; ^{1}H NMR: δ_H 2.86 (d, 2H, -NCH_2-, ^{3}J = 5.2 Hz), 3.38 (s, 6H, -OCH_3), 3.67 (s, 4H, -CH_2N-), 4.45 (t, 1H, -CH-, ^{3}J = 5.2 Hz); ^{13}C NMR: δ_C 54.6 (-OCH_3), 58.2 (-NCH_2-), 61.7 (-CH_2N-), 104.4 (-CH-), 125.9, 128.2 (-C=C-); MS: m/z 421 (14%), 419 (45), 417 (44), 415 (14, M^+-HBr), 390 (2), 388 (9), 386 (8), 384 (2, M^+-HBr-OMe), 340 (16), 338 (39), 336 (14, M^+-HBr-Br),

308 (12), 306 (21), 304 (10, M^+-HBr-HOMe-Br), 75 (100, $CH(OMe)_2$).

Anal. Calcd. for $C_{10}H_{13}O_2NBr_4$: C, 24.08; H, 2.63; N, 2.81; Br, 64.07. Found: C, 24.15; H, 2.92; N, 2.65; Br, 64.31.

With *n*-Butylamine.

The hexabromide (0.5 g, 0.9 mmol), potassium carbonate (0.13 g, 0.94 mmol) and *n*-butylamine (0.07 g, 0.9 mmol) were used in a manner similar to the previous experiments, over 48 h. Work-up and chromatography (silica, dichloromethane/hexane (1:1)) generated two liquid products.

Material of higher Rf: identified as ((1*Z*,3*Z*)-2,3,4,5-tetrabromohexa-1,3,5-trienyl)butylamine (**5**, R = Bu, R^1 - R^4 = Br) (0.14 g, 34%); IR: ν_{max}/cm^{-1} 3120, 3020, 2940, 1630, 1510, 1500, 1470, 1440, 1430, 980, 910, 750, 730, 700, 670; ^{1}H NMR: δ_H 0.60-1.70 (m, 7H, $-CH_2CH_2CH_3$), 3.92 (t, 2H, $-NCH_2-$, J = 7.3 Hz), 5.98 (d, 1H, J = 1.5Hz), 6.11 (d, 1H, J = 1.5Hz), 6.72 (s, 1H); ^{13}C NMR: δ_C 14.6 ($-CH_3$), 20.8, 34.6 ($-CH_2-$), 48.2 ($-NCH_2-$), 105.5, 102.7, 119.5, 124.1, 129.3, 135.2.

Material of lower Rf: identified as 3,4,5,6-tetrabromo-1-butyl-2,7-dihydro-1*H*-azepine (**4**, R = Bu, R^1 - R^4 = Br) (0.25 g, 60%); IR: ν_{max}/cm^{-1} 3040, 2960, 2920, 2820, 2800, 1580, 1560, 1460, 1440, 960, 830, 760, 710, 700, 660, 620; ^{1}H NMR: δ_H 0.80-1.72 (m, 7H, $-CH_2CH_2CH_3$), 2.50-2.78 (m, 2H, $-NCH_2-$), 3.58 (s, 4H, $-CH_2N-$); ^{13}C NMR: δ_C 14.4 ($-CH_3$), 21.4, 31.2 ($-CH_2-$), 55.6 ($-NCH_2-$), 61.0 ($-CH_2N-$), 129.2, 138.6 (-C=C-).

Anal. Calcd. for $C_{10}H_{13}NBr_4$: C, 25.73; H, 2.81; N, 3.00; Br, 68.46. Found: C, 25.92; H, 2.97; N, 3.09; Br, 68.22.

Reactions of (2*Z*,4*Z*)-1,6-Dibromo-2,3,4,5-tetrachlorohexa-2,4-diene (**3**, R^1 - R^4 = Cl) with Amines.

With *n*-Butylamine.

The dibromide (0.56 g, 1.5 mmol), potassium carbonate (0.21 g, 1.5 mmol) and *n*-butylamine (0.11 g, 1.5 mmol) were used in a manner similar to the previous experiments over 48 h. Evaporation of the solvent left a brown/yellow semi-solid, which was slurried in diethyl ether and the insoluble salts removed by filtration. The filtrate was evaporated to yield a light brown liquid which TLC analysis showed contained two products. These were separated by column chromatography (silica, hexane followed by dichloromethane/hexane (1:1)). However neither could be obtained pure enough for elemental analysis.

Material of higher Rf, a faint yellow/green liquid, identified as ((1*Z*,3*Z*)-2,3,4,5-tetrachlorohexa-1,3,5-trienyl)butylamine (**5**, R = Bu, R^1 - R^4 = Cl) (0.18 g, 42%); IR: ν_{max}/cm^{-1} 3140, 2960, 2940, 2880, 1630, 1520, 1490, 1450, 960, 750, 730; ^{1}H NMR: δ_H 0.70-1.90 (m, 7H, $-CH_2CH_2CH_3$), 3.90 (t, 2H, $-NCH_2-$, J = 7.3 Hz), 5.62 (d, 1H, J = 1.2 Hz), 5.83 (d, 1H, J = 1.2 Hz), 6.63 (s, 1H); ^{13}C NMR: δ_C 14.2 ($-CH_3$), 20.4, 33.6 ($-CH_2-$), 49.3 ($-NCH_2-$), 105.1, 105.7, 119.3, 123.0, 126.5, 128.2.

Material of lower Rf, a brown viscous liquid, identified as 1-butyl-3,4,5,6-tetrachloro-2,7-dihydro-1*H*-azepine (**4**, R = Bu, R^1 - R^4 = Cl) (0.22 g, 51%); IR: ν_{max}/cm^{-1} 2960, 2940, 2860, 2800, 1730, 1580, 1450, 970, 880, 780, 690, 590; ^{1}H NMR: δ_H 0.80-1.70 (m, 7H, $-CH_2CH_2CH_3$), 2.45-2.62 (m, 2H, $-NCH_2-$), 3.47 (s, 4H, $-CH_2-$); δ_C: 14.5 ($-CH_3$), 21.0, 30.7 ($-CH_2-$), 56.6 ($-NCH_2-$), 60.0 ($-CH_2N-$), 128.2, 137.5 (-CH=CH-).

With Toluene *p*-Sulfonamide.

The dibromide (0.78 g, 2 mmol), potassium carbonate (0.28 g, 4.1 mmol) and the sulfonamide (0.40 g, 2.3 mmol) were used in a manner similar to the previous experiments. After 60 h work-up gave a yellow semi-solid which TLC and NMR analysis showed to be mainly one product and some starting material. This crude product was subjected to column chromatography (silica, chloroform/pentane (1:1)) to give a yellow tinged solid material which was recrystallised with chloroform/pentane (1:1) to give a white solid, 3,4,5,6-tetrachloro-2,7-dihydro-1-[(4-methylphenyl)sulfonyl]-1*H*-azepine (**4**, R = Ts, R^1 - R^4 = Cl) (0.38 g, 48%) mp 166-168°C; IR: ν_{max}/cm^{-1} 1590, 1580, 1460, 920, 770, 690, 630, 580, 560, 53; ^{1}H NMR: δ_H 2.44 (s, 3H, $-CH_3$), 4.13 (s, 4H, $-CH_2N-$), 7.26-7.78 (m, 4H, Ar); ^{13}C NMR: δ_C 22.2 ($-CH_3$), 52.2 ($-CH_2N-$), 131.1 132.1 (-C=C-), 128.4, 130.6, 135.5, 145.1 (Ar); MS: m/z 389 (1%), 387 (2), 385 (2, M^+), 354 (1), 352 (2), 350 (1, M^+-Cl), 236 (5), 234 (22), 232 (46), 231 (11), 230 (34, M^+-$MeC_6H_4SO_2$), 229 (8, M^+-$MeC_6H_4SO_2H$), 199 (3), 198 (4), 197 (8), 196 (13), 195 (10, M^+-Cl-$MeC_6H_4SO_2$), 155 (29, $CH_3C_6H_4SO_2$), 91(100).

Anal. Calcd. for $C_{13}H_{11}NO_2SCl_4$: C, 40.34; H, 2.86; N, 3.62; S, 8.28; Cl, 36.63. Found: C, 40.08; H, 2.85; N, 3.50; S, 7.98; Cl, 36.85.

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