Tetrahedron Vol. 49, No. 13, pp. 2629-2640, 1993
Printed in Great Britain

0040-4020/93 $6 00+ 00

Novel Syntheses of Oxamides, Oxamates and Oxalates from Diisopropenyl Oxalate

Muriel Neveux, Christian Bruneau, Serge Lécolier†, Pierre H. Dixneuf *

Laboratoire de Chimie de Coordination Organique, Unité de Recherche Associée au CNRS 415
Campus de Beaulieu, Université de Rennes, 35042 Rennes (France)
† SNPE Centre de Recherche du Bouchet, BP 2, 91710 Vert Le Petit (France)

(*Received in Belgium* 11 *January* 1993)

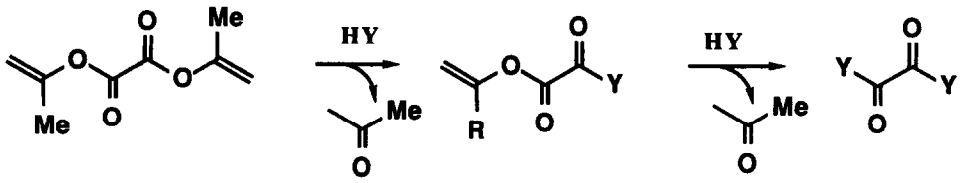
Key Words : Diisopropenyl Oxalate ; Oxamides ; Oxamates ; Oxalates; α-Dicarbonyl derivatives

Abstract : Diisopropenyl oxalate, obtained by catalytic addition of oxalic acid to propyne, is a useful reagent for the access to a variety of α-dicarbonyl compounds such as oxamides, oxamates and oxalates, under very mild conditions.

α-Dicarbonyl compounds are useful synthons in organic chemistry, and the α-dioxo bridge is a key functionality of many elaborated compounds. Esters and amides of general formula ZCOCOZ' (Z, Z'= OR, NR_2) have industrial uses as synthetic intermediates[1] or co-component in polymerization[2]. Some of them show biological activity as pesticides[3] or pharmaceutics.[4]

α-Ketoamides have been prepared by double carbonylation of organic halides with amines in the presence of palladium complexes.[5] Oxamides, oxalates and oxamates have been obtained by carbonylation of amines, alcohols or amino alcohols with palladium(II) catalysts.[6] These catalytic carbonylation reactions require the use of carbon monoxide and most of them are not selective since monocarbonylation occurs. Some reactive oxamides, oxalates or oxamates,[9] such as oxalyldiimidazole[1] or diacetyloxamide,[10] have been used for the synthesis of α-diketo derivatives. Because of the lack of selectivity of the direct carbonylation methods, oxalyl chloride is widely used and allows the access to a variety of α-dicarbonyl compounds, either *via* Friedel and Crafts reactions with aromatics[7] or *via* acylation of nucleophiles.[8] The use of oxalyl chloride produces hydrochloric acid and its trapping requires bases which are not tolerated for some pharmaceutical syntheses.

We have previously reported that enol esters were easily available in one step by regioselective addition of carboxylic acids to terminal alkynes, catalyzed by ruthenium(II) complexes.[11] We also have shown that these activated esters were efficient *O*- and *N*-acylation reagents.[12] We now wish to report on the use of diisopropenyl oxalate as a new acylating agent of nucleophiles, which presents the major advantage of releasing acetone as the only by-product on mono- or diacylation reactions under neutral conditions.

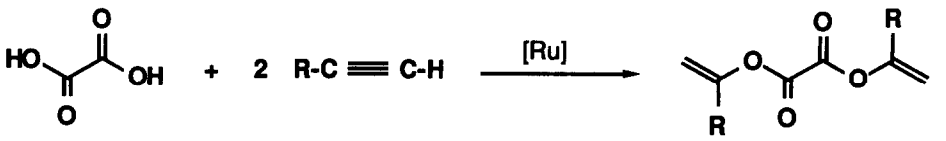


HY= R'NH_2, R'OH

SYNTHESIS OF DIISOPROPENYL OXALATE

In the presence of a catalytic amount of a ruthenium complex[11c] (0.4 mmol), the regioselective addition of oxalic acid (50 mmol) to hex-1-yne or propyne (110 mmol) in toluene (40 ml) at 100°C for 20 h afforded the symmetrical dienyl oxalates **1a** and **1b** in 60 and 40% yields, respectively (eq. 1). These new compounds were easily isolated by distillation under reduced pressure and characterized spectroscopically and by satisfactory elemental analyses. To our knowledge, only divinyl oxalate (**1**: **R** = H), prepared from chloromercuriacetaldehyde and oxalyl chloride was known.[13]

eq.1

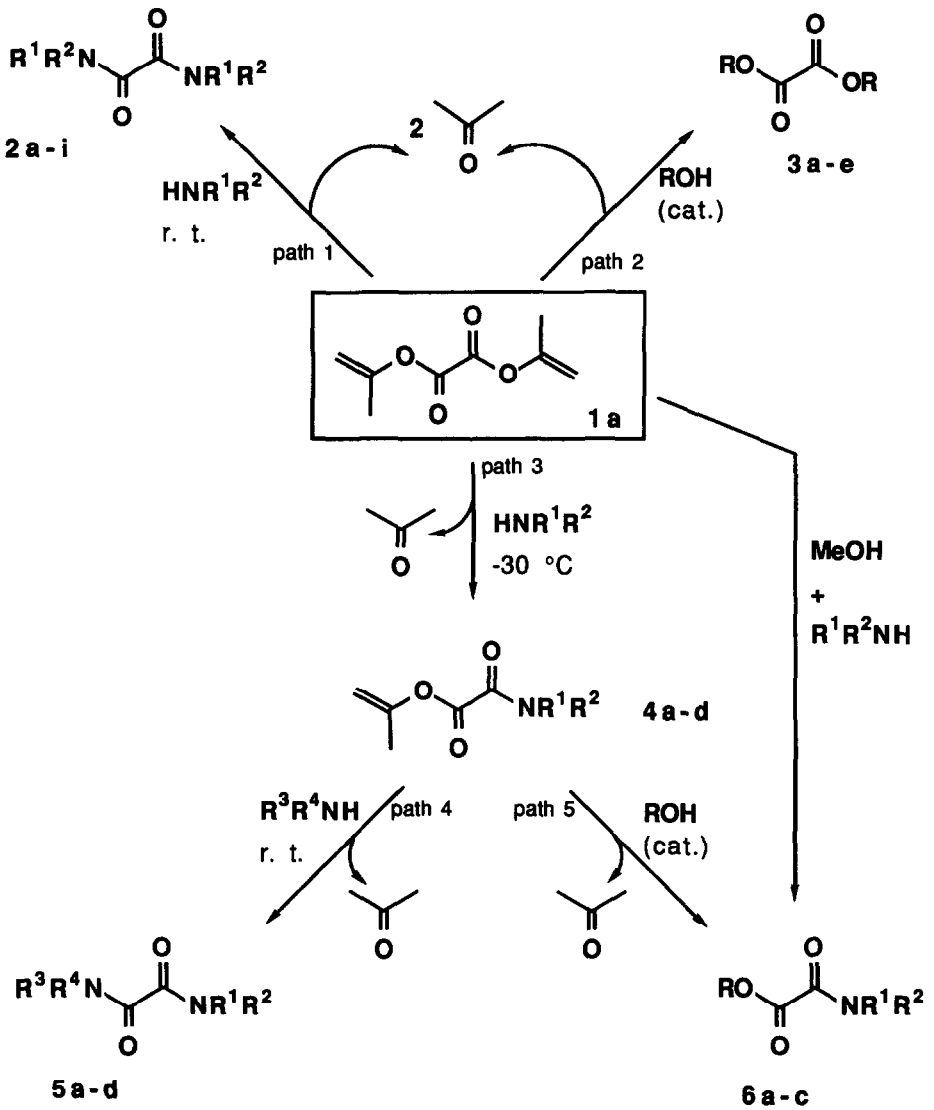


R= Me (**1a**) 60%
^{n}Bu (**1b**) 40%

DOUBLE ACYLATION: SYNTHESIS OF SYMMETRICAL OXAMIDES AND OXALATES

When 2 equivalents of a primary or secondary amine, or ammonia were reacted with diisopropenyl oxalate **1a** in ethylacetate at room temperature, a very fast conversion of the diester was observed by gas chromatography. An exothermic *N*-acylation reaction took place affording the symmetrical oxamides **2a-i** (Table 1) in good yields and acetone as the only by-product (Scheme, path 1). It was noteworthy that diisopropenyl oxalate **1a** was much more reactive than dialkyl oxalates since the acylation of morpholine with diethyloxalate at 40 °C reached 50% yield after 45 h, whereas the diacylation with **1a** was instantaneous at room

temperature. Moreover, with diethyloxalate no amide was formed with ethylglycinate at 40 °C for 15 h or aniline at 80 °C for 15 h.



cat.: Imidazole (10 mol%)

Scheme: New pathways for the access to α-dicarbonyl compounds from diisopropenyl oxalate

Functional oxamides such as 1,1'-oxalyldihydrazine **2d** or 1,1'-oxalyldiethanolamine **2h** were easily obtained by this method. Of special interest was the acylation of amino acid derivatives under mild conditions which led to the synthesis of peptide oxamides of type **2g** directly from the amino ester hydrochloride in the presence of Et_3N. With a heterocyclic primary amine such as 2-aminothiazole, the oxamide **2e** was isolated in 73% yield. This reaction provides a new and simple access to the oxalyldi(2-aminothiazole) unit encountered in biologically active substances.[4]

Table 1. Synthesis of Oxamides from Diisopropenyl Oxalate **1a**

Amine	Oxamide		Yield (%)
Ammonia	**2a**	$H_2NCOCONH_2$	95
n-Propylamine	**2b**	$Me(CH_2)_2NHCOCONH(CH_2)_2Me$	81
Aniline	**2c**	PhNHCOCONHPh	80
Hydrazine	**2d**	$H_2NNHCOCONHNH_2$	78
2-Aminothiazole	**2e**		73
Morpholine	**2f**		75
Ethyl glycinate	**2g**	$EtO_2CCH_2NHCOCONHCH_2CO_2Et$	75
2-Ethanolamine	**2h**	$HOCH_2CH_2NHCOCONHCH_2CH_2OH$	76
L(-)-α-Methylbenzylamine	**2i**	$Ph^*CH(Me)NHCOCONH^*CH(Me)Ph$	61

Acylation of secondary amines like morpholine, which required the presence of KCN as catalyst with classical enol esters[11c, 12b] was possible at room temperature without any additional catalyst and afforded 1,1'-oxalyldimorpholine **2f** in 75% yield within a few minutes. As detected by high resolution ^1H NMR, the diastereoisomerically pure oxamide **2i** was obtained starting from pure *L*-(-)-α-methylbenzylamine, which indicated that both acylation reactions took place without racemization. The primary diamines 1,2-diaminoethane and 1,10-diaminodecane reacted very rapidly with diisopropenyl oxalate **1a** to give insoluble polymeric oxamides exhibiting a strong IR absorption at 1630 cm^{-1}, but their composition was not elucidated.

Diisopropenyl oxalate **1a** and isopropenyl formate[12a] show similar behaviours towards the acylation of amines; both of them are better acylating reagents than alkyl oxalates or formates and also they are much more reactive than enol esters obtained from alkyl or aryl carboxylic acids, especially in the case of secondary amines for which no acylation catalyst is necessary to produce oxamides and formamides.

The synthesis of fragile functional or optically active oxalates under mild conditions was an attractive goal, but under the previous conditions, even simple alcohols like methanol or ethanol failed to react with diisopropenyl oxalate **1a**. Nevertheless, in the presence of a catalytic amount of imidazole (1 mmol) as acylation catalyst, the reaction of 10 mmol of ethanol, *n*-pentanol, propargyl or allyl alcohol, with 5 mmol of diisopropenyl oxalate **1a** at 50 °C for 20-30 h, (Scheme , path 2) gave the expected symmetrical oxalates **3a-d** in 65, 60, 77 and 83% yields, respectively (Table 2). The intermediate formation of the very reactive 1,1'-oxalyldiimidazole[1] usually produced from oxalyl chloride is suggested to explain this catalytic effect. The acylation of phenol was more difficult and only 40% yield of diphenyloxalate **3e** could be isolated.

Table 2. Synthesis of Oxalates from Diisopropenyl Oxalate **1a**

Alcohol		Oxalate	Yield (%)
Ethanol	**3a**	EtO_2CCO_2Et	65
n-Pentanol	**3b**	$C_5H_{11}O_2CCO_2C_5H_{11}$	60
Propargyl alcohol	**3c**	$HC{\equiv}CCH_2O_2CCO_2CH_2C{\equiv}CH$	77
Allyl alcohol	**3d**	$CH_2{=}CHCH_2O_2CCO_2CH_2CH{=}CH_2$	83
Phenol	**3e**	PhO_2CCO_2Ph	40

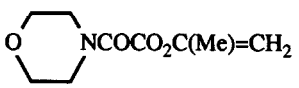
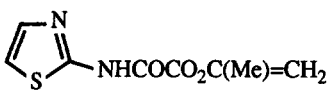
MONOACYLATION: SYNTHESIS OF ISOPROPENYL OXAMATES AND ACCESS TO UNSYMMETRICAL OXAMIDES AND ALKYL OXAMATES

In order to produce bifunctional compounds, attempts have been made to substitute only one enol group of diisopropenyl oxalate to form activated oxamates, precursors of amino acids[14].

When 8 mmol of amine diluted in 20 ml of solvent were slowly added to 8 mmol of diisopropenyl oxalate **1a** in 30 ml of the same solvent at -30 °C and stirred for 5 h, the new isopropenyl oxamates **4b-d** were obtained as major products (Scheme path 3 - Table 3). A small amount of oxamide (5 to 10%) was always formed, but

was easily removed by filtration before evaporation of the solvent. Gaseous ammonia was so reactive that $NH_2COCONH_2$ was formed and it was not possible to obtain the isopropenyl oxamate **4a** even at very low temperature. The use of a 7M solution of ammonia in methanol diluted in THF allowed the formation of **4a** in 60% yield, whereas the direct access to **4a** *via* the catalytic addition of oxamic acid to propyne was not possible. α-Dicarbonyl compounds **4a-d** are suitable intermediates for the access to a variety of unsymmetrical dicarbonyl precursors and useful derivatives: for example, the dehydration of ethyl oxamate by P_2O_5 affords ethylcyanoformate which is the starting material for numerous syntheses of substances of biological importance.[15]

Table 3. Synthesis of Isopropenyl Oxamates from Diisopropenyl Oxalate **1a**

Amine	Oxamate		Yield (%)
Ammonia	**4a**	$H_2NCOCO_2C(Me)=CH_2$	60
Aniline	**4b**	$PhNHCOCO_2C(Me)=CH_2$	60
Morpholine	**4c**		79
2-Aminothiazole	**4d**		69

Attempts to synthetize isopropenyl oxalates by reaction of one equivalent of alcohol with **1a** in diluted solutions were unsuccessful, but this reaction was possible in the presence of an acylation catalyst at 50 °C. Unfortunately, both mono- and diacylation took place and no selectivity was obtained. Thus, in the presence of 10 mol% of imidazole at 50 °C, allyl alcohol gave a 50/50 mol% mixture of allyl isopropenyl oxalate and diallyl oxalate.

The high reactivity of the enol oxamates **4** allowed the clean and easy access to α-dicarbonyl compounds usually produced from oxalyl chloride. Thus, 5 mmol of amine reacted with 5 mmol of isopropenyl oxamates **4** in 10 ml of THF or dichloromethane at 20 °C to give the unsymmetrical oxamides **5a-d** and acetone (Scheme path 4 - Table 4). The reaction of alcohols with the intermediates **4a-d** was not possible without the use of an

acylation catalyst. With 10 mol% of imidazole at 50 °C, oxamate **4c** reacted with ethanol to afford ethyl morpholine oxamate in 60% yield (Scheme path 5). However, we have shown that with a large excess of methanol used as solvent and one equivalent of amine, methyl oxamates **6a** and **6b** were obtained in one step at room temperature directly from diisopropenyl oxalate **1a** (Table 5).

Table 4. Synthesis of Unsymmetrical Oxamides from Isopropenyl Oxamates **4a-d**

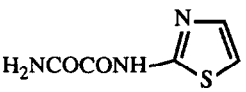
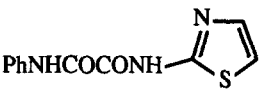
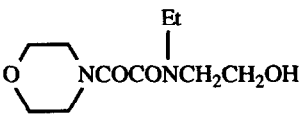
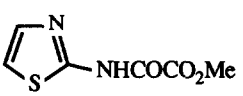
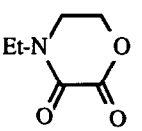
Isopropenyl Oxamide	Amine	Oxamate	Yield (%)
4a	2-Aminothiazole	**5a** 	65
4b	2-Aminothiazole	**5b** 	60
4c	2-(Ethylamino) ethanol	**5c** 	60
4d	Morpholine	**5d** 	61

Table 5. One Step Synthesis of Alkyl Oxamates from Diisopropenyl Oxalate **1a**

Amine	Alcohol	Oxamate	Yield (%)
Ammonia	Methanol	**6a** H_2NCOCO_2Me	60
2-Aminothiazole	Methanol	**6b** 	87
2-(Ethylamino) ethanol		**6c** 	75

When 8 mmol of 2-(ethylamino)ethanol were added dropwise to a solution containing 8 mmol of **1a** in 50 ml of dichloromethane cooled at -10 °C, 4-ethylmorpholine-2,3-dione **6c** was isolated in 75% yield. In these latter reactions, the amine serves as the basic catalyst for the acylation of the alcohol and the intermediate isopropenyl oxamates **4** seem to be more reactive towards the alcohol than the initial diisopropenyl oxalate **1a**.

These results show that diisopropenyl oxalate, prepared in one step from oxalic acid and propyne under ruthenium catalysis, is a versatile starting material for the access to α-dioxo compounds. It thus appears as a possible substitute of oxalyl chloride especially when mild and neutral conditions avoiding racemization are required.

EXPERIMENTAL SECTION

General. All the solvents were freshly distilled over dehydrating materials, and reactants were commercially available and used without further purification. Melting points were determined with a Reichert melting point apparatus and were uncorrected. IR spectra were carried out with a Nicolet 205 FTIR spectrometer and ^1H NMR spectra were performed with a Bruker AW 80 (80 MHz) or a Bruker AC 300 (300 MHz) spectrometer. Mass spectra were carried out with a Varian Mat 311 mass spectrometer at Le Centre Régional de Mesures Physiques de L'Ouest (Rennes) and elemental analyses were performed at Le Laboratoire Central de Microanalyses du CNRS (Vernaison).

*Diisopropenyl oxalate (**1a**).* 60% yield; colorless liquid, bp 64 °C (2 mm Hg); IR (film) ν/cm^{-1} 1775, 1750 (C=O) and 1680 (C=C); ^1H NMR δ (80 MHz, $CDCl_3$) 2.00 (s, 6 H, CH_3), 4.86 (m, 4 H, CH_2=C). Found: C, 56.03; H, 5.95; M$^+$, 170.058. Calcd for $C_8H_{10}O_4$: C, 56.45; H, 5.93; M, 170.058.
*Di(hex-1-en-2-yl) oxalate (**1b**).* 40% yield; colorless liquid, bp 95 °C (1 mm Hg); IR (film) ν/cm^{-1} 1780 (C=O), 1680 and 1670 (C=C); ^1H NMR δ (80 MHz, $CDCl_3$) 0.90 (t, 6 H, ^3J= 7.1 Hz, CH_3), 1.40 (m, 8 H, CH_2), 2.25 (m, 4 H, OCH_2), 4.80(m, 4 H, CH_2=C). Found: M$^+$, 254.152. Calcd for $C_{14}H_{22}O_4$: M, 254.152.

*Typical procedure for the preparation of oxamides **2a-i**.* 3 Mmol of diisopropenyl oxalate **1a** were slowly poured into a solution containing 6 mmol of amine in 10 ml of anhydrous ethylacetate, and the mixture was stirred for 0.5 h at room temperature. After removal of the solvents with a rotary evaporator, the solid oxamides were recrystallized from dichloromethane-diethylether mixtures. Although the starting product **1a** and the isopropenyl oxamate intermediate were no longer present (NMR, VPC), the elemental analyses of **2a-i** were not always satisfactory.
*Oxamide (**2a**).* 95% yield; white solid; m.p. > 360 °C (lit. 419 °C decomp.); IR (KBr) ν/cm^{-1} 1670 (C=O); Found: C, 28.86; H, 4.52; N, 30.76; M$^+$, 88.027. Calcd for $C_2H_4N_2O_2$: C, 27.26; H, 4.58; N, 31.82; M, 88.027.

N,N'-*Di*-n-*propyl oxamide (2b)*. 81% yield; white solid; m.p. 134-136 °C; IR (KBr) ν/cm^{-1} 1680 (C=O); ^{1}H NMR δ (80 MHz, $CDCl_3$) 0.92 (t, 6 H, ^{3}J= 7.2 Hz, CH_3), 1.57 (sext, 4 H, ^{3}J= 7.2 Hz, CH_2Me), 3.26 (q, 4 H, ^{3}J= 6.4 Hz, CH_2N), 7.30 (m, 2 H, NH). Found: C, 54.60; H, 9.48; N, 15.27; M$^+$, 172.121. Calcd for $C_8H_{16}N_2O_2$: C, 55.77; H, 9.37; N, 16.27; M, 172.121.

N,N'-*Diphenyl oxamide (2c)*. 80% yield; white solid; m.p. 253-255 °C; IR (KBr) ν/cm^{-1} 1680 (C=O); ^{1}H NMR δ (80 MHz, DMSO) 3.28 (s, 2 H, NH), 7.40 (m, 6 H, Ph meta- and para-H), 7.80 (m, 4 H, Ph ortho-H). Found: C, 69.50; H, 5.10; N, 11.38; M$^+$, 240.089. Calcd for $C_{14}H_{12}N_2O_2$: C, 69.97; H, 5.04; N, 11.66; M, 240.090.

1,1'-Oxalyldihydrazine (2d). 78% yield; white solid; m.p. 240 °C decomp.; IR (KBr) ν/cm^{-1} 1680 (C=O). Found: C, 21.04; H, 5.04; N, 46.48; M$^+$, 118.048. Calcd for $C_2H_6N_4O_2$: C, 20.33; H, 5.12; N, 47.45; M, 118.049.

1,1'-Oxalyldi(2-aminothiazole) (2e). 73% yield; white solid; m.p.>300 °C decomp.; IR (KBr) ν/cm^{-1} 1670 (C=O) and 1540 (C=N); ^{1}H NMR δ (300 MHz, DMSO) 7.38 (d, 2 H, ^{3}J= 3.2 Hz, C<u>H</u>=CH), 7.60 (d, 2 H, ^{3}J= 3.2 Hz, CH=C<u>H</u>), 13.00 (m, 2 H, NH). Found: C, 38.50; H, 2.84; N, 21.27; M$^+$, 253.992. Calcd for $C_8H_6N_4O_2S_2$: C, 37.80; H, 2.38; N, 22.05; M, 253.993.

1,1'-Oxalyldimorpholine (2f). 75% yield; white solid; m.p. 182-184 °C; IR (KBr) ν/cm^{-1} 1640 (C=O), ^{1}H NMR δ (300 MHz, DMSO) 3.30 (m, 4 H, ^{3}J= 4.8 Hz, CH_2), 3.50 (m, 4 H, ^{3}J= 4.8 Hz, CH_2), 3.60 (m, 8 H, ^{3}J= 4.9 Hz, CH_2). Found: C, 51.80; H, 7.20; N, 12.10; M$^+$, 228.111. Calcd for $C_{10}H_{16}N_2O_4$: C, 52.67; H, 7.20; N, 12.27; M, 228.111.

1,1'-Oxalyldi(ethylaminoacetate) (2g). 75% yield; white solid; IR (KBr) ν/cm^{-1} 1760 (C=O ester) and 1670 (C=O amide); ^{1}H NMR δ (80 MHz, CD_2Cl_2) 1.25 (t, 6 H, ^{3}J= 7.2 Hz, CH_3), 4.03 (d, 4 H, ^{3}J= 4.8 Hz, CH_2N), 4.20 (q, 4 H, ^{3}J= 7.2 Hz, CH_2Me), 7.30 (m, 2 H, NH). Found: C, 46.15; H, 6.04; N, 10.79; M$^+$, 260.102. Calcd for $C_{10}H_{16}N_2O_6$: C, 46.14; H, 6.20; N, 10.77; M, 260.101.

N,N'-*Di(2-hydroxyethyl) oxamide (2h)*. 76% yield; white solid; m.p. 128-130 °C; IR (KBr) ν/cm^{-1} 1660 (C=O); ^{1}H NMR δ (300 MHz, DMSO) 3.20 (q, 4 H, ^{3}J= 6.0 Hz, CH_2N), 3.44 (t, 4 H, ^{3}J= 6.0 Hz, OCH_2), 4.8 (m, 2 H, NH). Found: C, 41.15; H, 6.98; N, 15.53. Calcd for $C_6H_{12}N_2O_4$: C, 40.89; H, 6.87; N, 15.91.

1,1'-Oxalyldi(L(-)-α-methylbenzylamine) (2i). 61% yield, white solid, m.p. 200-202 °C; $[\alpha_D]^{20}$= -160 (c=1g/l, EtOH); IR (KBr) ν/cm^{-1} 1650 (C=O); ^{1}H NMR δ (300 MHz, DMSO) 1.45 (d, 6 H, ^{3}J= 7.1 Hz, CH_3), 4.97 (dq, 2 H, ^{3}J= 8.7 and ^{3}J= 7.2 Hz, CH), 7.30 (m, 10 H, Ph), 9.14 (d, 2 H, ^{3}J= 8.7 Hz, NH). Found: C, 73.27; H, 6.90; N, 9.55; M$^+$, 296.154. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.94; H, 6.80; N, 9.46; M, 296.152.

Typical procedure for the preparation of oxalates 3a-e. Imidazole (0.5 mmol) was added to a solution containing 5 mmol of diisopropenyl oxalate **1a** and 11 mmol of alcohol in anhydrous tetrahydrofuran (10 ml). The mixture was heated at 50 °C for 20-30 h and the solvents were removed with a rotary evaporator. Oxalates **3a** and **3b** were purified by distillation under reduced pressure, oxalate **3c** and **3e** were recrystallized from dichloromethane-ether-hexane mixtures, and oxalate **3d** was purified by column chromatography on silica (Merck Si 60) with hexane- ether (80:20) as eluent.

Diethyl oxalate (3a). 65%, colorless liquid; IR (film) ν/cm^{-1} 1770 and 1745 (C=O); ^{1}H NMR δ (80 MHz, $CDCl_3$) 1.30 (t, 6 H, ^{3}J= 7.2 Hz, CH_3), 4.30 (q, 4 H, ^{3}J= 7.2 Hz, CH_2).

Di-n-pentyl oxalate (3b). 60% yield; colorless liquid; IR (film) ν/cm^{-1} 1770 and 1750 (C=O); ^{1}H NMR δ (300 MHz, $CDCl_3$) 0.85 (t, 6 H, ^{3}J= 6.8 Hz, CH_3), 1.33 (m, 8 H, CH_2), 1.70 (quint, 4 H, ^{3}J= 6.9 Hz, $OCH_2C\underline{H}_2$), 4.23 (t, 4 H, ^{3}J= 7.0 Hz, OCH_2).

Di-(prop-2-ynyl) oxalate (3c). 77% yield; white solid; m.p. 99-101 °C; IR (KBr) ν/cm^{-1} 2130 (C≡C) and 1750 (C=O); ^{1}H NMR δ (300 MHz, CD_3OD) 3.07 (t, 2 H, ^{4}J= 4.5 Hz, HC≡), 4.77 (d, 4 H, ^{4}J= 4.5 Hz, CH_2). Found: C, 56.46; H, 3.67; M$^+$, 83.013. Calcd for $C_8H_6O_4$: C, 57.82; H, 3.64; M/2, 83.013.

Diallyl oxalate (3d). 83% yield; colorless liquid; IR (film) ν/cm^{-1} 1770, 1740 (C=O) and 1650 (C=C); ^{1}H NMR δ (300 MHz, CD_2Cl_2) 4.72 (dt, 4 H, ^{3}J= 5.9, ^{4}J= 1.3 Hz, CH_2), 5.29 (dq, 2 H, $^3J_{cis}$= 10.3, ^{4}J=1.2, ^{2}J= 1.2, =C$\underline{H}$H), 5.38 (dq, 2 H, $^3J_{trans}$= 17.1, ^{4}J= 1.4, ^{2}J= 1.2 Hz, =C$\underline{H}$H), 6 - 5.87 (4 t, 2 H, ^{3}J= 5.9, $^3J_{cis}$= 10.4, $^3J_{trans}$= 17.1 Hz, $CH_2C\underline{H}$=). Found: C, 56.17; H, 6.08; M$^+$, 170.157. Calcd for $C_8H_{10}O_4$: C, 56.45; H, 5.93; M, 170.158.

Diphenyl oxalate (3e). 40% yield; white solid; m.p. 138-140 °C; IR (film) ν/cm^{-1} 1780 and 1760 (C=O); ^{1}H NMR δ (300 MHz, CD_2Cl_2) 7.33 (m, 4 H, Ph, meta H), 7.34 (m, 2 H, Ph para H), 7.49 (m, 4 H, Ph ortho H). Found M$^+$, 242.057. Calcd for $C_{14}H_{10}O_4$: M, 242.058.

Typical procedure for the preparation of isopropenyl oxamates 4a-d. 8 Mmol of diisopropenyl oxalate **1a** in 20 ml of anhydrous tetrahydrofuran (or dichloromethane) were cooled to -30 °C and 8 mmol of amine diluted in 30 ml of the same solvent were added dropwise. The mixture was stirred for 5 h at -30 °C and after elimination of a small amount of oxamide by filtration, the volatile solvents were removed by evaporation. Isopropenyl oxamates **4a**, **4b** and **4d** were recrystallized from hexane-diethylether mixtures, and oxamate **4c** was chromatographied on silica with hexane-diethylether (50:50) as eluent.

Isopropenyl oxamate (4a). 60% yield; white solid; m.p. 120-122 °C; IR (KBr) ν/cm^{-1} 1750 (C=O ester), 1710 (C=O amide) and 1690 (C=C); ^{1}H NMR δ (80 MHz, CD_2Cl_2) 1.97 (s, 3 H, CH_3), 4.80 (m, 2 H, CH_2). Found: C, 45.94; H, 5.42; M$^+$, 129.043. Calcd for $C_5H_7NO_3$: C, 46.50; H, 5.47; M, 129.043.

Isopropenyl-N-phenyl oxamate (4b). 60% yield; white solid; m.p. 55-57 °C; IR (KBr) ν/cm^{-1} 1735 (C=O ester), 1705 (C=O amide) and 1680 (C=C); ^{1}H NMR δ (80 MHz, $CDCl_3$) 2.01 (s, 3 H, CH_3), 4.85 (m, 2 H, CH_2), 7.50 - 7.10 (m, 3 H, Ph), 7.90 - 7.60 (m, 2 H, Ph). Found: C, 64.05; H, 5.35; N, 6.83; M$^+$, 205.073. Calcd for $C_{11}H_{11}NO_3$: C, 64.37; H, 5.41; N, 6.83; M, 205.074.

Isopropenyl α-oxo-1H-morpholine-1-acetate (4c). 79% yield; pale yellow oil; IR (film) ν/cm^{-1} 1750 (C=O ester), 1665 (C=O amide) and 1660 (C=C); ^{1}H NMR δ (80 MHz, $CDCl_3$) 1.98 (s, 3 H, CH_3), 3.67 (m, 8 H, CH_2), 4.80 (m, 2 H, $=CH_2$). Found: M$^+$, 199.083. Calcd for $C_9H_{13}NO_4$: M, 199.084.

Isopropenyl-N-(2-thiazolyl) oxamate (4d). 69% yield; white solid; m.p. 240 °C decomp.; IR (KBr) ν/cm^{-1} 1760 (C=O ester), 1690 (C=O amide) and 1680 (C=C); ^{1}H NMR δ (300 MHz, DMSO) 1.92 (m, 3 H, CH_3), 4.88 (dd, 1 H, $^4J_{cis}$= 0.4 Hz, ^{2}J= 1.3 Hz, C$\underline{H}$H), 4.93 (quint., 1 H, ^{2}J= $^4J_{trans}$= 1.3 Hz, CH$\underline{H}$), 7.30 (d, 1 H, ^{3}J= 3.7 Hz, CH=C$\underline{H}$), 7.54 (d, 1 H, ^{3}J= 3.7 Hz, C$\underline{H}$=CH), 13.2 (s, 1 H, NH). Found: C, 45.02; H, 3.90; N, 13.18. Calcd for $C_8H_8N_2O_3S$: C, 45.28; H, 3.80; N, 13.20.

Typical procedure for the preparation of unsymmetrical oxamides 5a-d. 3 Mmol of amine were added to 3 mmol of isopropenyl oxamide **4** in 10 ml of tetrahydrofuran (or dichloromethane). The mixture was stirred at room temperature in the case of primary amines or at 50 °C with secondary amines. After elimination of the

solvents, the solid oxamides were washed with methanol (**5a** and **5b**) or recrystallized from methanol (**5c**) or a dichloromethane-ether-hexane mixture (**5d**).

N-*(2-Thiazolyl) oxamide (5a)*. 65% yield; pale yellow powder; m.p. 231-233 °C; IR (KBr) ν/cm^{-1} 1680 and 1675 (C=O); ^{1}H NMR δ (300 MHz, DMSO) 7.36 (d, 1 H, ^{3}J= 3.5 Hz, C<u>H</u>=CH), 7.58 (d, 1 H, ^{3}J= 3.5 Hz, CH=C<u>H</u>), 8.09 (s, 1 H, N<u>H</u>H), 8.44 (s, 1 H, NH<u>H</u>), 12.42 (m, 1 H, NH). Found: C, 35.17; H, 3.00; N, 23.70. Calcd for $C_5H_5N_3O_2S$: C, 35.09; H, 2.95; N, 24.57.

N-*Phenyl*-N'-*(2-thiazolyl) oxamide (5b)*. 60% yield; pale yellow powder; m.p. 234-235 °C; IR (KBr) ν/cm^{-1} 1690 and 1670 (C=O); ^{1}H NMR δ (300 MHz, DMSO) 7.14 (t, 2 H, ^{3}J= 7.4 Hz, arom. H), 7.38 (t, 1 H, ^{3}J= 7.4 Hz, arom. H), 7.40 (d, 1 H, ^{3}J= 3.5 Hz, C<u>H</u>=CH), 7.60 (d, 1 H, ^{3}J= 3.5 Hz, CH=C<u>H</u>), 7.80 (d, 2 H, ^{3}J= 7.6 Hz, arom. H), 11.00 (s, 1 H, NH). Found: C, 53.22; H, 3.53; N, 16.50. Calcd for $C_{11}H_9N_3O_2S$: C, 53.43; H, 3.67; N, 17.00

1,1'-Oxalyl-N-*(2-ethylaminoethanol)*-N'-*morpholine (5c)*. 60% yield; solid; m.p. 76-78 °C; IR (KBr) ν/cm^{-1} 1640 and 1620 (C=O); ^{1}H NMR δ (300 MHz, CD_2Cl_2) 1.15 (2 t, 3 H, ^{3}J= 7.1 Hz, CH_3), 3.33 (q, 1 H, ^{3}J= 7.1 Hz, CHMe), 3.38 - 3.35 (m, 4H, CH_2), 3.42 (q, 1 H, ^{3}J= 7.1 Hz, CHMe), 3.49 (t, 2 H, ^{3}J= 5.1 Hz, CH_2N), 3.60 - 3.71 (m, 4 H, CH_2), 3.73 (t, 2 H, ^{3}J= 5.1 Hz, OCH_2).

1,1'-Oxalyl-N-*(2-aminothiazole)*-N'-*morpholine (5d)*. 61% yield; solid; m.p. 172-174 °C; IR (KBr) ν/cm^{-1} 1655 and 1650 (C=O); ^{1}H NMR δ (300 MHz, DMSO) 3 7 - 3.4 (m, 8 H, CH_2), 7 35 (d, 1 H, ^{3}J= 3.6 Hz, C<u>H</u>=CH), 7.55 (d, 1 H, ^{3}J= 3.6 Hz, CH=C<u>H</u>), 12.90 (s, 1 H, NH). Found: C, 44.92; H, 4.85; N, 17.13; M$^+$, 241.052. Calcd for $C_9H_{11}N_3O_3S$: C, 44.81; H, 4.60; N, 17.43; M, 241.052.

Typical procedure for the preparation of methyl oxamates 6a-b. 5 Mmol of amine were added to a solution containing 3 mmol of diisopropenyl oxamate **1a** in 15 ml of anhydrous methanol. After stirring at room temperature for 5 h, methanol and acetone were removed with a rotary evaporator. Oxamates **6a** and **6b** were purified by recrystallization from methanol-hexane mixtures.

Methyl oxamate (6a). 60% yield; white solid, m.p 109-111 °C; IR (KBr) ν/cm^{-1} 1750 (C=O ester) and 1695 (C=O amide); ^{1}H NMR δ (80 MHz, CD_3OD) 3 84 (s, 3 H, CH_3). Found: M$^+$, 103.026. Calcd for $C_3H_5NO_3$: M, 103.027.

Methyl-N-(2-thiazolyl) oxamate (6b). 87% yield; solid; m.p. 209-210 °C; IR (KBr) ν/cm^{-1} 1750 (C=O ester) and 1690 (C=O amide); ^{1}H NMR δ (300 MHz, DMSO) 3.84 (s, 3 H, CH_3), 7.37 (d, 1 H, ^{3}J= 3.4 Hz, C<u>H</u>=CH), 7.59 (d, 1 H, ^{3}J= 3.4 Hz, CH=C<u>H</u>), 12.98 (s, 1 H, NH). Found: C, 38.23; H, 3.18; N, 15.39. Calcd for $C_6H_6N_2O_3S$: C, 38.71; H, 3.25; N, 15.06.

4-Ethylmorpholine-2,3-dione (6c). 8 Mmol of 2-(ethylamino)ethanol in 30 ml of dichloromethane were added dropwise to a solution of 8 mmol of diisopropenyl oxalate **1a** in 50 ml of dichloromethane cooled at -10 °C The mixture was stirred at -10 °C until complete conversion of **1a**. After concentration and filtration of a small amount of oxamide, **6c** was isolated as a white solid and purified by recrystallization from a dichloromethane-hexane mixture. 75% yield; solid; m.p. 69-71 °C; IR (KBr) ν/cm^{-1} 1755 (C=O ester) and 1685 (C=O amide); ^{1}H NMR δ (300 MHz, $CDCl_3$) 1.24 (t, 3 H, ^{3}J= 7.2 Hz, CH_3), 3.57 (q, 2 H, ^{3}J= 7.2 Hz, CH_2Me), 3.69 (t, 2 H, ^{3}J= 5.2 Hz, CH_2N), 4.54 (t, 2 H, ^{3}J= 5.2 Hz, CH_2O). Found: C, 50.30; H, 6.22; N, 9.82; M$^+$, 143.058. Calcd for $C_6H_9NO_3$: C, 50.33; H, 6.34; N, 9.79; M, 143.058.

Acknowledgements. The authors wish to thank the SNPE and CNRS for a grant to M. Neveux.

References

1. (a) Murata, S. *Chem. Lett.* **1983**, 1819-1820. (b) Kitagawa, T.; Kuroda, H.; Sasaki, H.; Kawasaki, K. *Chem. Pharm. Bull.* **1987**, *35*, 4294-4301.
2. (a) Deits, W.; Vogl, O. *Org. Coat. Plast. Chem.* **1980**, *42*, 386-389. (b) Hass, P.; Avar, G.; Grammes, H. *Ger. Offen.* DE 3,332,792 (1985); *Chem. Abstr.* **1985**, *103*, 38155n..
3. (a) Boger, M.; Drabek, J.; Neumann, R. BP 2,145,716 (1985); *Chem Abstr.* **1985**, *103*, 141636u. (b) Lunkenheimer, W.; Brandes, W. *Ger Offen.* 2,836,158; *Chem. Abstr.* **1980**, *93*, 168596t
4. (a) Nakagawa, A.; Tsuji, M.; Mizota, T. JP 61,271,265 (1985); *Chem Abstr* **1987**, *106*, 138091n. (b) Treuner, U.; Breuer, H. *U. S.* 4,113,943; *Chem. Abstr.* **1979**, *90*, 72217g.
5. (a) Tanaka, M.; Kobayashi, T.; Sakakura, T. *J. Chem. Soc., Chem. Commun.* **1985**, 837-838. (b) Ozawa, F.; Soyama, H.; Yamamoto, T.; Yamamoto, A. *Tetrahedron Lett.* **1982**, *23*, 3383-3386. (c) Kobayashi, T.; Tanaka, M. *J. Organomet. Chem* **1982**, *233*, C64-C66. (d) Ozama, F.; Soyama, H.; Yanagihara, H.; Aoyama, I.; Takino, H.; Izawa, K.; Yamamoto, T ; Yamamoto, A *J. Am. Chem. Soc.* **1985**, *107*, 3235-3245.
6. (a) Murahashi, S.; Mitsue, Y.; Ike, K. *J. Chem. Soc , Chem. Commun* **1987**, 125-127 (b) Fenton, D. M.; Steinwand, P. J. *J. Org. Chem.* **1974**, *39*, 701-704. (c) Tam, W. *J Org. Chem* **1986**, *51*, 2977-2981. (d) Pri-bar, I.; Alper, H. *Can. J. Chem.* **1990**, *68*, 1544-1547.
7. (a) Sokol, P. E. *Org. Synth.* **1964**, *44*, 69-71. (b) Psiorz, M.; Schmid, R. *Chem. Ber.* **1987**, *120*, 1825-1828.
8. (a) Stoffel, P. J. *J. Org. Chem.* **1964**, *29*, 2794-2796. (b) McDonald, R. N. *J. Org Chem.* **1959**, *24*, 1580-1581.
9. (a) Nimitz, J. S.; Mosher, H. S. *J. Org. Chem* **1981**, *46*, 211-213. (b) Vogl, O.; Stevenson, D. USP 471,513 (1974); *Chem. Abstr.* **1975**, *83*, 148028z.
10. Messina, G.; Sechi, G. M.; Lorenzoni, L.; Chessa, G. EP 338,386 (1989); *Chem. Abstr.* **1990**, *112*, 197644y.
11. (a) Ruppin, C.; Dixneuf, P. H. *Tetrahedron Lett.* **1986**, *27*, 6323-6324. (b) Ruppin, C.; Dixneuf, P. H.; Lécolier, S. *Tetrahedron Lett.* **1988**, *29*, 5365-5368. (c) Bruneau, C.; Neveux, M.; Kabouche, Z.; Ruppin, C.; Dixneuf, P. H. *Synlett* **1991**, *11*, 755-763.
12. (a) Neveux, M.; Bruneau, C.; Dixneuf, P. H. *J. Chem. Soc. Perkin Trans I* **1991**, 1197-1199. (b) Kabouche, Z.; Bruneau, C.; Dixneuf, P. H. *Tetrahedron Lett* **1991**, *32*, 5359-5362
13. Nishino, J.; Yoshida, T.; Makino, I.; Nanya, S.; Tamaki, K., Sakaguchi, Y *Kobunshi Ronbunshu* **1974**, *31*, 177-180, *Chem. Abstr.* **1974**, *81*, 91983j.
14. Bazureau, J. P.; Person, D.; Le Corre, M. *Tetrahedron Lett* **1989**, *30*, 3065-3068.
15. (a) Gronowitz, S. S.; Sjoberg, B. O.; Michael, U. *Ger. Offen.* 2,118,988 (1971); Chem. Abstr. **1972**, *76*, 59241b. (b) Nii, Y.; Okano, K.; Kobayashi, S.; Ohno, M. *Tetrahedron Lett* **1979**, *27*, 2517-2520. (c) Howe, R. K.; Gruner, T. A.; Franz, J. E. *J. Org Chem* **1977**, *42*, 1813-1814.