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Thermal Ene Reactions of Alloxan and 1,3-Dimethylalloxan

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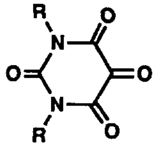
Abstract: *Both alloxan* ***1*** *and 1,3-dimethylalloxan* ***2*** *are conveniently prepared from their hydrates, respectively* ***3*** *and* ***4****, by either chemical removal of the water (acetic anhydride in boiling acetic acid) or by azeotropic drying using chlorobenzene as solvent. The central C=O groups of these triones are extremely electrophilic and ene addition occurs at these sites with a wide range of alkenes and with terminal alkynes in aprotic solvents at moderate temperatures (100–130°C). The ene adducts are 5-allyl-5-hydroxybarbituric acids or their N,N-dimethyl analogues. Stereoselectivity, when relevant, appears largely to be dictated by steric factors. Isoprene, however, reacted by Diels–Alder rather than by ene addition; the adducts are the expected regio-isomers* ***24****.*

INTRODUCTION

The ene reaction is, in effect, the intermolecular equivalent of a sigmatropic [1,5] H-shift. These reactions are also the central members of a pericyclic series of intermolecular reactions that extends from the well-known Diels–Alder reaction at one extreme to the rare homogeneous hydrogen transfer processes at the other. In comparison with Diels–Alder processes, ene reactions suffer from less favourable stereo-electronic and energetic factors, and are more difficult to promote. In frontier orbital terms a small HOMO–LUMO gap between the reaction partners is required. The enophile is generally the electron acceptor, and reactive species possess a low LUMO energy. The ene is the electron donor, and the most reactive possess a high HOMO energy.

There is more scope for reducing enophile LUMO energies than for increasing ene HOMO energies. We have shown[1] that enes may be placed in the following 'reactivity series': **Type 1** $RCH_2C(R^1)=CH_2$ ≥ $RCH_2C(R^1)=CHR^2$ > **Type 2** $RCH_2CH=CH_2$ > **Type 3** $RCH_2CH=CHCH_2R^1$ ≥ **Type 4** $RCH_2C\equiv CH$ > **Type 5** $ZCH_2CH=CH_2$ ≥ $RCH_2C(Z)=CH_2$, where R is hydrogen, alkyl or aryl, R^1 is alkyl or aryl, R^2 is alkyl, and Z an electron-withdrawing group. Our results have indicated an *approximate* order of magnitude fall in reactivity between adjacent members as this series is traversed.

The central C=O group is the reactive site in the enophile indane-1,2,3-trione. Reactivity is enhanced by the presence of two flanking and coplanar C=O groups, and we have shown recently that indanetrione may be regarded as a superenophile.[1] In a parallel study we also investigated alloxan **1** and 1,3-dimethylalloxan **2** as enophiles of potentially high reactivity. They also possess the two flanking C=O groups and both form stable hydrates (*i.e.* **3** and **4**) – indicating the electrophilic nature of their central C=O groups. We were interested to discover if the urea-type or amide-type resonance (*i.e.* respectively **A** and **B**) within these molecules appreciably attenuated the electron-deficiency at C-5.



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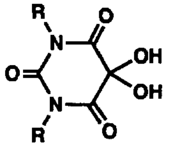
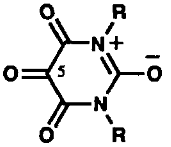
2 R = Me



3 R = H
4 R = Me



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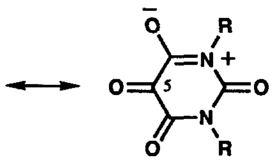
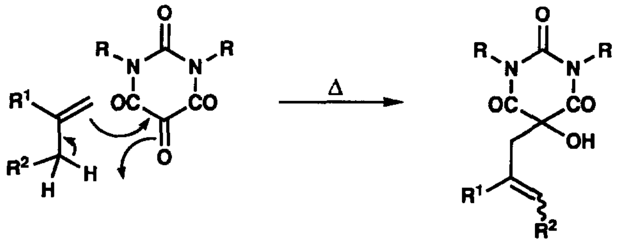


B

Successful ene additions to the alloxans would allow for the rather easy synthesis of 5-allyl-5-hydroxybarbituric acids, as indicated in equation (1) for the reaction with a 1,1-dialkylethylene. The HOMO of the ene possesses a large coefficient at the terminal C-atom, and the LUMO of the enophile has a large orbital coefficient on its C-atom also. Hence, the regiochemistry for the addition should be as shown. In such an addition it is likely that the transition state will be highly unsymmetrical with C–C bonding being more advanced than O–H bonding. In some ene reactions it is clear that the H-transfer lags so far behind that formal stepwise mechanisms are involved.[2,3]



(1)

RESULTS AND DISCUSSION

The Preparation of **1** *and* **2**.— Although alloxan is referred to frequently in the literature, it is clear in most cases that the monohydrate **3** is the reagent being utilised. Alloxan monohydrate is readily prepared by the oxidation of barbituric acid[4] or benzalbarbituric acid.[5] It is also available commercially. In the preparation of 1,3-dimethylalloxan monohydrate **4**, caffeine was first converted into tetramethylalloxantin[6] which was then oxidatively cleaved with nitric acid.[7]

Biltz noted that the loss of water from **3** occurs at about 130°C to give yellow, crystalline alloxan **1**.[8] He also reported that solutions of **3** in acetic acid assume a yellow colour[9] – presumably indicating that the conversion **3** → **1** is acid-catalysed, and that a significant quantity of **1** is present in the equilibrium. However, we found that removal of the acetic acid *in vacuo* merely led to the recovery of **3** through the recombination of **1** with the water eliminated. The water was therefore removed by chemical combination. Thus, heating a solution of **1** in acetic acid containing > 1 equiv. of acetic anhydride led to the formation of a homogeneous yellow solution in about 30 min. Evaporation of the solvent under reduced pressure then afforded yellow solid alloxan **1** in essentially quantitative yield. A similar procedure was also effective for the conversion of **4** into 1,3-dimethylalloxan **2**.

We found that direct heating of solid **3** or **4**, to effect conversion into **1** or **2**, was neither convenient nor efficient since a certain amount of decomposition usually also occurred. Although **3** is almost insoluble in chlorobenzene (b.p. 133°C), nevertheless the slow distillation of solvent from a suspension of **3** in boiling chlorobenzene led to the expulsion of all of the water and formation of a yellow solution containing suspended yellow alloxan **1**. The alloxan could be obtained simply by further concentration and then cooling of the solution to effect crystallisation, but it was usually more convenient to use the solution directly for the ene addition. 1,3-Dimethylalloxan **2** could be prepared similarly from **4**. Since transfers are avoided, yields are essentially quantitative. Both **1** and **2** are also obtained quantitatively by standing 1,2-dimethoxyethane solutions of **3** or **4** over dry 3 Å molecular sieves at room temperature.[10] Scale is somewhat limited in this method by solubility considerations, and again it was usually more convenient to use the solutions directly for the ene additions than to first isolate the triones.

Procedures for the Ene Reactions of **1** *and* **2**.— A number of procedures were developed, and are necessary to accommodate the wide range of boiling points and reactivities of the enes examined in this study. The simplest procedure of all involved boiling under reflux a mixture of the monohydrate **3** or **4** and the ene (*i.e.* b.p. > 130°C) in chlorobenzene until the yellow colour was discharged (Method A). Droplets of water collect in the condenser, and hence it is not necessary to pre-form the enophile. However, this procedure proved to be reliable only for the most reactive (*i.e.* **Type 1** enes) of high b.p. since prolonged heating in an open system generally led to the formation of red or brown by-products. These were invariably water soluble (*cf.* purpuric acid), and presumably result from the thermal hydrolytic decomposition of the alloxan.

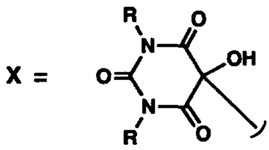
All of the other methods therefore used pre-formed **1** or **2**. A mixture of the enophile and ene in a dry aprotic solvent was placed, together with a magnetic follower, in a Carius tube fitted with a high vacuum Teflon® screw valve.[11] The tube was flushed with dry argon or nitrogen, sealed, and placed in a magnetically stirred and heated oil bath. The reactions were monitored by the fading of the yellow alloxan colour, and were deemed complete when fading to colourless had been reached. In several cases (especially with the less reactive **Type 3** and **4** enes) yellow, red or brown by-products were formed and estimation of the 'end point' by eye became very subjective. When colour fading could not be used as a satisfactory criterion for completion, the reaction was allowed to run somewhat longer than the time estimated by reference to the 'reactivity series' given above.

Suitable solvents for the Carius tube reactions were found to be toluene at 130°C (Method B), chlorobenzene at 130°C (Method C), and 1,2-dimethoxyethane at 110°C or 130°C (Methods D_1 and D_2, respectively). 1,2-Dimethoxyethane has the advantage that **1** and **2** are much more soluble in it than in toluene or chlorobenzene, but satisfactory results were only obtained when it was carefully purified. It is also likely that this solvent reduces the reactivities of the enophiles by complexation (*cf.* indane-1,2,3-trione in THF)[1], but this was counteracted to a certain extent since it allowed the employment of higher initial concentrations of the reagents. The results are summarised in the Table; yields are of purified products.

Type 1 enes.— β-Pinene, α-methylstyrene, methylenecyclopentane, methylenecyclohexane, 2-methyl-1-butene and 2-methyl-2-butene were taken as representative examples of this class. In our experience, β-pinene is the most reactive readily available ene. The C(3)–H σ-bond *anti* to the CMe_2 bridge is co-parallel with the adjacent p-π orbitals, an essential feature for concerted reaction, and there is a thermodynamic driving force for the movement of the C=C from an exocyclic to an endocyclic position. It was not too surprising to find that β-pinene reacted with **1** and **2** (whether pre-formed or generated *in situ*) cleanly and rapidly at 130°C. Isolation and purification of the adduct was achieved simply by evaporation of the solvent under reduced pressure, and recrystallisation of the solid residue. Assignment of the structures **5a** and **5b** follows from the analytical and spectroscopic data. Of particular interest in the ^1H NMR spectrum is the shielding (δ_H *ca.* 1.1, d) of the pinene 7-H_a by the pinene C=C to which it is *syn*. Because of approximate 90° dihedral angles for H_{7a}–C–C–H_1 and H_{7a}–C–C–H_5, the observed splittings of *ca.* 9 Hz can be assigned to the two bond couplings with 7-H_b.

Reactions of **1** or **2** with methylenecyclopentane, methylenecyclohexane, and 2-methyl-2-butene also proceeded rapidly to give the adducts **7a,b–9a,b** in high yield. Some variability was found in the ease of crystallising the crude adducts, which explains the variation in yield (Table) of purified products from fair to excellent. We have found previously that α-methylstyrene can behave as a borderline **Type 1** to **Type 2** ene, and it appeared to react with **1** or **2** more sluggishly than the other **Type 1** enes on the colour-fading criterion. However, the final solutions were a pale yellow colour indicating that the time for completion was over-estimated; the adducts **6a** and **6b** were obtained in good to excellent yield.

The reaction of 2-methyl-1-butene with alloxan **1** gave a 20 : 80 mixture of the adducts **10a** : **11a**, which could not be separated. The predominance of **11a** indicates the transfer of H occurred preferentially from the secondary allylic site which (assuming a concerted reaction) can be accommodated by differences in steric interactions in the alternative approach topologies (a) and (b) shown in Fig. 1. The major steric interactions appear to be between the C-4 carbonyl oxygen and any underlying alkyl group of the olefin (*i.e.* Me *versus* Et). Clearly (a) is less hindered, and reaction should afford predominantly **11a** – as observed. The stereoselectivity is similar to that observed in the reaction of 2-methyl-1-butene with indane-1,2,3-trione.[1]



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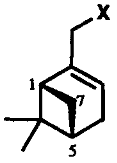
b R = Me



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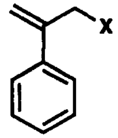

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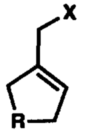
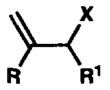
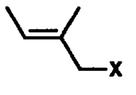


7 R = CH_2
8 R = $(CH_2)_2$



9 R = R^1 = Me
10 R = Et, R^1 = H



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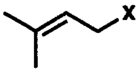

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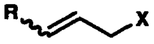
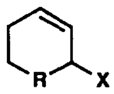
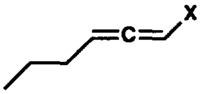


13 R = C_3H_7
14 R = C_4H_9
15 R = C_5H_{11}
16 R = $(CH_2)_7CO_2Me$
17 R = C_6H_5
18 R = $SiMe_3$
19 R = OC_6H_5



20 R = CH_2
21 R = $(CH_2)_2$
22 R = $(CH_2)_3$



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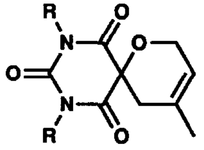
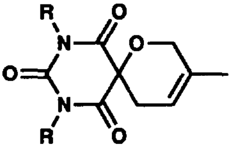


24 a R = H
b R = Me



25 a R = H
b R = Me

(a) **Figure 1** (b)

Other Type 1 enes such as (+)-limonene and caryophyllene also reacted with **1** and/or **2** to give product mixtures which we were unable to purify. We found in our studies of the Lewis acid-catalysed addition of chloral that isoprene reacted in part as a Type 1 ene and in part as a Diels–Alder diene.[12] In the thermal addition of isoprene to **1** or **2**, however, only a *ca.* 90 : 10 mixture of the two Diels–Alder adducts **24a,b** and **25a,b** were formed. Frontier orbital theory predicts a kinetic preference for the formation of isomers **24**, and the (4 + 2) addition product from alloxan **1** and isoprene has been assigned the structure **24a**.[13]

Table. Ene addition reactions of alloxan **1** and 1,3-dimethylalloxan **2**

Eno-phile	Ene	Adduct	Method (h)	Recryst. solvent[a]	Yield (%)	M.p. (°C)	Found (%) C	Found (%) H	Found (%) N	Requires (%) C	Requires (%) H	Requires (%) N	Formula
1	β-pinene	**5a**	A (1)	P_1–E	91	199–200	60.6	6.7	9.8	60.4	6.5	10.1	$C_{14}H_{18}N_2O_4$
2		**5b**	A (0.5)	P_2–B	95	117–118	62.7	7.3	8.95	62.7	7.2	9.1	$C_{16}H_{22}N_2O_4$
1	α-methylstyrene	**6a**	A (16)	P_1–E	80	180–181	60.1	4.7	10.7	60.0	4.7	10.8	$C_{13}H_{12}N_2O_4$
2		**6b**	A (24)	P_1–EA	91	122–123	62.5	5.7	9.5	62.5	5.6	9.7	$C_{15}H_{16}N_2O_4$
1	methylenecyclopentane	**7a**	D_2 (0.5)	P_3–EA	59	150–151	53.4	5.5	12.5	53.6	5.4	12.5	$C_{10}H_{12}N_2O_4$
2		**7b**	C (1)	P_2	80	112–113	57.3	6.7	10.9	57.1	6.4	11.1	$C_{12}H_{16}N_2O_4$
1	methylenecyclohexane	**8a**	D_1 (1)	P_1–E	94	190–192	55.3	6.0	11.9	55.5	5.9	11.8	$C_{11}H_{14}N_2O_4$
2		**8b**	C (3)	P_2	90	98.5–99	58.5	7.0	10.4	58.6	6.8	10.5	$C_{13}H_{18}N_2O_4$
1	2-methyl-2-butene	**9a**	C (2)	Ac–Ch	82	194–196	50.8	5.7	13.4	50.9	5.7	13.2	$C_9H_{12}N_2O_4$
2		**9b**	C (1)	P_3	56	82–84	55.1	6.8	11.9	55.0	6.7	11.7	$C_{11}H_{16}N_2O_4$
1	2-methyl-1-butene	**10a + 11a**	D_1 (5)	P_1–E	72	128–130[b]	----	----	----	50.9	5.7	13.2	$C_9H_{12}N_2O_4$
1	3-methyl-1-butene	**12a**	D_1 (4)	P_1–E	81	148–149	50.9	5.6	13.0	50.9	5.7	13.2	$C_9H_{12}N_2O_4$
1	1-hexene	**13a**	C (3)	P_2–EA	58[c]	133–135	53.1	6.2	12.2	53.1	6.2	12.4	$C_{10}H_{14}N_2O_4$
2		**13b**	B (3)	P_3	75[c]	96–104	56.4	7.3	11.1	56.7	7.1	11.0	$C_{12}H_{18}N_2O_4$
1	1-heptene	**14a**	D_1 (24)	P_2–EA	37[c]	112–114	55.0	6.9	11.4	55.0	6.7	11.7	$C_{11}H_{16}N_2O_4$
2		**14b**	C (47)	P_2	85[c]	73–74	58.1	7.6	10.6	58.2	7.5	10.4	$C_{13}H_{20}N_2O_4$
1	1-octene	**15a**	C (4)	P_2–EA	60[c]	110–112	56.4	7.4	11.2	56.7	7.1	11.0	$C_{12}H_{18}N_2O_4$
2		**15b**	C (5)	P_2	87[c]	58–60	59.6	7.85	10.2	59.6	7.85	9.9	$C_{14}H_{22}N_2O_4$
1	methyl undec-10-enoate	**16a**	D_1 (24)	Ch	79[c]	113–115	56.1	7.1	8.0	56.4	7.1	8.2	$C_{16}H_{24}N_2O_6$
2		**16b**	C (24)	P_2	66[c]	52.5–54.5	58.9	7.55	7.4	58.7	7.7	7.6	$C_{18}H_{28}N_2O_6$

1	allylbenzene	**17a**	C (21)	P_2–EA	60[c]	223–228	59.8	4.7	10.7	60.0	4.65	10.8	$C_{13}H_{12}N_2O_4$
2		**17b**	A (4.5)	P_2–EA	65[c]	123–124	62.3	5.65	9.6	62.5	5.6	9.7	$C_{15}H_{16}N_2O_4$
1	allyltrimethylsilane	**18a**	D_2 (4.5)	PhCl	86[c]	153–155	46.9	6.6	11.1	46.9	6.3	10.9	$C_{10}H_{16}N_2O_4Si$
2		**18b**	C (16)	P_2	50[c]	78.5–83	50.9	7.2	9.85	50.7	7.1	9.85	$C_{12}H_{20}N_2O_4Si$
1	allyl phenyl ether	**19a**	D_2 (72)	P_3–EA	37	154–158	56.6	4.6	9.9	56.5	4.4	10.1	$C_{13}H_{12}N_2O_5$
2		**19b**	C (72)	P_2–EA	1	68–73.5	----	----	----	59.2	5.3	9.2	$C_{15}H_{16}N_2O_5$
1	cyclohexene	**20a**	D_1 (48)	AM	53	218–220	53.4	5.4	12.1	53.6	5.4	12.5	$C_{10}H_{12}N_2O_4$
2		**20b**	C (48)	oil[d]	86	150–170#	57.0	6.5	10.9	57.1	6.4	11.1	$C_{12}H_{16}N_2O_4$
1	cycloheptene	**21a**	C (48)	P_2–EA	50	204–206	55.3	6.0	12.0	55.5	5.9	11.8	$C_{11}H_{14}N_2O_4$
1	cyclo-octene	**22a**	A (25)	PhCl	71	223–225	57.0	6.4	11.1	57.1	6.4	11.1	$C_{12}H_{16}N_2O_4$
2		**22b**	B (48)	P_2	66	118–119	60.1	7.1	9.8	60.0	7.2	10.0	$C_{14}H_{20}N_2O_4$
1	1-hexyne	**23a**	D_2 (72)	oil[d]	74	----	----	----	----	53.6	5.4	12.5	$C_{10}H_{12}N_2O_4$
2		**23b**	C (72)	P_1	62	52.5–53.5	57.0	6.5	11.0	57.1	6.4	11.1	$C_{12}H_{16}N_2O_4$

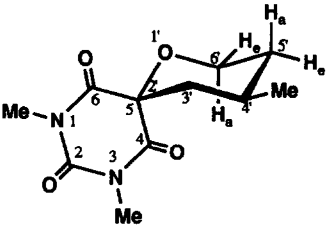
[a] Solvents: Ac = acetone; AM = aq. methanol; B = benzene; Ch = chloroform; E = diethyl ether; EA = ethyl acetate; P_1, P_2, P_3 = light petroleum b.p. respectively 40–60°C, 60–80°C, 80–100°C.

[b] A 20 : 80 mixture of compounds which could not be separated.

[c] Mixture of stereoisomers; the following ratios were obtained for the crude (unpartitioned) product mixtures from the average, when possible, of ^1H and ^{13}C NMR analyses (excluding C atoms with long relaxation times). Values given are in the sense $E : Z$.— **13a** 77 : 23; **13b** 77 : 23; **14a** 80 : 20; **14b** 80 : 20; **15a** 79.5 : 20.5; **15b** 80 : 20; **16a** 80 : 20; **16b** 83 : 17 (recrystallisation gave the E-isomer, m.p. 56.5–57.5°C); **17a** 85 : 15 (*nb.* the Z-isomer was not detected by ^{13}C NMR); **17b** 93 : 7 (*nb.* the Z-isomer was not detected by ^{13}C NMR); **18a** 52 : 48; **18b** 54 : 46; **19a** 82 : 18.

[d] These oils were purified by dissolving the crude adduct in P_1–EA; the impurities were largely insoluble. The solvent was then removed *in vacuo*. For **20b** (#) signifies kugelrohr b.p. (bath)/0.5 torr; **23a** decomposed on attempted distillation.

However, this regiochemistry was not proven conclusively. The ^1H NMR spectrum of **24b/25b** was not particularly illuminating, and even at 400 MHz lacked fine structure. Hence the purified adduct was hydrogenated (10% Pd/C, methanol solution) to give a dihydro-compound (*i.e.* **26** or **27**). The 6'-H_a and 6'-H_e signals were resolved from all other resonances in the ^1H NMR spectrum of the dihydro-compound – even at 90 MHz; at 400 MHz these signals (at δ 4.52 and δ 4.06) were amenable to first order analysis. The downfield signal at δ 4.52 (ddd) is assigned to 6'-H_a. This hydrogen atom is deshielded by *ca.* 1 p.p.m. by the 4-C carbonyl group. The signal at δ 4.06 (ddd) is assigned to 6'-H_e. The δ 4.52 resonance is characterised by the couplings $J_{6'a5'a}$ = 12.9, $J_{6'a6'e}$ = 11.3, and $J_{6'a5'e}$ = 2.7 Hz, whereas the δ 4.06 resonance is characterised by the couplings $J_{6'e6'a}$ = 11.3, $J_{6'e5'a}$ = 5.2, and $J_{6'e5'e}$ = 1.4 Hz. The signals for the other ring hydrogens were not first order, but could also be assigned (see Experimental). The presence of the five couplings $J_{6'a5'a}$, $J_{6'a6'e}$, $J_{6'a5'e}$, $J_{6'e5'a}$, and $J_{6'e5'e}$ for the two 6'-H hydrogens means, of course, that 5'-C must be unsubstituted. Hence, structure **27** is ruled out, and the Diels–Alder product from dimethylalloxan **2** and isoprene must possess structure **24b**. In similar fashion, it follows that **24a** is the structure of the analogous adduct from alloxan **1**.



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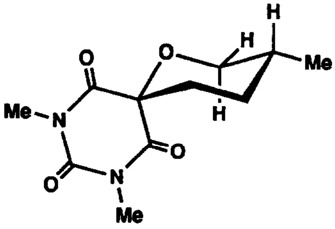

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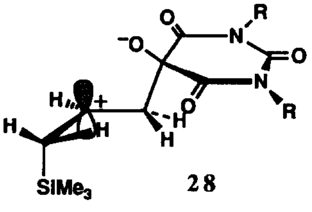
Type 2 enes.— The simple terminal olefins 3-methyl-1-butene, 1-hexene, 1-heptene and 1-octene were chosen as representatives of **Type 2** enes; all gave adducts (**12a–15a,b**). With all except 1-heptene colour-fading in the reactions with **1** or **2** occurred fairly rapidly (3–5 h). In some cases, the alloxan adducts **a** proved to be difficult to crystallise, and this is reflected in the yields obtained; otherwise the yields of adducts were good. The anomaly of the 1-heptene results was possibly due to an impurity in the olefin since the final reaction solutions were a yellow–brown colour. Similarly, the ene additions of **1** or **2** to methyl undec-10-enoate also gave final pale yellow–brown solutions, indicating that the reaction time of 24 h was an over-estimate. The adducts **16a** and **16b** were obtained in reasonable yield. In this case, however, some slowing of the reaction was expected on entropic grounds. The remote CO_2Me should have no adverse effect on the reaction rate. Furthermore, substitution at the allylic carbon atom of the 1-alkene by Ph or Me_3Si (*i.e.* allylbenzene and allyltrimethylsilane) likewise had did not deactivate the ene towards addition since the adducts **17a,b–18a,b** were formed on a similar time scale. Hence, all of these olefins are properly regarded as **Type 2** enes.

The products (excluding **12a**) are mixtures of stereoisomers (see Table, footnote c, for isomer ratios), and for all except those from allyltrimethylsilane the *E*-isomer predominated. These results can be accommodated by appropriate modification of our steric model (*cf.* Fig. 1) as shown in Fig. 2, and again assuming concerted reactions. The allylic substituent R^1 can be placed either in the W-type conformation (a), or in the more congested U-type conformation (b) where there would be a loss of rotational entropy within the substituent R^1 as the transition state is approached. Hence, topology (a) should be favoured, and the *E*-adducts should predominate – as observed.

(a) **Figure 2** (b)

However, the reasons for the complete loss of stereoselectivity for the additions to allyltrimethylsilane (*E* : *Z* *ca.* 53 : 47) are not at all clear on the basis of this model. The R^1 group (*i.e.* Me_3Si) with free rotation about the C–R^1 bond is sterically demanding. Severe steric compressions would exist in (b) between R^1 and the *syn* vinylic H-atom as well as between R^1 and the overlying alloxan molecule. These compressions are greatly alleviated in topology (a), predicting the almost exclusive formation of the *E*-adducts. Since we were unable to obtain pure samples of the *E*- or *Z*-adduct from either **18a** or **18b**, the possibility of isomer equilibration following upon the (concerted) ene addition could not be tested. If the isomer ratios are not the result of subsequent equilibration, then in the case of the allyltrimethylsilane additions at least the concerted addition mechanism must be open to question. The lowest energy addition pathway could involve the zwitterionic intermediate **28** in which the empty p-orbital at C-2 of the olefin is stabilised by electron donation from the co-parallel C–Si σ-orbital. The collapse of this intermediate to products would require a 60° rotation about the olefinic C-2/C-3 bond, and hence could generate both the *E*- and *Z*-adducts.



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Type 3 enes.— The simple cycloalkenes – cyclohexene, cycloheptene and cyclo-octene – were chosen as representatives of this class. All reacted with both **1** and/or **2** under typical reaction conditions to give fair to good yields of the adducts **20a,b–22a,b**. However, all were appreciably less reactive than the **Type 1** or **2** enes, and it is our experience that with enophiles of moderate reactivity the **Type 3** enes usually mark the limits for successful reaction.

Type 4 enes.— 1-Hexyne appeared to react rather sluggishly with either **1** or **2** on the colour-fading criterion. However, the final solutions were a yellow-brown colour, and the reactions appeared to reach that colour intensity after about 48 h. That time would place the reactivity of 1-hexyne on a par with the cycloalkenes, and a similar conclusion was reached in the ene additions of these olefins to indane-1,2,3-trione.[1] Successful ene additions of 1-alkynes have rarely been recorded. Removal of the solvent from the reaction mixtures gave rather unpromising dark-coloured oils. The product from **2** responded to recrystallisation, and pure **23b** was isolated in fair yield. The alloxan adduct **23a** was only obtained as an oil. The IR (*ca.* 1960 cm^{-1}) and ^{13}C NMR (*ca.* δ_C 197 p.p.m.) spectra clearly establish the presence of the allene unit in compounds **23a,b**.

Type 5 enes.— Although we felt that the **Type 4** enes marked the limits of reactivity for the alloxans, nevertheless the reactions of a few **Type 5** enes were examined. Ene additions to olefins such as methacrylonitrile, methyl methacrylate, allyl bromide, allyl cyanide, methyl 3-butenoate, or allyl phenyl ether have been achieved very rarely. Of these only allyl phenyl ether appeared to react; prolonged heating gave the products **19a,b** moderate yield; removal of dark coloured by-products led to appreciable losses on recrystallisation.

The failure of **1** or **2** to react with a more representative selection of **Type 5** enes means that they cannot be regarded as 'superenophiles' – unlike indane-1,2,3-trione. Nevertheless, they are enophiles of unusually high reactivity. At this stage we have not explored the chemistry of adducts **5a,b–23a,b** for synthetic purposes.

EXPERIMENTAL

General Procedures.— The enes and all solvents were distilled before use. Light petroleum refers to the fraction b.p. 40–60°C. 1,2-Dimethoxyethane was fractionally distilled from sodium and a small quantity of benzophenone. Alloxan monohydrate **3** was either the commercial material (Lancaster) or it was prepared according to standard procedures.[4,5] 1,3-Dimethylalloxan monohydrate **4** was prepared from caffeine which was first converted into tetramethylalloxantin;[6] this compound was oxidatively cleaved with nitric acid to give **4** following the literature procedure for the conversion of alloxantin into alloxan monohydrate[7] (yield 50%).

Analytical and spectroscopic methods and instrumentation have been noted previously.[1] In the determination of NMR spectra (shifts are expressed in p.p.m. downfield from Me_4Si as internal standard), unless stated otherwise, CD_3OD solutions were used for the **a** series ene adducts **5a–23a**, whereas solutions in $CDCl_3$ were used for the **b** series ene adducts **5b–23b**. The ^{1}H signals were singlets unless specified otherwise: *i.e.* d, doublet; dd, double doublet; ddd, double doublet of doublet; dt, double triplet; q, quartet; m, multiplet; br., broad. Assignments in the ^{1}H spectra were consistent with signal intensities and in the ^{13}C spectra with the results of the DEPT pulse sequence.

***Preparation of Alloxan* 1.**— (a) Alloxan monohydrate **3** (5.00 g, 31.25 mmol) was suspended in a mixture of acetic acid (100 cm^3) and acetic anhydride (3.267 g, 32 mmol). The mixture was boiled under reflux, with occasional swirling, until the solid dissolved giving a yellow solution (*ca.* 30 min). The solution was cooled and then rotary eveporated to near dryness. The solid yellow residue was broken up with the aid of a spatula and washed with dry ether (2 x 20 cm^3). The ether was removed with the aid of a pipette and discarded. The yellow solid alloxan **1** after drying *in vacuo* (4.395 g, 99%) had m.p. 256°C [(dec. – after turning pink at 230°C); lit.[9,14] m.p. 256°C (dec.)]. The material could be stored in a plastic stoppered vial in a desiccator for several months without apparent deterioration.

(b) Alloxan monohydrate **3** (5.00 g, 31.25 mmol) was suspended in chlorobenzene (100 cm^3) and the mixture boiled under reflux for 3 h, during which time most of the solid dissolved, the solution turned yellow, and droplets of water collected in the condenser. The mixture was then distilled (all of the water collected in the *ca.* 10 cm^3 fore-run) to low bulk (*ca.* 10 cm^3), and then cooled to precipitate any remaining dissolved alloxan. The solvent was removed with the aid of a pipette. The residue of yellow crystalline alloxan **1** was then treated with ether and dried as in (a) to give material of comparable purity and yield. Solutions of alloxan in chlorobenzene were also prepared by this method by stopping the distillation of the solvent at the desired point. These solutions were used immediately.

(c) Alloxan in 1,2-dimethoxyethane was prepared by Schonberg and Singer's procedure:[10] alloxan monohydrate (3.20 g, 20 mmol) in purified and dried 1,2-dimethoxyethane (200 cm^3) was treated with dry 3 Å molecular sieve pellets (50 g). The solution quickly turned yellow. After 2 h the solution was filtered, and the filtrate used immediately.

***Preparation of 1,3-Dimethylalloxan* 2.**— The methods (a), (b) and (c), above, gave strictly comparable results for the preparation of 1,3-dimethylalloxan **2** from its monohydrate **4**. From procedure (a), for example, the yellow prismatic crystals of 1,3-dimethylalloxan **2** (99%) had m.p. 254–255°C (dec.) [lit.[14] 252°C (dec.)]. Found C, 42.3; H, 3.7; N, 16.8%. Calculated for $C_6H_6N_2O_4$: C, 42.4; H, 3.6; N, 16.5%.

***Methods for Conducting the Ene Reactions of* 1 *and* 2.**— The following specific procedures are illustrative of the general methods, the results of which are summarised in the Table.

Method A: A mixture of 1,3-dimethylalloxan monohydrate **4** (0.94 g, 5 mmol), β-pinene (1.36 g, 10 mmol), and chlorobenzene (60 cm^3) was boiled under reflux. The initially yellow solution became colourless within 0.5 h, and droplets of water were retained in the condenser. The bulk of the solvent was removed by distillation or rotary evaporation and then allowed to cool. The oily residue thus obtained was triturated with a small quantity of light petroleum; spontaneous crystallisation occurred after *ca.* 30 min to give a solid mass of colourless crystals. The small quantity of liquor was discarded. The crystals were dissolved in the minimum quantity of boiling benzene and 60–80° light petroleum (*ca.* 40 cm^3) added to incipient turbidity. The mixture was boiled briefly and allowed to cool overnight. *The product* **5b**, plus a second crop obtained by concentration, was obtained as small colourless needles (total 1.46 g, 95%), m.p. 117–118°C.

Method B: Into a heavy-walled Schlenk tube of *ca.* 100 cm^3 capacity and fitted with a high vacuum Teflon® screw valve,[11] was added a small magnetic follower, 1,3-

dimethylalloxan **2** (0.85 g, 5 mmol), 1-hexene (1.26 g, 15 mmol), and dry toluene (50 cm^3). The tube was flushed with dry nitrogen or argon, sealed and suspended in a magnetically stirred oil bath heated to 130°C (**CAUTION**, see ***Safety Note*** below). When the initially yellow solution had become colourless (3 h), the tube was removed and allowed to regain room temperature before it was opened. The reaction mixture was rotary evaporated to give a colourless oil which was triturated with a small quantity of 60–80° light petroleum to induce crystallisation. A further quantity of 60–80° light petroleum was then added and the mixture boiled under reflux. Ethyl acetate (*ca.* 8 cm^3) was added in small portions until the crystals just dissolved. The solution was allowed to cool overnight. *The product* **13b**, plus a second crop obtained by concentration, was obtained as colourless fibrous crystals (total 0.95 g, 75%), m.p. 96.5–104.5°C.

Method C: Allylbenzene (1.18 g, 10 mmol), alloxan **1** (0.71 g, 5 mmol) and dry chlorobenzene (50 cm^3) was heated in a Schlenk tube at 130°C as in Method B. [The required quantity of alloxan in chlorobenzene could also be obtained as in procedure (b), above]. The solution did not decolourise completely, and reaction was terminated after 21 h (pale brown). Removal of the solvent as in Method B afforded a brown solid which was recrystallised as before from 60–80° light petroleum/ethyl acetate to give *the product* **17a** as an off-white powder (total 0.78 g, 60%), m.p. 223–228°C.

Methods D_1 and D_2: A solution of alloxan **1** (0.71 g, 5 mmol) in 1,2-dimethoxyethane (25 ml) [prepared as in procedure (c) above or by dissolving pre-formed alloxan in 1,2-dimethoxyethane] and allyltrimethylsilane (1.14 g, 10 mmol) was heated at 110°C (Method D_1) or 130°C (Method D_2) in a Schlenk tube as in Method B. The reaction was terminated after 4.5 h when the solution had reached a very pale yellow colour. Removal of the solvent by rotary evaporation afforded a creamy-coloured solid which was recrystallised from chlorobenzene to give *the product* **18a** as a white powder (1.10 g, 86%), m.p. 153–155°C.

(***Safety Note:*** We have not experienced the rupture of a single tube in over a hundred such reactions. However, it is essential that these processes be conducted behind suitable safety screens, and the tubes filled to only about 50% of their capacity. The unfilled section of the tube is not immersed in the oil bath, and acts as a condenser for the more volatile enes. Handling the hot sealed tube can be avoided by clamping it in such a way that lifting the clamp stand allows the tube to clear the oil bath – otherwise heavy gloves should be worn. The tube should be allowed to cool to room temperature – either undisturbed or cooled in a water bath once the temperature of the contents has fallen to *ca.* 50°C – before opening).

***Spectroscopic Data for the Ene Adducts* 5a,b–23a,b**.— The moieties **X** (*i.e.* 5-hydroxyalloxanyl or 1,3-dimethyl-5-hydroxyalloxanyl) in these adducts give rise to fairly consistent features in the IR spectra; these are summarised at the beginning of each set of data. The ^{1}H NMR spectra for analogous ene adducts (*e.g.* **5a** and **5b**) were very similar except for differences arising from the NH *versus* NMe absorptions – hence, only one set of data is given.

IR Spectra (KBr/ cm^{-1}). *General features of* **a** *series compounds* — 3450–3350, 3300–3200, 3125–3050, 2960–2840, 1720–1700, 1370–1320, 1290–1250, 1230–1200, and 1160–1120. *Other notable absorptions*: **5a** 840; **6a** 1500, 930, 810, 780; **7a** 1030; **8a** 780; **9a** 1650 (sh), 1020, 920; **10a**

+ **11a** 1660 (sh); **12a** ---; **13a** 1660 (sh), 970; **14a** 1640 (sh), 970; **15a** 980, 780; **16a** ---; **17a** 1665 (sh 965, 810, 775; **18a** 1610, 845, 770; **19a** 1670 (sh), 1590, 1495, 820, 760, 690; **20a** 840, 780; **21a** 1645 (sh); **22a** 1650 (sh), 805; **23a** (film) 1960, 1100. *General features of* **b** *series compounds* — 3500–3300 (br), *ca.* 3050 (sh), 2960–2840, 1760–1745 (sh.z), 1695–1670, 1385–1355, and 1295–1280. *Other notable absorptions*: **5b** 1165, 1105, 1065, 755; **6b** 1160, 1125, 1075, 930, 920, 800, 780, 750, 700; **7b** 1170, 1100, 1070, 750; **8b** 1175, 1105, 1075, 850, 750; **9b** 1330, 1205, 1115, 1075, 920; **13b** 1345, 1095, 1080, 1060, 975, 750; **14b** 1170, 1070, 980, 750; **15b** 1070, 970, 750; **16b** 1255, 1220, 1170, 1100, 1080, 970, 900, 750; **17b** 1495, 1155, 1105, 1065, 980, 760, 740; **18b** 1610, 1245, 1110, 1075, 865, 845, 750; **20b** (film) 1110, 1075; **22b** 1240, 1190, 1065, 825, 755; **23b** 1975, 1180, 1145, 1070, 1110, 755.

^1H NMR Spectra (δ_H/p.p.m.; 90 MHz, unless specified otherwise) — **5a** 5.43 (br. s, =CH), 4.76 (br. s, 2 x NH + OH), 2.80 (d, *J* 12.5, $C\underline{H}HCOH$), 2.55 (d, *J* 12.5, $CH\underline{H}COH$), 2.50–2.15 (m, 5H), 2.10–1.95 (m, 2H), 1.26 (*anti*-Me), 1.10 (d, *J* 9, *syn* 7-H), 0.80 (*syn*-Me); **6b** 7.42–7.30 (m, Ph), 5.45 (br. s, $=C\underline{H}H$), 5.21 (br. s, $=CH\underline{H}$), 3.89 (br. s, OH), 3.30 (br. s, CH_2), 2.89 (2 x NMe); **7a** 5.60 (br. s, =CH), 4.83 (br. s, 2 x NH + OH), 2.83 (br. s, $C\underline{H}_2COH$), 2.45–2.15 (m, $C\underline{H}_2C{=}CHC\underline{H}_2$), 2.00–1.75 (m, $C\underline{H}_2CH_2C{=}$); **8a** 5.56 (br. s, =CH), 4.72 (br. s, 2 x NH + OH), 2.61 (br. s, $C\underline{H}_2COH$), 2.15–1.85 (m, $C\underline{H}_2C{=}CHC\underline{H}_2$), 1.75–1.50 (m, $C\underline{H}_2C\underline{H}_2CH_2C{=}$); **9b** 4.98 (m, $=C\underline{H}H$), 4.74 (br. s, $=CH\underline{H}$), 3.77 (br. s, OH), 3.37 (NMe), 3.35 (NMe), 2.76 (q, *J* 7.5, $C\underline{H}Me$), 1.70 (br. s, $\underline{Me}C{=}CH_2$), 1.19 (d, *J* 7.5, $CH\underline{Me}$); **10a** + **11a** (a 1 : 4 mixture) 5.62–5.32 (1H, m *ca.* q, *J* 7.5, $=C\underline{H}Me$), 5.01 and 4.91 (0.5H, 2 x br. s, $=CH_2$), 4.69 [3.75H, br. s, 2 x (2 x NH + OH)], 2.84–2.71 [2.5H, m, 2 x ($C\underline{H}_2COH$)], 2.11 (0.5H, q, *J* 7.5, $C\underline{H}_2Me$), 1.76–1.56 (6H, m, $\underline{Me}CH{=}C\underline{Me}$), 1.02 (0.75H, t, *J* 7.5, $CH_2\underline{Me}$); **12a** 5.14 (br. t, *J* 8, =CH), 4.76 (br. s, 2 x NH + OH), 2.75 (d, *J* 8, CH_2), 1.75 and 1.64 ($=C\underline{Me}_2$); *E*-**13a** (250 MHz) 5.60 (*ca.* dt, *J* 15.2 and 6.9, $CH{=}C\underline{H}CH_2COH$), 5.33 (*ca.* dt, *J* 15.2 and 7.6, $C\underline{H}{=}CH$), 4.87 (2 x NH + OH), 2.62 (d, *J* 7.3, $C\underline{H}_2COH$), 1.97 (m, $C\underline{H}_2CH{=}$), 1.37 (m, $C\underline{H}_2Me$), 0.88 (t, *J* 7.3, Me): {*Z*-**13a** was detected by satellite peaks at δ 2.72 (d, *J* 8.1, $C\underline{H}_2COH$) and 0.90 (t, *J* 7.3, Me) – in the crude adduct *E* : *Z* = 77.5 : 22.5}; **14b** 5.80–5.05 (m, $C\underline{H}{=}C\underline{H}$), 3.67 (br. s, OH), 3.34 (2 x NMe), 2.65 (d, *J* 8, $C\underline{H}_2COH$), 2.10–1.80 (m, $CH_2C\underline{H}_2CH{=}$), 1.40–1.10 (m, $MeC\underline{H}_2C\underline{H}_2$), 0.88 (t, *J* 7, Me): {*Z*-**14b** was detected by a satellite peak at δ 2.74 (d, *J* 8, $C\underline{H}_2COH$) – in the crude adduct *E* : *Z* = *ca.* 80 : 20}; *E*-**15b** (250 MHz) 5.58 (dt, *J* 15.2 and 7.0, $CH{=}C\underline{H}CH_2COH$), 5.25–5.11 (m, $C\underline{H}{=}CH$), 3.77 (br. s, OH), 3.30 (2 x NMe), 2.63 (d, *J* 7.4, $C\underline{H}_2COH$), 2.01–1.93 (m, $CH_2C\underline{H}_2CH{=}$), 1.36–1.21 (m, $MeC\underline{H}_2C\underline{H}_2C\underline{H}_2$), 0.88 (t, *J* 7.1, Me): {*Z*-**15b** was detected by satellite peaks at δ 3.29 (2 x NMe) and 2.73 (d, *J* 8.4, $C\underline{H}_2COH$) – in the crude adduct *E* : *Z* = 77 : 23}; *E*-**16b** (250 MHz) 5.57 (dt, *J* 15.2 and 6.8, $CH{=}C\underline{H}CH_2COH$), 5.18 (dt, *J* 15.2 and 7.5, $C\underline{H}{=}CH$), 3.67 (OMe), 3.30 (2 x NMe), 2.63 (d, *J* 7.5, $C\underline{H}_2COH$), 2.30 (t, *J* 7.5, CH_2COO), 1.98–1.91 (m, $CH_2C\underline{H}_2CH{=}$), 1.64–1.55 (m, CH_2), 1.27 (br. s, 4 x CH_2): {*Z*-**16b** was detected by a satellite peak at δ 2.73 (d, *J* 8.1, $C\underline{H}_2COH$) – in the crude adduct *E* : *Z* = 83 : 17. Recrystallisation led to the accumulation of *E*-**16b** in the mother liquor}; *E*-**17a** (250 MHz) 7.36–7.15 (m, Ph), 6.52 (d, *J* 15.7, $=C\underline{H}Ph$), 6.14 (dt, *J* 15.7 and 7.6, $C\underline{H}{=}CHPh$), 4.88 (br. s, 2 x NH + OH), 2.83 (d, *J* 7.6, CH_2): {*Z*-**17a** was detected by satellite peaks at δ 6.67 (d, *J* 11, $=C\underline{H}Ph$) and 2.93 (dd, *J* 7.4

and 1.6, CH$_2$) – in the crude adduct *E* : *Z* = 85 : 15. Recrystallisation afforded *E*-**17a**}; *E*-**18b** (250 MHz; CD$_3$COCD$_3$ – no TMS added) 6.00 (dt, *J* 18.5 and 6.1, C$\underline{H}$=CHSiMe$_3$), 5.87 (d, *J* 18.5, CH=C$\underline{H}$SiMe$_3$), 5.25 (br. s, OH), 3.31 (2 x NMe), 2.84 (d, *J* 6.1, CH$_2$), 0.13 (Si$\underline{Me}_3$): {*Z*-**18b** 6.29 (dt, *J* 14.3 and 7.4, C$\underline{H}$=CHSiMe$_3$), 5.79 (dt, *J* 14.3 and 1.3, CH=C$\underline{H}$SiMe$_3$), 5.34 (br. s, OH), 3.33 (2 x NMe), 2.92 (dd, *J* 7.4 and 1.3, CH$_2$), 0.20 (Si$\underline{Me}_3$); in the crude adduct *E* : *Z* = 55 : 45}; *E*-**19a** 7.35–6.95 (m, OPh), 6.63 (d, *J* 13.5, CH=C$\underline{H}$OPh), 5.16 (dt, *J* 13.5 and 8.5, C$\underline{H}$=CHOPh), 4.78 (br. s, 2 x NH + OH), 2.67 (d, *J* 8, CH$_2$): {*Z*-**19a** was detected by a satellite peak at δ 2.88 (d, *J* 8, CH$_2$) – in the crude adduct *E* : *Z* = 82 : 18}; **20b** (250 MHz) 5.99–5.91 (m, *ca.* dq, *J* 10.3 and 3.4, CH$_2$C$\underline{H}$=CHCH), 5.49 (m, *ca.* dq, *J* 10.3 and 2.0, CH$_2$CH=C$\underline{H}$CH), 3.64 (br. s, OH), 3.32 and 3.31 (2 x NMe), 2.68–2.62 (m, =CHC$\underline{H}$COH), 2.01–1.93 (m, C$\underline{H}_2$CH=), 1.77–1.45 (m, C$\underline{H}_2$C$\underline{H}_2$); **21b** (250 MHz) 5.97–5.87 (m, CH$_2$C$\underline{H}$=CHCH), 5.65 (*ca.* dd, *J* 11.3 and 4.6, CH$_2$CH=C$\underline{H}$CH), 3.72 (br. s, OH), 3.32 and 3.31 (2 x NMe), 2.78–2.73 (m, =CHC$\underline{H}$COH), 2.21–1.96 (m, 3H), 1.73–1.60 (m, 2H), 1.53–1.25 (m, 3H); **22a** 6.05–5.42 (m, C$\underline{H}$=C$\underline{H}$), 4.75 (br. s, 2 x NH + OH), 3.20–3.00 (m, =CHC$\underline{H}$COH), 2.25–2.00 (m, C$\underline{H}_2$CH=), 1.85–1.20 (m, 4 x CH$_2$); **23b** 5.70–5.40 (m, C$\underline{H}$=C=C$\underline{H}$), 3.97 (br. s, OH), 3.38 (2 x NMe), 2.18–1.86 (m, C$\underline{H}_2$CH=), 1.55–1.20 (m, MeC$\underline{H}_2$), 0.93 (t, *J* 7, Me).

^{13}C NMR Spectra (δ$_C$/p.p.m.)— *E*-**13a** 173.1 (2 x CO), 151.2 (NCON), 138.6 (=CH), 121.5 (=CH), 77.1 (COH), 45.2 ($\underline{C}$H$_2$COH), 35.5 ($\underline{C}$H$_2$CH=), 22.1 ($\underline{C}$H$_2$Me), 13.9 (CH$_2\underline{Me}$); *Z*-**13a** 173.3 (2 x CO), 151.2 (NCON), 137.1 (=CH), 120.5 (=CH), 76.5 (COH), 39.8 ($\underline{C}$H$_2$COH), 30.1 ($\underline{C}$H$_2$CH=), 23.5 ($\underline{C}$H$_2$Me), 14.0 (CH$_2\underline{Me}$) – in the crude adduct *E* : *Z* = 76 : 24; *E*-**13b** 170.7 (2 x CO), 151.1 (NCON), 138.1 (=CH), 120.1 (=CH), 76.7 (COH), 45.8 ($\underline{C}$H$_2$COH), 34.6 ($\underline{C}$H$_2$CH=), 28.6 (2 x NMe), 22.3 ($\underline{C}$H$_2$Me), 13.6 (CH$_2\underline{Me}$); *Z*-**13b** 170.8 (2 x CO), 151.1 (NCON), 136.5 (=CH), 119.2 (=CH), 76.2 (COH), 40.2 ($\underline{C}$H$_2$COH), 29.1 ($\underline{C}$H$_2$CH=), 28.8 (2 x NMe), 22.6 ($\underline{C}$H$_2$Me), 13.6 (CH$_2\underline{Me}$) – in the crude adduct *E* : *Z* = 78 : 22; *E*-**15a** 172.9 (2 x CO), 151.1 (NCON), 138.7 (=CH), 121.1 (=CH), 77.0 (COH), 45.0 ($\underline{C}$H$_2$COH), 33.2 ($\underline{C}$H$_2$CH=), 32.1 (CH$_2$), 29.6 (CH$_2$), 23.2 ($\underline{C}$H$_2$Me), 14.2 (CH$_2\underline{Me}$); *Z*-**15a** 173.2 (2 x CO), 151.1 (NCON), 137.2 (=CH), 120.0 (=CH), 76.5 (COH), 39.6 ($\underline{C}$H$_2$COH), 32.3 ($\underline{C}$H$_2$CH=), 29.9 (CH$_2$), 27.9 (CH$_2$), 23.2 ($\underline{C}$H$_2$Me), 14.2 (CH$_2\underline{Me}$) – in the crude adduct *E* : *Z* = 76 : 24; *E*-**15b** 170.6 (2 x CO), 151.1 (NCON), 138.3 (=CH), 120.0 (=CH), 76.7 (COH), 45.8 ($\underline{C}$H$_2$COH), 32.5 ($\underline{C}$H$_2$CH=), 31.3 (CH$_2$), 28.8 (CH$_2$), 28.6 (2 x NMe), 22.5 ($\underline{C}$H$_2$Me), 13.9 (CH$_2\underline{Me}$); *Z*-**15b** 170.8 (2 x CO), 151.1 (NCON), 136.8 (=CH), 119.0 (=CH), 76.2 (COH), 40.2 ($\underline{C}$H$_2$COH), 31.4 ($\underline{C}$H$_2$CH=), 29.1 (CH$_2$), 28.6 (2 x NMe), 27.2 (CH$_2$), 22.5 ($\underline{C}$H$_2$Me), 13.9 (CH$_2\underline{Me}$) – in the crude adduct *E* : *Z* = 83 : 17; *E*-**17a** 173.1 (2 x CO), 151.2 (NCON), 138.2 (quat. aryl =C-), 136.9 (olef. =CH), 129.5 (2 x aryl =CH), 128.8 (aryl =CH), 127.5 (2 x aryl =CH), 121.5 (olef. =CH), 77.2 (COH), 45.4 (CH$_2$) – in the crude, unpartitioned adduct there was no definite evidence for the presence of *Z*-**17a**; *E*-**17b** 170.2 (2 x CO), 150.8 (NCON), 136.4 (olef. =CH), 136.2 (quat. aryl =C-), 128.6 (2 x aryl =CH), 128.0 (aryl =CH), 126.4 (2 x aryl =CH), 119.6 (olef. =CH), 76.5 (COH), 45.8 (CH$_2$), 28.8 (2 x NMe) –in the crude, unpartitioned adduct there was no definite evidence for the presence of *Z*-**17b**; *E*-**18a** (CD$_3$COCD$_3$, no TMS added) 171.9 (2 x CO), 150.5 (NCON), 139.4 (=CH), 138.8 (=CH), 77.0 (COH), 48.9 ($\underline{C}$H$_2$COH), 0.6 (Si$\underline{Me}_3$); *Z*-

18a (CD_3COCD_3, no TMS added) 171.8 (2 x CO), 150.5 (NCON), 138.0 (=CH), 136.0 (=CH), 76.6 (COH), 44.9 ($\underline{C}H_2COH$), –1.0 ($Si\underline{Me}_3$) – in the crude adduct *E* : *Z* = 53 : 47; *E*-**18b** (no TMS added) 170.0 (2 x CO), 150.4 (NCON), 138.8 (=CH), 135.5 (=CH), 76.0 (COH), 49.2 ($\underline{C}H_2COH$), 28.4 (2 x NMe), –2.0 ($Si\underline{Me}_3$); *Z*-**18b** (no TMS added) 170.0 (2 x CO), 150.5 (NCON), 136.7 (=CH), 135.9 (=CH), 75.6 (COH), 44.8 ($\underline{C}H_2COH$), 28.1 (2 x NMe), –0.3 ($Si\underline{Me}_3$) – in the crude adduct *E* : *Z* = 54 : 46.

EI Mass Spectra [*m*/*z*, (%)] – **5a** 279 (5), 257 (2), 235 (13), 217 (12), 135 (85), 134 (77), 119 (100), 91 (100); **5b** 288.1460 (0.5) (M – H_2O req. 288.1474), 245 (15), 173 (8), 172 (37), 135 (30), 134 (15), 119 (33), 91 (100); **6a** 260 (58), 144 (12), 126 (11), 120 (39), 118 (86), 117 (100), 116 (40), 115 (100), 91 (90); **8a** 237 (15), 236 (32), 191 (11), 179 (10), 160 (11), 159 (5), 144 (36), 96 (100); **8b** 266.1266 (1) ($C_{13}H_{18}N_2O_4$ req. 266.1266), 248 (3), 247 (2), 173 (10), 172 (88), 157 (1), 143 (3), 95 (100); **9a** 145 (2), 144 (13), 142 (1), 69 (100); **12a** 212 (1), 197 (7), 173 (30), 144 (85), 136 (14), 69 (100); **13a** 227 (5), 179 (8), 165 (48), 145 (30), 144 (100), 83 (100); **14a** 240 (1), 215 (1.5), 214 (1), 201 (2), 156 (10), 145 (35), 97 (100); **14b** 269.1536 (6.5) (M + H req. 269.1501), 221 (2), 207 (4), 194 (4), 193 (25), 174 (2.5), 173 (19), 172 (100); **15a** 255 (20), 207 (12), 193 (35), 165 (13), 145 (15), 144 (100), 111 (75), 69 (100); **16a** 309 (100), 290 (20), 262 (10), 197 (33), 166 (85), 147 (53), 144 (47), 123 (65), 95 (32), 61 (100); **20b** 234.0990 (5) (M – H_2O req. 234.1004), 233 (9), 206 (1), 174 (1), 173 (10), 172 (69), 170 (1), 143 (1), 142 (2), 81 (100); **21a** 220 (10), 219 (18), 191 (20), 144 (35), 96 (70), 95 (100); **21b** 248.1164 (6) (M – H_2O req. 248.1161), 247 (5), 219 (8), 173 (12), 172 (90), 95 (100); **22a** 235 (9), 206 (12), 191 (32), 176 (13), 145 (33), 144 (85), 109 (100); **22b** 262.1333 (3) (M – H_2O req. 262.1317), 219 (7), 173 (9), 172 (100), 109 (42); **23a** 207 (100), 195 (35), 165 (50), 164 (25), 136 (12), 124 (25), 122 (25), 109 (23), 81 (60).

Reaction of 1,3-Dimethylalloxan 2 with Isoprene: (1,3-Dimethyl-2,4,6-trioxo-hexahydropyrimidine)-5-spiro-2'-(4'-methyl-3',6'-dihydro-2'H-pyran) 24b — A mixture of dimethylalloxan **2** (1.7012 g, 10 mmol), isoprene (1.7030 g, 25 mmol) in dry chlorobenzene (40 cm^3) was heated at 95°C using the sealed tube described above (Method B). After the fading of the yellow colour (*ca.* 30 min), the reaction mixture was worked-up as in Method B to give a colourless solid (2.38 g, 100%). The ^1H NMR spectrum indicated an 88 : 12 mixture of isomers: δ_H (major isomer **24b**; 250 MHz) 5.49 (br. s, =CH), 4.48 (m, OCH_2), 3.23_4 and 3.23_1 (2 x NMe), 2.37 [d, *J* 1.0, $C\underline{H}_2C(Me)=$], 1.70 (=CMe); the minor isomer **25b** exhibited satellite resonances at δ_H 5.38 (br. s), 2.47 (m), and 1.61. Recrystallisation from ethanol led to the removal of the minor isomer giving the *title compound* **24b** (1.679 g, 70.5%), m.p. 140–141°C: ν_{max}(KBr/cm^{-1}) 2970, 2920, 2870, 1760, 1706, 1685, 1369, 1281, 1255, 1200, 1165, 1108, 754; δ_H (400 MHz) 5.56 (m, 3'-H), 4.45 (m, 6'-H_2), 3.31 (s, 2 x NMe), 2.45 (m, 5'-H_2), 1.79 (br. s, =CMe); δ_C (100 MHz) 168.5 (4-C + 6-C), 150.9 (2-C), 126.8 (4'-C), 118.4 (3'-C), 73.7 (5-C ≡ 2'-C), 64.5 (6'-C), 33.3 (5'-C), 29.0 (2 x NMe), 22.9 (=C$\underline{Me}$); *m*/*z* (%) 238 (2), 221 (9), 220 (60), 211 (5), 210 (46), 209 (20), 208 (4), 207 (36), 195 (33), 192 (44), 169 (20), 163 (23). Found C, 55.6; H, 6.0; N, 11.7%; M^+ , 238.0968: $C_{11}H_{14}N_2O_4$ requires C, 55.5; H, 5.9; N, 11.8%; $M^{+\cdot}$, 238.0953.

The similar reaction of **1** with isoprene gave **24a** and **25a** as a *ca.* 90 : 10 mixture; recrystallisation from ethanol afforded (2,4,6-trioxo-hexahydropyrimidine)-5-spiro-2'-(4'-methyl-3',6'-dihydro-2'H-pyran) **24a**, m.p. 255–256°C (dec.) [lit.[13] m.p. 255–256°C (dec.)].

***(1,3-Dimethyl-2,4,6-trioxo-hexahydropyrimidine)-5-spiro-2'-(4'-methyl-tetrahydropyran)* 26** — The Diels–Alder adduct **24b** (0.953 g, 4 mmol) in methanol (100 cm^3) was hydrogenated at atmospheric pressure in the presence of 10% Pd/C (0.1 g). The theoretical uptake of hydrogen took place within 1 h. The mixture was then filtered through a short column of silica gel, which was rinsed with methanol (30 cm^3). The combined methanolic solution was rotary evaporated to give a white solid (0.961 g, 100%). Recrystallisation from hexane afforded colourless prisms of *the title compound*(0.82 g, 85%), m.p. 93–95°C: ν_{max}(KBr/cm^{-1}) 2965, 1755, 1698(sh), 1679, 1375, 1098, 1080, 752; δ_H (400 MHz) 4.52 (ddd, $J_{6'a5'a}$ 12.9, $J_{6'a6'e}$ 11.3, $J_{6'a5'e}$ 2.7, 6'-H$_a$), 4.06 (ddd, $J_{6'e6'a}$ 11.3, $J_{6'e5'a}$ 5.2, $J_{6'e5'e}$ 1.4, 6'-H$_e$), 2.02 (complex m, 4'-H$_a$), 1.85 (non first order ddd, $\underline{J}$ 13.5, 3.7, 1.8, 5'-H$_e$), 1.67 (non first order dd, $\underline{J}_{3'a3'e}$ 13.5, $\underline{J}_{3'a4'a}$ 12.5, 3'-H$_a$), 1.67 (non first order br. d, $\underline{J}_{3'a3'e}$ 13.5, 3'-H$_e$), 1.38 (non first order ddd or dq, $\underline{J}$ 13.1, 12.1, 5.2, 5'-H$_a$), 0.96 (d, J 6.5, CH$\underline{\text{Me}}$); δ_C (100 MHz) 170.3 (4-C/6-C), 169.3 (6-C/4-C), 150.8 (2-C), 75.8 (5-C ≡ 2'-C), 65.6 (6'-C), 40.4 (3'-C), 32.8 (5'-C), 29.3 (1-NMe/3-NMe), 28.7 (3-NMe/1-NMe), 24.4 (4'-C), 22.0 (CH$\underline{\text{Me}}$); *m/z* (%) 240 (1), 238 (3), 222 (11), 212 (11), 197 (9), 196 (31), 172 (54), 171 (7), 170 (78), 169 (100), 157 (7). Found C, 54.7; H, 6.8; N, 11.7%; $M^{+\cdot}$, 240.1090: $C_{11}H_{16}N_2O_4$ requires C, 55.0; H, 6.7; N, 11.7%; $M^{+\cdot}$, 240.1110.

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