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ELECTROPHILIC AMINATION OF 2-AZADIENES

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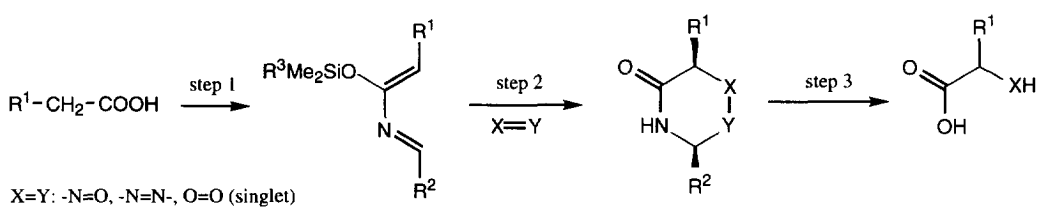
Abstract : 2-Azadienes **1** bearing a trialkylsilyloxy group on position 3 can be regarded as carboxylic acid synthons. Their cycloadditions with several classes of nitroso compounds have been studied in details as well as the transformation of the adducts into α-amino acids. This study showed that arylnitroso compounds such as nitrosobenzene reacted with 2-azadienes to give adducts that are potential precursors of α-N-arylamino acids. We have outlined an important limitation to the use of α-chloronitroso compounds. They are not compatible with highly functionalized dienes like 2-azadienes. On the other hand α-cyanonitroso and acylnitroso compounds reacted with azadienes to give adducts which were readily converted into α-amino acid derivatives. Copyright © 1996 Elsevier Science Ltd

Key words : electrophilic amination, Diels-Alder reaction, nitroso compound, 2-azadiene, α-amino acid.

INTRODUCTION

Studies from these laboratories have shown that carboxylic acid chlorides can be readily transformed into 2-azadienes by reaction with N-silylimines.[1] These heterodienes have been successfully used as cycloaddition reagents for the preparation of pyridones and pyrimidones with a defined substitution pattern and for the diastereo- and enantioselective synthesis of piperidine derivatives.[2]

In this context, we became interested in the possibility of using 2-azadienes **1** as carboxylic acids synthons. The cycloaddition of **1** with an heterodienophile X=Y could yield an adduct which, after reduction and hydrolysis, would produce a carboxylic acid derivative functionalized at the α-carbon atom (scheme 1).



Scheme 1

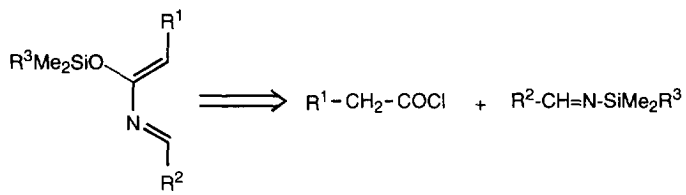
We first envisaged a potential route to α-aminoacids using nitroso compounds as dienophiles. These are known to react with conventional dienes allowing the simultaneous formation of a carbon-nitrogen bond and a carbon-oxygen bond at the two ends of the diene as well as for the creation of two stereogenic centers.[3] The Diels-Alder cycloadditions of chiral nitroso compounds to dienes followed by the reductive cleavage of the

N-O bond have been used for the preparation of enantiomerically pure 1,4-aminoalcohols.[4] Thus, the use of a chiral nitroso compound in the sequence outlined in Scheme 1 would provide a Diels-Alder strategy for the asymmetric amination of carboxylic acids. Preliminary results have demonstrated the feasibility of this approach.[5] This paper represents a full study of the scope and limitation of the Diels-Alder reactions of 2-azadienes with nitroso compounds and the transformation of the products into α-amino acid derivatives.

RESULTS AND DISCUSSION

Step 1 : Conversion of the Carboxylic Acids into 2-Azadienes

2-Azadienes **1** have been prepared from the corresponding acid chlorides and various imine derivatives as described in a recent paper (Scheme 2).[1] This strategy allows the introduction of a wide variety of substituents R^1 and R^2. For the following studies we selected a phenyl or an isopropoxy group on carbon 1. The latter group enhances the reactivity of the azadiene.



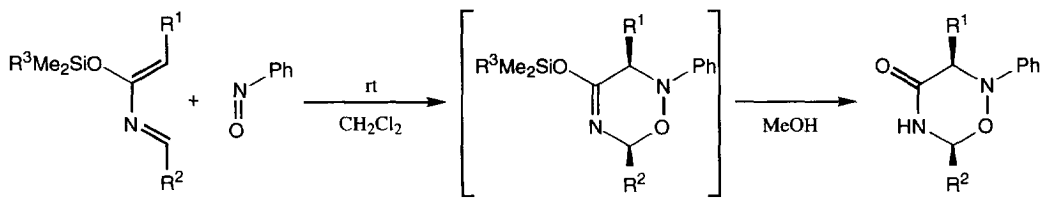
1

Scheme 2

Step 2 : Cycloadditions

1. Nitrosobenzene

Nitrosobenzene reacted at room temperature with 2-azadienes **1a-i**. The reaction could be monitored by the disappearance of the blue colour of the dienophile. The primary adducts were directly desilylated in an excess of methanol to give good yields of 1-oxa-2,5-diaza-4-oxo-cyclohexanes **2** as colourless stable crystals (Scheme 3, Table 1).



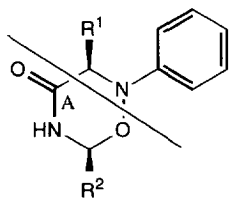
1 **2**

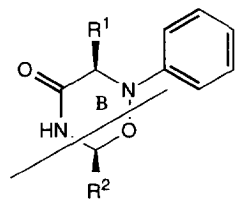
Scheme 3

Table 1 : Cycloadditions with Nitrosobenzene

Diene	R^1	R^2	R^3	Product	Yield (%)
1a	H	Ph	Me	**2a**	78
1b	Me	Ph	Me	**2b**	83
1c	Me	OPr^i	Bu^t	**2c**	75
1d	Ph	Ph	Me	**2d**	82
1e	Ph	OPr^i	Bu^t	**2e**	63
1f	CH_2Ph	Ph	Me	**2f**	82
1g	CH_2Ph	OPr^i	Bu^t	**2g**	65
1h	$CH{=}CH_2$	Ph	Me	**2h**	75
1i	$CH_2Ph(OMe)_2$m,p	Ph	Me	**2i**	41

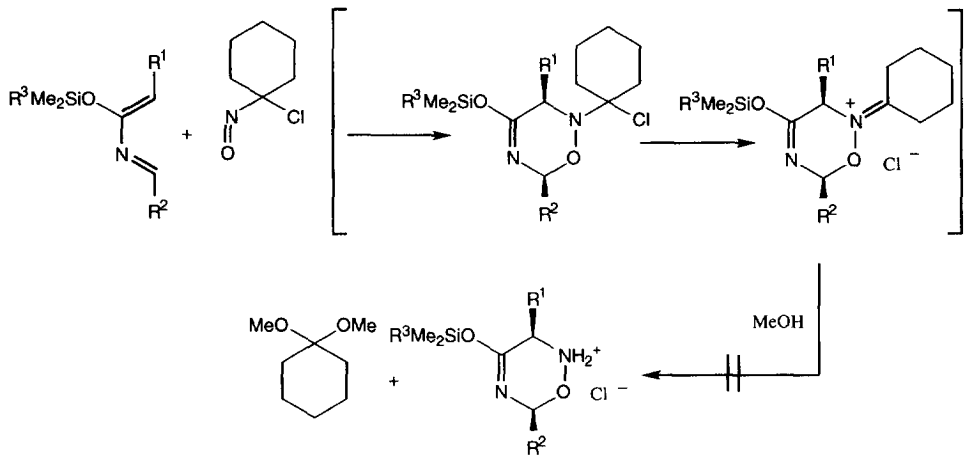
All cycloadditions yielded a single isomer as shown by the ^1H NMR spectra of crude **2**. The mass spectra of **2** showed fragmentations **A** and **B** and thus confirmed that the C-N bond had been formed at the carbon atom bearing R^1. These observations are consistent with earlier results on nitrosobenzene cycloadditions with electron-rich dienes.[6] An X-ray diffraction analysis[7] confirmed the structure of **2i** and the anticipated cis-relationship between substituents R^1 and R^2.





2. *α–Chloronitroso Compounds*

The introduction of a free amino group according to the strategy of Scheme 1 requested a nitroso dienophile bearing a removable group. To this end, we first considered α-chloronitroso compounds which are potent dienophiles.[8] However, we were unable to achieve cycloadditions of 1,1-chloronitrosocyclohexane with 2-azadienes **1b** and **1c**. A fast reaction occured yielding a complex mixture of products even when methanol was added to trap the intermediate iminium salt. This failure was probably due to side reactions between the highly nucleophilic azadiene and the electrophilic iminium salt intermediate (Scheme 4).

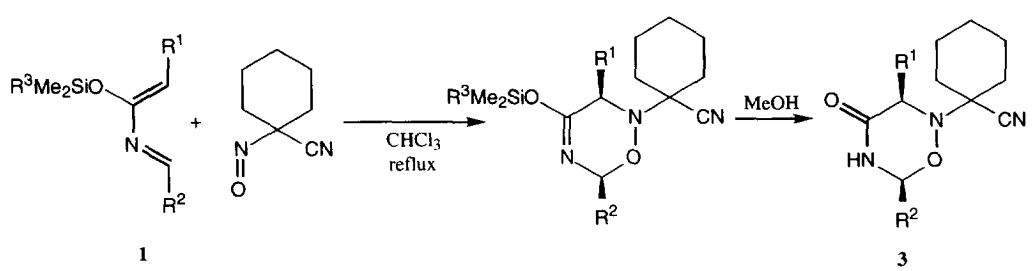


Scheme 4

3. α–Cyanonitroso Compounds

The problem was solved by the use of α-cyanonitroso compounds as dienophiles. Indeed, the replacement of the chlorine atom by the cyano group leads to a stable primary adduct since the cyano group is not a good leaving group.

Reaction of 1,1-cyanonitrosocyclohexane with 2-azadienes in refluxing chloroform yielded stable primary adducts which could be desilylated in methanol (Scheme 5, Table 2). This observation confirmed that the problems encountered with the use of 1,1-chloronitrosocyclohexane were due to the lability of the chlorine atom α to the nitrogen in the primary adduct.



1 3

Scheme 5

Table 2 : Cycloadditions with 1,1-Cyanonitrosocyclohexane

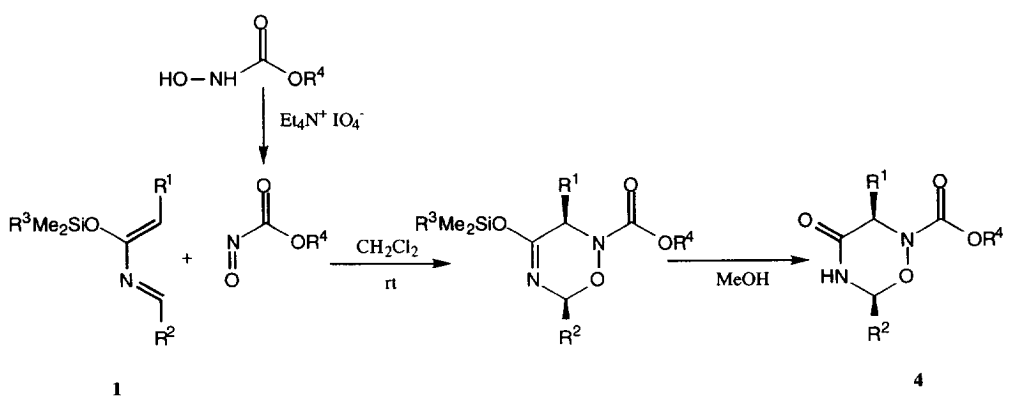
Diene	R^1	R^2	R^3	Product	Yield (%)
1b	Me	Ph	Me	**3b**	79
1c	Me	OPr^i	But	**3c**	71
1d	Ph	Ph	Me	**3d**	68
1f	CH_2Ph	Ph	Me	**3f**	74
1h	$CH{=}CH_2$	Ph	Me	-	(a)
1i	$CH_2Ph(OMe)_2m,p$	Ph	Me	**3i**	70

(a) traces of adduct have been detected on the ^1H NMR spectrum of the crude mixture

All the adducts obtained from 1,1-cyanonitrosocyclohexane could be kept at room temperature. No adduct was obtained from triene **1h**. We only observed a slow degradation of the triene. The ^1H NMR spectra of the crude mixtures showed that only one regioisomer had been formed. The regiochemistry was again assigned by mass spectroscopy. The presence of fragment **A** confirmed that the carbon-nitrogen bond had been formed α to the lactam function as we had already observed for the adducts prepared from nitrosobenzene. By analogy with adducts **2**, we have assigned a cis relationship between substituents R^1 and R^2.

4. Acylnitroso compounds

N-Acylnitroso compounds can also be regarded as free amine synthons. They are very reactive heterodienophiles which undergo hetero Diels-Alder reactions at low temperatures.[9] They are produced *in situ* by oxidation of the corresponding hydroxamic acid with a solution of tetraethylammonium periodate in dichloromethane. Acylnitroso compounds reacted at room temperature with 2-azadienes. The primary adducts were desilylated in an excess of methanol to give compounds **4** as colourless oils or solids (Scheme 6, Table 3).



Scheme 6

Table 3 : Cycloadditions with Acylnitroso Compounds

Diene	R^1	R^2	R^3	R^4	Product	Yield (%)
1f	CH_2Ph	Ph	Me	CH_2Ph	**4a**	30
1g	CH_2Ph	OPr^i	Bu^t	CH_2Ph	**4b**(a)	73
1e	Ph	OPr^i	Bu^t	CH_2Ph	**4c**	67
1e	Ph	OPr^i	Bu^t	Ph	**4d**	40

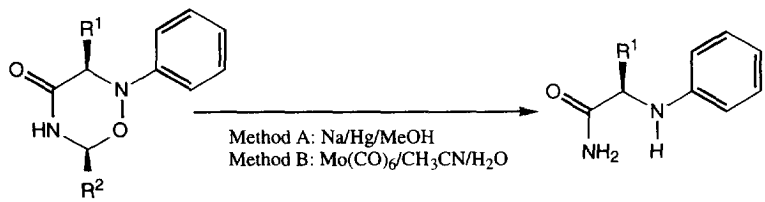
(a) this compound was contaminated by 10% of the other regioisomer

Yields were higher with the more reactive 2-azadienes bearing two electrodonating groups on position 1 and 3. All the adducts could be kept at room temperature. For most cycloadditions, only one stereoisomer was obtained as demonstrated by ^1H NMR on the crude mixtures. We observed only one set of signals for protons positioned on carbons 3 and 6. For compound **4b** contaminated with 10 % of the other regioisomer, two sets of signals were clearly observed. The regiochemistry has been assigned by mass spectroscopy. By analogy with adducts **2**, we have assigned a cis-relationship between substituents R^1 and R^2.

Step 3 : Reductive Cleavage of the Adducts into α-amino Acids or Amides

1. Reductive Cleavage of Adducts 2

We have tested several reagents for the reductive cleavage of adducts **2**. The best results have been obtained with Na/Hg[10] and $Mo(CO)_6$.[11] The expected α-N-phenylamino amides **5** were obtained in good yields (Scheme 7, Table 4).



2 5

Scheme 7

Table 4 : Reductive Cleavage of Adducts **2**

Adducts	R_1	R_2	Products	Yield (%) Method A	Yield (%) Method B
2a	H	Ph	**5a**	74	75
2b	Me	Ph	**5b**	73	69
2c	Me	OPr^i	**5b**	53	71
2d	Ph	Ph	**5c**	93	91
2e	Ph	OPr^i	**5c**	67	65
2f	CH_2Ph	Ph	**5d**	72	68
2g	CH_2Ph	OPr^i	**5d**	75	78
2h	$CH=CH_2$	Ph	**5e**	(a)	56
2i	$CH_2Ph(OMe)_2$ m,p	Ph	**5f**	83	-

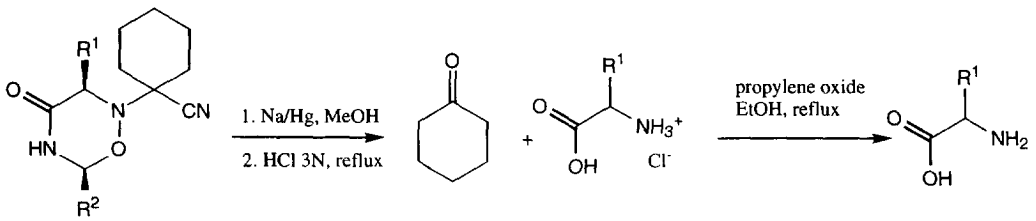
(a) this reaction gived 2-anilino-butanamide

For adduct **2h** sensitive to isomerisation and over reduction, we used $Mo(CO)_6$, a smoother reagent than sodium amalgam. Indeed, the use of Na/Hg for the reductive cleavage of the N-O bond of adduct **2h** lead to 2-anilinobutanamide probably via reduction of 2-anilino-2-butenamide formed as an intermediate.

2. Reductive Cleavage of Adducts 3 and 4

Adducts **3** were converted into the corresponding α-amino acids by reductive cleavage of the N-O bond and cleavage of the 1-cyanocyclohexyl group. We have choosen acidic conditions to cleave the cyanocyclohexyl group.[12]

The successive treatment of adducts **3** by Na/Hg in methanol and HCl 3N directly yielded the expected α-amino acids as their hydrochloride salts. The free amino acids were obtained by treatment of the salts with propylene oxide in refluxing ethanol (Scheme 8, Table 5).[13] They were identical with authentic samples.



3 6

Scheme 8

Table 5 : Reductive Cleavage of Adducts **3**

Adducts	R_1	R_2	Product	Yield (%)
3b	Me	Ph	**6a**	31
3c	Me	OPr^i	**6a**	42
3d	Ph	Ph	**6b**	64
3f	CH_2Ph	Ph	**6c**	70

Adducts **4** derived from acylnitroso compounds are also precursors of free amino acids as already described in the literature.[5]

CONCLUSION

We have undertaken a systematic study of the Diels-Alder reaction between differently substituted 2-azadienes and several classes of nitroso compounds. This study shows that nitrosobenzene, 1,1-cyanonitrosocyclohexane and acylnitroso compounds do react with 2-azadienes to give moderate to good yields of adducts. All those reactions give stable adducts obtained in most cases as single stereoisomers. We have also outlined an important limitation to the use of α-chloronitroso compounds as we have shown that this class of dienophile is not compatible with very functionalized dienes like 2-azadienes.

Asymmetric amination of carboxylic acid using the sequence outlined in Scheme 1 should be feasible starting with a chiral azadiene bearing the chiral auxiliary on position 1 or with a chiral nitroso compound. Preliminary results on a new asymmetric synthesis of α-amino acids using the strategy outlined here have been published in a preliminary communication.[5]

EXPERIMENTAL SECTION

^{1}H NMR spectra were recorded in $CDCl_3$ (unless otherwise noted) on VarianT-60 (^{1}H NMR, 60 MHz), Varian Gemini-200 (^{1}H NMR, 200 MHz), Varian XL-200 and VXR 200 (^{13}C NMR, 50 MHz) spectrometers. Chemical shifts (δH) are reported in parts per million (p.p.m) and are referenced to tetramethylsilane (0 ppm). Multiplicities are reported as broad (br), singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). Coupling constants (J) are reported in Hertz (Hz) to the nearest 0.1 Hz. Infra-red spectra were recorded in $CHCl_3$ solution using a Perkin-Elmer 681 spectrometer and are referenced to polystyrene (1601 cm^{-1}). Only selected peaks are reported and absorption maxima are given in cm^{-1}. Microanalysis were performed by the microanalytical service of Dr Bieler (University of Vienna) and A.Stones (University College London). Mass spectra (m/z) were recorded on Varian-Mat-44 and Finnigan Mat-TSQ70 spectrometers using electronic impact (70 eV) or chemical ionisation (100eV, isobutane). Melting points were recorded on a Leitz-Wetzlar HM-LUX microscop and are uncorrected. X-Ray diffraction analysis were performed on an automatic Synthex diffractometer. The structures are resolved using the Multan-80 system and Shelx-76 program. Thin layer chromatography (t.l.c.) was performed using Merck plastic backed sheets precoated with Kieselgel (70-230 Mesh). Plates were visualised using uv light (254 nm), iodine vapour or a solution of $FeCl_3$ in ethanol. Solvents were distilled prior to use using standard literature procedures.

1,1-chloronitrosocyclohexane[14], 1,1-cyanonitrosocyclohexane[15], N-benzyloxycarbonylhydroxylamine[16] and N-phenoxyhydroxylamine[17] have been prepared according to the procedures reported in the literature.

CYCLOADDITIONS

All the reactions are performed under a positive pressure of Argon.

General procedure for nitrosobenzene

To a solution of 2-azadiene (1eq) in dry CH_2Cl_2(1M) was added dropwise at room temperature a solution of nitrosobenzene (1eq, 1M in CH_2Cl_2). When the blue colour of the dienophile has disappeared, a large excess of methanol was added to the reaction mixture. After complete methanolysis, solvents were evaporated under vacuum and the oily residue was triturated in ether. The compound solidified and was purified by recristallisation.

2,6-diphenyl-1-oxa-2,5-diaza-4-oxo-cyclohexane 2a

2-azadiene **1a** (0.96g, 4.4 mmol), nitrosobenzene (0.47g, 4.4 mmol); yield: 0.87g, 78%; Rf=0.75 (ethyl acetate); $\bar{\nu}$ max (cm^{-1}) 3400 (NH), 1685 (CONH); δH (200 MHz, $CDCl_3$) 7.56-7.01 (10H, m), 6.77 (1H, br s), 6.24 (1H, s), 4.21-3.93 (2H, dxd (AB), ^{2}J=15.93); δC (50 MHz, $CDCl_3$) 167.5, 148.0, 136.0, 131.1, 129.6, 129.5, 128.1, 124.4, 116.8, 87.5, 57.4; m/z (E.I.) 254 ($M^{+\cdot}$, 2%), 167 (38%), 149 (100%), 122 (34%); E.A ($C_{15}H_{14}N_2O_2$) %C (70.85, found 70.83), %H (5.55, found 5.61), %N (11.02, found 11.03); mp 166.5°C

3-methyl-2,6-diphenyl-1-oxa-2,5-diaza-4-oxo-cyclohexane 2b

2-azadiene **1b** (0.88g, 3.7 mmol), nitrosobenzene (0.4g, 3.7 mmol); yield : 0.8g, 83%; Rf=0.18 (ethyl acetate:cyclohexane, 1:1); $\bar{\nu}$ max (cm^{-1}) 3400 (NH), 1700 (CONH); δH (200 MHz, $CDCl_3$) 7.59-6.98 (10H, m), 6.66 (1H, br s), 6.18 (1H, s), 4.41 (1H, q, ^{3}J=6.8), 1.39 (3H, d, ^{3}J=6.8); δC (50 MHz, $CDCl_3$) 171.2, 145.1, 136.2, 130.7, 129.2, 129.1, 127.7, 122.8, 115.8, 87.2, 61.5, 11.9; m/z (E.I.) 268 ($M^{+\cdot}$,3%), 167 (22%), 149 (56%), 136 (34%), 119 (16%); E.A ($C_{16}H_{12}N_2O_2$) %C (71.62, found 71.73), %H (6.12, found 6.01), %N (10.44, found 10.50); mp 184°C

3-methyl-6-isopropoxy-2-phenyl-1-oxa-2,5-diaza-4-oxo-cyclohexane 2c

2-azadiene **1c** (0.15g, 0.58 mmol), nitrosobenzene (0.057g, 0.58 mmol); yield : 0.1g, 75%; oil; $\bar{\nu}$ max(cm^{-1}) 3400 (NH), 1680 (CONH); δH (200 MHz, $CDCl_3$) 7.37-7.02 (5H, m), 6.57 (1H, br s), 5.91 (1H, s), 4.13 (1H, h, ^{3}J=6.22), 4.15 (1H, q, ^{3}J=6.81), 1.31 (3H, d, ^{3}J=6.23), 1.26 (6H, d, ^{3}J=6.63); δC (50 MHz, $CDCl_3$) 172.2, 147.1, 129.6, 124.2, 117.8, 101.3, 71.7, 62.1, 23.7, 22.9, 12.1; m/z (E.I.) 250 ($M^{+\cdot}$, 4%), 136 (76%), 119 (28%), 77 (100%), 43 (73%)

2,3,6-triphenyl-1-oxa-2,5-diaza-4-oxo-cyclohexane 2d
2-azadiene **1d** (2.1g, 7 mmol), nitrosobenzene (0.75g, 7 mmol); yield : 1.89g; 82%; Rf=0.51 (ethyl acetate:cyclohexane,7:3); $\bar{\nu}$ max (cm^{-1}) 3320 (NH), 1650 (CONH); δH (200 MHz, $CDCl_3$) 7.62-6.88 (16H, m), 6.30 (1H, s), 5.36 (1H, s); δC (50 MHz, $CDCl_3$) 169.1, 147.0, 136.0, 134.9, 131.1, 129.9, 129.6, 129.3, 128.8, 128.7, 128.1, 123.3, 116.9, 87.7, 69.9; m/z (E.I.) 330 ($M^{+\cdot}$,12%), 223 (43%), 198 (100%), 180 (42%), 118 (79%), 77 (68%) E.A ($C_{21}H_{18}N_2O_2$) %C (76.34, found 76.39), %H (5.49, found 5.51), %N (8.48, found 8.62); mp 179-181°C

2,3-diphenyl-6-isopropoxy-1-oxa-2,5-diaza-4-oxo-cyclohexane 2e
2-azadiene **1e** (0.3g, 0.94 mmol), nitrosobenzene (0.1g, 0.94 mmol); yield : 0.185g, 63%; Rf=0.71 (ethyl acetate); $\bar{\nu}$ max (cm^{-1}) 3400 (NH), 1690 (CONH); δH (200 MHz, $CDCl_3$) 7.37-6.93 (11H, m), 6.03 (1H, s), 5.11 (1H, s), 4.18 (1H, h, ^3J=6.23), 1.34 (3H, d,^3J=6.23), 1.29 (3H, d,^3J=6.19); δC (50 MHz, $CDCl_3$) 169.4, 146.7, 133.9, 129.7, 128.7, 128.2, 128.1, 123.6, 117.8, 100.7, 71.1, 70.4, 23.4, 22.5; m/z (E.I.) 312 ($M^{+\cdot}$), 198 (23%), 181 (100%), 77 (43%); E.A ($C_{24}H_{24}N_2O_4$) %C (69.21, found 69.24), %H (6.45, found 6.47), %N (8.97, found 9.01); mp 149°C

3-benzyl-2,6-diphenyl-1-oxa-2,5-diaza-4-oxo-cyclohexane 2f
2-azadiene **1f** (1.4g, 4.5 mmol), nitrosobenzene (0.53g, 4.9 mmol); yield : 1.3g, 82%; Rf=0.91 (ethyl acetate); $\bar{\nu}$ max (cm^{-1}) 3400 (NH), 1685 (CONH); δH (200 MHz, $CDCl_3$) 7.45-6.97 (15H, m), 6.57 (1H, br s), 6.05 (1H, s), 4.64 (1H, t, ^3J=5.3), 3.25 (2H, d, ^3J=5.3); δC (50 MHz, $CDCl_3$) 169.6, 146.9, 138.5, 135.7, 130.8, 130.5, 129.5, 129.2, 128.6, 127.9, 126.6, 122.8, 115.9, 87.1, 66.5, 34.8; m/z (E.I.) 344 ($M^{+\cdot}$,12%), 194 (100%), 106 (36%), 91 (20%), 77 (18%); E.A ($C_{22}H_{20}N_2O_2$) %C (76.72, found 76.8), %H (5.85, found 5.84), %N (8.13, found 8.15); mp 159-162°C

3-benzyl-6-isopropoxy-2-phenyl-1-oxa-2,5-diaza-4-oxo-cyclohexane 2g
2-azadiene **1g** (0.3g, 0.94 mmol), nitrosobenzene (0.1g, 0.94 mmol); yield : 0.2g, 65%; oil; Rf=0.31 (ethyl acetate:cyclohexane, 3:7); $\bar{\nu}$ max (cm^{-1}) 3400 (NH), 1680 (CONH); δH (200 MHz, $CDCl_3$) 7.28-6.97 (11H,m) , 5.87 (1H, s), 4.40 (1H, t, ^3J=5.54), 3.98 (1H, h, ^3J=6.23), 3.11 (1H, d, ^3J=5.13), 1.28 (3H, d, ^3J=6.13), 1.24 (3H, d, ^3J=6.08); δC (50 MHz, $CDCl_3$) 170.6, 146.3, 138.1, 129.3, 128.9, 127.9, 125.9, 125.9,122.9, 116.5, 100.7, 70.7, 66.5, 34.2, 23.4, 22.7

3-vinyl-2,6-diphenyl-1-oxa-2,5-diaza-4-oxo-cyclohexane 2h
2-azadiene **1h** (1.0g, 4.1 mmol), nitrosobenzene (0.43g, 4.1 mmol); yield : 0.86g, 75%; Rf=0.66 (ethyl acetate); $\bar{\nu}$ max (cm^{-1}) 3400 (NH), 1685 (CONH); δH (200 MHz, $CDCl_3$) 7.6-6.96 (10H, m), 6.58 (1H, br s), 6.20 (1H, s), 5.97 (1H, dxdxd, ^3J=10.4, ^3J=17.3, ^3J=7.1), 5.48 (1H, d,^3J=17.3), 5.36 (1H, d, ^3J=10.4), 4.80 (1H, d, ^3J=7.1); δC (50 MHz, $CDCl_3$) 168.5, 147.3, 135.8, 131.2, 130.6, 129.53, 129.4, 128.2, 123.3, 122.6, 116.4, 87.8, 68.9; m/z (E.I.) 280 ($M^{+\cdot}$, 2%), 173 (12%), 131 (24%), 106 (24%), 77 (100%) E.A ($C_{21}H_{18}N_2O_2$) %C (72.84, found 72.90), %H (5.75, found 5.84), %N (9.99, found 10.07); mp 154°C

3-(m,p-dimethoxybenzyl)-2,6-phenyl-1-oxa-2,5-diaza-4-oxo-cyclohexane 2i
2-azadiene **1i** (2.1g, 5.6 mmol), nitrosobenzene (0.6g, 5.6 mmol); yield : 0.9 g, 41%; Rf=0.75 (ethyl acetate); $\bar{\nu}$ max (cm^{-1}) 3400 (NH), 1675 (CONH); δH (200 MHz, $CDCl_3$) 7.46-6.94 (10H, m), 6.69 (2H, s), 6.58 (1H, s), 6.43 (1H, br s), 6.04 (1H, s), 4.61 (1H, t, ^3J=4.6), 3.80 (3H, s), 3.70 (3H, s), 3.21 (2H, d, ^3J=4.8) ; δC (50 MHz, $CDCl_3$) 169.7, 149.1, 148.0, 147.1, 135.8, 131.2, 131.1, 129.6, 129.4, 128.1, 122.9, 122.5, 116.1, 113.9, 111.4, 87.2, 66.8, 56.2, 56.0, 34.7; m/z (E.I.) 404 ($M^{+\cdot}$, 36%), 272 (50%), 253 (100%), 151 (47%), 77 (30%) E.A ($C_{24}H_{24}N_2O_4$) %C (71.29, found 71.30), %H (5.94, found 6.00), %N (6.93, found 6.95); mp 172°C; X-Ray (cristallographic parameters): spatial group (P21/a), paramaters (a=8.712 Å, b=21.768 Å, c=11.840 Å, β=107.41°, v= 2142.5 $Å^3$, Z= 4

General procedure for 1,1-cyanonitrosocyclohexane
A mixture of 2-azadiene (1eq) and 1,1-cyanonitrosocyclohexane (1eq) in dry $CHCl_3$ (1M) was refluxed until complete disappearance of the dienophile. A large excess of methanol was then added to the reaction mixture. After complete methanolysis, solvents were evaporated under vacuum and the oily residue was purified by column and/or recrystallisation.

3-methyl-2(1'-cyanocyclohexyl)-6-phenyl-1-oxa-2,5-diaza-4-oxo-cyclohexane 3b
2-azadiene **1b** (0.7g, 3.0 mmol), 1,1-cyanonitrosocyclohexane (0.4g, 3.0 mmol); yield : 0.7g, 79%; Rf=0.28 (ethyl acetate:cyclohexane, 1:1); $\bar{\nu}$ max (cm^{-1}) 3400 (NH), 2240 (CN, weak), 1685 (CONH); δH (200MHz, $CDCl_3$) 7.40 (5H, br s), 6.78 (1H, br s), 5.91 (1H, s), 3.93 (1H, q, ^3J=6.80), 1.69 (3H, d, ^3J=6.80), 2.35-1.21 (10H, m); δC (50 MHz,$CDCl_3$) 171.5,135.7, 131.7, 129.43, 127.9, 120.7, 88.1, 60.1, 59.5, 35.9, 31.7, 25.0, 22.1, 21.7, 12.4; m/z (E.I.) 299 ($M^{+\cdot}$, less than 1%), 151 (13%), 106 (37%), 77 (100%); E.A ($C_{17}H_{21}N_3O_2$) %C (68.20, found 68.27), %H (7.07, found 7.10), %N (14.04, found 14.09); mp 177°C

3-methyl-2(1'-cyanocyclohexyl)-6-isopropoxy-1-oxa-2,5-diaza-4-oxo-cyclohexane 3c
2-azadiene **1c** (0.74g, 2.9 mmol), 1,1-cyanonitrosocyclohexane (0.4g, 2.9 mmol); yield : 0.6g, 71%; Rf=0.39 (ethyl acetate:cyclohexane, 1:1); $\bar{\nu}$ max (cm^{-1}) 3400 (NH), 2240 (CN, weak), 1680 (CONH); δH (200 MHz, $CDCl_3$) 6.39 (1H, br s), 5.77 (1H, s), 4.10 (1H, h, ^3J=5.43), 3.80 (1H, q, ^3J=7.13), 1.62 (3H, d, ^3J=7.02), 1.26 (6H, d, ^3J=5.66), 2.50-1.23 (10H, m); δC (50 MHz, $CDCl_3$) 172.3,120.5, 101.5, 71.3, 60.1, 58.8, 36.0, 31.7, 24.9, 23.8, 23.0, 21.7, 22.1, 12.1; m/z (E.I.) 281 ($M^{+\cdot}$, less than 1%), 167 (6%), 43 (100%); E.A ($C_{14}H_{28}N_3O_3$) %C (59.79, found 59.80), %H (8.18, found 8.21), %O (17.08, found 17.09); mp 137°C

3,6-diphenyl-2(1'-cyanocyclohexyl)-1-oxa-2,5-diaza-4-oxo-cyclohexane 3d
2-azadiene **1d** (0.56g, 1.9 mmol), 1,1-cyanonitrosocyclohexane (0.26g, 2.0 mmol); yield : 0.46g, 68%; Rf=0.29 (ethyl acetate:cyclohexane, 1:1); $\bar{\nu}$ max (cm^{-1}) 3400 (NH), 2240 (CN, very weak), 1680 (CONH); δH (200 MHz, $CDCl_3$) 7.65-7.28 (10H, m), 6.91 (1H, br s), 6.12 (1H, s), 4.86 (1H, s), 2.41-1.15 (10H, m); δC (50 MHz,$CDCl_3$) 169.2, 135.9, 134.4, 131.1, 130.9, 129.9, 129.6, 129.2, 127.9, 118.6, 87.8, 68.1, 61.9, 35.5, 32.5, 24.9, 22.1, 21.9; m/z (E.I.) 361 ($M^{+\cdot}$, 13%), 334 (9%), 255 (16%), 223 (85%), 118 (100%), 106 (49%), 77 (26%); E.A.($C_{22}H_{23}N_3O_2$) %C (73.11, found 73.01), %H (6.41, found 6.65), %N (11.63, found 11.75); mp 226°C (dec)

3-benzyl-2(1'-cyanocyclohexyl)-6-phenyl-1-oxa-2,5-diaza-4-oxo-cyclohexane 3f
2-azadiene **1f** (0.9g, 2.9 mmol), 1,1-cyanonitrosocyclohexane (0.44g, 3.2 mmol); yield : 0.8g, 74%; Rf=0.33 (ethyl acetate:cyclohexane, 1:1); $\bar{\nu}$ max (cm^{-1}) 3400 (NH), 2240 (CN, very weak), 1685 (CONH); δH (200 MHz, $CDCl_3$) 7.47-7.25 (10H, m), 6.35 (1H, br s), 6.00 (1H, s), 4.09 (1H, t), 3.63 and 3.45 (2H, ABX, $^2J_{AB}$=14.50, $^3J_{AX}$=3.94, $^3J_{BX}$=2.55), 2.35-1.21 (10H, m); δC (50 MHz,$CDCl_3$) 168.9,138.3, 135.5, 130.9, 130.3, 129.2, 128.7, 127.8, 126.8, 120.7, 87.7, 64.5, 60.0, 35.9, 33.7, 31.8, 24.8, 21.9, 21.4; m/z (E.I.) 375 ($M^{+\cdot}$, 25%), 348 (5%), 284 (37%), 243 (47%), 106 (49%); E.A.($C_{23}H_{25}N_3O_2$) %C (73.58, found 73.56), %H (6.71, found 6.24), %N (11.19, found 11.20); mp 191°C (dec)

3-(m,p-dimethoxybenzylbenzyl)-2(1'-cyanocyclohexyl)-6-phenyl-1-oxa-2,5-diaza-4-oxo-cyclohexane 3i
2-azadiene **1i** (0.77g, 2.1 mmol), 1,1-cyanonitrosocyclohexane (0.3g, 2.1 mmol); yield : 0.94g, 70%; Rf=0.18 (ethyl acetate:cyclohexane, 1:1); $\bar{\nu}$ max (cm^{-1}) 3400 (NH), 2240 (CN, very weak), 1685 (CONH); δH (200 MHz, $CDCl_3$) 7.45-7.21 (5H, m), 7.06 (1H, d, ^3J=1.98), 6.97 (1H, dxd, ^3J=1.98, ^3J=8.14), 6.81 (1H, d, ^3J=8.20), 6.58 (1H, br s), 5.98 (1H, s), 4.07 (1H, t=dxd, ^3J=4.99), 3.89 (3H, s), 3.81 (3H, s), 3.54 and 3.38 (2H, ABX, $^2J_{AB}$=14.80, $^3J_{AX}$=5.68, $^3J_{BX}$=4.71), 2.29-1.27 (10H, m); δC (50 MHz, $CDCl_3$) 169.2 ,148.8, 147.8, 135.2, 130.9, 130.6, 128.9, 127.5, 122.2, 120.7, 113.9, 111.1, 87.5, 64.4, 59.8, 55.8, 35.8, 32.9, 31.5, 24.5, 21.7, 21.2; m/z (E.I.) 455 ($M^{+\cdot}$, 3%), 408 (4%), 287 (12%), 151 (100%), 121 (17%); E.A.($C_{25}H_{29}N_3O_2$) %C (68.95, found 68.90), %H (6.71, found 7.00), %N (6.65, found 6.81); mp 175°C

General procedure for acylnitroso compounds
To a solution of 2-azadiene (1.1eq) and tetraethylammonium periodate (1eq) in dry dichloromethane (0.5M) was added dropwise the hydroxamic acid dissolved (1eq) in dry dichloromethane at room temperature. When the reaction was over (complete disappearance of the hydroxamic acid by TLC), the mixture was diluted with dichloromethane, washed with $Na_2S_2O_3$ (5%) and water. The organic layer was diluted with methanol, dried with anhydrous $MgSO_4$, filtered, and evaporated to dryness. The residue was purified by column chromatography.
3-benzyl-2-benzyloxycarbonyl-6-phenyl-1-oxa-2,5-diaza-4-oxo-cyclohexane 4a
0.5 mg (1.6 mmol) of azadiene **1f**, 270mg (1.6 mmol) of N-benzyloxycarbonylhydroxylamine, 541mg (1.6 mmol) of tetraethylammonium periodate; yield: 191mg (30%); colourless oil; Rf=0.43 (ethyl acetate:

cyclohexane/ 1:1); $\bar{\nu}$ max (cm^{-1}) 3220 (NH), 1685 (CONH), 1690 (NCOO); δH (200 MHz, $CDCl_3$) 7.51 (15H, m), 6.45 (1H, br s), 5.97 (1H, s), 4.95 (2H, m), 4.78 (1H, t=dxd, ^3J=6.01), 3.23 (2H, d, ^3J=6.18); δC (50 MHz, $CDCl_3$) 167.9, 154.2, 136.8, 135.6, 134.1, 131.2, 130.1, 129.1, 128.8, 128.6, 128.4, 128.1, 127.9, 127.1, 88.5, 68.1, 61.8, 37.3; m/z (E.I.) 402 (M^+)

3-benzyl-2-benzyloxycarbonyl-6-isopropoxy-1-oxa-2,5-diaza-4-oxo-cyclohexane 4b
0.366 mg (1.1 mmol) of azadiene **1g**, 167mg (1 mmol) of N-benzyloxycarbonylhydroxylamine, 356mg (1 mmol) of tetraethylammonium periodate; yield: 280.5mg (73%); colourless oil; Rf=0.35 (ethyl acetate: hexane, 4:6); $\bar{\nu}$ max (cm^{-1}) 3220 (NH), 1685 (CONH), 1690 (NCOO); major regioisomer: δH (200 MHz, $CDCl_3$) 7.45-7.11 (11H, m), 5.86 (1H, s), 4.90 (2H, m), 4.71 (1H, dxd, ^3J=5.12, ^3J=9.14), 4.15 (1H, h, ^3J=6.22), 3.20 (2H, m), 1.33 (3H, d, ^3J=6.22), 1.25 (3H, d, ^3J=6.20); δC (50 MHz, $CDCl_3$) 168.4,153.5, 136.5, 135.0, 129.5, 128.3, 128.4, 128.2, 128.1, 127.9, 101.5, 72.7, 67.9, 60.8, 36.6, 23.0, 22.4; m/z (E.I.) 384 (M^+, < 1 %), 205, 176, 148, 91 (100 %); calculated exact mass $C_{20}H_{24}N_2O_5$: 384.168522 (found : 384.168300)

3-phenyl-2-benzyloxycarbonyl-6-isopropoxy-1-oxa-2,5-diaza-4-oxo-cyclohexane 4c
0.351 mg (1.1 mmol) of azadiene **1e**, 167mg (1 mmol) of N-benzyloxycarbonylhydroxylamine, 356mg (1 mmol) of tetraethylammonium periodate; yield: 248.0mg (67%); Rf=0.33 (ethyl acetate: hexane, 4:6); $\bar{\nu}$ max (cm^{-1}) 3240 (NH), 1690 (CONH, NCOO); δH (200 MHz, $CDCl_3$) 7.54-7.18 (11H, m), 5.92 (1H, s), 5.56 (1H, s), 5.20 (2H, m), 1.28 (3H, d, ^3J=6.20), 1.19 (3H, d, ^3J=6.20); δC (50 MHz, $CDCl_3$) 167.1, 153.8, 135.1, 134.9, 128.5, 128.1, 127.9, 101.8, 72.9, 68.3, 62.5, 23.0, 22.4; m/z (E.I.) 370 (4%), 212, 176, 118, 91, 77, 65, 43; E.A. ($C_{20}H_{22}N_2O_5$) %C (64.85, found 64.50), %H (5.99, found 5.85), %N (7.56, found 7.46)

3-phenyl-2-phenoxycarbonyl-6-isopropoxy-1-oxa-2,5-diaza-4-oxo-cyclohexane 4d
0.351 mg (1.1 mmol) of azadiene **1e**, 153mg (1 mmol) of N-phenoxycarbonylhydroxylamine, 356mg (1 mmol) of tetraethylammonium periodate; yield: 140.0mg (40%); colourless oil; Rf=0.29 (ethyl acetate: hexane, 4:6); $\bar{\nu}$ max (cm^{-1}) 3220 (NH), 1730 (CONH), 1690 (NCOO); δH (200 MHz, $CDCl_3$) 7.81-7.06 (11H, m), 6.08 (1H, s), 5.59 (1H, s), 4.24 (1H, h, ^3J=6.20), 1.37 (3H, d, ^3J=6.20), 1.28 (3H, d, ^3J=6.20), δC (50 MHz, $CDCl_3$) 167.2, 152.2, 150.3, 134.8, 129.4, 128.7, 127.9, 126.1, 121.2, 102.0, 73.2, 62.6, 23.1, 22.4; m/z (E.I.) 356 (5%), 242, 134, 104, 77; calculated exact mass $C_{19}H_{20}N_2O_5$; 356.137222 (found : 356.138000)

REDUCTIVE HYDROLYSIS

Method A : sodium amalgam in methanol
In a dry flask, the cycloadduct (1eq) was dissolved in dry methanol (0.1M) (if required, the solution was heated for complete dissolution). Sodium/amalgam (10 eq in weight) was added portionwise through an additionnal funnel for solid. After addition, the reaction was stirred until disappearance of the starting material (TLC). The crude mixture was filtered on celite and the precipitate washed several times with methanol. The filtrate was then evaporated and the residue treated with HCl 1M. After two hours, the solution was neutralized with sodium carbonate and extracted several times with ethylacetate. The organic phase was dried over $MgSO_4$, filtered and evaporated under vacuum. The residual oil solidified in ether and was purified by recristallisation.

Method B : molybdenum hexacarbonyl
In a flask equipped with a condenser, the cycloadduct (1eq) was dissolved in a mixture acetonitrile/water (15/1). Molybdene hexacarbonyl (0.7eq) was added and the mixture refluxed. After 15-20 minutes, the mixture was completely black. This colour indicated that the reaction was taking place. When the reaction was over (disappearance of the starting material), the product was purified by column chromatography.

α-N-phenyl-glycinamide 5a
Method A: 0.4g (1.5 mmol) of adduct **2a**, 4g (10 eq. in weight) of 5% Na/Hg; 30 ml of CH_3OH; yield: 0.184g (74%); *Method B*: 0.2g (0.79 mmol) of adduct **2a**, 0.15g (0.55 mmol) of $Mo(CO)_6$, 13 ml of CH_3CN, 1ml of H_2O, yield:0.089g (75%); Rf=0.35 (ethyl acetate); $\bar{\nu}$ max (cm^{-1}) 3520 and 3400 (NH), 1690 (CONH); δH (200 MHz, $CDCl_3$) 7.26-6.63 (6H, m), 5.55 (1H, br s), 4.30 (1H, s), 3.82 (2H, s); δC (50 MHz, $CDCl_3$) 173.7, 147.6, 129.6, 119.3, 113.2, 48.3; m/z (E.I.) 150 ($M^{+\cdot}$, 20%), 106 (87%), 77 (34%), 58 (100%)

2–anilino-propionamide 5b
Method A: 0.27g (1 mmol) of adduct **2b**, 2.8g (10 eq in weight) of Na/Hg 5%, 25 ml of MeOH; yield: 0.11g (73%); *Method B*: 0.25g (0.93 mmol) of adduct **2b**, 0.17g (0.65 mmol) of $Mo(CO)_6$, 15 ml of CH_3CN, 1ml of H_2O, yield:0.11g (69%); *Method A*: 0.15g (0.6 mmol) of adduct **2c**, 1.5g (10 eq in weight) of Na/Hg 5%, 25 ml MeOH; yield: 0.052g (53%); *Method B*: 0.1g (0.4 mmol) of adduct **2c**, 0.074g (0.28 mmol) of $Mo(CO)_6$, 7ml of CH_3CN, 0.5ml of H_2O, yield:0.047g (71%); Rf=0.46 (ethyl acetate:cyclohexane, 1:1); $\bar{\nu}$ max (cm^{-1}) 3510 and 3400 (NH), 1695 ($CONH_2$); δH (200 MHz, $CDCl_3$) 7.25-6.59 (5H, m), 6.78 (1H, br s), 5.55 (1H, br s), 3.93 (1H, br s), 3.77 (1H, q,^{3}J=7.10), 1.53 (3H, d, ^{3}J=6.96); δC (50 MHz, $CDCl_3$) 177.3, 146.6, 129.5, 119.1, 113.5, 54.8, 19.3; m/z (E.I.) 164 ($M^{+\cdot}$, 11%), 120 (100%), 77 (14%)

2–anilino-2-phenyl-acetamide 5c
Method A: 0.15g (0.45 mmol) adduct **2d**, 1.5g (10 eq in weight) of Na/Hg 5%, 5 ml of MeOH; yield: 0.095g (93%); *Method B*: 0.171g (0.5 mmol) of adduct **2d**, 0.096g (0.36 mmol) of $Mo(CO)_6$, 7.5 ml of CH_3CN, 0.5ml of H_2O, yield:0.11g (91%); *Method A*: 0.15g (0.48 mmol) of adduct **2e**, 1.5g (10 eq in weight) of Na/Hg 5%, 30 ml of MeOH; yield: 0.073g (67%); *Method B*: 0.15g (0.48 mmol) of adduct **2e**, 0.089g (0.34 mmol) of $Mo(CO)_6$, 8 ml of CH_3CN, 0.5 ml of H_2O, yield:0.071g (65%) Rf=0.76 (ethyl acetate); $\bar{\nu}$ max (cm^{-1}) 3500 and 3400 (NH), 1700 ($CONH_2$); δH (200MHz, $CDCl_3$) 7.49-6.65 (10H, m), 6.53 (1H, br s), 5.70 (1H, br s), 4.78 (1H, s), 4.66 (1H, br s); δC (50 MHz, $CDCl_3$) 173.5, 146.2, 138.4, 129.4, 129.0, 128.4, 127.1, 118.8, 113.5, 63.4; m/z (E.I.) 226 ($M^{+\cdot}$, 11%), 182 (100%), 104 (24%), 77 (47%)

2–anilino-3-phenyl-propionamide 5d
Method A: 0.07g (2.00 mmol) of adduct **2f**, 0.7g (10 eq in weight) of Na/Hg 5%, 10 ml of MeOH; yield: 0.035g (72%); *Method B*: 0.1g (0.3 mmol) of adduct **2f**, 0.053g (0.2 mmol) of $Mo(CO)_6$, 5ml of CH_3CN, 0.3ml of H_2O, yield:0.049g (68%); *Method A*: 0.15g (0.46 mmol) of adduct **2g**, 1.5g (10 eq in weight) of Na/Hg 5%, 10 ml of MeOH; yield: 0.082g (75%); *Method B*: 0.15g (0.46 mmol) of adduct **2g**, 0.085g (0.32 mmol) of $Mo(CO)_6$, 8 ml of CH_3CN, 0.5 ml of H_2O, yield:0.086g (78%); Rf=0.74 (ethyl acetate); $\bar{\nu}$ max (cm^{-1}) 3510 and 3400 (NH), 1695 ($CONH_2$); δH (200 MHz, $CDCl_3$) 7.40-6.54 (10H, m), 6.62 (1H, br s), 5.49 (1H, br s), 4.01 (1H, br s), 3.95 (1H, dxd, ^{3}J=4.58, ^{3}J=8.83), 3.34 (1H, dxd, ^{2}J=14.2, ^{3}J=4.44), 3.06 (1H, dxd, ^{2}J=14.1, ^{3}J=8.79); δC (50 MHz, $CDCl_3$) 169.0, 146.5, 135.7, 129.1, 128.9, 127.3, 125.9, 119.4, 113.9, 59.9, 38.7; m/z (E.I.) 240 (20%), 196 (100%), 149 (96%), 119 (24%), 104 (54%), 91 (22%), 77 (34%), 43 (52%); E.A.($C_{15}H_{16}N_2O$) %C (74.97, found 74.34), %H (6.71, found 6.65), %N (11.66, found 11.50); mp 151-152°C

2–anilino-2-vinyl-acetamide 5e
Method B: 0.1g (0.36 mmol) of adduct **2h**, 0.066g (0.25 mmol) of $Mo(CO)_6$, 6 ml of CH_3CN, 0.4 ml of H_2O, yield:0.036g (56%) ; Rf=0.49 (ethyl acetate); $\bar{\nu}$ max (cm^{-1}) 3510 and 3400 (NH), 1695 ($CONH_2$); δH (200MHz, $CDCl_3$) 6.70 (5H, m), 6.50 (1H, br s), 5.60 (1H, br s), 4.30 (1H, br s, NH), 6.05 (1H, dxdxd, ^{3}J=10.1, ^{3}J=17.0, ^{3}J=6.5), 5.52 (1H, dxd, ^{2}J=16.95), 5.36 (1H, dxd,^{3}J=10.04), 4.25 (1H, dxd, ^{3}J=6.60); m/z (E.I.) 176 ($M^{+\cdot}$, 23%), 132 (100%), 105 (10%), 83 (6%)

2–anilino-butanamide
Method A: 0.13g (0.45mmol) of adduct **2h**, 1.58g (10 eq in weight) of Na/Hg 5%, 15 ml of MeOH; yield: 0.045g (56%); Rf=0.28 (ethyl acetate:cyclohexane, 7:3); $\bar{\nu}$ max (cm^{-1}) 3510 and 3400 (NH), 1695 ($CONH_2$); δH (200 MHz, $CDCl_3$) 7.30-6.60 (6H, m), 5.48 (1H, br s), 3.95 (1H, br s), 3.61 (1H, dxd, ^{3}J=4.50, ^{3}J=8.20), 2.01 (1H, m), 1.82 (1H, m), 1.50 (3H, t, ^{3}J=7.50); m/z (E.I.) 178 ($M^{+\cdot}$; 15%), 134 (100%), 118 (16%), 77 (6%)

2–anilino-3-(3',4'-dimethoxyphenyl)-propionamide 5f
Method A: 0.106g (0.26 mmol) of adduct **2f**, 1.1g (10 eq in weight) of Na/Hg 5%, 15 ml of MeOH; yield: 0.065g (83%); Rf=0.54 (ethyl acetate); $\bar{\nu}$ max (cm^{-1}) 3500 and 3400 (NH), 1695 ($CONH_2$); δH (200 MHz, $CDCl_3$) 7.40-6.50 (9H, m), 6.65 (1H, br s), 5.47 (1H, br s), 3.95 (1H, dxd, ^{3}J=4.54, ^{3}J=8.26), 3.87 (3H, s,), 3.83 (3H, s,), 3.29 (1H, dxd, ^{2}J=14.61, ^{3}J=4.54), 3.01 (1H, dxd, ^{2}J=14.1, ^{3}J=8.28); δC (50 MHz,

$CDCl_3$) 176.5, 149.2, 148.2, 146.4, 129.3, 128.8, 121.1, 119.3, 113.9, 111.9, 111.3, 59.9, 55.8, 38.7; m/z (E.I.) 300 ($M^{+\cdot}$, 2%), 256 (5%), 149 (4%), 107 (100%), 77 (51%)

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REFERENCES

1. Ghosez, L.; Bayard, Ph.; Nshimyumukiza, P.; Gouverneur, V.; Sainte, F.; Beaudegnies, R.; Rivera, M.; Frisque-Hesbain, A.-M. and Wynants, C. *Tetrahedron* **1995**, *51*, 11021.
2. Ghosez, L.; Serckx-Poncin, B.; Rivera, M.; Bayard, P.; Sainte, F.; Demoulin, A.; Hesbain-Frisque, A.-M.; Mockel, A.; Munoz, L.; Bernard-Henriet, C. *Lect. Het. Chem.* **1985**, *8*, 69; Bayard, P.; Ghosez, L. *Tetrahedron Lett.* **1988**, *29*, 6115; Bayard, P.; Sainte, F.; Beaudegnies, R.; Ghosez, L. *Tetrahedron Lett.* **1988**, 3799; Rivera, M.; Lamy-Schelkens, H.; Sainte, F.; Mbiya, K.; Ghosez, L. *Tetrahedron Lett.* **1988**, 4573; Lamy-Schelkens, H.; Giomi, D.; Ghosez, L.; *Tetrahedron Lett.* **1988**, 5887; Lamy-Schelkens, H.; Ghosez, L. *Tetrahedron Lett.* **1989**, 5891; Gouverneur, V.; Ghosez, L. *Tetrahedron:Asymmetry* **1991**, 5349.
3. Boger, D.L.; Weinreb, S.N. " Hetero Diels-Alder Methodology in Organic Synthesis", Academic Press Inc. **1987** and references therein.
4. Defoin, A.; Fritz, H.; Schmidlin, C.; Streith, J. *Helv. Chim. Acta* **1987**, *70*, 554; Kirby, G.W.; Nazeer, M. *Tetrahedron Lett.* **1988**, 6173; Miller, A.; Mc Paterson, T.C.; Procter, G. *Synlett* **1989**, 32; Braun, H.; Charles, R.; Kresze, G.; Sabuni, M.; Winkler, J. *Liebigs Am. Chem.* **1987**, 1129; Feller, H.; Kresze, G.; Prewo, R.; Vasella, A. *Helv. Chim. Acta* **1986**, *69*, 1137; Sabrini, M.; Kresze, G.; Braun, H. *Tetrahedron Lett.* **1979**, *27*, 3597; Felber, H.; Kresze, G.; Braun, H.; Vasella, A. *Tetrahedron Lett.* **1986**, *27*, 1895.
5. Gouverneur, V.; Ghosez, L. *Tetrahedron Lett.* **1991**, *32*, 5349.
6. Mc Clure, K.F.; Danishefsky, S.F. *J. Org. Chem* . **1991**, *56*, 850; Ried, W.; Reiher, U.; Bats, J.W. *Helv. Chim. Acta* **1987**, *70*, 1255; Taylor, E.C.; Mc Daniel, K.; Skotnicki, J.S. *J. Org. Chem.* **1984**, *42*, 2500.
7. We thank Dr J.-P.Declercq, J. Feneau-Dupont and Dr B.Tinant for the crystallographic study.
8. Kresze, G.; Weiss, M.M.; Dittel, W. *Liebigs Ann. Chem.* **1984**, 203; Leonard, N.J.; Playtis, A.J.; Skoog, F.J.; Schmitz, R.Y. *J. Am. Chem. Soc.* **1971**, *93*, 3056; Leonard, N.J., Playtis, A.J. *J. Chem. Soc. Chem. Commun.* **1972**, *133* .
9. Kirby, G.W.; Mc Guigan, H.; Mac Kinnon, J.W.N.; Mc Lean, D.; Sharma, R.P. *J. Chem. Soc. Perkin Trans I* **1985**, 1437; Defoin, A.; Pires, J.; Streith, J. *Synlett* **1990**, 111; Boger, D.L.; Patel, M. *J. Org. Chem.* **1984**, *49*, 4098; Boger, D.L.; Patel, M.; Takusagawa, F. *J. Org. Chem.* **1985**, *50*, 1911; Baldwin, J.E.; Otsuka, M.; Wallace, P.M. *Tetrahedron* **1986**, *42*, 3097; Keck, G.E. *Tetrahedron Lett.* **1978**, 4767; Keck, G.E.; Nickell, D.G. *J. Am. Chem. Soc.* **1980**, *102*, 3632.
10. Boger, D.L.; Patel, M.; Takusagawa, F. *J. Org.Chem* **1985**, *50*, 1911.
11. Cicchi, S.; Goti, A.; Brandi, A.; Guarna, A., De Sarbo, F. *Tetrahedron lett.* **1990**, *31*, 3351; Baraldi, P.G.; Barco, A.; Benetti, S.; Mangredini, S.; Simoni, D. *Synthesis* **1987**, 276.
12. Zenders, D.; Lotter, H.; Maigrot, N.; Maleyrat, J.P.; Welvart, Z. *Nouveau Journal de Chimie* **1984**, *7*, 747.
13. See for example Schollkopft, U.; Neubauer, H.J. *Synthesis* **1982**, 861.
14. Kresze, G. *Org. Prep. Proced. Int.* **1987**, *19*, 329.
15. Porter, C.C.; Hellerman, L. *J. Am. Chem. Soc.* **1944**, *66*, 1652; Winterle, O.; Gregor, V.; Dubansky, A.; Seidl, V. *Chem. Listy* **1957**, *51*, 605.
16. Boyland, E.; Nevy, R. *J. Chem. Soc.(C)* **1966**, 354.
17. Stewart, A.O.; Brooks, D.W. *J. Org. Chem.* **1992**, *57*, 5020.

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