SYNTHESIS OF SOME NOVEL TRICYCLIC α- AMINOACID ESTERS AND POTENTIAL BIOACTIVE COMPOUNDS *VIA* 1,2-PROTOTROPY AND 1,3-APT CASCADE REACTIONS

H. Ali Dondas[a]* and Naciye Yaktubay Dondas[b]

a. Mersin University, Faculty of Pharmacy, Department of Chemistry, Mersin, 33342, Turkey

b. Çukurova University, Faculty of Medicine, Department of Pharmacology, 01330 Adana-Turkey

Abstract: Some novel cyclic α -aminoacid esters and potential bioactive compounds were prepared via thermal 1,2-prototropy- and 1,3-APT oxime nitrone-1,3-dipolar cycloaddition cascades reactions. This substrate allows the influence of the new stereocentres on the cascade to be assessed with respect to the configuration of the nitrone that is generated and the facial selectivity of the subsequent cycloaddition.

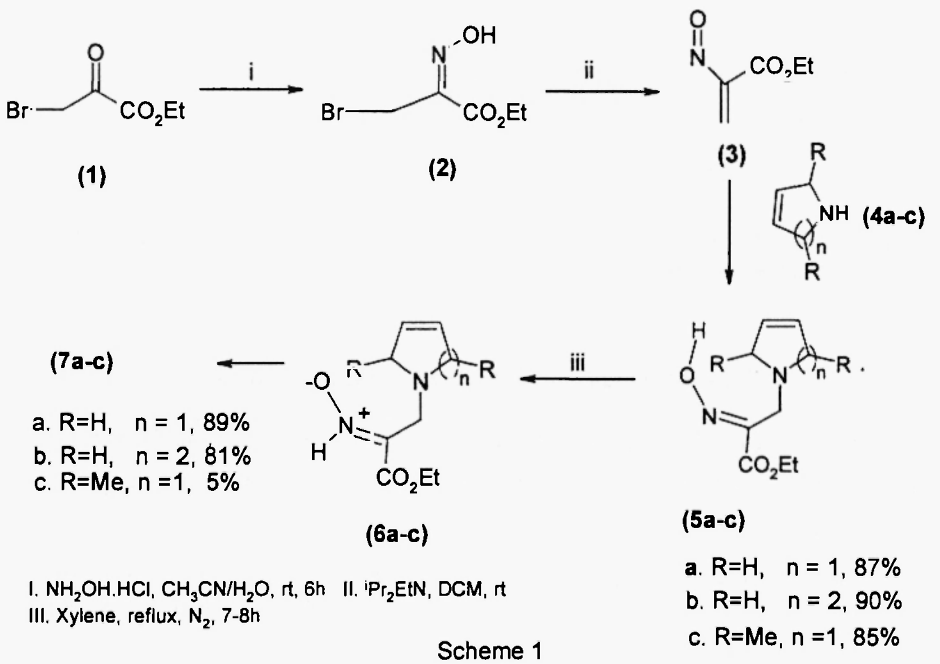
Introduction: 1,3-Dipolar cycloaddition (1,3-DC) reactions have developed considerably in recent years; stereochemistry of the cycloaddition reaction can be controlled by either choosing appropriate substrates or by using a metal complex as a catalyst. Several examples of 1,3-dipolar cycloadditions catalyzed by metal cations or metal complexes can be found in the literature[1-4].

The use of 1,2-prototropy-cycloaddition cascades for the synthesis of fused rings containing a bridgehead nitrogen atom, such as pyrrolizidines, indolizidines and quinolizidines is important as they occur in a number of alkaloids[4-6]. Over the past decade, Grigg and co-workers have developed a range of oxime based tandem nitrone generation/cycloaddition reactions in which the nucleophilicity of the nitrogen atom has been extensively exploited to assemble a broad spectrum of complex fused- bridged-, and spiro-cyclic isoxazolidine[7-18]. When an oxime reacts in either an inter- or an intra-molecular fashion with an alkene two tandem processes are possible in which involves tandem 1,2-prototropy/1,3-dipolar cycloaddition[8,9] and 1,3-azaprotio cyclotransfer (APT)/1,3-dipolar cycloaddition cascade.[10,11] Aspect of both these processes were studied as part of this work and the results are discussed.

Results and Discussion: In this paper, we report a series of 1,2 prototropy- and 1,3 APT- 1,3-dipolar cycloaddition reactions of a series of oximes which would produce potential bioactive compounds in one pot cascade reactions. In the case of 1,2-prototropy-cycloaddition route to novel cyclic α -aminoacid esters, oximes (**5a-c**) were prepared from corresponding amines (**4a-c**) as outlined in scheme 1 in good to excellent yield. The oximes (**5a,b**) were then smoothly underwent 1,2-prototropy followed intramolecular 1,3-dipolar cycloaddition to give aza-tricyclic compounds when heated in xylene at reflux temperature under nitrogen furnishing the isoxazolidines (**7a,b**) in 81-89% overall yield. The stereochemistry of cycloadducts were assigned by ^{1}Hnmr, ^{2}D COSY studies; n.O.e data and decoupling experiments (see experimental). When oxime (**5c**), which were prepared from 2,5-dimethyl-pyrroline, was boiled under reflux in xylene after 7h starting material along with trace amount (5%, ^{1}Hnmr) of desired product (**7c**) were present whilist 18h the mixture comprised starting material, trace amount of the desired product and decomposition products. Examination of the molecular model indicates that in this case the transition states for NH nitrone (**6c**) cycloaddition are imposible due to extreme steric deformations required for an effective overlap of the reactive centres.

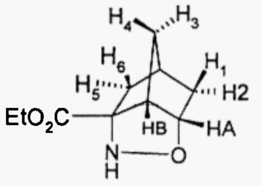
The key step of the proposed route in scheme 1 is a tandem 1,2-prototropy/intramolecular cycloaddition reaction of oximes (**5a-c**). The formation of single stereoisomers in these thermodynamically controlled cycloaddition indicates stereospecific formation of a single dipole (scheme 1) *via* 1,2-prototropy and intramolecular 1,3-dipolar cycloaddition which proceeds with high regio- and stereo-selectivity. This substrates allows the influence of the new stereocentres on the cascade to be assessed with respect to the configuration of nitrone that is generated and the facial selectivity of the subsequent cycloaddition.

We were also interested in the reactivity and reaction selectivity of competitive 1,2-prototropy and 1,3-APT in the systems such as outlined in scheme 2. Thus inactivated alkenyl oximes (**17**) were prepared *via* an ene reaction[22] on (**8**) afforded (**10**) which in turn gave oxime (**11**) as a 1:1 *E/Z*-isomer mixture in 90 % yield from (**8**).

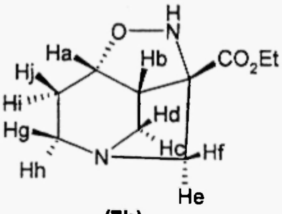


I. $NH_2OH.HCl$, CH_3CN/H_2O, rt, 6h II. $^{i}Pr_2EtN$, DCM, rt
III. Xylene, reflux, N_2, 7-8h

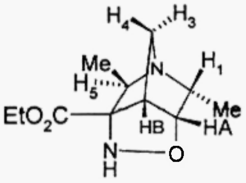
Scheme 1



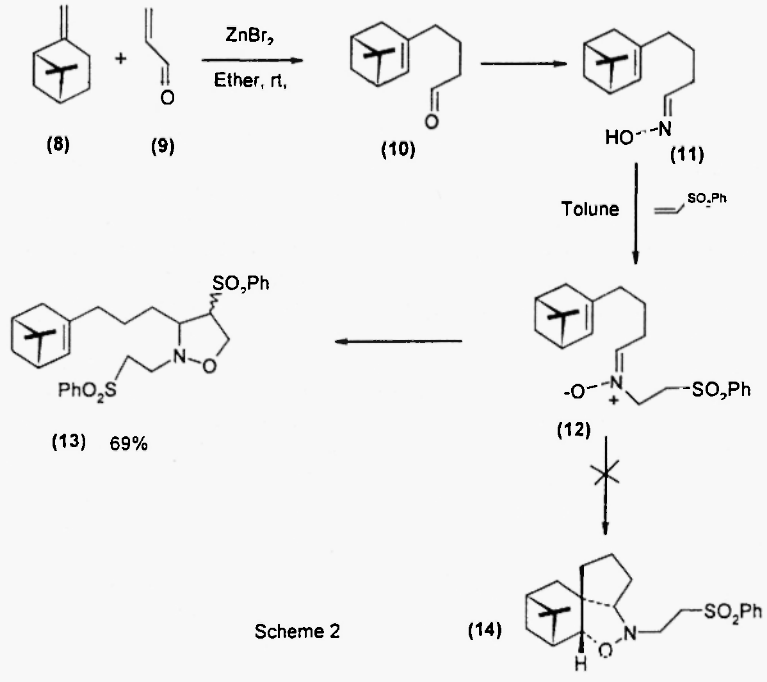
(7a)



(7b)



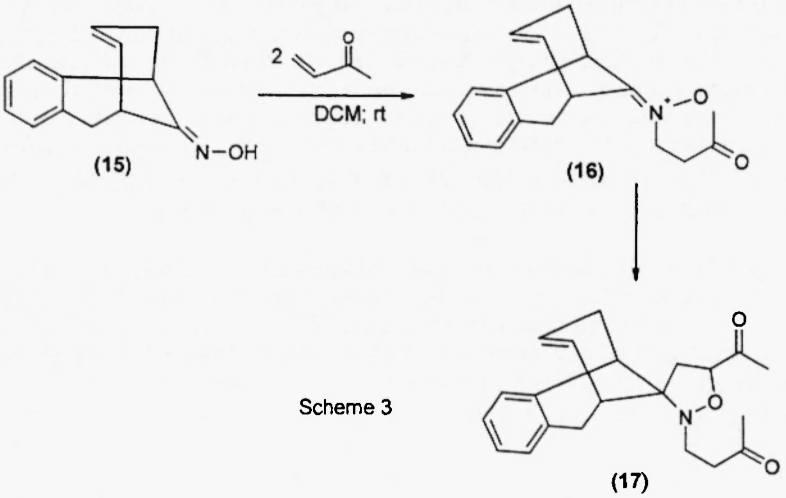
(7c)



Scheme 2

When oxime **(11)** treated with phenyl vinyl sulphone (toluene, 110 °C) produced intermediate nitrone **(12)** generated via 1,3-APT which cycloadds to another molecule of dipolarophile through tandem intermolecular 1,3 dipolar cycloaddition leading to isoxazolidines system **(13)** in 69% yield as 2:1 mixture of isomers. No intramolecular cycloadduct **(14)** was observed, showing the intermolecular process to be faster with the activated dipolarophile than intramolecular cycloaddition with a non-activated dipolarophile. Close inspection of molecular models reveals that in the pre-transition state of **(12)**, the geometry of the oximes nitrogen lone pair makes 1,2-prototropy imposible. Thus, the intermediate nitrone **(12)** generated via 1,3-APT, proceeds through 1,3 dipolar cycloaddition with another molecule of phenyl vinyl sulphone leading to compound **(13)**

Another example of the 1,3-APT reaction of oxime **(15)**[9] with methylviny ketone (2equiv) (DCM; rt; N_2, 7d) furnished intermediate nitrone **(16)** which subsequently undergo intermolecular cycloaddition to afford **(17)** in 76% yield as 2:1 mixture of isomers. Amines of **(15)** is known to show anorectic and antidepressant activities[20].



Scheme 3

In conclusion, some novel tricyclic α -aminoacid esters and potential bioactive compounds were obtained in good to excellent yield *via* the technically simple thermal 1,2-prototropy- and 1,3-APT oxime nitrone-1,3-dipolar cycloaddition cascades reactions. The reactivity and reaction selectivity of competitive 1,2-prototropy and 1,3-APT were also studied as part of this work.

Acknowledgement: We thank The Scientific and Technical Research Council of Turkey (TUBITAK) (TBAG-2154, 102T033), Mersin University and Çukurova University for support.

EXPERIMENTAL:

Microanalyses were obtained using a Carlo - Erba Model 1106 instrument. Mass spectra were recorded at 70 ev on a VG Autospec mass spectrometer. Nuclear magnetic resonance spectra and decoupling experiments were determined at 300 MHz. on a Q.E 300 instrument and at 400 MHz on a Bruker AM400 spectrometer as specified. Chemical shifts are given in parts per million (□) downfield from tetramethylsilane as internal standard. Spectra were determined in deuteriochloroform except where otherwise stated. The following abbreviations are used; s= singlet, d= doublet, t= triplet, q= quartet, m= multiplet, br= broad and brs= broad singlet. Flash column chromatography was performed using silica gel 60 (230-400 mesh). Kieselgel columns were packed with silica gel GF_{254} (Merck 7730).

Petroleum ether refers the fraction with b.p 40-60 °C unless otherwise specified. Melting points were determined on a Kofler hot stage apparatus and are uncorrected.

3-bromo-2-hydroxyiminopropanoate(2). Prepared according to the literature procedure[21] in 85% yield.

3-(2,5-Dihydro-pyrrol-1-yl)-2-hydroxyimino-propionic acid ethyl ester (5a). 3-Bromo-2-hydroxyiminopropanoate **(2)** (1.52g, 7.23 mmol) was added to a mixture of 3-pyroline (0.5g, 7.23mmol) and Hunig's base (2.53ml, 14.46mmol), in dichloromethane (50ml) at room temperature. After overnight stirring at room temperature, the reaction mixture was washed with water and the solvent was removed in vacuo. The residue was subjected to column chromatograpy on slica eluting with ether-petroleum ether 2:1 v/v to afford the product (5a) (1.25g, 87%) as a colourless solid, which comprised a single isomer, m.p. 82-84 °C. Found: C, 54.55; H, 7.15; N, 13.9. $C_9H_{14}N_2O_3$ requires: C, 54.55; H, 7.1; N, 14.15 %.. (300 MHz): 13.5-13.2(br, 1H, OH), 5.77(brs, 2H, CH=CH), 4.33(q, 2H, $O\underline{CH_2}Me$), 3.99(s, 2H, $N\underline{CH_2}CN$), 3.64(s, 4H, NCH_2) and 1.39(t, 3H, $OCH_2\underline{Me}$). m/z (%) (FAB): 199 (M+1, 100), 82(24) and 68(11).

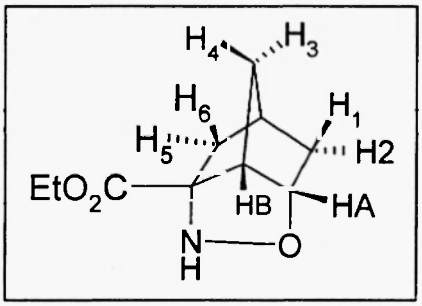
3-(3,6-Dihydro-2H-pyridin-1-yl)-2-hydroxyimino-propionic acid ethyl ester (5b). Oxime (2) (2.3g, 10.95mmol) was added to a mixture of 1,2,3,6-tetrahydropyridine (0.91g, 10.95mmol.) and Hunig's base (3.8ml, 20.90mmol), in dichloromethane (100ml) at room temperature. After overnight stirring at room temperature, the reaction mixture was washed with water and the solvent removed in *vacuo*. The residue was subjected to column chromatograpy on slica eluting with 3:1 v/v ether- petroleumether to afford the product (5b) (2.11g, 90 %) as colourless prisms, which comprised a single isomer, m.p. 79-81 °C. Found: C, 56.3; H, 7.75; N, 13.05. $C_{10}H_{16}N_2O_3$ requires: C, 56.55; H, 7.6; N, 13.2 %. (300 MHz): 13.5-13.9(br, 1H, OH), 5.76-5.62(m, 2H, CH=CH), 4.31(m, 2H, OCH_2), 3.8(s, 2H, NCH_2CN), 3.11-2.22(m, 6H, CH_2) and 1.24(t, 3H, Me). m/z (%): 212(M^+, 2), 195(11), 121(21), 96(100), 82(81), 67(19), 54(22) and 42(49).

3-(2,5-Dimethyl-2,5-Dihydro-pyrrol-1-yl)-2-hydroxyimino-propionic acid ethyl ester (5c).. 3-Bromo-2-hydroyiminopropanoate (2) (1.52g, 7.23 mmol) was added to a mixture of 2,5-dimethyl-3-pyroline (mixture of cis- and trans isomers), (0.5g, 7.23mmol) and Hunig's base (2.53ml, 14.46mmol), in dichloromethane (50ml) at room temperature. After overnight stirring at room temperature, the reaction mixture was washed with water and the solvent was removed in vacuo. The residue was subjected to column chromatograpy on slica eluting with ether-petroleum ether 3:1 v/v to afford the product (5c) (1.25g, 85%) as a colourless solid, which comprised a mixture of isomer, m.p. 82-84 °C. (300 MHz): 12.8-11.9(br, 1H, OH), 5.44(brs, 2H, CH=CH), 4.33(m, 2H, OCH_2Me), 1.25(m, 9H, OCH_2Me + 2Me). m/z (%) (FAB): 227 (M^+, 95), 133(100), 110(96), 94(54), 81(32) and 69(44).

4-Oxa-5-aza-tricyclo|4.2.1.0*3,7*|nonane-6-carboxylic acid ethyl ester (7a). A solution of the oxime (5a) (0.1g) in degassed xylene was boiled under reflux under a nitrogen atmosphere for 7h. After cooling the solvent was removed in *vacuo* and the residue was subjected to column chromatography on slica, eluting with 5:1 v/v ether-methanol to afford the product (7a) (0.089 g, 89%) as a pale yellow thick oil. HRMS: 198.1004 . $C_9H_{14}N_2O_3$ requires: 198.1003. (400 MHz): 6.4(br, 1H, NH), 4.73(t, 1H, J 5.5 Hz, Ha), 4.2(q, 2H, OCH_2), 3.57-3.54(dd, 1H, J 13.3 and 2.3Hz, H5), 3.07(d, 1H, J 5.0 Hz, Hb), 3.02-2.98(dd, 1H, J 2.88 and 10.4 Hz, H3), 2.81(ddd, 1H, J 2.6, 6.0, 13.5 Hz, H1), 2.61-2.65 (m, 2H, H4 and H6), 2.53 and 2.57(dd, 1H, J 3.05 and 13.05 Hz, H2) and 1.26(t, 3H, J 7.12 Hz, OCH_2Me). m/z(%) (FAB): 199(M+1, 55), 197(11), 95(29), 81(36), 69(59), 57(74) and 55(100).
Coupling constants (Hz): Ja,1 = 6.0, Ja,2 = 0, Ja,b= 5.0, J1,2 = 13.5, Jb,3 = 0, Jb,4 = 0, J3,4 = 10.4, J5.6 = 12.0, J5.3 = 2.9, J2,4 = ,3.05, J1,6= 2.6
n.O.e. data for (7a)

Enhancement(%)

Signal irradiated	H_A	H_B	H1	H2	H3	H4,6	H5
H_A		4.3	2.5				
H_B	5.2					1.5	
H1	10.7			12.5			7.3
H2	2.3						
H3	1.2					14.1	2.4
H4,H6	1.7				18.8		14.7
H5						15.2	

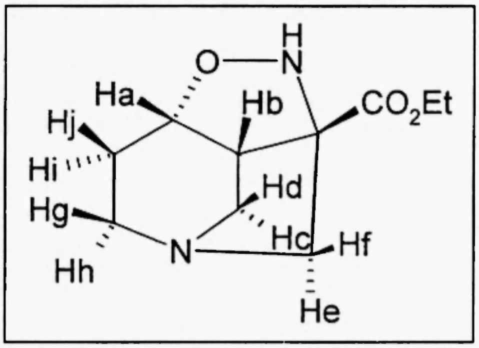


5-Oxa-1,6-diaza-tricyclo|5.2.1.0*4,8*|decane-7-carboxylic acid ethyl ester (7b). A solution of the oxime (5b) (0.1g) in xylene was boiled under reflux under a nitrogen atmosphere for 8h. After cooling, the solvent was removed in *vacuo* and the residue was subjected to column chromatography on silica, eluting with 4:1 v/v ether - methanol to afford the product (7b) (0.081g, 81%) as a pale yellow thick oil. HRMS: 212.1160. $C_{10}H_{16}N_2O_3$ requires: 212.1155. (400 MHz): 6.2(br, 1H, NH), 4.55(d, 1H, J 9.3 Hz, Ha), 4.19(q, 2H, OCH_2), 3.66(d, 1H, J 13.3 Hz, He), 3.35(dd, 1H, J 8.4 and 13.8 Hz, Hg), 2.98 and 2.95(dd, 1H, J 2.5 and 12.4 Hz, Hc), 2.86-2.75(m, 3H, Hd, Hb, Hh), 2.71 and 2.67(dd, 1H, J 2.5 and 13.2 Hz, Hf), 1.7-1.5(m, 2H, Hi) and 1.25(t, 3H, J 7.1 Hz, OCH?Me). m/z(%): 213(M+1, 3), 212(7), 211(24), 183(46), 168(23), 139(100) and 128(28).

Coupling constants (Hz): Ja,b = 9.5, Ja,i = small, Ja,j= 2.8, Jb,c = 2.5, Jb,d = 0, Jc,d = 12.0, Jg,h = 14, Jg,i = 2.0, Jg,j = 8.5, Jh,i = 7.0, Jh,j = 11.2, Ji,j= 15, Je,f = 13.3
n.O.e. data for (7b)

Enhancement(%)

Signal irradiated	**Ha**	**Hb,Hh, Hd**	**Hc**	**He**	**Hf**	**Hg**	**Hi**
Ha		**9.8**					**7.3**
Hb,Hh, Hd	**4.2**		**7.4**	**2.5**		**7.1**	
Hc	**1.7**	**10.3**					**7.3**
He					**25.5**		
Hf	**2.5**		**4.9**	**26.8**			
Hg	**1.1**	**23.2**					**5.5**
Hi	**8.7**		**5.0**			**3.5**	



4-(6,6-Dimethyl-bicyclo[3.1.1]hept-2-en-3-yl)-butyraldehyde(10). Prepared according to the literature procedure[22] in 30% yield. The material was used without further purification for the next stage. □(300 MHz): 9.78(t, 1H, J 1.9 Hz, CHO), 5.20(m, 1H, CH=), 1.35-2.7(m, 12H, CH_2), and 1.23 and 0.83 (2xs, 2x3H, Me).

4-(6,6-Dimethyl-bicyclo[3.1.1]hept-2-en-3-yl)-butyraldehyde oxime (11). A solution of aldehyde (10) (0.5g, 2.6mmol) in acetonitrile (25ml) was added to a solution of hydroxylamine hydrochloride (199mg, 1.2 equiv.) and sodium acetate (256mg, 1.2equiv) in water (25ml). The resulting solution was stirred at ambient temperature for 3 h and then extracted with chloroform (2x50 ml). The combined organic layer was dried ($MgSO_4$) and concentrated under reduced pressure and the residue subjected to column chromatography on silica eluting with 2:1 v/v petroleum ether-ether. The product (0.49g, 51%) was a pale yellow thick oil, which comprised a 1:1 mixture of *E*- and *Z*- isomers.
[ ]$_D$ = -36.8 (c.1g/100 ml, $CHCl_3$). Found: C, 75.5; H, 10.2; N, 6.7. $C_{13}H_{21}NO$ requires: C, 75.3; H, 10, 2; N, 6.75 %.
(300 MHz): 9.8 and 9.2(br, 1H, OH, isomers), 7.41(t, 1H, E-CH=N), 6.69(t, 1H, Z-CH=N), 5.2(br, s, 1H, C=CH, isomer), 2.4 -1.5(m. 12H, isomers), 1.25(s, 3H, Me, isomers) and 0.80(s, 3H, Me, isomers). m/z(%): 207(M^+, 2), 190(36), 173(16), 131(53), 105(83), 91(100) and 41(74).

4-Benzenesulfonyl-2-(2-benzenesulfonyl-ethyl)-3-[3-(6,6-dimethyl-bicyclo[3.1.1]hept-2-en-3-yl)-propyl]-isoxazolidine (13). A solution of oxime (11) (0.2g, 0.96mmol) and phenylvinyl sulphone (0.32g, 1.83 mmol) in toluene (20ml) was stirred and boiled under reflux for two dy. Upon cooling the solvent was removed in *vacuo* and the residue was subjected to column chromatography on silica eluting with 1:1 v/v ethylacetate-hexane. The product (13) (0.36g, 69%) was obtained as a colourless gum which comprised a 2:1 mixture of isomers. Found: C, 63.95; H, 6.7; N, 2.6. $C_{29}H_{37}NO_5S_2$ requires: C, 64.0; H, 6.8; N, 2.6 %.
(400 MHz): 7.95-7.50(m, 10H, ArH, isomers), 5.07 and 5.11(2xbr, 1H, H15), 4.1(m, 1H, H2, isomers), 3.58-3.52(m, 2H, H1, isomers), 3.4(m, 3H, H5, H3, isomers), 3.2(m, 3H, H4, H11, isomers), 2.4(m, 1H, H7, isomers), 2.2(m, 2H, H14, isomers), 2.1(m, 1H, H7, isomers), 2.0-1.8(m, 3H, H8, H13, isomers), 1.4(m, 2H, H12, isomers), 1.21(s, 3H, Me, isomers), 1.26 and 1.0(m, 2H, H9, isomers) and 0.75(s, 3H, Me, isomers).
m/z(%): 544 (M+1,42), 402(29), 358(13), 97(29), 83(39), 57(93), 55(100) and 54(62).

Benzo-bicyclonenone oxime (15): were praperad according to litterature procedure[9].

Cycloadduct 17. A solution of oxime (15) (0.5g, 2.5mmol), and methyl vinyl ketone (0.39g, 5.52 mmol) in dichloromethane (40 ml) was stirred under N_2, at room temperature for 7 dy. The solvent was then removed in *vacuo* and the residue subjected to column chromatography eluting with 3:1 v/v ether - petroleum ether to afford the product (0.65g,76%) as a brown gum which comprised a 2:1 mixture of isomers (^{1}Hn.m.r). Found: C, 72.2 ; H, 7.4 ; N, 3.9. $C_{21}H_{25}NO_3.1/2H_2O$) requires: C, 72.35 ; H, 7.5; N, 4.0 %.. □(300 MHz): 7.21-7.0(m, 4H, Ar-H), 5.7(m, 2H, CH=CH), 4.6(m, 1H, CHO), 3.45-1.80(m, 12H), 2.25(s, 3H, Me) and 2.18(2xs, 3H, Me, isomers). m/z(%): 339M$^+$, 28), 296(15), 282(5), 222(9), 181(16), 167(65), 141(19), 115(20), 84(56), 71(19) and 43(100).

REFERENCES:

1. (a) Kanemasa, S.; Ueno, N.; Shirahase, M.; *Tetrahedron Lett.*, **2001**, 42, 6715-6717. (b) Gardiner, M.; Grigg, R.; Kordes, M.; Sridharan, V.; Vicker, N.; *Tetrahedron*, **2001**, 57, 7729-7735. (c) Bayon, P.; De March, P.; Espinosa, M.; Figueredo, M.; Font, J.; *Tetrahedron Asymmetry.*, **2000**, 11, 1757-1765. (d) Tanaka, J.; Kanemasa, S., *Tetrahedron*, **2001**, 57,899-905.Gothelf, K.V.; Jorgensen, K.A.; *Chem.Rev.*, **1998**, 863-909.
2. Gothelf, K.V.; Jorgensen, K.A.; *Chem. Commun.*, **2000**, 1449-1458.
3. Breuer, E.; Aurich, H.G.; Nielsen, A.; *Nitrones, Nitronates and Nitroxides*, John Willey and Sons Ltd., **1989**, p 141
4. Padwa, A.; *1,3-Dipolar Cycloaddition Chemistry*, ed. Wiley, New York, **1984**, vol. 2, p.83; Torssell, K.B.G.; *Nitrile Oxides, Nitrones and Nitronates in Organic Synthesis*, VCH, Weinheim, **1988**.
5. Iwasa, S.; Tsushima, S.; Shimada, T.; Nishiyama, H.; T*etrahedron Lett.*, **2001**, 42, 6715-6717.
6. (a) Frank, E.; Wölfling, J.; Aukszi, B.; König, V.; Schneider, T. R.; Schneider, G.; *Tetrahedron*, **2002**, 58, 6843-6849. (b) Kanemasa, S.; Tsuruoka, T.; Yamamoto, H.; T*etrahedron Lett.*, **1995**, 36, 5019-5022. (c) Kanemasa, S.; Tsuruoka, T.; *Chem. Lett.*, **1995**, 49-50.
7. Grigg, R., *Chem. Soc. Rev.*, **1987**, 16, 89. Frederickson, M.; Grigg, R.; *Org. Prep. Procedures*, **1997**, *29*, 33-62 and 63-115; Frederickson, M.; *Tetrahedron*, **1997**, *53*, 403-425.
8. Grigg, R.; Markandu, J.; Perrior, T.; Surendrakumar, S.; Warnock, W. J.; *Tetrahedron*, **1992**, 48, 6929.
9. Dondas. H. A, PhD thesis submitted to Leeds University, 1997
10. Dondas. H.A.; Fiswick, C. W.G; Grigg, R.; Thornton-Pett, M.; Tetrahedron, **2003**, 59, 9997-10007
11. (a). Grigg, R.; Heaney, F.; Markandu, J.; Surendrakumar, S.; Thornton-Pett, M; Warnock, W. J.; *Tetrahedron*, **1991**, 47, 4007-4030.(b). Heaney, F.; Bourke S.; *J.Cem.Soc.Perkin Trans.1*, **1998**, 955-964 and references there in.
12. Dondas, H.A.; Yaktubay, N.; *Heterocyclic Commun.*, **2003**, 9, 337-344.
13. Dondas. H.A.; Grigg, R.; Hadjisoteriou, M.; Markandu, J.; Thomas, W.A.; Kennewell, P.; *Tetrahedron*, **2000**, *56*, 10087-10096.
14. Dondas, H.A.; Grigg, R.; Hadjisoteriou, M.; Markandu, J.; Kennewell, P.; Thornton-Pett, M.: *Tetrahedron*, **2001**, *57*, 1119-1128;
15. Dondas, H.A.; Grigg, R.; Thibault, S.; *Tetrahedron*, **2001**; *57*, 7035-7045. Durust, Y.; Dondas, H.A.; Ozkoru, N.; *Heterocyclic Commun.*, **1999**, 5, 173-178.
16. Dondas, H.A.; Grigg, R.; Markandu, J.; Perrior, T., Suziki, T.; Thibault, S.; Thomas, W.A.; Thornton-Pett, M.; *Tetrahedron* , **2002**, *58*, 161-173.
17. Dondas, H.A.; Grigg, R.; Frampton, C.S.; *Tetrahedron Lett.*, **1997**, *38*, 5719-5722. ; Dondas, H.A.; Frederickson, M.; Grigg, R.; Markandu, J.; Thornton-Pett M.; *Tetrahedron* , **1997**, *53*, 14339-14354.
18. Markandu, J.; Dondas, H.A.; Frederickson, M.; Grigg, R., Thornton-Pett, M.; *Tetrahedron*, **1997**, *53*, 13165-13176.
19. Dondas, H.A.; Cummins, J.E.; Grigg, R.; Thornton-Pett, M.; *Tetrahedron* **2001**, *57*, 7951-7964
20. (a). Hawlett, C.L.; Savage, D.S.; *British patent, B.P.1504694/1978* (Chem. Abstr., 1976, 84, 105298r). (b). Matsuhashi, K.; Shiotani, S.; *Chem. Pharm Bull.*, **1970**, 18, 75-79.
21. Gilchrist, T., L.; Lingham, D. A.; Roberts, J.; *J. Chem. Soc. Chem. Commun.*, 1979, 66, 1089
22. Snider, B. B.; *J. Org. Chem.*, **1974**, 39, 255-261.

Received on March 10, 2004.