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X=Y-ZH Systems as Potential 1,3-Dipoles. Part 45.[1,2] Proton Sponge Effects on the 1,2-Prototropic Formation of Azomethine Ylides from Arylidene Benzylamines.

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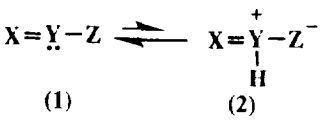
Abstract: A strong rate enhancing effect of an ortho-methoxy or an ortho-dimethylamino group on the 1,2-prototropic generation of azomethine ylides from arylidene arylmethylamines is demonstrated. In the absence of such functionality azomethine ylide formation fails to occur in boiling xylene. The reactions generate the E,E- or syn-azomethine ylide stereoselectively if a single ortho- OMe or -NMe_2 group is present or stereospecifically if either bifurcated H-bonding or push-pull stabilisation of the dipole is possible. Cycloadducts with N-phenylmaleimide are obtained in 78-95% yield.

A new general type of prototropy, 1,2-prototropy was discovered[3] and exploited[4] by us as a facile means for generating 1,3-dipoles (1) ⇌ (2) from X=Y-ZH systems in which Y is a nitrogen atom e.g. imines,[1,4] hydrazones[5] and oximes.[6] We showed that for imines (3) the 1,2-prototropy was facilitated by electron donating R substituents (which increase the basicity of the imine nitrogen atom) and electron withdrawing R^1 substituents [which lower the pKa of the proton H_A in (3)].[7] Subsequently we identified a range of groups Z in (4) which could replace the ester group in (3) and which also promote 1,2-prototropy (e.g. Z = ketones, phosphonates, 2-pyridyl, 2-thiazolyl, 9-fluorenyl, etc).[8] French workers[9] introduced the cyano activating group (4, Z=CN) and this has been subsequently exploited, in particular, by Tsuge et al.[10]



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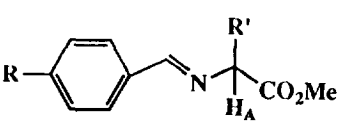

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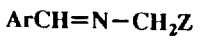

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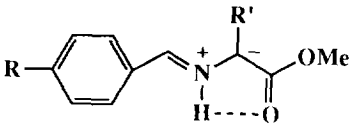

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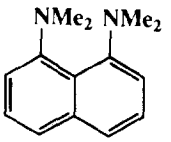

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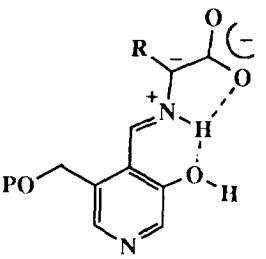
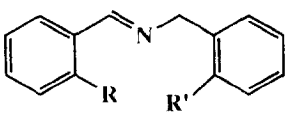
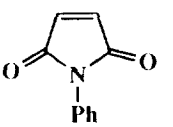


(8)

The well established 1,3-prototropic processes fall into three broad categories involving proton transfer from a carbon atom to a carbon atom (e.g. alkene isomerisation), from a carbon carbon atom to a heteroatom or the reverse (e.g. keto ⇌ enol) or from a heteroatom to a heteroatom (e.g. triazene isomerisation). Normally such prototropic processes involve equilibria between two neutral species. In contrast 1,2-prototropic processes differ in that they create charge separated species, 1,3-dipoles, from uncharged precursors. In this respect they resemble prototropic processes which produce zwitterions such as amino acids (5). There are two categories of 1,2-prototropic processes involving either proton transfer from a carbon atom to a heteroatom or from a heteroatom to a heteroatom. Imines fall into the first category, and oximes and hydrazones into the second. The location of the proton on the central nitrogen atom of (2) potentially offers a third approach to promoting a dipole forming 1,2-prototropic process in addition to those illustrated by variation of R and R' in (3).[7] This latter approach involves stabilising the resultant 1,3-dipole by hydrogen bonding. Thus our earlier studies on (3) proposed that intramolecular hydrogen bonding is responsible for the kinetically controlled stereospecific formation of (6). The 1,4-relationship of the imine and carbonyl oxygen lone pairs responsible for the hydrogen bonding in (6) taken together with the 1,5-lone pair relationship in the well known "Proton Sponge" (7)[11] suggested similar geometrical arrays of lone pairs could stabilise 1,3-dipoles. Such arrays of lone pairs may be important in promoting 1,3-dipole formation in pyridoxal and pyruvate dependant enzymes.[12] Thus (8) has the potential for 1,4- and a 1,5- lone pair/anion participation in 1,3-dipole formation by H-bonding. Related carboxylate anion participation in hydrogen bonding is found, for example, at the active site of aspartate proteases.[13]



(9) **a.** R = R' = H
b. R = OMe, R' = H
c. R = H, R' = OMe
d. R = NMe_2, R' = H
e. R = H, R' = NMe_2
f. R = R' = OMe
g. R = OMe, R' = NMe_2
h. R = NMe_2, R' = OMe
i. R = R' = NMe_2



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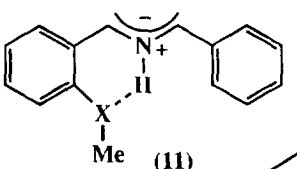

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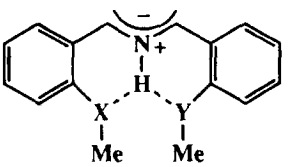

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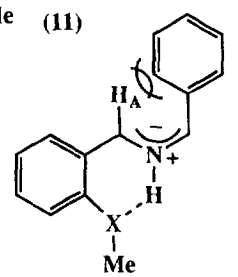


(13)

Table 1. Cycloaddition of (9b-h) to (10) in xylene at 140°C.

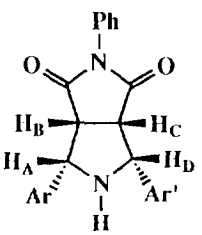
Imine	Reaction Time (h)[a]	Yield (%)[b]	Product Ratio
9b	72	94	2.2(14a):1.4(15a):1(16a)
9c	24	91	2.8(14a):1.7(15a):1(17a)
9d	58	85	1.3(14b):1(15b)[c]
9e	37	87	1.5(14b):1(15b)[c]
9f	36	95	2(14c):1(15c)
9g	24	90	1.1(14d):1(15d)
9h	28	78	1.2(14d):1(15d)

a. Reaction times not optimised.

b. Isolated yield of mixed isomers.

c. ^{1}H n.m.r. monitoring shows 3 isomers are formed initially but the minor isomer disappears on prolonged reaction.

In order to test the ability of suitable arrays of lone pairs to promote 1,2-prototropic formation of azomethine ylides via a "proton sponge" effect we selected (9a) as a reference compound and prepared the related imines (9b-h). Imine (9a) does not react with N-phenylmaleimide in boiling xylene. In contrast (9b-h) all react with (10) in boiling xylene to give good yields of mixtures of stereoisomeric cycloadducts (Table). Imines (9b-e) can form hydrogen bonded dipoles (11) whilst (9f-h) can form 3-centred or bifurcated hydrogen bonded species (12). Support for these ideas is provided by the observations that whilst (9f-h) give rise to mixtures of endo- and exo-cycloadducts only of the E,E- or syn-dipole (12), the imines (9b-e) give cycloadducts derived from both the E,E- or syn- (11)- and E,Z- or anti- (13)-dipoles (Table).



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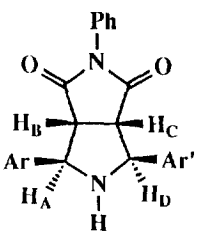

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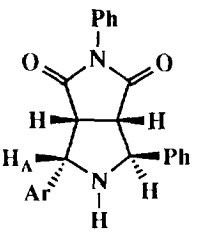

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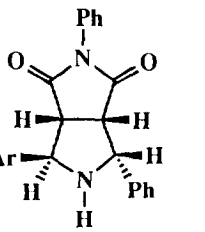
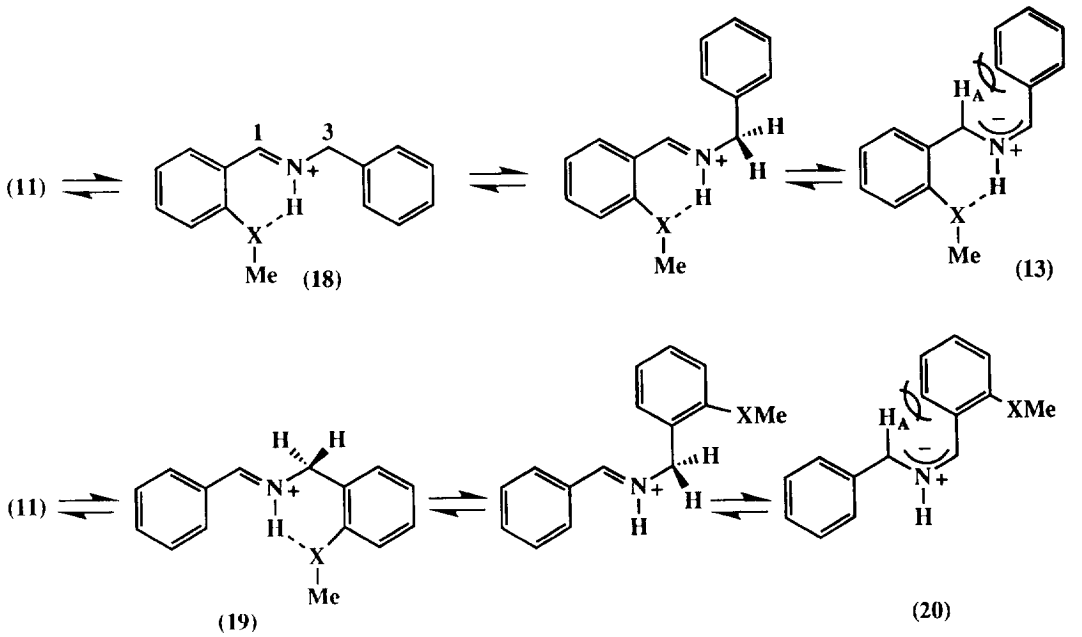


(17)

a. Ar = 2 - $MeOC_6H_4$, Ar' = Ph
b. Ar = 2 - $Me_2NC_6H_4$, Ar' = Ph
c. Ar = Ar' = 2 - $MeOC_6H_4$
d. Ar = 2 - $MeOC_6H_4$, Ar' = 2 - $Me_2NC_6H_4$

The different cycloadduct isomer mixtures obtained from (9b)/(9c) and (9d)/(9e) arise from differences in the transition states for the azomethine ylide formation. Assuming hydrogen bonding plays a role then the formation of the azomethine ylides involves initial protonation to give either (18) [from (9b) or (9d)] or (19) [from (9c) or (9e)]. Deprotonation of the appropriate conformers of (18) leads to dipoles (11) and (13) whilst (19) similarly gives (11) and (20). Stereoelectronic factors require the proton lost to be coplanar with the imine and aryl π- systems. Both (9b)/(9c) and (9d)/(9e) show a strong kinetic preference for the syn-dipole



(11) reflecting the steric retardation of the deprotonations forming the anti-dipoles (13) and (20) due to the developing H_A-Ar interactions in the transition states. Note that the formation of the azomethine ylides involves two molecules of the imine, one of which functions as the base. Evidence accumulated by us over a number of years has established that N-substituted maleimides trap the dipole(s) formed under kinetic control before dipole equilibration can occur.[4,14]. The stereochemistry of the cycloadducts (14) - (17) is based on n.O.e. data. A typical set of selected data for (14a) - (17a) is collected in Table 2.

Table 2. N.O.e. data ($CDCl_3$) for (14a) - (17a).

Cycloadduct	Proton Irradiated	n.O.e.(%)			
		H_A	H_B	H_C	H_D
14a	H_A	-	19	-	10
	H_D	10	-	13	-
15a	H_A	-	*	-	13
	H_D	9	*	-	-
16a	H_A	-	20	2	-
17a	H_A	-	-	-	-
	H_D	-	-	19	-

* Signal obscured.

Thus isomers (14a) and (15a) arise from the syn-dipole (11, X=O) by endo- and exo-cycloaddition respectively. Cycloadduct (16a) is formed by endo-cycloaddition to anti-dipole (13) whilst (17a) arises from

endo-cycloaddition to anti-dipole (20). The ratio of syn: anti dipole cycloadducts is thus 3.6:1 for imine (9b) and 4.5:1 for imine (9c).

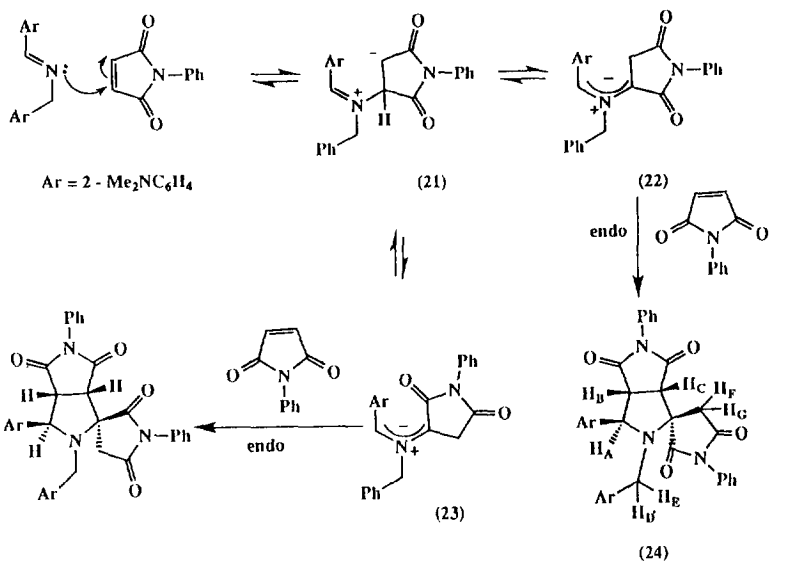
The transient appearance of a minor third isomer in the cycloaddition reactions of imines (9d) and (9e) is puzzling since both cycloreversion - readdition or epimerisation to (14b)/(15b) seem unlikely explanations for these observations. The former because the major cycloadducts are stable under the reaction conditions, the latter because epimerisation presumably involves the 2-$Me_2NC_6H_4$ moiety in some role (radical cation?) and would in the case of (17b) produce (14b) which is more sterically congested. The nature and fate of the transient "third isomer" in these cases therefore remains unresolved. The assignment of stereochemistry of the cycloadducts (14b) and (15b) is based on n.O.e. data and selected data is summarised in Table 3.

Table 3. N.O.e. data ($CDCl_3$) for (14b) and (15b).

Cycloadduct	**Proton Irradiated**	**n.O.e.(%)**			
		H_A	H_B	H_C	H_D
14b	H_A	-	14	-	8
	H_B	14	-	13	-
	H_C	-	6	-	10
	H_D	8	-	15	-
15b	H_A	-	2	1	9
	H_B	-	-	8	-
	H_C	-	10	-	-
	H_D	8	-	-	-

N.O.e data supporting the assigned stereochemistry was also obtained for cycloadducts (14c), (14d), (15c) and (15d) and these data are collected in the experimental section.

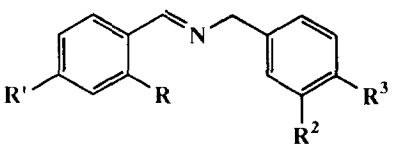
Imine (9i), in contrast to imines (9b-h), reacts under the same conditions to give an unusual 2:1 adduct (24) in 82% yield (Scheme 1).



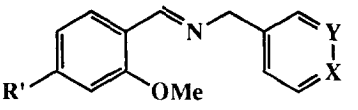
Scheme 1

Michael addition of (9i) to N-phenylmaleimide initially give (21). Formal 1,2-prototropy then furnishes an azomethine ylide for which two configurations (22) and (23) are possible. The stereochemistry of the product (24) together with the preference for an endo-cycloaddition transition state identifies (22) as the product forming dipole. Inspection of molecular models confirms the severe steric hindrance between the Ar and C=O moieties in (23) and implicates developing steric strain in the 1,2-prototropy transition state as the cause of stereospecific generation of (22). There is literature precedent for 1,2-prototropy of the type involved in (21) → (22)/(23).[15] The trans-relationship between H_A and H_B in (24) was established by n.O.e. studies. Thus irradiation of H_B causes a minor enhancement of the signals for H_A (3%) but a substantial enhancement of H_C (12%).

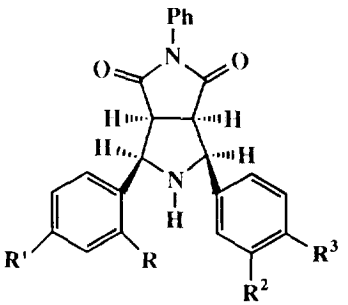
A further series of arylidene benzylamines were prepared in which either an electron withdrawing group is located in the benzylamine moiety (25a-e) or it is replaced by a 3- or 4-pyridylmethyl group (26a, b).



(25) a. R = R' = R^2 = H, R^3 = NO_2
b. R = R^2 = H, R' = OMe, R^3 = NO_2
c. R = R' = OMe, R^2 = H, R^3 = NO_2
d. R = OMe, R' = R^2 =H, R^3 = NO_2
e. R = R' =OMe, R^2 = NO_2, R^3 = H



(26) a. R'= OMe, X= N, Y= CH
b. R'= H, X= CH, Y= N



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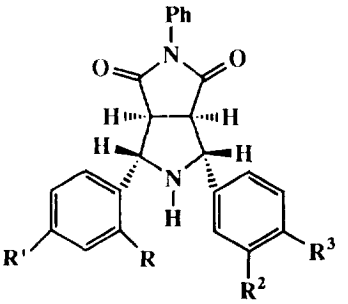

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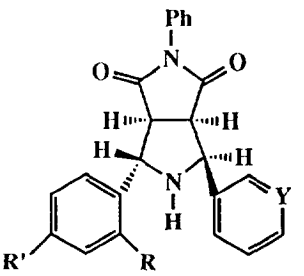
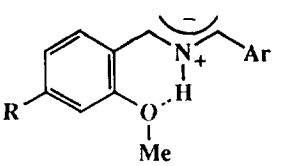


(29)

a. R = R' = OMe, R^2 = H, R^3 = NO_2
b. R = OMe, R' = R^2 = H, R^3 = NO_2
c. R = R' = OMe, R^2 = NO_2, R^3 = H

a.R = OMe, Y = CNO_2
b.R = H, Y = N



(30)

Table 4. Cycloaddition of (25c-e), (26) and (27) to (10) in xylene at 140°C.

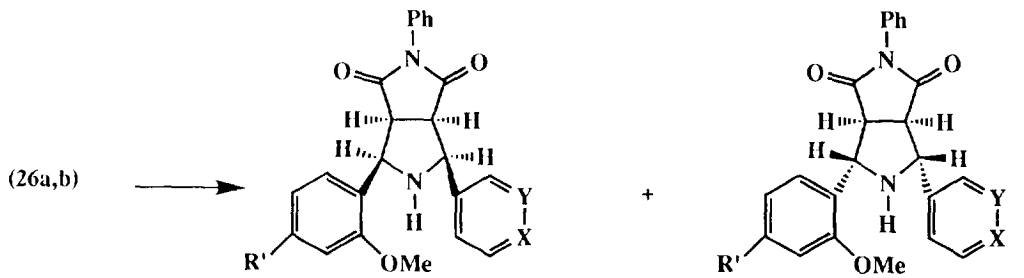
Imine	Reaction Time(h)	Yield(%)[a]	Product Ratio.[b]
25c	12	90	4(27a) : 1(28a)
25d	12	80	4(27b) : 1(28b)
25e	36	81	3(27c) : 1(28c)[c]
26a	12	88	4(31a) : 1(32a)
26b	48	88	1.6(31b) : 3.8(32b) : 1(29b)

a. Isolated yield of the mixed isomers.

b. Determined by integration of the ^{1}H n.m.r. spectra of the reaction mixtures.

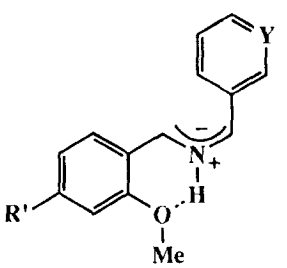
c. Trace amounts (<5%) of (29a) present.

Heating imines (25a) and (25b) with N-phenylmaleimide in toluene or xylene under an atmosphere of argon failed to give any cycloadduct. However, imines (25c-e), which possess a methoxy substituent ortho to the imine moiety, underwent cycloaddition with N-phenylmaleimide on heating in boiling xylene for 12-48h. The products (Table 4) comprised mixtures of endo-(27) (major) and exo-(28) (minor) cycloadducts of the E,E- or syn-azomethine ylide (30). Imines (26a) and (26b) underwent analogous reactions with N-phenylmaleimide to give mixtures of endo-(31) (major) and exo-(32) (minor) cycloadducts which are also derived from azomethine ylides (30) (Table 4).



(31) (32)

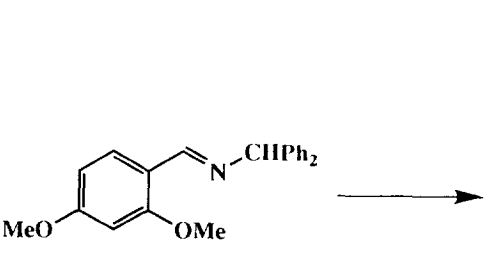
a. R' = OMe, Y = CH, X = N
b.R' = H, Y = N, X = CH



(33) **a. R' = OMe, Y = CNO_2**
b. R' = H, X = CH, Y = N

Imine (25e) gave a trace amount of a cycloadduct derived from the anti-dipole (33a) and imine (26b) also furnished a small amount of a third cycloadduct (29b) (Table 4) derived from the corresponding anti-dipole (33b). These minor cycloadducts (29a) and (29b) are derived from their respective anti-dipole precursors via an exo-transition state.

The imine (34) derived from diphenylmethylamine also undergoes cycloaddition with N-phenylmaleimide in boiling xylene over 24h. to afford a single cycloadduct (35) in 80% yield.



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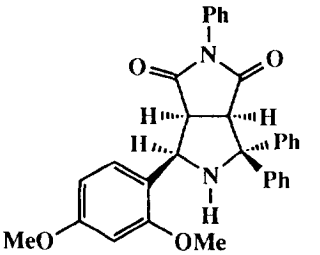
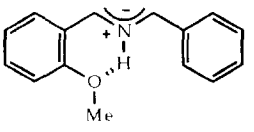
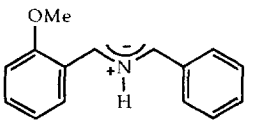


(35)

Proton Sponge Mechanism. The introduction of ortho-methoxy or-dimethylamino moieties in one or both aryl rings of arylidene arylmethylamines promotes azomethine ylide formation in boiling xylene. The effectiveness of this arrangement of conjugated 1,5-lone pairs in the imine precursors has been clearly demonstrated. However the imine functions as both dipole precursor and base. The ability of the pyrrolidine product to assume the role of base is compromised by the steric hindrance occasioned by the 2,5-diaryl substitution. It was therefore of interest to calculate the heats of formation of the two E,E- dipole conformers (11) and (36). These were found to be 39.4 and 40.9k.cal/mol respectively. Thus conformer (11) in which the proton sponge effect is operative is calculated to be more stable by ca. 1.5 k.cal/mol.



(11)



(36)

The preference for the E,E- dipoles, e.g. (11)/(36), in 1,3-diaryl azomethine ylides parallels observations for 1,3-diaryl allyl anions and factors influencing this latter case and their relevance to azomethine ylides have been discussed by us previously.[16] The small energy difference between (11) and (36) is compatible with a pre-equilibrium followed by a rate determining step and suggests a rate difference of a factor of 10 or less for the formation (11) and (36). Thus the operations of a proton sponge effect on dipole stability (favouring dipole formation) has not been clearly established but the rate enhancing effect of ortho-methoxy or - dimethylamino moieties have been clearly demonstrated. We have previously shown[7] that para-NMe_2 and -OMe groups substantially increase the rate of 1,2-prototropic formation of azomethine ylides in (3) and the results reported herein could be mainly a reflection of the increased basicity of the ortho-OMe and -NMe_2 imines although such an effect would also clearly influence dipole stability.

Experimental. General experimental details were as previously described.[17] Calculations were performed using SPARTAN (SGI version 3.1.3GL) (Wavefunction Inc., Irvine, CA) on a Silicon Graphics 4D480S with optimisations by Semi-Empirical calculations at the AM1 level.

General Methods for the Preparation of Imines

Method A. Free amine (0.02 mol) and the appropriate aldehyde (0.02 mol) were dissolved in dry methylene chloride (80 ml). Anhydrous sodium sulphate (10g) was added and the mixture stirred at room temperature for 12-24h. The sodium sulphate was then removed by filtration and the filtrate concentrated to give the crude imine.

Method B. The appropriate amine hydrochloride (0.02 mol) was stirred in dry methylene chloride (100 ml) and triethylamine (0.022 mol) was added. The stirring was continued for 10 min. and then the aldehyde (0.02 mol) and anhydrous sodium sulphate (10g) were added and the mxture stirred at room temperature for 12-14h. The sodium sulphate was then removed by filtration and the filtrate washed with water (3 x 50 ml), dried, (Na_2SO_4) and concentrated to give the crude imine.

2-Methoxybenzylidene benzylamine (9b). 2-Methoxybenzaldehyde (13.6g, 0.1 mol) and benzylamine (10.7g, 0.1 mol) were reacted over 24h by method A. The resulting pale yellow oil was distilled *in vacuo* to afford the **product** (17.2g, 76%) as a colourless oil, b.p. 124-126 °C/0.01 mmHg. (Found: C, 79.9; H, 6.6; N, 6.15. $C_{15}H_{15}NO$ requires C, 80.0; H, 6.7; N, 6.2%); m/z(%) 225 (M^+, 37), 196(10), 121(100) and 91(96); ν_{max} (film) 1640, 1590, 1440, 1240 and 1030 cm^{-1}; δ 8.85 (s, 1H, CH=N), 7.4-6.99 (m, 9H, ArH), 4.8(s, 2H, CH_2) and 3.8(s, 3H, Ome).

Benzylidene-2-methoxybenzylamine (9c). Benzaldehyde (5.3g, 0.05 mol) and 2-methoxybenzylamine (6.8g, 0.05 mol) were reacted over 24h by method A. The resulting yellow oil was distilled *in vacuo* to afford the **product** (8.4g, 75%) as a pale yellow oil, b.p. 132-134°C/0.1 mmHg. (Found: C, 80.1; H, 6.95; N, 6.1. $C_{15}H_{15}NO$ requires C, 79.95; H, 6.7; N, 6.2%); m/z(%) 225(M^+, 11) 224(13), 195(26), 134(50) and 91(100); ν_{max} (film) 1640, 1590, 1480, 1250 and 1030 cm^{-1}; δ 8.44(s, 1H, HC=N), 7.9-6.95(m, 9H, ArH), 4.95(s, 2H, CH_2) and 3.87(s, 3H, OMe).

2-Dimethylaminobenzylidene benzylamine (9d) 2-Dimethylaminobenzaldehyde (3.73g, 0.025 mol) and benzylamine (2.67g, 0.025 mol) were reacted over 12h by method A. The resulting brown oil was distilled *in vacuo* to yield the **product** (4.9g, 84%) as a colourless oil, b.p. 140-144°C/0.05 mmHg. (Found: C, 80.85; H, 7.65; N, 11.5. $C_{16}H_{18}N_2$ requires C, 80.65; H, 7.6; N, 11.75%); m/z(%) 238 (M^+,10), 147(79), 132(100), 118(12) and 91(56); ν_{max} (film) 1630, 1590, 1480, 1450 and 1280 cm^{-1}; δ 8.72(s, 1H, CH=N), 7.97-6.97 (m, 9H, ArH), 4.81(s, 2H, CH_2) and 2.71(s, 6H, NMe_2).

Benzylidene 2-dimethylaminobenzylamine (9e). Benzaldehyde (2.12g, 0.02 mol) and 2-dimethylaminobenzylamine (3g, 0.02 mol) were reacted over 18h by method A. The resulting brown oil was distilled *in vacuo* to yield the **product** (4.6g, 96%) as a colourless oil, b.p. 130-135°C/0.01 mmHg. (Found: C, 80.9; H, 7.8; N, 11.55, $C_{16}H_{18}N_2$ requires C, 80.65; H, 7.6; N, 11.75%); m/z(%) 238(M^+,25), 195(10), 150(12), 135(19), 134(66), 132(100) and 118(39); ν_{max} (film) 1640, 1600, 1580, 1490, 1450 and 1310; δ 8.33(s, 1H, HC=N), 7.73-6.93(m, 9H, ArH), 4.85(s, 2H, CH_2) and 2.67(s, 6H, Nme_2).

2-Methoxybenzylidene 2-methoxybenzylamine (9f). 2-Methoxybenzaldehyde (13.6g, 0.1 mol) and 2-methoxybenzylamine (13.7g, 0.1 mol) were reacted over 24h by method A. The resulting dark yellow oil was distilled *in vacuo* to yield the **product** (20.1g, 79%) as a colourless oil, b.p. **148-150°C/0.1 mmHg.** (Found: C, 75.05; H, 6.95; N, 5.35. $C_{16}H_{17}NO_2$ requires C, 75.25; H, 6.7; N, 5.5%); m/z(%) 255(M^+,20) 254(11), 134(96), 121(100) and 91(93); ν_{max} (film) 1630, 1600, 1480, 1460, 1440 and 1240 cm^{-1}; δ **8.84**(s, 1H, CH=N), 8.0(m, 1H, CHOMe), 7.36-6.8 (m, 7H, ArH), 4.82(s, 2H, CH_2) and 3.78(s, 6H, 2 x OMe).

2-Methoxybenzylidene 2-dimethylaminobenzylamine (9g). 2-Methoxybenzaldehyde (1.81g, 0.013 mol) and 2-dimethylaminobenzaldehyde (2g, 0.013 mol) were reacted over 18h by method A. The resulting dark oil was distilled *in vacuo* to yield the **product** (3.2g, 89%) as a pale yellow oil b.p. 154-156°C/0.05 mmHg. (Found: C, 75.8; H, 7.65; N, 10.55. $C_{17}H_{20}N_2O$ requires C, 76.1; H, 7.5; N, 10.45%); m/z(%) 268(M^+,24) 147(20), 134(47), 132(100) and 118(39); ν_{max} (film) 1635, 1480, 1445 and 1010 cm^{-1}; δ 8.94(s, 1H, CH=N), 8.1-6.98(m, 8H, ArH), 4.97(s, 2H, CH_2), 3.90(s, 3H, OMe) and 2.80(s, 6H, Nme_2).

2-Dimethylaminobenzylidene-2-methoxybenzylamine (9h). 2-Dimethylaminobenzaldehyde (7.46g, 0.05 mol) and 2-methoxybenzylamine (6.86g, 0.05 mol) were reacted over 24h by method A. The resulting yellow oil was distilled *in vacuo* to furnish the **product** (7.02g, 52%) as a viscous yellow oil b.p. 145-147°C/0.05 mmHg. (Found: C, 76.05; H, 7.75; N, 10.25. $C_{17}H_{20}N_2O$ requires C, 76.1; H, 7.5; N, 10.45%); m/z(%) 268(M^+,2), 148(11), 147(100), 146(4) and 145(7); ν_{max} (film) 1640, 1600, 1510, 1460 and 1300 cm.$^{-1}$; δ 8.61(s, 1H, CH=N), 7.21-6.7(m, 8H, ArH), 4.74(s, 2H, CH_2), 3.67(s, 3H, OMe), and 2.62(s, 6H, NMe_2).

2-Dimethylaminobenzylidene-2-dimethylaminobenzylamine (9i). 2-Dimethylaminobenzaldehyde (1.98g, 0.013 mol) and 2-dimethylaminobenzylamine (2.0g, 0.013 mol) were reacted over 18h by method A. The resulting dark oil was distilled *in vacuo* to yield the **product** (2.1g, 56%) as a yellow oil, b.p. 140-145°C/0.2 mmHg. $C_{18}H_{23}N_3$ requires 281.1892 H.R.M.S. found 281.1893 ± 0.002 m/z(%) 281(0.6,M^+), 150(57), 133(69), 132(100), 120(26) and 118(60); ν_{max} (film), 1650, 1590, 1550 and 1440 cm^{-1}; δ 8.80(s, 1H, CH=N), 7.99-7.01(m, 8H, ArH), 4.96(s, 2H, CH_2) 2.80(s, 6H, NMe_2) 2.80(s, 6H, NMe_2) and 2.78(s, 6H, NMe_2).

2,4-Dimethoxybenzylidene-4-nitrobenzylamine (25c). 2,4-Dimethoxybenzaldehyde (3.32g, 0.02 mol) and 4-nitrobenzylamine hydrochloride (3.76g, 0.02 mol) were reacted over 2 dy by method B. The resulting pale yellow solid was crystallized from ether - petroleum ether to give the **product** (5g, 83%) as colourless plates, m.p. 78-80°C (Found: C, 63.8; H, 5.2; N, 9.05. $C_{16}H_{16}N_2O_4$ requires C, 64.0; H, 5.35; N, 9.35%). δ 8.77(s, 1H, CH=N), 8.20-6.46(m, ArH, 7H), 4.86(s, 2H, NCH_2), and 3.87 and 3.86(2 x S, 2 x 3H, 2 x OMe); m/z(%) 300 (M^+,24), 164(73), 149(100, 136(19), 121(19) and 90(20); ν_{max} 1630, 1600, 1500 and 1350 cm^{-1}.

2-Methyoxybenzylidene-4-nitrobenzylamine (25d). 2-Methoxybenzaldehyde (2.04g, 0.015 mol) and 4-nitrobenzylamine hydrochloride (2.82g, 0.015 mol) reacted over 2 dy using method B. The resulting pale yellow solid was crystallized from ether - petroleum ether to give the **product** (2g, 74%) as colourless rods, m.p. 75-76°C. (Found: C, 66.5; H, 5.10; N, 10.45. $C_{15}H_{14}N_2O_3$ requires C, 66.65; H, 5.22; N, 10.35%); δ 8.89(s, 1H, CH=N), 8.20-6.94(m, ArH, 8H), 4.90(s, 2H, NCH_2) and 3.90(s, 3H, OMe); m/z(%) 271(2.5), 270(M^+,1), 134(100), 119(70), 91(23), 90(19), 89(20) and 78(19); ν_{max} 1630, 1610, 1420 and 1350 cm^{-1}.

2,4-Dimethoxybenzylidene-3-nitrobenzylamine (25e). 2,4-Dimethoxybenzaldehyde (3.32g, 0.02 mol) and 3- nitrobenzylamine hydrochloride (3.76g, 0.02 mol) reacted over 2 dy using method B. The resulting pale brown solid was crystallized from ether - petroleum ether to give the **product** (4.2g, 70%), as pale brown rods, m.p. 70-71°C (Found: C, 63.7; H, 5.45; N, 9.2. $C_{16}H_{16}N_2O_4$ requires C64.0; H, 5.35; N, 9.35%); δ 8.78(s,

1H, CH=N), 8.21-6.45(m, ArH, 7H), 4.85(s, 2H, NCH_2), and 3.87 and 3.85(2xs, 2x3H, OMe); m/z(%) 300(M^+,24), 164(73), 149(100), 136(19), 121(19) and 90(20); ν_{max} 1630, 1610, 1420 and 1250 cm^{-1}.

2,4-Dimethoxybenzylidene-4-aminomethylpyridine (26a). 2,4-Dimethoxybenzaldeyde (1.66g, 0.01 mol) and 4-aminomethyl pyridine (1.08g, 0.01 mol) reacted over 1 dy using method A. The resulting colourless solid was crystallized from ether - petroleum ether to give the **product** (2g, 78%) as colourless rods, m.p. 100°C. (Found: C, 70.45; H, 6.3; N; 10.75 $C_{15}H_{16}N_2O_2$ requires C, 70.3; H, 6.3; N, 10.9%); δ 8.75(s, 1H, CH=N), 8.54-6.45(m, ArH, 7H), 4.77(s, 2H, NCH_2), and 3.86 and 3.85(2xs, 2x3H, OMe). m/z(%) 256(M^+,26), 164(94), 149(100), 93(26), 92(40) and 65(24); ν_{max} 1630, 1610, 1410 and 1360 cm^{-1}.

2-Methoxybenzylidene-3-aminomethylpyridine (26b). 2-Methoxybenzaldehyde (2.72g, 0.02 mol) and 3-aminomethylpyridine (2.16g, 0.02 mol) reacted over 1 dy using method A. The resulting crude oil was distilled in vacuo to give the **product** (2.95g, 60%) as a pale yellow oil, b.p. 140-142°C/0.1mmHg. (Found: C, 74.7; H, 6.15; N, 12.5. $C_{14}H_{14}N_2O$ requires C, 74.3; H, 6.25; N, 12.4%); δ 8.88(s, 1H, CH=N), 8.8-6.99(m, 8H, ArH), 4.81(s, 2H, NCH_2), and 3.87(s, 3H, OMe); m/z(%) 226(M^+,58), 225(41), 134(100) and 92(25); ν_{max} (film) 1630, 1600, 1580, 1380, 1360 and 1180 cm^{-1}.

2.4-Dimethoxybenzylidene-aminodiphenylmethane (27). 2,4-Dimethoxybenzaldehyde (4.15g, 0.025 mol) and aminodiphenylmethane (4.5g, 0.025 mol) reacted over 1 dy using method A. The resulting colourless solid was crystallized from ether - petroleum ether to give the **product** (6.2g, 81%) as colourless plates, m.p. 82-83°C. (Found: C, 79.95; H, 6.45; N, 4.2. $C_{22}H_{21}NO_2$ requires C, 79.75; H, 6.4; N, 4.25%); δ 8.79(s, 1H, CH=N), 8.12-6.41(m, ArH, 13H), 5.55(s, 1H, NCH), and 3.83 and 3.82(2xs, 2x3H, 2xOMe); m/z(%) 331(M^+,19), 200(18), 167(100), 165(29) and 164(39); ν_{max} 1630, 1600, 1500, 1490 and 1380 cm^{-1}.

Cycloadducts.

2-(2'-Methoxyphenyl)-4,7-diphenyl-6,8-dioxo-3,7-diazabicyclo[3.3.0]octane (14a), (15a) and (16a). Imine (9b) (3.37g, 0.015 mol) and N-phenylmaleimide (2.6g, 0.015 mol) were boiled under reflux in xylene (40 ml) for 3 dy. T.l.c. monitoring showed no N-phenylmaleimide remained at this time. The solvent was removed under reduced pressure to leave a dark brown gum whose ^1H n.m.r spectrum showed it to comprise a 2.23 : 1.4:1 mixture of (14a), (15a) and (16a) respectively. This gum was triturated with ether to give a pale yellow solid (94%). The isomers were separated (with difficulty) by flash chromatography eluting with 15:4 v/v ether-hexane. Cycloadduct (14a) was obtained pure whilst (15a) and (16a) were obtained as a mixture. [Found: (mixed isomers) C, 74.9; H, 5.3; N, 6.8. $C_{25}H_{22}N_2O_3$ requires C, 75.35; H, 5.55; N, 7.05%]; m/z(%) (mixed isomers) 398(M^+,2), 255(17), 226(18) and 225(100); ν_{max} (mixed isomers) 1720, 1610, 1510, 1400 and 1260 cm^{-1}.

14a. Obtained as colourless rods m.p. 188-189°C from ether-hexane. δ 7.6-6.85(m, 14H, ArH), 4.72(d, 1H, 4-H, J6.4Hz), 4.63(d, 1H, 2-H, J6.3Hz), 3.87(s, 3H, OMe), 3.75(dd, 1H, 5-H, J6.3, 7.7Hz), 3.50(dd, 1H, 1-H, J6.4, 7.6Hz) and 2.1(s, 1H, NH) (exchanges with D_2O).

15a/16a. Obtained as a mixture (colourless solid).

15a. δ 7.71-6.80(m, 14H, ArH), 4.57(d, 1H, 4-H, J5.9Hz), 4.40(d, 1H, 2-H, J6.0Hz), 3.79(s, 3H, OMe) and 3.55(m, 3H, 1-H, 5-H, NH).

16a. δ 7.71-6.80(m, 14H, ArH), 5.09(s, 1H, 4-H), 4.78(d, 1H, 2-H, J7.1Hz), 3.75(s, 3H, OMe) and 3.61(m, 3H, 1-H, 5-H, NH).

2-(2'-Methoxyphenyl)-4,7-diphenyl-6,8-dioxo-3,7-diazabicyclo[3.3.0]octane. Isomer (17a). Imine (9c) (3.37g, 0.015 mol) and N-phenylmaleimide (2.6g, 0.015 mol) were heated in boiling xylene (40 ml) for 24h.

The solvent was removed under reduced pressure to yield a dark yellow oil whose ^{1}H n.m.r. spectrum showed it to comprise a 2.79 : 1.69 :1 mixture of (14a), (15a) and (17a) respectively. The oil was triturated (ether) to yield a colourless solid (91%). The isomers were separated (with difficulty) by flash chromatography eluting with 75:20 v/v ether-hexane. Cycloadduct (14a) was obtained pure, (15a) and (17a) were obtained as a mixture. [Found (mixed isomers): C, 75.0; H, 5.55; N, 6.65. $C_{25}H_{22}N_2O_3$ requires C, 75.35; H, 5.55; N, 7.05%], m/z(%) (mixed isomers). Cycloadduct (14a) was obtained pure whilst (15a) and (17a) were obtained as a mixture. [Found (mixed isomers):C, 398(M^+,1), 255(29), 226(18) and 225(100); ν_{max} (mixed isomers) 1720, 1605, 1510, 1410 and 1260 cm^{-1}].

17a. δ 7.70-6.92(m, 14H, ArH), 5.40(s, 1H, 4-H), 5.31(d, 1H, 2-H, J6.5Hz), 3.64(s, 3H, OMe) and 3.5-3.2(m, 3H, 1-H, 5-H + NH).

(14a) and (15a) were identical to those reported above.

2-(2'-Dimethylaminophenyl)-4,7-diphenyl-6,8--dioxo-3,7-diazabicyclo[3.3.0]octane (14b) and (15b).

NMR run: Imine (9d) (35mg, 1.46 x 10^{-4} mol) and N-phenylmaleimide (25mg, 1.46x10^{-4} mol) were dissolved in d^{10}-xylene (1ml) and placed in an n.m.r. tube. The solution was heated in the probe of a 250 MHz spectrometer at 140°C and spectra were recorded at 60 min. intervals. During the course of the reaction the formation of three isomers (14b), (15b) and (tentatively) (16b) was observed. However, on further heating the minor isomer (16b) disappears to yield only the two major isomers (14b) and (15b) in the ratio 1.3:1 after 58h.

Preparative scale. Imine (9d) (3.5g, 14.6 mmol) and N-phenylmaleimide (2.53g, 14.6 mmol) were heated in boiling xylene (40ml) for 58h. The solvent was removed under reduced pressure to yield a yellow gum who ^{1}H n.m.r. spectrum show it to comprise a 1.3:1 mixture of (14b) and (15b). Trituration (ether) yielded a yellow solid (85%) which was separated by flash chromaography eluting with 3:1 v/v ether-hexane. [Found (mixed isomers): C, 75.45; H, 6.0; N, 9.95. $C_{26}H_{25}N_3O_2$ requires C, 75.9; H, 6.1; N, 10.2%].

14b. Eluted first and formed colourless needles, m.p. 205-206°C, from ether-hexane. m/z(%) 411(M^+,100), 397(16), 396(58), 320(36) and 147(47); ν_{max} 1720, 1510, 1400 and 1300 cm^{-1}; δ 7.66-7.18(m, 14H, ArH), 5.03(d, 1H, 4-H, J7.4Hz), 4.55(d, 1H, 2-H, J6.5Hz), 3.67(dd, 1H, 5-H, J7.7, 9.3Hz), 3.54(dd, 1H, 1-H, J7.13, 9.4Hz) and 2.71(s, 6H, NMe_2).

15b. Obtained as colourless rods m.p. 119-121°C (ether/hexane). m/z(%) 412(30), 411(M^+,100), 397(24), 396(79), 320(96), and 147(96); ν_{max} 1710, 1500, 1390 and 1250 cm^{-1}; δ 7.60-6.81(m, 14H, ArH), 5.00(s, 1H, 4-H), 4.80(s, 1H, 2-H), 3.92(d, 1H, 5-H, J6.1Hz), 3.54(d, 1H, 1-H, J6.5Hz) and 2.82(s, 6H, NMe_2).

Attempts to separate the minor isomer (16b) after 24h failed.

The same products were obtained from imine (9e) although the transient cycloadduct was different as noted below:

NMR run: Imine (9e) (35mg, 1.46 x 10^{-4}mol) and N-phenylmaleimide (25mg, 1.46 x 10^{-4}mol) were dissolved in d^{10}-xylene (1ml) and placed in an n.m.r. tube. This solution was heated in the probe of a 250 MHz spectrometer at 140°C and spectra were recorded at 60 min. intervals. During the course of the reaction the formation of three isomers (14b), (15b) and (tentatively) (17b) was observed. However, on further heating the minor isomer (17b) disappears to yield a 1.5:1 mixture of (14b) and (15b) after 37h.

Preparative scale: Imine (9e) (3.5g, 14.6 mmol) and N-phenylmaleimide (2.53g, 14.6 mmol) were heated in boiling xylene (40ml) for 37h. The solvent was removed under reduced pressure to yield a brown oil whose ^{1}H n.m.r. spectrum showed it to comprise a 1.5:1 mixture of (14b) and (15b). Trituration (ether) yielded a colourless solid (87%) from which cycloadducts (14b) and (15b) were separated as described above.

2-(2'-Methoxyphenyl)-4-(2'-methoxyphenyl)-7-phenyl-6,8-dioxo-3,7-diazabicyclo[3.3.0]octane (14c) and (15c). Imine (9f) (2.55g, 0.01 mol) and N-phenylmaleimide (1.7g, 0.01 mol) were boiled under reflux in dry xylene (40ml) for 36h. The solvent was removed under reduced pressure to yield a yellow solid (100%) whose ^{1}H n.m.r. spectrum show it to comprise a 2:1 mixture of (14c) and (15c). The isomers were separated by flash chromatography eluting with 70:30 v/v ether-hexane.

14c. Eluted first and was obtained as fine colourless needles, m.p. 266-268°C (ether-hexane) [Found (mixed isomers): C, 72.8; H, 5.65; N, 6.55. $C_{26}H_{24}O_4N_2$ requires C, 72.9; H, 5.65; N, 6.5%]; m/z(%) 428(M^+,1), 256(17), 255(100), and 240(11); ν_{max} 1720, 1605, 1500, 1460 and 1400 cm^{-1}; δ 7.66-6.89(m, 13H, ArH), 4.87(d, 2H, 2-H, 4-H, J3.7Hz), 3.89(s, 6H, 2 x OMe), 3.77(dd, 2H, 1-H, 5-H, J3.0, 5.4Hz) and 1.9(brs, 1H, NH); n.O.e.(%): irradiation of 2-H/4-H effected enhancement of 1-H/5-H (16%).

15c. Obtained as colourless fine needles, m.p. 219-220°C (ether-hexane); m/z(%) 428(M^+,3), 427(5), 256(17), 255(100), and 240(11); ν_{max} 1720, 1610, 1500, 1460, 1400 and 1250 cm^{-1}; δ 7.45-6.88(m, 13H, ArH), 4.53(brs, 2H, 2-H, 4-H), 3.86(s, 6H, 2 x OMe) and 3.84(br d, 2H, 1-H, 5-H, J5.1Hz); n.O.e.(%): irradiation of 2-H/4-H effected no enhancement of H-1/H-5.

2-(2'-Dimethylaminophenyl)-4-(2'-methoxyphenyl)-7-phenyl-6,8-dioxo-3,7-diazabicyclo[3.3.0]octane (14d) and (15d). Imine (9g) (5.36g, 0.02 mol) and N-phenylmaleimide (3.46g, 0.02 mol) were heated in boiling xylene (75ml) for 24h. The solvent was removed under reduced pressure to yield a brown solid (90%) whose ^{1}H n.m.r. spectrum showed it to comprise a 1.1:1 mixture of (14d) and (15d). The isomers were separated by flash chromatography eluting with 3:1 v/v ether-hexane. Cycloadduct (14d) eluted first. The same products were obtained from imine (9h) in essentially the same ratio after a reaction time of 28h. [Found (mixed isomers): C, 73.05; H, 6.35; N, 9.45. $C_{27}H_{27}N_3O_3$ requires C, 73.45; H, 6.15; N, 9.5%]; m/z(%) (mixed isomers) 441(M^+,10), 256(18), 255(100), 240(10) and 132(10); ν_{max} (mixed isomers) 1720, 1500, 1380, 1200 and 1175cm^{-1}.

14d. Obtained as colourless needles m.p. 233-237°C (ether-hexane) δ7.77-6.92(m, 13H, ArH), 5.14(br d, 1H, 4-H, J4.5Hz), 4.91(br d, 1H, 2-H, J5.3Hz), 3.93(s, 3H, OMe), 3.85(t, 2H, 1-H, 5-H, J4.8Hz) and 2.78(s, 6H, NMe_2); n.O.e.(%): irradiation of 2-H effected enhancement of 4-H(9) and 1-H/5-H(17), irradiation of 1-H/5-H effected enhancement of 2-H(8) and 4-H(8).

15d. Obtained as colourless needles m.p. 238-240°C (ether-hexane) δ7.56-6.79(m, 13H, ArH), 4.80(brs, 2H, 2-H, 4-H), 3.81(s, 3H, OMe), 3.71(d, 2H, 1-H, 5-H, J5.6Hz) and 2.65(s, 6H, NMe_2); n.O.e.(%) irradiation of 1-H/5-H effected enhancement of 2-H/4-H(2).

Cycloadduct (24). Imine (9i) (1.81g, 0.01 mol) and N-phenylmaleimide (1.73g, 0.01 mol) were heated in boiling xylene (60ml) for 12h. Removal of the solvent under reduced pressure yielded a brown oil whose ^{1}H n.m.r. spectrum showed it to comprise ca. 1:1 mixture of starting imine (9i) and a single cycloadduct (24). Flash chromatography eluting with 3:1 v/v ether-hexane furnished (24) (2.6g, 82% based on recovered N-phenylmaleimide) as colourless needles m.p. 224-226°C (ether-hexane). (Found: C, 72.55; H, 5.75. $C_{38}H_{37}N_5O_4$ requires C, 72.7; H, 5.95%). $C_{38}H_{37}N_5O_4$ requires 627.2845 H.R.M.S. found 627.2863; m/z(%) 627(M^+,2), 494(33), 493(100), 346(12) and 147(52); ν_{max} 1715, 1600, 1495, 1360 and 1250 cm^{-1}; δ(C_6D_6) 8.0-6.80(m, 18H, ArH), 6.11(d, 1H, H_A, J10Hz), 4.30(d, 1H, H_D or H_E, J15Hz), 4.19(d, 1H, H_F or H_G, J19Hz), 4.08(dd, 1H, H_B, J8.2, 10Hz), 3.60(d, 1H, H_D or H_E, J15Hz), 2.81(s, 6H, NMe_2), 2.78(d, 1H, H_F or H_G, J19Hz), 2.37(d, 1H, H_C, J8.2Hz) and 2.03(s, 6H, NMe_2).

General Procedure for Cycloaddition of Imines (25c-e), (26a,b) and (34) with N-Phenylmaleimide. The imine (0.01 mol) and N-phenylmaleimide (0.01 mol) were dissolved in dry xylene (80ml) and boiled under reflux for 12-48h. (Table 2). On cooling the major cycloadducts (Table 2) precipitated whilst concentration of the mother liquors afforded mainly the other isomers.

4-(2',4'-Dimethoxyphenyl)-2-(4'-nitrophenyl)-7-phenyl-6,8-dioxo-3,7-diazabicyclo[3.3.0]octane. (27a) and (28a). Obtained (90%) as 4:1 mixture of isomers (27a) and (28a).

27a. Pale yellow needles from ether - petroleum ether, m.p. 254-255°C. (Found: C, 66.0; H, 4.8; N, 8.75; $C_{26}H_{23}N_3O_6$ requires C, 65.9; H, 4.85; N, 8.8%); δ : 8.25-6.48(m, 12H, ArH), 4.93(d, 1H, 2-H, J7.96Hz), 4.81(d, 1H, 4-H, J7.52Hz), 3.90 and 3.81(2xs, 2x3H, 2xOMe), 3.81(t, 1H, 1-H, J8.37Hz), 3.66(t, 1H, 5-H, J7.73Hz), and 2.1(br, 1H, NH); ν_{max} 3320, 1710, 1590, 1500 and 1380 cm^{-1}; m/z(%) 473(M^+,1.5), 300(100), 285(13), 270(5), 269(6), 239(6) and 149(6).

28a. This isomer was not purified but its structure was assigned on the basis of the ^1H n.m.r. spectrum of the pale yellow solid residue obtained from the mother liquors of (27a). δ ($CDCl_3$ + one drop D_2O): 8.28-6.44(m, 12H, ArH), 4.68(d, 1H, 2-H, J7.95Hz), 4.60(d, 1H, 4-H, J7.15Hz), 3.83 and 3.82(2xs, 2x3H, 2xOMe), 3.82(m, 1H, 1-H), 3.48(dd, 1H, 5-H, J7.22Hz and 9.49Hz).

4-(2'-Methoxyphenyl)-2-(4'-nitrophenyl)-7-phenyl-6,8-dioxo-3,7-diazabicyclo[3.3.0}octane (27b) and (28b). Obtained (80%) as a 4:1 mixture of isomers (27b) and 28(b).

(27b). Obtained as colourless prisms from methanol, m.p. 232-234°C. (Found: C, 67.4, H, 4.7; N, 9.2; $C_{25}H_{21}N_3O_5$ requires C, 67.7; H, 4.75, N, 9.5%); δ 8.27-6.94(m, 12H, ArH), 4.99(d, 1H, 2-H, J 7.99Hz), 4.83(d, 1H, 4-H, J7.72Hz), 3.94(s, 3H, OMe), 3.88(t, 1H, 1-H, J7.99Hz), 3.67(t, 1H, 5-H, J7.8Hz), and 1.57(br, 1H, NH); ν_{max} 3300, 1710, 1600, 1510 and 1380 cm^{-1}; m/z(%) 443(M^+, 3), 270(100), 240(16), 85(14), and 83(22).

28b. The structure of this isomer was assigned on the basis of the ^1H n.m.r. spectrum of the yellow residual solid obtained from the mother liquors of (27b). δ ($CDCl_3$ + 1 drop D_2O) 8.24-6.82(m, 12H, ArH), 4.76(d, 1H, 2-H), 3.93(d, 1H, 4-H), 3.88(s + m, 3H, OMe overlapping with N-H and 1-H) and 3.62(dd, 1H, 5-H).

4-(2',4'-Dimethoxyphenyl)-2-(3'-nitrophenyl)-7-phenyl-6,8-dioxo-3,7-diazabicyclo[3.3.0]octane (27c) and (28c). Obtained (81%) as a 3:1 mixture of (27c) and (28c).

27c. Crystallized from chloroform - petroleum ether as pale yellow prisms, m.p. 240-242°C (Found: C, 65.75, H, 5.05; N, 8.6; $C_{26}H_{23}N_3O_6$ requires C, 65.95; H, 4.9; N, 8.9%); δ 8.44-6.49(m, 12H, ArH), 4.92(d, 1H, 2-H, J7.9Hz), 4.80(d, 1H, 4-H, J7.9Hz), 3.91 and 3.81(2xs, 2x3H, 2xOMe), 3.81(t, 1H, 1-H), 3.64(t, 1H, 5-H, J7.7Hz) and 0.09(br, 1H, NH); ν_{max} 3310, 1710, 1610, 1500, 1530 and 1380 cm^{-1}; m/z(%) 473(M^+,2), 300(100), 285(15), 270(19), and149(11).

(28c). δ 8.77-6.16(m, 12H, ArH), 4.66(d, 1H, 2-H, J7.82Hz), 4.58(d, 1H, 4-H, J7.13Hz), 3.87 and 3.86(2 x s + m, 2x3H, 2xOMe, overlapping with 1-H) and 3.51(dd, 1H, 5-H, J7.19Hz and 9.52Hz).

4-(2',4'-Dimethoxyphenyl)-2-(4'-pyridyl)-7-phenyl-6,8-dioxo-3,7-diazabicyclo[3.3.0]octane (31a) and (32a). Obtained as a 4:1 mixture (88%) of (31a) and (32a).

(31a). Obtained as colourless rods from chloroform-petroleum ether, m.p. 235-236°C. (Found: C, 69.7; H, 5.4; N, 9.8; $C_{25}H_{23}N_3O_4$ requires C, 69.9; H, 5.4; N, 9.8%); δ 8.63-6.47(m, 12H, ArH), 4.88(d, 1H, 2-H, J7.94Hz), 4.66(d, 1H, 4-H, J7.45Hz), 3.90 and 3.81(2 x s, 2x3H, 2xOMe), 3.76(t, 1H, 1-H, J7.90Hz), 3.63(t, 1H, 5-H, J7.70Hz and 2.14(br, 1H, NH); ν_{max} 3320, 1705, 1590, 1500 and 1380 cm^{-1}; m/z(%) 429(M^+,2.5), 428(31), 427(7), 257(15), 256(90) and 83(21).

32a. Obtained as an impure yellow solid residue from the mother liquors of (31a). The compound was not further purified and its structure was assigned on the basis of the ^{1}H n.m.r. spectrum of the crude solid. δ 8.63-6.45(m, 18H, ArH), 4.63(d, 1H, 2-H, J7.88Hz), 3.95(d, 1H, 4-H), 3.80 and 3.78(2xs + m, 2x3H, 2xOMe, overlapping with 1-H), and 3.71(dd, 1H, 5-H).

4-(2'-Methoxyphenyl)-2-(3'-pyridyl)-7-phenyl-6,8-dioxo-3,7-diazabicyclo[3.3.0]octane (29b), (31b) and (32b). Obtained (88%) and a 1.6:3.8:1 mixture of (31b), (32b) and (29b).

31b. Obtained as colourless prisms from chloroform -petroleum ether, m.p. 200-202°C. (Found: C, 71.45; H, 5.25; N, 9.9; $C_{24}H_{21}N_3O_3$ requires C, 72.2; H, 5.25; N, 10.5%); δ 8.05-6.93(m, ArH, 13H), 4.94(d, 1H, 2-H, J7.87Hz), 4.73(d, 1H, 4-H, J6.69Hz), 3.94(s, 3H, OMe), 3.88(t, 1H, 1-H, J7.8Hz), 3.61(t, 1H, 5-H, J7.8Hz) and 2.3(br, 1H, NH); ν_{max} 3330, 1710, 1590 and 1500 cm^{-1}); m/z(%) 399(M^+,1.5), 226(100), 227(16), 211(11), 195(7), 119(8) and 91(8).

The structures of isomers (31b) and (29b) were assigned on the basis of the ^{1}H n.m.r. spectra of variously enriched mixtures of both isomers.

32b. 8.9-6.9(m,ArH, 13H), 4.72(d, 1H, 2-H, J7.74Hz), 4.55(d, 1H, 4-H, J7.3Hz), 3.88(s, 3H, OMe), 3.8-3.7(dd, 1H, 1-H), 3.57(dd, 1H, 5-H, J7.3 and 9.5Hz) and 2.01(br, 1H, NH).

29b. 8.9-6.9,(ArH, 13H), 5.22(s, 1H, 2-H), 4.94(d, 1H, 4-H, J8.36Hz), 3.83(s, 3H, OMe), 3.88-3.7(m, 2H, 1-H and 5-H) and 2.01(br, 1H, NH).

4-(2',4'-Dimethoxyphenyl)-2,2,7-tri(phenyl)-6,8-dioxo-3,7-diazabicyclo[3.3.0]octane (35). Obtained (80%) as colourless prisms from chloroform -petroleum ether, m.p. 254-255°C. (Found: C, 75.7; H, 5.6; N, 5.4. $C_{32}H_{28}N_2O_4$ requires C, 76.15; H, 5.6; N, 5.55%); δ 7.63-6.44(m, 18H, ArH), 4.52(d, 1H, 2-H, J8.41Hz), 4.20(d, 1H, 1-H, J7.62Hz), 3.79(s, 6H, 2xOMe), and 3.78(dd, 1H, 5-H, J7.58 and 8.14Hz); ν_{max} 3310, 1710, 1610, 1500 and 1380 cm^{-1} m/z(%) 503(M-1,5), 427(9), 331(100), 316(13), 167(8) and 165(9).

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