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1,3-Dipolar Cycloaddition Reaction of α,β-unsaturated Esters and Lactones with Diazomethane.

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Abstract: 1,3-Dipolar cycloaddition of diazomethane to the α,β-unsaturated esters and lactones such as **2-4, 6-8, 10** and **13** occurs in a stereoselective manner affording conjugated Δ^2-pyrazolines. E and Z isomers of D-mannitol lead to identical product which was cyclised to investigate the absolute stereochemistry of the product. The regiospecificities of all the reactions are consistent with **FMO** coefficients obtained through **AM1** calculations.

To introduce asymmetry in the 1,3-dipolar cycloaddition, a number of approaches have been used,[1a-1c] including reaction of the 1,3-dipole and dipolarophile in an inter[1b] and intramolecular[1d,1e] fashion. Recently, we reported the 1,3-dipolar cycloaddition of nitrone to enantiomerically pure esters and lactones[1f] with alkoxy-substitutent in γ-position leading to the regio and stereoselective formation of the isoxazolidines.

These results, as well as the interesting results of Fraser-Reid and co-workers[2] for the antithrombic activity of pyrazoline derivatives prompted us to investigate the addition of diazomethane to various unsaturated esters and lactones and thereby to observe the diastereoselectivity. Apart from selectivity aspects, the pyrazolines formed should be of interest as precursors for the synthesis of cyclopropane derivatives.

To the best of our knowledge, there are only a few examples of the cycloaddition of diazomethane derivatives, to open chain α,β-unsaturated esters and carbon bearing a chiral alkoxy substitutent at γ-position. Patzel and co-workers[3] report on the addition of diazo derivatives to α,β-unsaturated γ-alkoxy or γ-amino-ketones. Cycloaddition of nitrone, nitrile oxide and diazo derivatives to the menthyloxy furanone were carried out by Feringa and co-workers.[4] In all the cases cycloaddition leads to mixture of diastereomers.

In continuation of our effort to utilise the heterocyclic compounds as dipolarophiles in 1,3-dipolar cycloaddition reaction, we have investigated the cycloaddition of stereogenic unsaturated esters and lactones with diazomethane. In case of **2** and **3**, the absolute stereochemistry of the product as well as the facial selectivity was established by performing cyclisation experiments.

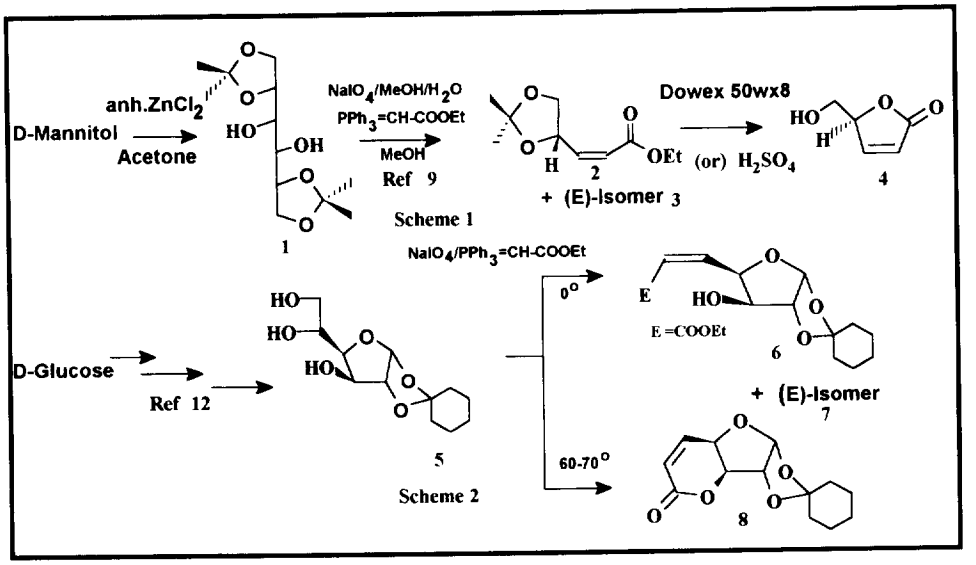
Results and Discussion:

The addition of an unsymmetrical olefin can, in principle occur in two directions and frequently does so even when the double bond is strongly polarized by substituents. In most of the cycloadditions, the diazoalkane carbon atom being more nucleophilic adds to the electron deficient centre of the dipolarophile to yield, in normal sense, the 3-substituted cycloadduct. The formation of other regiomer by cycloaddition via abnormal or inverse sense is thought to arise due to steric effects since this phenomenon occurs mainly in cycloadditions involving disubstituted diazomethanes such as diphenyl diazomethane. The *syn-anti* and *exo-endo* isomerism in diazoalkanes have been dealt in several papers[5-7] including the more sophisticated π-α* effect proposed by Franck Neumann.[8]

In this work, the influence of regio-, stereo- and facial selectivity in diazomethane cycloadditions has been studied. For this purpose, some stereochemically well defined dipolarophiles were synthesized (scheme 1-4) and condensed with diazomethane. The choice of dipolarophiles was governed by the following considerations;

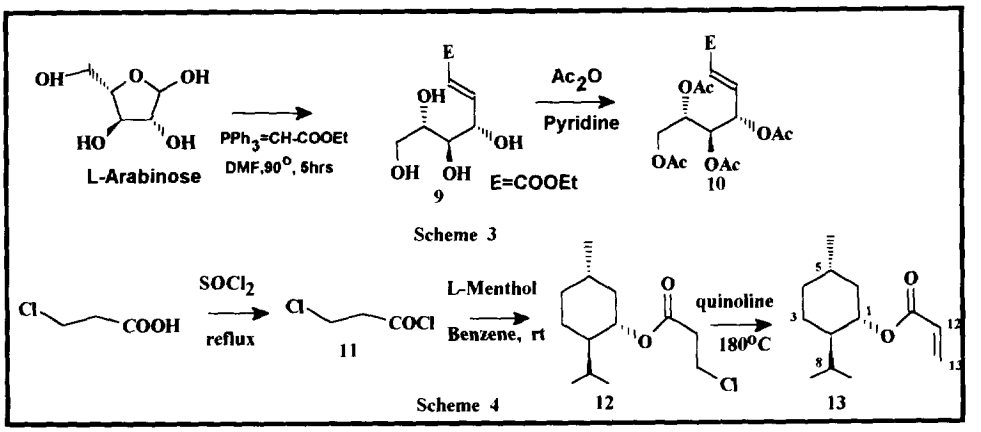
a. the remoteness of the stereogenic center from the site of addition, **b**. nature and geometry of electrophilic olefins (E and Z) and **c**. the presence or absence of allylic acyloxy or alkoxy groups.

Compound **2-4**[9], **10**[10] and **13**[11] were synthesized according to the literature procedure with slight modification. The dipolarophiles **6-8** were synthesized from D-glucose following our previously described method.[12]



As expected from the regiochemistry of diazomethane addition, in all the cases only one regiomer was formed viz, the carbon bearing the electron withdrawing carboxy group becomes attached to the

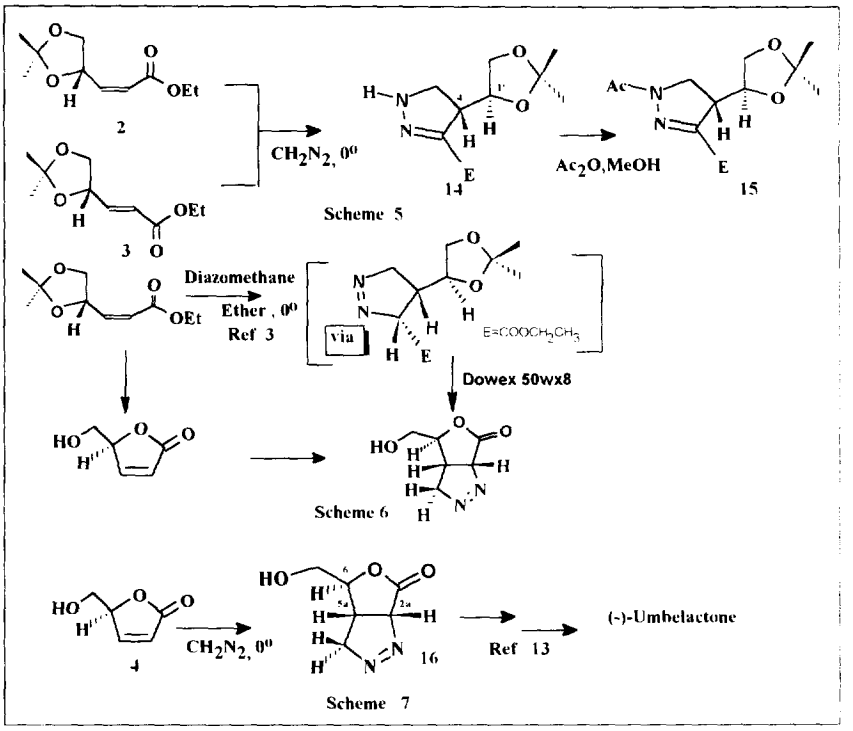
nitrogen of the diazomethane thereby forming 3-substituted regiomers exclusively. Taking the regiospecificity into consideration, two diastereomeric products were anticipated in each case of cycloaddition of dipolarophiles except in case of **13**.



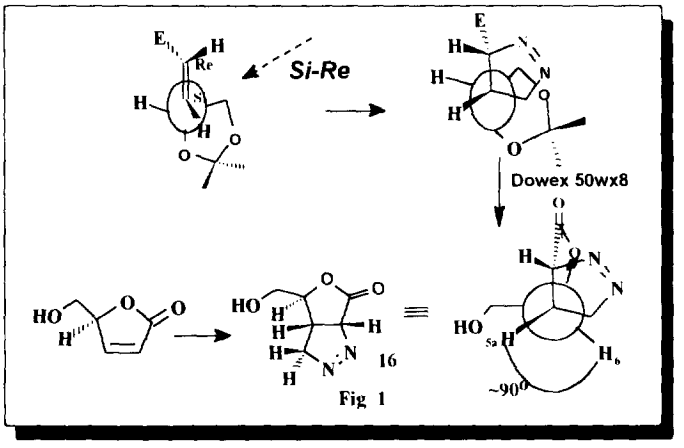
The dipolarophiles **2** and **3** were treated with 1.5 eq of diazomethane as an ethereal solution at 0°C. The pyrazolines obtained were immediately N-acetylated, purified and crystallized to give the corresponding N-acetyl-2-pyrazolines (scheme 5).

In the previous work, Patzel and co-workers[3] reported the formation of two diastereomers in different ratios, at different temperatures, but we could isolate only one of the two isomers. ^{1}H NMR of the adduct **15** showed a multiplet at δ 3.60 ppm which integrates for one proton was assigned to the H-4 proton. The proton on C-5 , H_a, H_b appeared as double doublets at δ 3.96 ppm and 4.20 ppm respectively. A one proton multiplet at δ 4.62 ppm was assigned to H-1' proton. The relative configurations at C-4 and C-1' in the adduct **14** could not be determined by spectroscopic means. Hence, the adduct was lactonised using Dowex. The dipolarophile **2**, after the addition of diazomethane at 0°C was treated with Dowex resin (scheme 6) to provide the cyclic adduct **16**, which is the main precursor for the synthesis of naturally occurring α,β-butenolide, (+)-Umbelactone.[13] The lactonisation should be easier when the alkoxycarbonyl and alcohol functions are *cis*-disposed about the pyrazoline ring. This was confirmed by reacting diazomethane with the furanone **4**, synthesised by acid cyclisation of **2** (scheme 7).

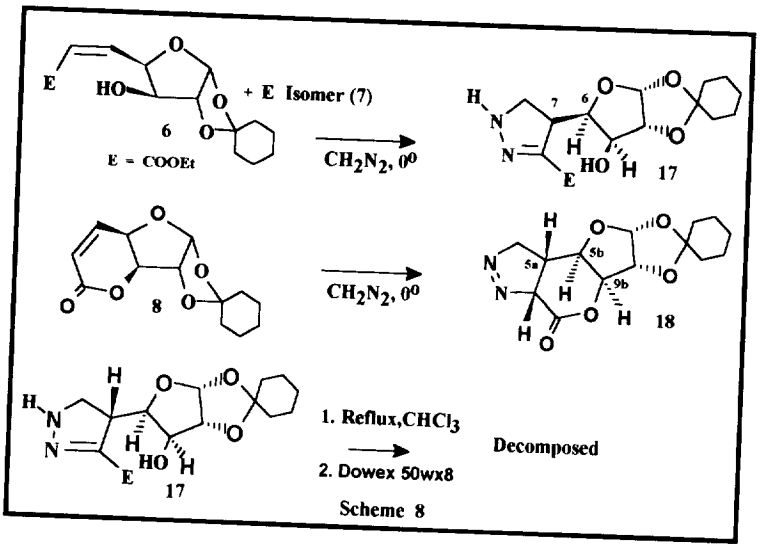
The proton H-6 of the adduct **16** appears as doublet of double doublet at δ 5.05 ppm with $J_{5a,6}$ 1.46 Hz. The small value (1.46 Hz) implies a dihedral angle of ~90° between H-5a and H-6 (fig 1). This implicitly confirms the *trans* relationship between these two protons and hence this adduct arises from an *antifacial* approach of the reactant in the transition state.



The formation of **16** in turn supports structure **14**, which accrues from the ***Si-Re*** face of the dipolarophile (fig 1). This finding clearly demonstrates that the primarily formed Δ^1-pyrazoline must have undergone cyclisation to the expected pyrazoline **16**.



Encouraged by the above results, our attention was next turned to chiral six-membered unsaturated lactone **8** and esters **6** and **7** derived from D-glucose which could serve as models for the synthesis of several optically active compounds. Very similar results were obtained in the cycloaddition of diazomethane to lactones and esters under identical conditions (scheme 8).



Scheme 8

Esters **6** and **7** provided the cycloadduct **17,** in which the proton H-7 absorbs at δ 3.56 ppm as a doublet of triplet with $J_{7,6}$ 3.20 Hz indicating the *trans* relationship between these protons (H-7 & H-6), which in turn indicates an *antifacial* approach of the reactant in the transition state. Pyranone **8** provided a single adduct **18** . In this case, appearance of H-5b as a triplet with $J_{5a,5b\ \&5b,9b}$ 1.2 Hz indicates the *trans* relationship. All these assignments were corroborated by **NOESY** experiments. The observed **2D** nuclear Overhauser effect (**nOe,** mixing time,1.0 sec) interactions are indicated in fig 2. The product decomposed while attempting the cyclisation in the case of the Z-ester **6**.

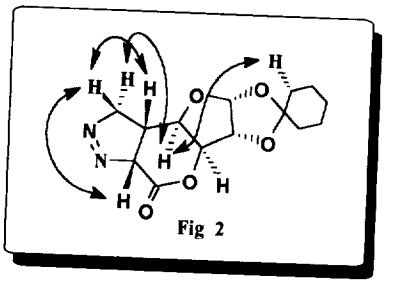
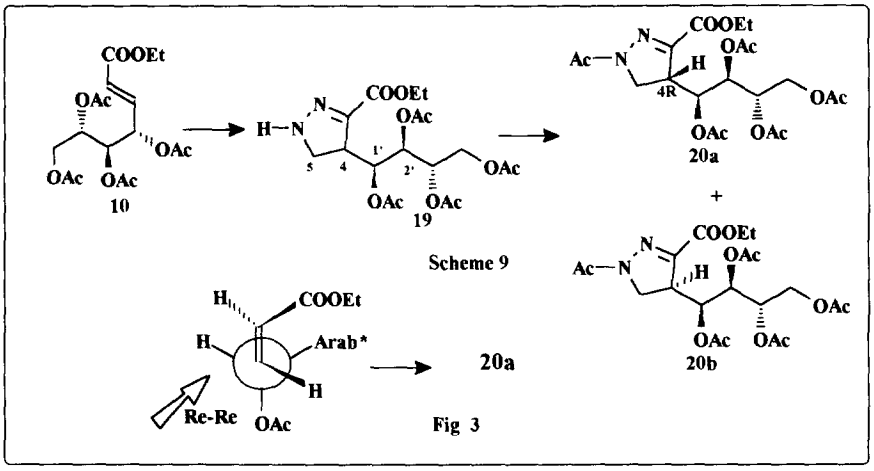


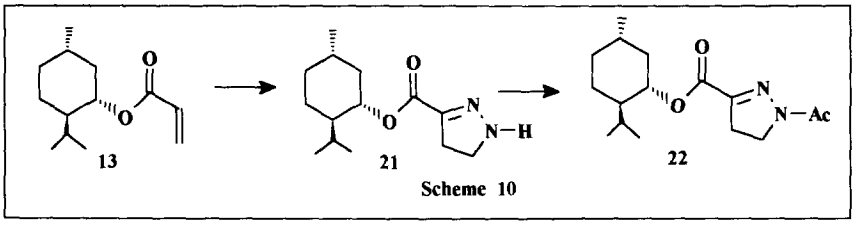
Fig 2

A four-fold excess of diazomethane was allowed to react with dipolarophile **10** in dry ether at 0°C (scheme 9). The only product formed quantitatively was immediately acetylated, purified and crystallised.

^{1}H NMR spectrum of compound **20** showed a multiplet at δ 3.85 ppm which was assigned to the H-4 proton. The gem methylene protons of C-5 appeared together as multiplet at δ 4.28 ppm. The methyl of N-acyl appeared downfield as a sharp singlet at δ 2.4 ppm compared to the four acetate singlets. Although, the absolute stereochemistry on C-4 has not been determined, we believe that only one of the diastereomers **20a** was obtained, which could be the 4R isomer, originated by addition of diazomethane to the less hindered ***Re-Re*** face of the dipolarophile **10** (fig 3). ^{13}C NMR of the compound **20a** further justified the structure proposed which is comparable with the diazoadduct of D-galactose derivative reported by Galbis and co-workers.[14,15]



Since dipolarophile **13** is mono substituted and the dipole cannot differentiate between its two faces, two diastereomers would still result. However, since the products obtained from the dipolarophiles are all homogenous by **HPLC**, and only one product is formed in each case, we believe that originally the 1-pyrazolines are obtained, which finally rearrange to 2-pyrazoline. In the case of menthyl acrylate (scheme 10), ^{1}H NMR analysis of the adduct **22** showed a triplet at δ 4.0 ppm integrating for two protons which was assigned to the H-5 proton. In addition, a triplet integrating for two protons appeared at δ 3.1 ppm which was unambiguously assigned to protons on C-4.



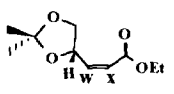
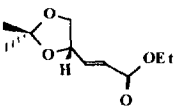
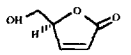
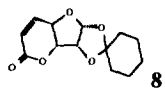
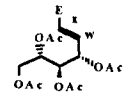
In previous studies, the diastereoselectivities of the cycloaddition of various 1,3-dipoles to several α,β-unsaturated esters were investigated.[3,16,17] However, based on theoretical calculations, it was

predicted that these reactions should be "almost stereorandom".[17] On the basis of the results obtained, it can be emphasized that the allylic hetero-atom is playing the important role of directing the incoming nucleophile *anti* with respect to its geometry, whereas, the bulky group is playing less important role compared to that of the heteroatom. This confirms the fact that transition state geometry having allylic hetero-atom in *anti* disposition with respect to the incoming diazomethane is preferred because of the analogous results obtained during the cycloaddition of nitrones to the said dipolarophiles. Furthermore due to immolation of one of the stereogenic centres in the 1-pyrazoline derivatives, the number of stereoisomers obtained will be reduced to half the number of originally anticipated products i.e. one each, for each case because of the prototropic rearrangement of initially formed 1-pyrazolines to the respective 2-pyrazolines.

AM1 Studies:

In order to rationalise the observed regioselectivities during the addition of diazomethane to dipolarophiles qualitatively, we have performed **FMO** analysis[18] on the **AM1** calculated frontier orbitals to determine HOMO-LUMO control of the 1,3-dipolar addition reaction.[4] All HOMO-LUMO orbital energies (table 1) were obtained from **AM1** optimised geometries.

Table 1: **AM1** calculated **FMO** energies and atomic contributions

Dipole/Dipolarophile		ΔE(ev)	W	X
CH_2=N=N	HO	-8.822	0.760	-0.627
	LU	1.072	0.561	0.515
 **2**	HO	-10.449	0.262	0.343
	LU	-0.216	-0.649	0.488
 **3**	HO	-10.574	-0.347	-0.420
	LU	-0.198	-0.611	0.467
 **4**	HO	-10.857	0.434	0.523
	LU	-0.467	-0.66	0.533
 **8**	HO	-10.576	0.069	0.079
	LU	-0.541	0.645	-0.525
 **10**	HO	-10.869	0.225	-0.216
	LU	-0.216	0.467	-0.443

The computed frontier orbital energies of diazomethane and the dipolarophiles **2-4,8** and **10** (table 1), reveal that the smaller HOMO-LUMO gap involves the LUMO of the dipolarophile and HOMO of the dipole. Hence the reaction is predicted to be dipole HOMO controlled in all the cases. With electron deficient dipolarophiles, this leads to 3-substituted pyrazoles.

The atom with the larger HOMO coefficient on the dipole consistently prefers to approach the atom with the larger LUMO coefficient on the dipolarophile. Thus, the observed regiochemistry is correctly predicted by the FMO's derived from AM1 calculations.

EXPERIMENTAL :

All the solvents were dried and distilled before use. The organic extracts were dried over anhydrous Na_2SO_4. IR spectra were recorded on a Perkin Elmer 688 Spectrometer. NMR spectra were recorded on a Varian VXR 300S, Varian FT 60A or Varian 100 spectrometer using $CDCl_3$ as the solvent containing TMS as an internal standard. Chemical shifts (δ) are expressed as ppm down field with respect to TMS. J values are expressed in Hz. Optical rotations were measured with a Shimadzu digital polarimeter. HPLC purifications and analyses were performed on a Dupont 8800 series chromatographic system with gradient controller. GLC analyses were carried out on Shimadzu 15A chromatograph. Mass spectra were recorded on a CEC-21-110B double focusing mass spectrometer operating at 70 eV using the direct inlet system. Analytical samples were dried in vacuum desiccator at room temperature for 12h. Microanalyses were performed on Carlo Erba Mode; 1106 elemental analyser.

Diazomethane was generated by treating N-nitroso-N-methyl-*p*-toluene sulphonamide with KOH in ethanol.

Ethyl 3-[3a(R), 5(R), 6(S), 6a(R)-tetrahydro-6-hydroxy spiro[cyclohexane-1,2-furo[2,3-d][1,3]-dioxalan-5-yl]propionate.(6,7) & 3a(R),4a(R),8a(S),8b(R)-tetrahydro spiro[cyclohexane-1',2-[7H][1,3]dioxalo[5',4':4,5]furo[3,3-b]pyran-7-one (8) :

To a slurry of 2.5g (10.6mmol) of triol **5** in 45 ml of 6% $NaHCO_3$ solution (4:1 EtOH/H_2O) at 0°C was added dropwise 2.7g(1.27mmol) of $NaIO_4$ in 10ml of 1:1 EtOH/H_2O solution. The mixture was stirred at room temperature for 2h and cooled to 0°C. To this cooled mixture was added a slurry of 10.62g (31.8mmol) of (carbethoxymethylene)triphenylphosporane in 20ml of ethanol. The mixture was stirred at 0°C for 24h and extracted four times with 100ml of $CHCl_3$. The combined extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford a viscous yellow oil. This oil was taken up in 300ml of 80% hexane-ether solution, the precipitated triphenylphosphine oxide was filtered, and the filtrate was concentrated under reduced pressure to afford a pale yellow oil. Flash chromatography on silica gel with hexane-50% ether-hexane gradient afforded 3.1g(94%) of mixture of (E), (Z) isomer and cyclised compound.

Z-Isomer (6):

$[\alpha]_{D^{28}}$ =-39.0(c12.9,$CHCl_3$); vmax (thin film)/cm^{-1}: 3400, 2950,2900, 1630, 1650, 1390, 850; ^{1}HNMR

(300 MHz) δ : 6.29(dd, J =11.9,6.4 Hz, 1H, 5-H), 5.96(m, 2H, 1-H, 6-H), 5.54 (m, 1H, 4-H), 4.55(d, J = 3.7 Hz, 1H, 2-H), 4.50(bs, 1H, 3-H), 4.14(q, 2H, $OC\underline{H}_2CH_3$), 2.42(bs, OH), 1.39-1.93(m, 10H, CH_2), 1.30(t, 3H, $OCH_2C\underline{H}_3$).
13C-NMR (75 MHz) δ: 165.68(s), 143.91(d), 122.1(d), 112.49(s), 104.41(d),85.12(d), 78.86(d), 77.18(d), 60.62(t),36.48(t), 35.82(t), 24.89(t), 23.88(t),23.57(t),14.12(q);
MS: m/z 99(M+1, 12.6%), 298(4.7), 255(12.9), 253(11.2), 209(17.8), 112(40.9), 99(21.1), 81(40.7), 55(100).

Cyclic isomer 8:

$[\alpha]_D^{28}$ =+44.0(2.27,$CHCl_3$); ν_{max} (thin film)/cm^{-1}: 3100, 3000, 2900, 1760, 1650, 1390, 850; ^{1}HNMR (300 MHz) δ : 6.96(dd, J= 9.7, 5.7 Hz, 1H ,5-H), 6.23(d, J= 9.7 Hz, 1H, 6-H), 6.02(d, J= 3.7 Hz, 1H, 1-H), 4.81(m, 2H, 2-H, 3-H), 4.62(dd, J= 5.7, 3.1 Hz, 1H, 4-H), 1.41-1.75(m, 10H) ;
^{13}C-NMR(75 MHz) δ: 166.644(s), 138.58(d), 125.02(d), 113.01(s), 104.64(d), 83.30(d),82.313(d), 67.39(d), 36.21(t), 35.46(t), 24.55(t), 23.61(t), 23.27(t); MS: m/z 252 (M+,4.8%), 209(23), 137 (13.5), 85(81), 42(100).

Ethyl 4,5,6,7-tetra-O-acetyl (E) 2,3-dehydro 2,3 dideoxy L-arabino heptenoate (10) :

On heating L(+)-arabinose (15g;100mmol) with (carbethoxymethylene)triphenylphosporane (34.79g; 100 mmol) in DMF at 90°C for six hours, an excellent yield of Ethyl 2,3 decahydro-2,3 dideoxy L arabino heptenoate was obtained. Yield 70%, m.p. 133-135°C[Lit[10] 133-135°C], $[\alpha]_D^{20}$=-14.45°(c,2.77 H_2O) t.l.c., Rf.0.52, Solvent system nC_4H_9OH-H_2O-CH_3COOH, 4:2:1. Ethyl 2,3 dehydro-2,3 dideoxy -L-arabino heptenoate (10g) was dissolved in dry pyridine at room temperature and the solution cooled in ice water. To this was added gradually acetic anhydride (12 ml) at 0°C with stirring. The solution was allowed to stand overnight at room temperature. At the end of this period, it was poured slowly with stirring into ice water. A heavy oil separated out, which crystallised immediately. Recrystallisation from ethanol gave the dipolarophile **10** as needle shaped crystals. m.p 84°C (Lit[10], 84°C); $[\alpha]_D^{20}$ = -35.9 (c 5.25, $CHCl_3$).
ν_{max} (KBr)/cm^{-1}: 1750, 1720, 1668, 980, 960 ;
^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.1 (t, $COOCH_2C\underline{H}_3$), 2.02, 2.04 and 2.14 (4s, 12H, 4-OAc's), 4.2 (m,4H, 7-Ha, Hb, -$COOC\underline{H}_2CH_3$), 5.2 (m, 1H, H-6), 5.4 (dd, 1H, $J_{4,5}$=3.0, $J_{5,6}$=9 Hz, H-5), 5.7 (m, 1H, H-4), 5.9 (dd, 1H, $J_{2,3}$ =17.7, $J_{2,4}$= 1.5 Hz, H-2), 6.8 (dd, 1H, $J_{2,3}$ =17.7, $J_{3,4}$ =3 Hz, H-3,).

General procedure for diazomethane cycloaddition reaction.

A solution of dipolarophile(2.5mmol) in dry ether (25ml) was added dropwise to a solution of diazomethane(prepared from N-methyl-N-nitroso-p-toluenesulphonamide, 0.5g,12.5mmol) in ether

(30ml). After 4h at 0°C, the excess ether was removed under reduced pressure. The syrupy material obtained was N-acylated with acetic anhydride (5ml) in methanol (20ml) at refluxing temperature. The reaction was worked up to remove the traces of acid by washing with brine solution. Later, some of the products (**20a,22**) were purified by preparative HPLC (ODS column, 20%H_2O-MeOH).

Ethyl 1-acetyl-4(R)-4-4(S)-2,2-dimethyl-[1,3]-dioxolane-4yl)-4,5-dihydro-1H-pyrazole-3-carboxylate (15).

Yield 80%; ν_{max} (thin film)/cm^{-1}: 1740, 1710, 1680, 1210, 1050; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.29 and 1.48 (2s,6H, H-6',7'), 1.39(t, 3H, H-4'), 2.4(s, 3H -$NCOCH_3$), 3.60 (m, 1H, H-4), 3.66(dd, 1H, J = 8.5 and 7, H-2'a), 3.96 (t, 1H, J= 11.5 , H-5a), 4.12(dd, 1H, J=8.5 and 7.2, H-2'b), 4.20(dd, 1H, J=11.5 and 6.3, H-5b), 4.36(q, 2H, H-3'), 4.62(m,1H, H-1').; ^{13}C-NMR(75 MHz) δ: 13.9(c-4'), 21($NCO\underline{C}H_3$), 24.5, 25.89(C-6',7'), 45.9(c-4), 47.5(C-5), 61.6(C-3'), 67.6(C-2'), 73.21(C-1'), 109.6(C-5'), 147.04(C-3), 161.4(C=O), 169.9(N-C=O)

Anal. Calcd. for $C_{13}H_{20}N_2O_5$ (284,31): C: 54.92%, H: 7.09%, N: 9.85%, Found: C: 54.74%, H: 7.27%, N: 9.64%.

Cyclisation experiment:

After addition of diazomethane for 4h at 0°C, the reaction mixture was stirred in the presence of Dowex 50Wx8 resin until T.L.C. showed completion of the cycloaddition as well as cyclisation. After filtration and evaporation of the solvent, the crude material was chromatographed using 30% EtOAc-hexane to provide the cycloadduct .

Cycloadduct 16

Yield: 72%; νmax (neat)/cm^{-1}: 2990, 1755, 1575 ; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.14(m,1H, H-5a), 3.82 (dd, 1H, J=3.11 and 12.26, H-7'), 3.96(dd,1H, J=2.93, 12.26, H-7''), 4.44(dd, 1H, J=3.29, 6.59, H-5'), 4.67(m, 1H, H-5'), 5.05 (ddd, 1H, J=3.84, 4.03 and 1.46, H-6), 5.85(m,1H, H-2a); ^{13}C-NMR(75 MHz) δ: 34.91(d), 63.91(t), 86.52(t), 87.53(d), 95.41(d), 171.06(s); MS, m/e 156(95), 98(61), 97(100), 84(27), 69(51), 68(40), 55(8), 41(21), 38(18).

Anal. Calcd. for $C_6H_8N_2O_3$ (156.14): C: 46.15%, H: 5.60%, N: 17.94%, Found: C: 46.45%, H: 5.29%, N: 17.76%.

Cycloadduct 17

Yield: 63%; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.38(t,3H, J=7.17, $COOCH_2\underline{C}H_3$), 1.52-1.67(m,10H), 3.56(dt, 1H,J=10.68, 3.20, H-7), 3.79(t, 1H, J=10.68, H-8'), 3.98(s, 1H, H-5), 4.06(dt, 1H, J=10.68, 3.20, H-8''), 4.33(q,2H, $COO\underline{C}H_2CH_3$), 4.55(d,1H, J=3.20, H-6), 4.59(d, 1H, J=3.81, H-4a), 5.90(d,1H,

J=3.81, H-1a), 6.42(bs,1H, N-H); ^{13}C-NMR(75 MHz) δ: 14.35(q), 23.76-25.07(5t), 35.88(t), 36.53(d), 75.75(d), 82.43(d), 104.86(d), 112.53(s), 138.00(s), 160.15(s);
Anal. Calcd. for $C_{16}H_{24}N_2O_6$ (340.38): C: 56.46%, H: 7.11%, N: 8.23%, Found: C: 56.17%, H: 7.27%, N: 8.35%.

Cycloadduct 18

Yield: 71%; ν_{max} (neat)/cm^{-1}: 2995, 1745, 1570; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.35-1.72(m,10H), 2.97(m,1H, H-5a), 4.03(dd, 1H, J=1.22 and 0.61, H-9b), 4.33(t, 1H, J=1.22, H-5b), 4.65(dd, 1H, J-3.66, 0.61, H-9a), 4.83(dd, 1H, J=0.98 , 2.29, H-5'), 4.85(d, 1H, J=2.44, H-5"), 5.07(dt, 1H, J= 2.44, 9.02, H-2a), 5.85(d, 1H, J=3.66, H-6a);
Anal. Calcd. for $C_{14}H_{18}N_2O_5$ (294.31): C: 57.14%, H: 6.16%, N: 9.52%, Found: C: 57.59%, H: 5.87%, N: 9.45%.

Ethyl 1-acetyl-4,5-dihydro-4-(1',2',3',4'-tetraacetoxy butyl)-1-H-pyrazole-3-carboxylate (20a):

Yield: 98%; mp. 98°C; ν_{max} (KBr)/cm^{-1}: 3000, 1740, 1680, 1380, 1210, 1000; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.4(t, $COOCH_2C\underline{H}_3$), 2.02, 2.04 and 2.14(4s, 12H, 4x-$COCH_3$), 2.40(N-$COCH_3$), 3.85(m,2H, H-4), 4.28, 4.10(dd, 2H, H-4'a,4'b), 4.28(m,1H, H-5), 4.37(q, 2H, $COOC\underline{H}_2CH_3$), 5.13(m, 1H, H-3'), 5.3(dd, 1H, H-2'), 5.5(dd, 1H, H-1') ; ^{13}C-NMR(75 MHz) δ: 13.9($COOCH_2\underline{C}H_3$), 20.18, 20.41, 21.0(4, $COOCH_3$, N-$COCH_3$), 45.1(C-4), 47.8(C-5), 61.4($COO\underline{C}H_2CH_3$), 61.88(C-4'), 68.1(C-3'), 68.6(C-2'), 69.79(C-1'), 149.0(C-3), 161.0(-$\underline{C}OOCH_2$), 169.2(4-$COOCH_3$).

1-Acetyl-44,5-dihydro-1H-pyrazole-3-L(-)-menth-3'yl-carboxylate (22):

Yield: 85%; ν_{max} (thin film)/cm^{-1}: 1720, 1680, 1385, 1210, 1100, 1050 ; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.8(d, 3H, H-7', CH_3), 0.9(2s, 6H, H-9' and H-10')=2xCH_3), 2.40(N-$COCH_3$), 3.1(t,2H, H-4), 4.0(t,2H, H-5), 4.8(dt, 1H, H-3'); ^{13}C-NMR(75 MHz) δ: 16.45(C-9'), 20.38(C-10'), 21.7(C-7'), 23.6(C-5), 26.46(C-8'), 31.24(C-5), 31.3(N-COCH3), 33.9(C-6'), 40.5(C-2'), 44.8(C-4'), 46.7(C-4), 76.0(C-3'), 148(C-3), 161(-COO), 170(N-CO).

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