Tetrahedron Vol 46, No 5, pp 1599-1610, 1990
Printed in Great Britain

0040-4020/90 $3 00+ 00
Pergamon Press plc

X=Y-ZH Systems as Potential 1,3-Dipoles. Part 26.[1,2] 1,5-Electrocyclisation and Tandem 1,5-Electrocyclisation-Aldol Type Condensation Processes in Imines.

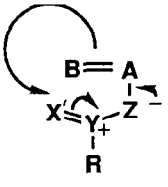
Ronald Gngg,[a,*] H Q Nimal Gunaratne,[b]
Deirdre Henderson,[b] and Visuvanathar Sridharan [a]

a School of Chemistry, University of Leeds, Leeds LS2 9JT
b Chemistry Department, Queen's University, Belfast, Northern Ireland BT9 5AG

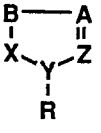
(*Received in UK 7 November* 1989)

Abstract A 1,2- prototropy route and an iminium ion route to vinyl azomethine ylides are described In both cases the vinyl azomethine ylides undergo 1,5-electrocyclisation to dihydropyrroles In the former case the 1,5-electrocyclisation is solvent sensitive and competes with a prototropic process giving the imine of an α, β-unsaturated α-amino ester The mechanism and solvent sensitivity are discussed In the latter case the dihydropyrrole reacts further with aldehydes via an aldol type condensation

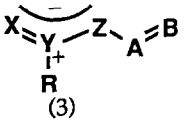
1,3-Dipolar cycloaddition reactions represent the most ubiquitous method for the synthesis of 5-membered heterocycles [3,4] In cases where the 1,3-dipolar species is conjugated to a double bond (homo-or hetero polar) (1) an intermolecular process, 1,5-electrocyclisation (1) ⇌ (2), may occur[5] provided the 1,3-dipole and the additional double bond moiety have, or can achieve, the required configuration [i e (1) as opposed to (3)] There are also analogous 1,5-electrocyclisations involving the corresponding anionic[6] and cationic[7] species (4) and (5)



(1)



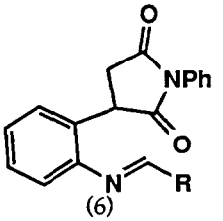
(2)



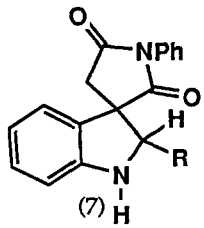
(3)

(4)

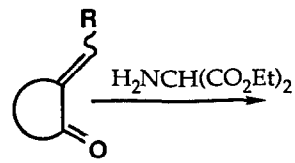
(5)



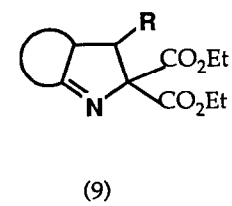
(6)



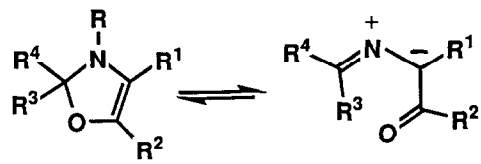
(7)



(8)



(9)



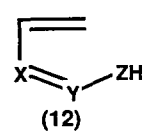
(10) (11)

All these 1,5-electrocyclisations involve 6π-electron disrotatory ring closures[8] [apart from (5) which is a 4π-electron system], and the general scope of such processes was reviewed some ten years ago [9] More recent developments include the utilisation of such processes in photochromic systems,[10] the 1,5-electrocyclisation of (6) -> (7), [11] and of (8) -> (9) [12] Vedejs has used the reverse process, the ring opening of oxazolines (10) -> (11) to generate azomethine ylides [13] 1,5-Electrocyclisations forming oxazolines[8] and oxazoles[14] have been known for some time

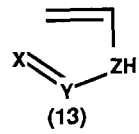
Our interest in 1,5-electrocyclisations arose from our ongoing program of devising simple new methods for generating 1,3-dipoles [15-19] For example we have demonstrated that certain X=Y-ZH systems undergo thermal equilibration with their 1,3-dipolar tautomers [X=Y(H)-Z] via 1,2-prototropy [15] Vinylogues of such systems are potential sources of 1,5-dipoles (1) and there are two types of vinylogous X=Y-ZH systems, (12) and (13) Location of the vinyl moiety on the sp^3 - centre in (13) obviates stereochemical problems However, location of the vinyl group on the sp^2 centre permits both favourable (12) and unfavourable (14) configurations

The recently reported conversion of (8) -> (9) would appear to be an example of the 1,5-electrocyclisation of a dipole derived from a precursor of type (12) although it was not interpreted in these terms We prepared imines (15) and (16) from phenylglycine methyl ester and the appropriate aldehydes These imines exist as single stereoisomers, presumably the E-isomers, i e these precursors are of type (14) It was hoped that thermal equilibration with the corresponding dipole (3) might subsequently lead to a further equilibration with small amounts of the derived dipole of configuration (1) In the event the imines (15) and (16) were recovered unchanged on heating in boiling toluene and showed a tendency to decompose at higher temperatures Evidence that the corresponding azomethine ylides were forming in boiling toluene was obtained from trapping experiments with N-phenylmaleimide Thus (15) gives (17) as a single stereoisomer in 79% yield whilst (16) gives (18) in 90% yield

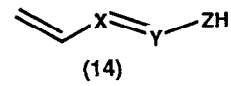
The acid (19)[20] was esterified and condensed with 2-naphthaldehyde to afford imine (20), a type (13) dipole precursor, in good yield When (20) was heated in xylene - d_{10} at 110°C in an n m r tube experiment it afforded a mixture of the 1,5-electrocyclisation product (22) and the double bond isomer (24) of the original imine (Table 1) (Scheme 1)



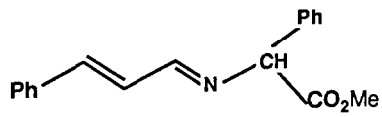
(12)



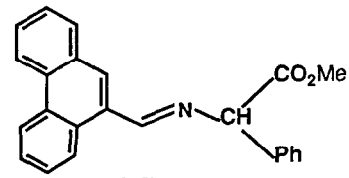
(13)



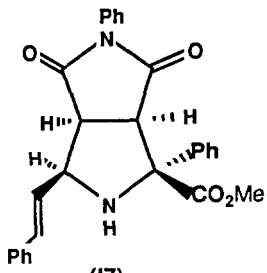
(14)



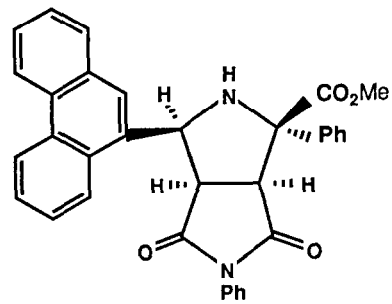
(15)



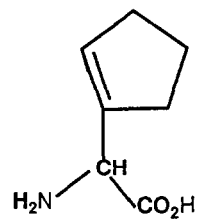
(16)



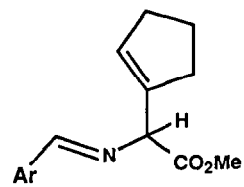
(17)



(18)

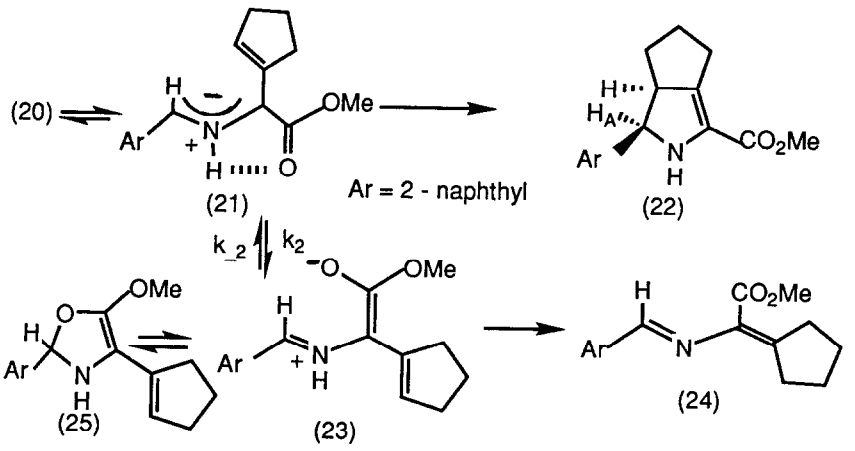


(19)



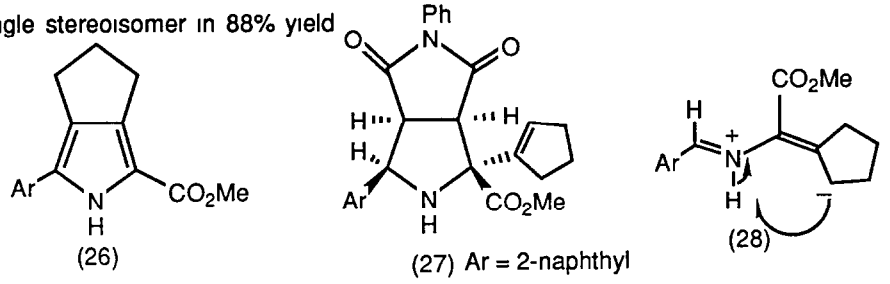
(20)

We have ample evidence[21,22] that thermal 1,2-prototropy in imines of α-amino esters is a kinetically controlled process and generates dipoles with configurations analogous to (21) Reasons for the stereospecific generation of a single dipole have been discussed [21,22] Dipole (21) has the correct configuration for a 1,5-electrocyclisation which is expected to occur in a disrotatory manner The product (22) is obtained as a single stereoisomer and is readily separated from (24) by preparative t l c (silica) The latter compound decomposes (hydrolysis) on silica The stereochemistry of (22) is assigned on the basis of the Woodward-Hoffmann rules [7] The dihydropyrrole (22) was further characterised by oxidation to the pyrrole (26) (90%) with DDQ Further evidence for formation of



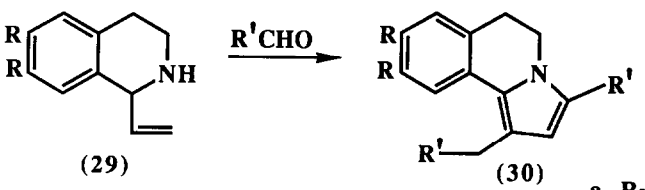
Scheme 1

azomethine ylide (21) was obtained by trapping the dipole with N-phenylmaleimide to give (27) as single stereoisomer in 88% yield



The double bond isomer (24) of the original imine could arise by an inter- or intra-molecular proto transfer An intramolecular proton transfer (28, arrows) requires stereomutation of the dipole (21) , (23) Such dipole stereomutation has been observed[21,22] although it usually requires aryl substituent at both the 1- and 3- positions of the dipole moiety 1- Aryl-3-alkyl substituted azomethine ylide usually show very little tendency to stereomutate [21,22] However, (21) is a 1-aryl-3-vinyl substitute azomethine ylide and would be expected to resemble the 1,3-diaryl case The 1,5-electrocyclisatio step is slow compared to the rate of dipole formation as shown qualitatively by the reaction times fc the conversion of (20) to (22)/(24) (17 5h, 110°C, xylene) compared to that for formation of (27) (<1h 110°C, toluene) Moreover, both the half life for the overall conversion of (20) to a mixture of (22) an (24) and the ratio of (22) to (24) are solvent dependent (Table 1)

The results presented in Table 1 show that addition of acids or bases promote intermolecular proto transfer leading to short half lives and to predominant or exclusive formation of (24) Non-polar aproti solvents (toluene, xylene) result in slower reaction and a modest predominance of (22) Acetonitrile a polar aprotic solvent, results in the slowest reaction and the highest proportion of (22) The resu for DMF appears atypical and may reflect traces of water or amine in the solvent A possibl explanation for the results with acetonitrile, toluene, and xylene, as solvent is that in these cases

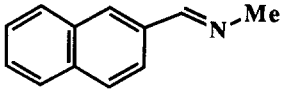


(29)

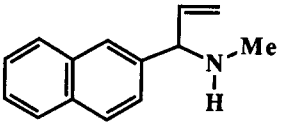
a.R=H
b.R=OMe

(30)

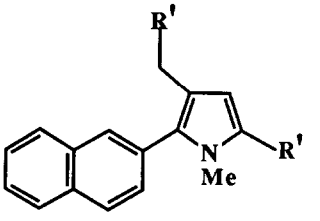
a. R=H, R'=2-pyridyl
b. R=H, R'=2-furyl
c. R=H , R'=PhCO
d. R=H, R'=CO_2Et
e. R=H, R'=2-thienyl
f. R=H, R'=p-$MeO_2C_6H_4$
g. R=H, R'=2-pyridyl



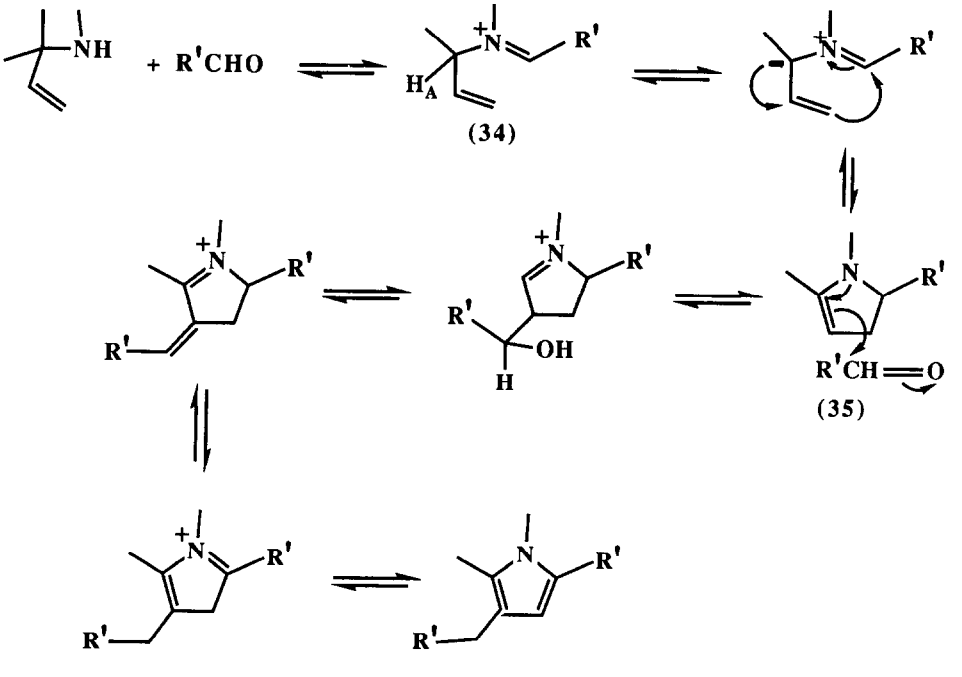
(31)



(32)



(33) R'=2-pyridyl



(34)

(35)

Scheme 2

Table 1 Half life of (20) and effect of solvent on competing 1,5-electrocyclisation and double bond migration

Solvent[a]	$t_{1/2}$(h)	Product ratio (22) (24)
MeCN	109	5 5 1
xylene[b]	ca 2h	1 93 1
toluene	43	1 20 1
pyridine	5 7	1 24
DMF	3 7	1 32
toluene/$MeCO_2H$(1eq)	0 63	c
toluene/DABCO(1eq)[d]	0 48	c

a Substrate concentration 0 137M, and reactions carried out at 80°C unless otherwise noted

b Substrate concentration 0 14M, reaction temperature 110°C Reaction complete in 17 5h

c Sole product (24)

d DABCO = 1,4-diazobicyclo[2 2 2]octane

proton transfer leading to (24) is wholly intramolecular (28, arrows) and proceeds via the dipole (23) (Scheme 1) Thus in acetonitrile the initially formed more polar dipole (21) is stabilised by the polar solvent relative to (23) and both the electrocyclisation (21) -> (22) and the isomerisation (21) -> (23) are relatively slow but the former is faster i e k_1, k_{-2}, > k_2, k_3 In a non-polar solvent (toluene, xylene) the less polar (23) is more stable than (21) and both the isomerisation rate and the 1,5-electrocyclisation rate are enhanced with the latter still marginally the greater The reduced polarity of (23) results from the favourable juxtaposition of the electronegative oxygen atom to the electrophilic iminium carbon atom It may well be that the oxazolidine (25) participates in the equilibrium

A second series of 1,5-electrocyclisation reactions has been developed based on our iminium ion route to azomethine ylides [16] The l-vinyltetrahydroisoquinoline (29a) was prepared by addition of vinylmagnesium bromide to the corresponding 3,4-dihydroisoquinoline Reaction of (29a) with a range of aldehydes afforded the 4,5-dihydropyrrolo[1,2-a]isoquinolines (30) (Table 2) The dimethoxy derivative (29b) reacts similarly (Table 2) The acyclic 2-vinyl secondary amine (32) was prepared from (31) by reaction with vinylmagnesium bromide Reaction of (32) with pyridine-2-carboxaldehyde afforded (33) (Table 2)

The genesis of the pyrrolic products (30a-g) and (33) is outlined in Scheme 2 Imine formation labilises proton H_A in (34) and deprotonation furnishes a 1,5-dipole which undergoes a 1,5-electrocyclisation to the enamine (a dihydropyrrole) (35) The enamine condenses with a second mole of aldehyde and subsequent dehydration, prototropy, and deprotonation furnishes the pyrrolic products Thus the latter arise from a tandem 1,5-electrocyclisation-aldol type condensation process Attempts to stop the reaction at the dihydropyrrole (35) stage were unsuccessful

Table 2 Pyrroles derived from the reaction of 2-vinyl secondary amines with aldehydes (toluene, 110°C)

Amine	Aldehyde(R^1)[a]	Reaction Time(h)	Product	Yield(%)
29a	2-pyridyl	3 5	30a	80
29a	2-furyl	5 0	30b	40
29a	PhCO	5 0	30c	47
29a	EtO_2C	2 75	30d	58
29a	2-thienyl	8 0	30e	53
29a	p-$MeO_2CC_6H_4$	7 0	30f	77
29b	2-pyridyl	6 0	30g	60
32	2-pyridyl	12 0	33	40

a All reactions employed two moles of aldehyde to 1 mol of the appropriate amine

Experimental General experimental details were as previously noted [23] Petroleum ether refers to the fraction with b p 40-60°C

Imines

Methyl N-(cinnamylidene)phenylglycinate (15) Phenylglycine methyl ester (1 65g, 0 01 mol) and cinnamaldehyde (1 32g, 0 01 mol) were dissolved in dry benzene (50ml) and molecular sieves (4A, 3g) added and the mixture stirred at room temperature for 16h The mixture was filtered and the filtrate evaporated under reduced pressure to leave the product as a thick pale yellow oil (2 5g) which decomposed on attempted distillation and was therefore used directly for the next stage Accurate mass 279 1259 $C_{16}H_{17}NO_2$ requires 279 1259, δ 8 05(d, 1H, J8 15Hz, CH=N), 7 49-6 92(m, 12H, ArH + 2 x olefinic H), 5 08(s,1H, CHN) and 3 72(s, 3H, OMe), ν_{max} (film) 3020, 2950, 1730, 1630, 1600, 750, 735 and 700cm $^{-1}$, m/z(%) 279(M^+,3) 221(19), 220(100), 194(13), 116(7), 115(36), 106(54), 91(11) and 77(17)

Methyl N-(9-phenanthrylidene)phenylglycinate (16) Prepared from phenylglycine methyl ester hydrochloride (1 03g, 5 mmol) and 9-phenanthraldehyde (1 01g, 5 mmol) using method B [23] The product (1 5g, 85%) crystallised as colourless plates from methanol, m p 132-134°C (Found C, 81 4, H, 5 45, N, 3 75 C_{24} $H_{19}NO_2$ requires C, 81 55, H, 5 4, N, 3 95%), δ 8 98(s, 1H, CH=N), 9 17-7 31(m, 14H, ArH), 5 33(s,1H, CHN) and 3 79(s, 3H, OMe), ν_{max} 3080, 2940, 2840, 1740, 1645, 1450, 770, 750, 730 and 720cm^{-1}, m/z(%) 353(M^+,26), 294(100), 216(31), 204(67), 191(22), 176(12), 91(11) and 77(9)

Cyclopent-1-enylglycine methyl ester hydrochloride Cyclopent-1-enylglycine (2 0g, 14 mmol)[20] was suspended in dry methanol (50 ml) and saturated with dry hydrogen chloride The mixture was kept at room temperature for 16h The methanol was then removed under reduced pressure and the residue crystallised from methanol to afford the product (2 4g, 90%) as colourless rods, m p 170-174°C(d) (Found C, 45 4, H, 7 85, N, 6 5 C_8 $H_{14}ClNO_2$ H_2O requires C,45 85, H, 7 7, N, 6 7%) δ(DMSO-d_6)

8 80(br s, 3H, NH_3), 5 92(s,1H, C=CH), 4 68(s, 1H, CH), 3 76(s, 3H, OMe) and 2 68-1 68(m, 6H, 3 x CH_2), ν_{max} 3400, 2900, 1750, 1510, 1260 and 1245cm^{-1}

Methyl N-(2-naphthylidene)cyclopent-1-enylglycinate (20) Cyclopent-1-enylglycine methyl ester hydrochloride (575mg, 3 mmol) was dissolved in dry methanol (30ml) containing sodium methoxide [from sodium (69mg)] 2-Naphthaldehyde (468mg, 3 mmol) was added and the resulting mixture stirred at ambient temperature for 16h The mixture was then filtered and the filtrate evaporated under reduced pressure The resulting residue was extracted with chloroform, the extracts combined, dried (Na_2SO_4) and evaporated under reduced pressure to leave a pale yellow solid which was crystallised from methanol to give the product (750mg, 85%), as colourless plates, m p 119-120°C (Found C, 77 6, H, 6 55, N, 4 65 $C_{19}H_{19}NO_2$ requires C, 77 8, H, 6 55, N, 4 75%), δ 8 45(s, 1H, CH=N), 8 12-7 50(m, 7H, ArH), 5 78(dd, 1H, C=CH), 4 85(s, 1H, CH), 3 80(s, 3H, OMe), 2 40(m, 4H, 2 x CH_2C=C) and 1 96(m, 2H, CH_2), ν_{max} 3040, 2925, 2820, 1735, 1630, 1430, 860, 830 and 750 cm^{-1}, m/z(%) 293(M^+,26), 235(19), 234(100), 154(16), 141(9), 127(6) and 81(26)

N-Phenylmaleimide Cycloadducts

Methyl c-4-styryl-2,7-diphenyl-6,8-dioxo-3,7-diazabicyclo[3 3 0]octane-r-2-carboxylate(17) Methyl N-(cinnamylidene)phenylglycinate (56mg, 0 2 mmol) and N-phenylmaleimide (38mg, 0 22 mmol) were dissolved in toluene(0 5ml) and the solution heated in a sealed tube at 110°C for 1h The product (71mg, 79%) crystallised from toluene as colourless needles, m p 249-251°C(Found C, 74 3, H, 5 3, N, 5 95 $C_{28}H_{24}N_2O_4$ requires C, 74 3, H, 5 35, N, 6 2%), δ 7 70-7 22(m, 15H, ArH), 6 76(d, 1H, J 16 9Hz, Ph CH=CH), 6 37(dd, 1H, Ph CH=CH), 4 21(d, 1H, J 7 7Hz, 1-H), 4 00(br t, 1H, 4-H), 3 77(s, 3H, OMe) and 3 48(dd, 1H, J 7 7 and 7 35Hz, 5-H), ν_{max} 3440, 1765, 1710, 1630, 1490, 965, 730 and 690cm^{-1}, m/z(%) 452(M^+, 6), 394(30), 393(100), 279(12), 246(11), 220(9), 115(10), 91(3) and 77(3)

Methyl c-4-(9-phenanthryl)-2,7-diphenyl-6,8-dioxo-3,7-diazabicyclo[3 3 0]octane-r-2-carboxylate(18) Prepared in analogous manner to that described above from methyl N-(9-phenanthrylidene) phenylglycinate (71mg) and N-phenylmaleimide (38mg) (reaction time 12h) The product (95mg, 90%) crystallised from toluene as colourless prisms, m p 290°C(Found C, 77 9, H, 4 95, N, 5 35 $C_{34}H_{26}N_2O_4$ requires C, 77 55, H, 5 0, N, 5 3%), δ 8 71-6 84(m, 19H, ArH), 5 07(d, 1H, J10Hz, 4-H), 4 38(d, 1H, J 6 25Hz, 1-H), 3 88(dd, 1H, 5-H) and 3 85(s, 3H, OMe), ν_{max} 3310, 3060, 2950, 1775, 1735, 1715, 1500, 1380, 750, 745 and 720cm^{-1}, m/z(%) 526(M^+, 3), 468(11), 354(26), 353(96), 293(100), 278(17), 221(21) and 189(20)

Methyl c-4-(2^1-naphthyl)-2-(cyclopent-1-enyl)-7-phenyl-6,8-dioxo-3,7-diazolbicyclo[3 3 0]octane-r-2-carboxylate(27) Prepared as above from methyl N-(2-naphthylidene) cyclopentenylglycinate(59mg) and N-phenylmaleimide(38mg) with a reaction time of 1h The cycloadduct crystallised out on cooling the reaction mixture and was recrystallised from methanol to yield the product (81mg, 88%) as colourless prisms, m p 226-228°C(Found C, 74 8, H, 5 65, N, 5 95 $C_{29}H_{26}N_2O_4$ requires C, 74 65, H, 5 6, N, 6 0%), δ 7 99-7 0(m, 12H, ArH), 5 86(t, 1H, C=CH), 4 67(d, 1H, J 9 17Hz, 4-H), 3 95(d, 1H, J 7 43Hz, 1-H), 3 89(s, 3H, OMe), 3 62(dd, 1H, 5-H) and 2 58-1 98(m, 6H, 3 x CH_2), ν_{max} 3310, 3050, 2940, 2840, 1770, 1735, 1710, 1490, 750 and 695cm^{-1}, m/z(%) 466(M^+, 11), 407(100), 239(39), 233(49),

173(20), 127(5) and 77(14)

1,5-Electrocyclisation Reactions

Methyl 3-aza-4-(2[1]-naphthyl)bicyclo[3 3 0]oct-1-ene-2-carboxylate(22) Methyl N-(2[1]-naphthylidene) cyclopent-1-enylglycinate (150mg) was dissolved in dry toluene (1 5ml) and heated at 110°C in a sealed tube under an atmosphere of argon for 24h The solvent was then removed under reduced pressure to leave a thick oil whose p m r spectrum showed it to comprise a 1 2 1 mixture of (22) and (24) Separation by preparative t l c on silica eluting with 3 2 v/v petroleum ether-ether resulted in decomposition of (24) and afforded (22) as a gum (110mg, 73%) which resisted attempted crystallisation Accurate mass 293 1419 $C_{19}H_{19}NO_2$ requires 293 1416, δ 7 90-7 20 (m, 7H, ArH), 5 45(dd, 1H, J2 55 and 8 63Hz, 4-H), 3 92 (s, 3H, OMe), 3 13(m, 1H, 5-H) and 1 97-0 88(m, 6H, 3 x CH_2), ν_{max} 3400, 2920, 2840, 1710, 1625, 1445, 1430, 1300 and 740cm^{-1}, m/z(%) 293(M^+, 100), 262(8), 261(29), 234(80), 233(53), 225(28), 166(49) and 127(22)

Oxidation of (22) Compound (22) (100mg, 0 34 mmol) and DDQ(77mg, 0 34 mmol) were dissolved in dry benzene and the solution stirred at ambient temperature for 16h The reaction mixture was then filtered and filtrate evaporated under reduced pressure to give a thick brown oil which afforded a colourless solid on trituration with ether Crystallisation of this solid from methanol afforded the product(26) (89mg, 92%) as colourless needles, m p 200-201°C(Found C, 78 2, H, 5 95, N, 4 85 $C_{19}H_{17}NO_2$ requires C, 78 35, H, 5 9, N, 4 8%), δ 9 00 (br s, 1H, NH), 7 93-7 43(m, 7H, ArH), 3 88(s, 3H, OMe), 2 99 and 2 90(2 x t, 2 x 2H, 2 x pyrrole-CH_2) and 2 48(m, 2H, CH_2), ν_{max} 3270, 3040, 2940, 1660, 1620, 1445, 1100, 850, 805 and 740cm^{-1}, m/z(%) 291(M^+, 100), 259(57), 232(6), 231(13) and 127(3)

1-Vinyl-1,2,3,4-tetrahydroisoquinoline(29a) A solution of 3,4-dihydroisoquinoline (13 1g, 0 1 mol) in dry THF(100ml) was stirred and cooled to 0°C Vinylmagnesium bromide (1M solution in THF, 250ml) was added dropwise under an atmosphere of nitrogen maintaining the temperature at O°C The mixture was then stirred at ambient temperature for 2 5 days Saturated ammonium chloride solution was then added dropwise to destroy the excess vinylmagnesium bromide and the THF removed under reduced pressure The residual oil was partitioned between water (200ml) and chloroform (100ml), and the aqueous layer extracted with chloroform (2 x 100ml) The combined chloroform layers were washed with brine, dried (anhy Na_2SO_4) and evaporated under reduced pressure to afford a pale yellow oil which upon distillation gave the product (11g, 70%) as a colourless oil, b p 70-72°C/0 05mm (Found C, 83 1, H, 8 2, N, 8 85 $C_{11}H_{13}N$ requires C, 83 0, H, 8 15, N, 8 8%), δ 7 29(m, 4H, ArH), 5 95(m, 1H, CH_2=C<u>H</u>), 5 26(m, 2H, <u>CH_2</u>=CH), 4 46(d, 1H, ArCHN), 3 28 and 3 16(2 x m, 2 x 1H, NCH_2), and 2 84 and 2 78(2 x m, 2 x 1H, $ArCH_2$), m/z(%) 159(M^+, 32), 132(100), 130(19), 115(14) and 77(10)

1-Vinyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline(29b) Prepared in an analogous manner to that described above The product (60%) was a thick pale yellow oil and was admixed with a byproduct (30%) which appeared to be the corresponding N-methylated compound Attempted distillation led to decomposition and so the crude product was used directly for the next stage making allowances for the

contaminant

(29b) δ 6 5(s, 2H, ArH), 6 0(m, 1H, CH=CH_2), 5 25(m, 2H, CH=CH_2), 4 4(d, 1H, ArCHN), 3 83 and 3 80(2 x s, 2 x 3H, 2 x OMe), 3 2(m, 2H, NCH_2) and 3 0(m, 2H, $ArCH_2$)

1-(2^1-Naphthyl) allyl methylamine (32) Prepared in an analogous manner to that described above The product (40%) was a pale brown oil which decomposed on attempted distillation and was therefore used directly for the next stage (below) δ 7 8-7 4(m, 7H, ArH), 5 99(m, 1H, CH=CH_2), 5 3 and 5 23(2 x d, 2 x 1H, CH=CH_2), 4 22(d,1H, ArCH) and 2 39(s, 3H, NMe), m/z(%) 197(M^+, 59), 196(32), 182(13), 170(100), 128(18) and 70(42)

General Procedure for Reaction of 2-Vinyl Secondary Amines with Aldehydes The 2-vinyl secondary amine (0 5 mmol) and the aldehyde (1 mmol) were dissolved in dry toluene (75ml) and the solution boiled under reflux using a Dean-Stark trap for the period shown in Table 2 The solvent was then removed under reduced pressure Crude products were purified by flash chromatography and/or crystallisation or by distillation as appropriate Yields are collected in Table 2

1-(2^1-Pyridylmethyl)-3-(2^1-pyridyl)-4,5-dihydropyrrolo[1,2-a]isoquinoline(30a) Colourless prisms from ether-petroleum ether, m p 110-111°C(Found C, 78 5, H, 5 65, N, 11 7 $C_{23}H_{19}N_3$ requires C, 78 15, H, 5 4, N, 11 9%), δ 8 61-7 03(m, 12H, ArH), 6 48(s, 1H, 2-H), 4 68(t, 2H, NCH_2), 4 37(s, 2H, pyridyl-CH_2), and 3 02(t, 2H, $ArCH_2$), m/z(%) 337(M^+, 100), 260(47), 259(52), 130(35) and 92(31)

1-(2^1-Furylmethyl)-3-(2^1-furyl)-4,5-dihydropyrrolo[1,2-a] isoquinoline(30b) Colourless prisms from ether-hexane, m p 85-87°C(Found C, 80 0, H, 5 5, N, 4 25 $C_{21}H_{17}NO_2$ requires C, 80 0, H, 5 4, N, 4 45%), δ 7 13-7 53(m, 6H, ArH and furyl α-H), 6 04-6 46(m, 4H, furyl β-H), 6 34(s, 1H, 2-H), 4 25(t, 2H, $ArCH_2$), 4 12(s, 2H, furyl-CH_2) and 3 02(t, 2H, NCH_2), ν_{max} 3142, 2888, 1600, 1472, 1421, 1326, 1007, 788, 754 and 738 cm^{-1}, m/z(%) 315(M^+, 100), and 248(11)

1-Benzoyl-3-benzoylmethyl-4,5-dihydropyrrolo[1,2-a]isoquinoline(30c) Orange prisms from ether-petroleum ether, m p 45-47°C(Found C, 82 85, H, 5 8, N, 3 8 $C_{27}H_{21}NO_2$ requires C, 82 85, H, 5 35, N, 3 4%), δ 7 25-8 04(m, 14H, ArH), 6 66(s, 1H, 2-H), 4 75(t, 2H, $ArCH_2$), 4 48(s, 2H, $COCH_2$) and 3 10(t, 2H, NCH_2), ν_{max} 2923, 1683, 1615, 1446, 1408, 1261 and 688 cm^{-1}, m/z(%) 391(M^+, 3), 286(12), 272(6), 258(5), 186(12) and 105(100)

Ethyl 3-ethoxycarbonylmethyl-4,5-dihydropyrrolo[1,2-a]isoquinoline-1-carboxylate(30d) Colourless oil, b p 180-186°C/0 2mm(Found C, 70 0, H, 6 55, N, 4 65 $C_{19}H_{21}NO_4$ requires C, 69 7, H, 6 4, N, 4 3%), δ 7 63(d, 1H, ArH), 7 19-7 30(m, 3H, ArH), 6 98(s, 1H, 2-H), 4 60(t, 2H, $ArCH_2$), 4 29 and 4 19(2 x q, 2 x 2H, 2 x OCH_2Me), 3 75(s, 2H, CH_2CO), 3 00(t, 2H, NCH_2) and 1 36 and 1 26(2 x t, 2 x 3H, 2 x OCH_2Me), ν_{max} 2977, 2935, 1731, 1697, 1244, 1083, 1029 and 766cm^{-1}, m/z(%) 327(M^+, 50), 255(100), 241(50), 226(28), 186(56) and 103(67)

1-(2^1-Thienyl)-3-(2^1-thienylmethyl)-4,5-dihydropyrrolo[1,2-a]isoquinoline(30e) Pale yellow needles from ether-petroleum ether, m p 117-119°C(Found C, 72 75, H, 4 65, N, 3 8 $C_{21}H_{17}NS_2$ requires C, 72 6, H, 4 9, N, 4 05%), δ 6 89-7 52(m, 10H, ArH + thienyl-H), 6 30(s, 1H, 2-H), 4 31(s, 2H, thienyl CH_2), 4 19(t, 2H, $ArCH_2$) and 3 00(t, 2H, NCH_2), ν_{max} 2923, 1599, 1482, 1460, 1417, 766, 748, 736 and 691 cm^{-1}, m/z(%) 347(M^+,100), 264(35), and 250(6)

1-(4[1]-Methoxycarbonylphenyl)-3-(4[1]-methoxycarbonylbenzyl)-4,5-dihydropyrrolo[1,2-a]isoquinoline(30f) Colourless plates from ether, m p 155-157°C(Found C, 77 5, H, 5 7, N, 3 3 $C_{29}H_{25}NO_4$ requires C, 77 2, H, 5 55, N, 3 1%), δ 8 06 and 7 98(2 x d, 2 x 2H, ArH), 7 21-7 45(m, 8H, ArH), 6 17(s, 1H, 2-H), 4 23(s, 2H, $ArCH_2$), 4 18(t, 2H, $ArCH_2$), 3 93 and 3 90(2 x s, 2 x 3H, 2 x OMe), and 2 99(t, 2H, NCH_2), ν_{max} 2948, 1716, 1607, 1428, 1274, 1101 and 766cm^{-1}, m/z(%) 451(M^+, 100), 420(3), 392(4), 316(29) and 210(9)

1-(2[1]-Pyridylmethyl)-3-(2[1]-pyridyl)-7,8-dimethoxy-4,5-dihydropyrrolo[1,2-a]isoquinoline(30g) Colourless plates from methanol-petroleum ether, m p 159-160°C(Found C, 75 25, H, 5 05, N, 10 45 $C_{25}H_{23}N_3O_2$ requires C, 75 55, H, 5 83, N, 10 55%), δ 8 58-6 74(m, 10H, ArH), 6 5(s, 1H, 2-H), 4 67(t, 2H, NCH_2), 4 36(s, 2H, pyridyl CH_2), 3 86 and 3 68(2 x s, 2 x 3H, 2 x OMe) and 2 96(t, 2H, $ArCH_2$), m/z(%) 397(M^+, 100), 382(13), 230(13), 192(24), 170(33) and 169(49)

1-Methyl-2-(2[1]-naphthyl)-3-(2[1]-pyridylmethyl)-5-(2[1]-pyridyl)pyrrole(33) Obtained as a pale brown oil by flash chromatography of the crude product Accurate mass 375 1748 $C_{26}H_{21}N_3$ requires 375 1735, δ 8 6-7 03(m, 14H, ArH), 6 53(s, 1H, 2-H), 4 04(s, 2H, pyridyl CH_2) and 3 80(s, 3H, NMe), m/z(%) 375(M^+, 29), 263(40), 235(11), 214(10), 212(17), 196(34), 107(70) and 79(100)

We thank the Department of Education for Northern Ireland, I C I Colours and Fine Chemicals, Queen's University and Leeds University for support

References

1 Part 25 Grigg, R , Armstrong, P , *Tetrahedron*, 1989, 45, 7581-7586

2 A portion of this work has appeared in preliminary form Grigg, R , Gunaratne, H Q N , *Tetrahedron Letters*, 1983, 24, 4457-4460

3 Huisgen, R , *Angew Chem Int Edn Engl*, 1963, 2, 565-598 and 633-645

4 1 3-Dipolar Cycloaddition Reactions, Edit , Padwa, A , Pub, Wiley, 1984, vols 1 and 2

5 Reinhoudt, D N , Visser, G W , Verboom, W , Benders, P H , and Pennings, M L M , *J Am Chem Soc* , 1983, 105, 4775-4781, Gesche, P , Klinger, F , Riesen, A , Tschamber, T , Zehnder, M , and Streith, J , *Helv Chim Acta*, 1987, 70, 2087-2097, Klarner, F G , Schroer, D , *Agnew Chem , Int Edn Engl* , 1987, 26, 1294-1295, Saalfrank, R W , Ackerman, E , Fischer, M , and Wirth, U , *Chem Ber*, 1987, 120, 2003-2006, Boyd, G V , Cobb, J , Lindley, P F , Mitchell, J C , and Nicolau, G A , *J Chem Soc , Chem Commun* , 1987, 99-101

6 Hunter, D H , Sim, S K , *J Am Chem Soc* , 1969, 91, 6202-6203, idem, *Can J Chem* , 1972, 50, 678-689, Hunter, D H , Steiner, R P , *ibid*, 1975, 53, 355-365, Shoppee, C W , Henderson, G N , *J Chem Soc , Chem Commun* , 1974, 561-562

7 Shopee, C W , Cooke, B J A , *J Chem Soc , Perkin Trans 1*, 1974, 189-192

8 Woodward, R B , Hoffmann, R , *Angew Chem , Int Edn Engl* , 1970, 8, 781-854

9 Taylor, E C , Turchi, I J , *Chem Rev* , 1979, 79, 181-231, Huisgen, R , *Angew Chem , Int Edn Engl* , 1980, 19, 947-973

10 Durr, H , *Angew Chem , Int Edn Engl*, 1989, 28, 413-431

11 Veenstra, S J , Fortgens, H P , Vijn, R J , DeJong, B S , and Speckamp, W N , *Tetrahedron*, 1987, 43, 1147-1156, Dijkink, J , Zonjee, J N , de Jong, B S , and Speckamp, W N , *Heterocycles*, 1983, 20, 1255-1258

12 Itoua, G B , Laronze, J -Y , *Synthesis*, 1987, 353-357

13 Vedejs, E , Grissom, J W , *J Org Chem*, 1988, 53, 1876-1882 and 1882-1887, *idem*, *J Am Chem Soc*, 1988, 110, 3238-3246

14 Hofle, G , Steglich, W , *Chem Ber*, 1971, 104, 1408-1419

15 Grigg, R , *Quart Rev Chem Soc*, 1987, 16, 89-121, Grigg, R , Dowling, M , Jordan, M W , and Sridharan, V , *Tetrahedron*, 1987, 43, 5873-5886

16 Ardill, H , Grigg, R , Sridharan, V , Surendrakumar, S , Thianpatanagul, S , and Kanajun, S , *J Chem Soc , Chem Commun*, 1986, 602-604

17 Grigg, R , Heaney, F , *J Chem Soc , Perkin Trans* 1, 1989, 198-200

18 Aly, M F , Grigg, R , Thianpatanagul, S , and Sridharan, V , *J Chem Soc , Perkin Trans* 1, 1988, 949-955 Grigg, R,, Surendrakumar, S , Thianpatanagul, S , and Vipond, D , *ibid*, 1988, 2693-2701 Grigg, R , Idle, J , McMeekin, P , Surendrakumar, S , and Vipond, D , *ibid*, 1988, 2703-2713 Ardill, H , Grigg, R , Sridharan, V , and Surendrakumar, S , *Tetrahedron*, 1988, 44, 4953-4966 Ardill, H , Grigg, R , Sridharan, V , and Malone, J F , *J Chem Soc , Chem Commun*, 1987, 1296-1298

19 Armstrong, P , Grigg, R , and Warnock, W J , *J Chem Soc Chem Commun*, 1987, 1325-1327, Armstrong, P , Grigg, R , Surendrakumar, S , and Warnock, W J , *ibid*, 1987, 1327-1328,Grigg, R , Dorrity, M R J , Heaney, F , Malone, J F , Rajviroongit, S , Sridharan, V , and Surendrakumar, S , *Tetrahedron Letters*, 1988, 29, 4323-4324, Grigg, R , Markandu, J , *ibid*, 1989, 30, 5489-5492

20 Nunami, K , Suzuki, M , and Yoneda, N , *J Chem Soc , Perkin Trans* 1, 1979, 2224-2229

21 Grigg, R , Kemp, J , and Warnock, W J , *J Chem Soc ,Perkin Trans* 1, 1987, 2275-2283, Grigg, R , Jordan, M W , Malone, J F , and Armstrong, P , *Tetrahedron*, 1985, 41, 3547-3558

22 Amornraksa, K , Grigg, R , Gunaratne, H Q N , Kemp, J , and Sridharan, V , *J Chem Soc , Perkin Trans* 1, 1987, 2285-2296

23 Grigg, R , Gunaratne, H Q N , and Kemp, J , *J Chem Soc , Perkin Trans* 1, 1984, 41-46