Pergamon

Tetrahedron, Vol. 53, No. 8, pp. 3005-3014, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00055-0

Synthesis of Pyrazole-containing Azacrown Ethers by Intramolecular Nitrilimine Cycloadditions†

Gianluigi Broggini, Luisa Garanti, Giorgio Molteni and Gaetano Zecchi*

Dipartimento di Chimica Organica e Industriale dell'Università and Centro CNR,
Via Golgi 19, 20133 Milano, Italy

Abstract: Intramolecular cycloadditions of suitably functionalised nitrilimines have been exploited to prepare a number of crown azaethers having a medium or large ring annulated to pyrazole unit(s).
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The use of intramolecular 1,3-dipolar cycloadditions for the construction of macrocyclic compounds is documented.[1-8] On continuing our interest in this field, we describe here an application of the intramolecular nitrilimine cycloaddition methodology to the synthesis of azacrown ethers having the nitrogen incorporated in the pyrazole ring. Such molecules, in the light of some recent reports,[9] are attractive as potential ligands towards metal cations.

Results and Discussion

We considered two series of functionalised nitrilimines having a different kind of connection between the dipole and dipolarophile groups. According to the usual procedure,[10] both nitrilimines **4** and **10** were generated *in situ* upon basic treatment of the corresponding hydrazonyl chlorides **3** and **9**, respectively. The synthetic sequences leading to the desired hydrazonyl chlorides are illustrated in Schemes 1 and 2.

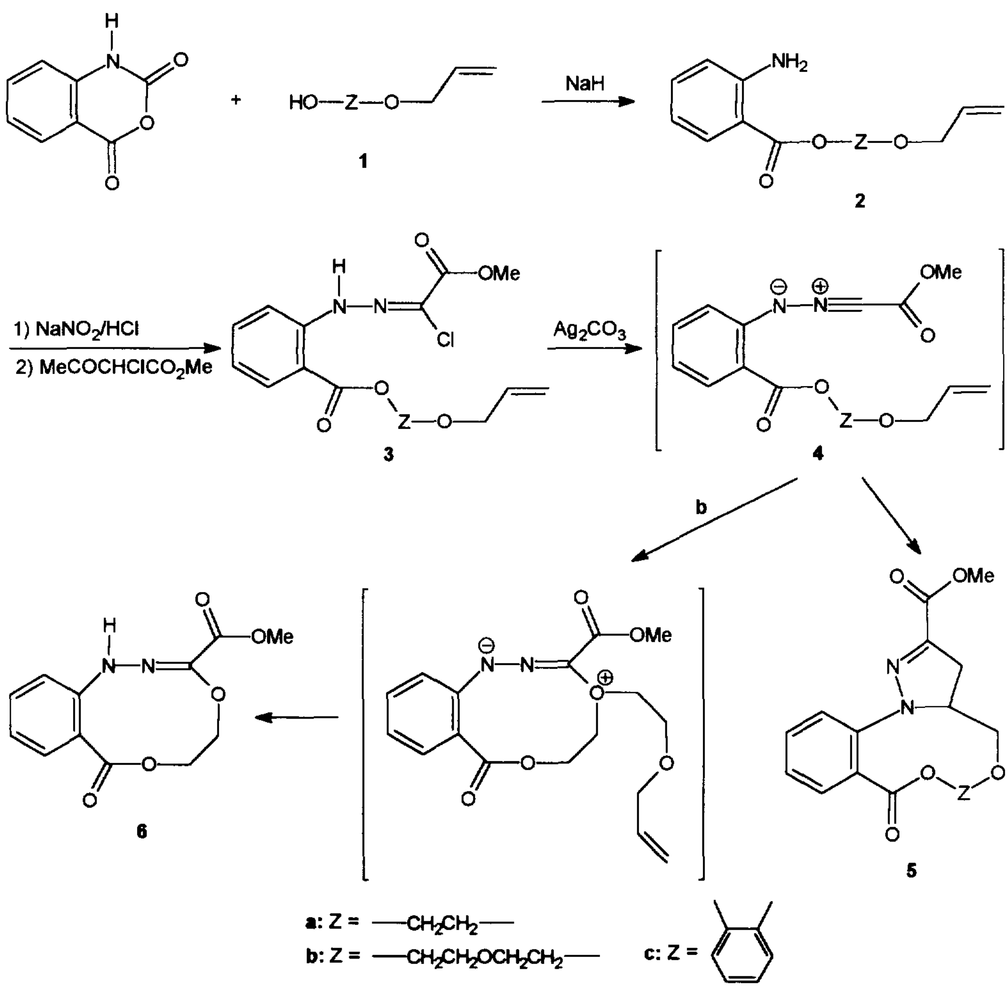
All substrates **3** and **9** were treated with an excess of silver carbonate in dioxane at room temperature. Reactions times, products and isolated yields are collected in Table 1. Long times, low temperature and heterogeneous conditions were found necessary to depress the formation of resinous material in favour of the intramolecular cycloaddition products. Structural assignments of the products rely upon analytical and spectral data (see Experimental Section). In the case of **13** which possesses two stereogenic centres, the choice of the racemic form (rather than the achiral mesoform) came from the fact that splitting of the ^{1}H-NMR signals was observed in the presence of *tris*[heptafluoropropyl-hydroxymethylene-(+)-camphorato] europium-(III).

†Dedicated to Professor Paolo Grünanger on the occasion of his 70th birthday.

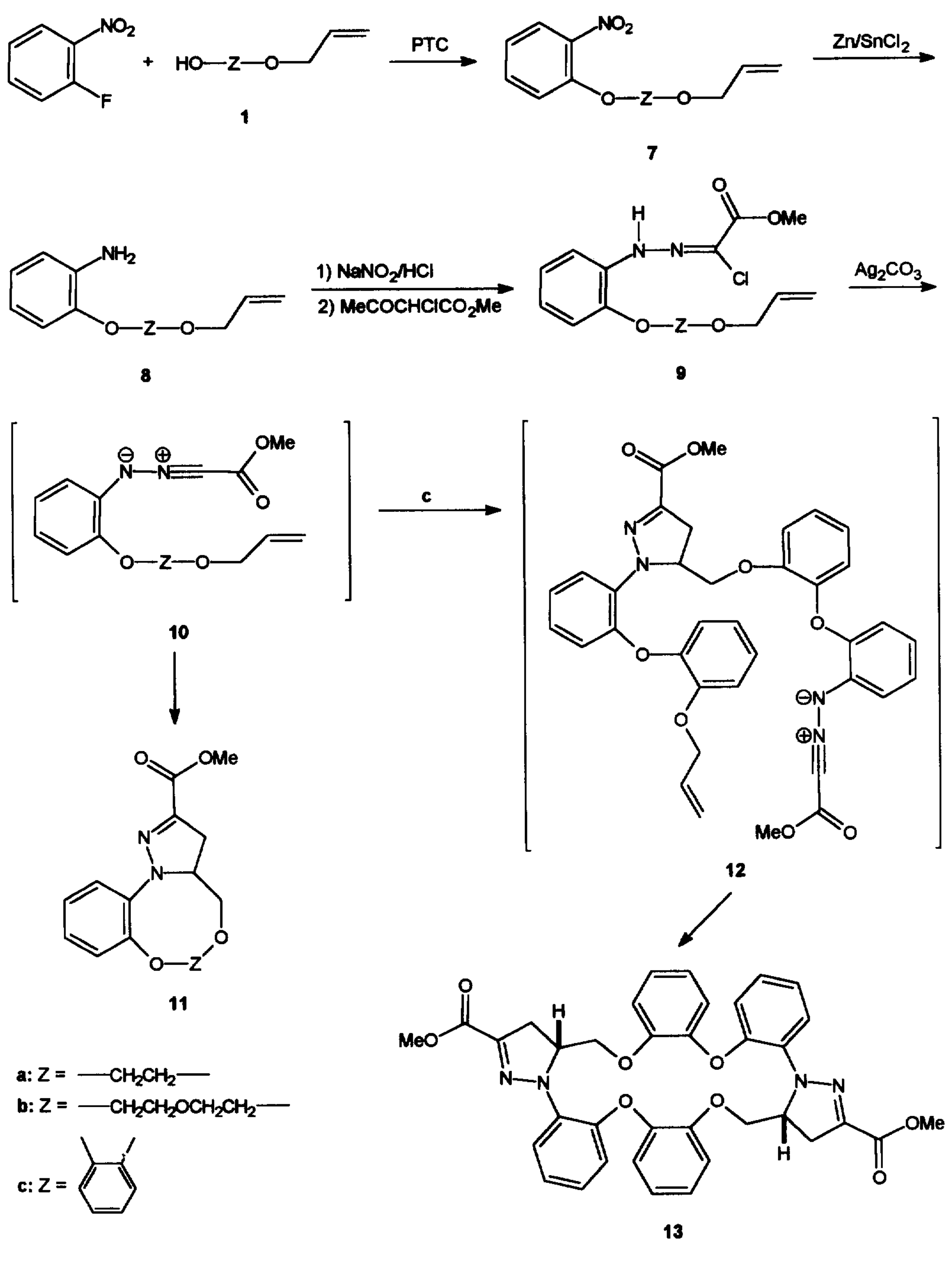
Table 1. Reaction of hydrazonyl chlorides **3** and **9** with silver carbonate in dioxane

Compd	Time[a] (days)	Product(s)[b,c] (% yield)	Eluant[d]
3a	9	**5a** (11%)	AcOEt/LP 2:1
3b	23	**5b** (17%) + **6** (8%)	Et_2O/CH_2Cl_2 1:1
3c	10	**5c** (28%)	AcOEt/LP 1:1
9a	4	**11a** (46%)	Et_2O
9b	7	**11b** (39%)	AcOEt/LP 1:1
9c	4	**11c** (56%) + **13** (18%)	AcOEt/LP 1:2

[a]At room temperature. [b]In order of elution. [c]Some quantity of the starting hydrazonyl chloride was recovered. [d]LP = light petroleum b.p. 40-60°C.

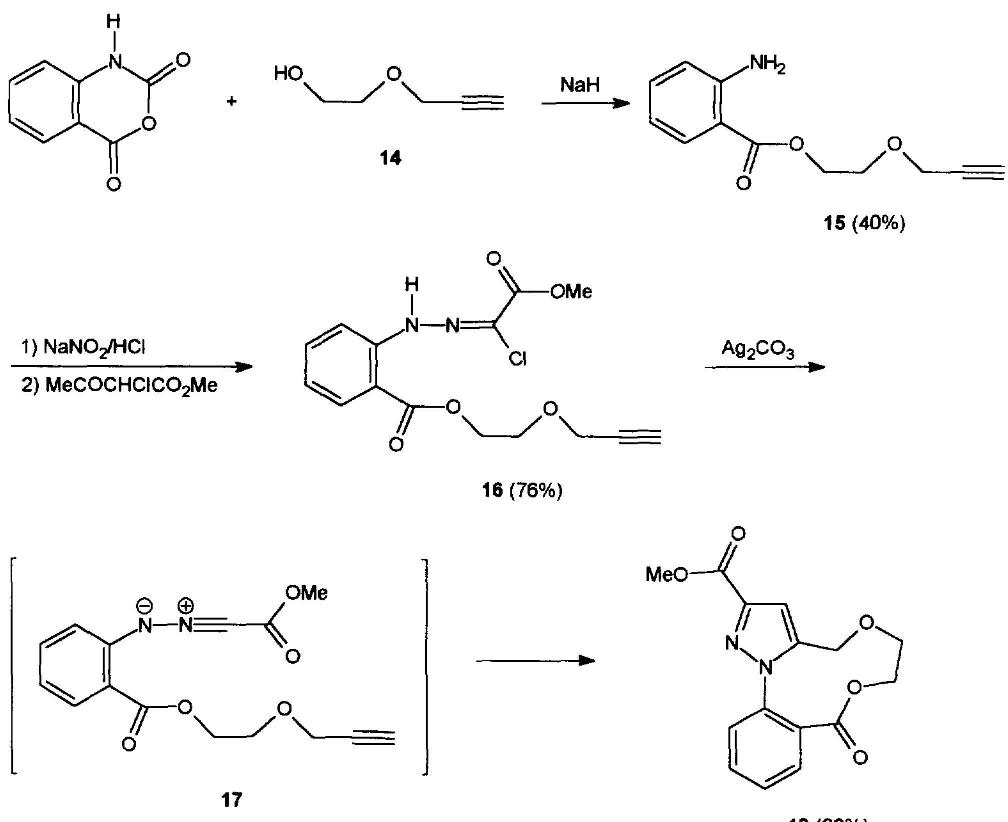


Scheme 1


NO2
F
HO—Z—O
1
PTC
7
Zn/SnCl2
NH2
8
1) NaNO2/HCl
2) MeCOCHClCO2Me
OMe
Cl
9
Ag2CO3
10
c
12
11
13
a: Z = —CH2CH2—
b: Z = —CH2CH2OCH2CH2—
c: Z =

Scheme 2

The above results deserve a few comments. The intramolecular cycloadditions leading to **11a-c** are very satisfactory in the light of both reaction rates and product yields. However, the intramolecular cycloadditions leading to **5a-c** require longer times and proceed to a lower extent. This means that the conformational freedom more than the length of the tether between the addends determines the energy barrier of the intramolecular cycloaddition. It may be that structures **4a-c** are less flexible than **10a-c** due to the presence of an ester functionality in place of the ethereal linkage. A second point worthy of noting is the formation of the macrocyclic compound **13** through an intresting cascade reaction sequence, *i.e.* intermolecular followed by intramolecular cycloaddition. Finally, a plausible pathway giving the side-product **6** is illustrated in Scheme 1.



Scheme 3

As a further developement of our work, in order to widen the variety of available substrates for a future evaluation of the complexating properties, we performed the reaction sequence outlined in Scheme 3, which led to compound **18** having a fully unsaturated (rather than 4,5-dihydrogenated) pyrazole ring.

Experimental Section

Melting points were determined with a Büchi apparatus and are uncorrected. IR spectra (in nujol unless otherwise indicated) were recorded with a Perkin-Elmer 298 spectrophotometer. Mass spectra were determined with a VG-70EQ apparatus. ^{1}H-NMR spectra were taken with a Bruker AC 300 instrument (in $CDCl_3$ solutions, unless otherwise stated). Chemical shifts are given as ppm from tetramethylsilane and coupling constant are given in Hz.

Compounds **1a**[11], **1b**[12], **1c**[13] and **14**[14] were prepared according to the literature methods.

General procedure for the preparation of alkenyl anthranilates 2. A solution of **1** (0.10 mol) in anhydrous benzene (70 mL) was treated with sodium hydride (2.64 g, 0.11 mol) and then refluxed for 1 h. Isatoic anhydride (16.3 g, 0.10 mol) in pyridine (60 mL) was added and the solution was refluxed for 5 h. The mixture was poured into ice-water (600 mL) and extracted with diethylether. The organic layer was dried over sodium sulfate and evaporated to give **2**.

2a (7.89 g, 36% yield) thick oil; IR (neat): 3490, 3370, 1700 (cm^{-1}); ^{1}H-NMR: δ 3.70 (2H, t, J=5.7), 4.06 (2H, dt, J=5.8, 1.1), 4.38 (2H, t, J=5.7), 5.05-5.38 (2H, m), 5.70 (2H, br s), 5.62-6.15 (1H, m), 6.45-7.93 (4H, m); MS: m/z 221 (M$^+$). Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.13; H, 6.84; N, 6.33. Found: C, 65.20; H, 6.90; N, 6.40.

2b (9.80 g, 37% yield) thick oil; IR (neat): 3480, 3370, 1696 (cm^{-1}); ^{1}H-NMR: δ 3.50-3.65 (4H, m), 3.76 (2H, t, J=5.2), 3.95 (2H, dt, J=5.6, 1.1), 4.39 (2H, t, J=5.2), 5.02-5.33 (2H, m), 5.61 (2H, br s), 5.63-6.10 (1H, m), 6.45-7.92 (4H, m); MS: m/z 265 (M$^+$). Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.47; H, 7.30; N, 5.40.

2c (11.6 g, 43% yield) m.p. 54°C (from diisopropylether); IR: 3460, 3360, 1694 (cm^{-1}); ^{1}H-NMR: δ 4.52 (2H, dt, J=5.7, 1.3), 5.02-5.41 (2H, m), 5.68 (2H, br s), 5.70-6.15 (1H, m), 6.56-8.18 (8H, m); MS: m/z 269 (M$^+$). Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.31; H, 5.54; N, 5.33.

General procedure for the preparation of nitroderivatives 7. A solution of *ortho*-fluoro nitrobenzene (6.40 g, 45.4 mmol) and **1** (68.1 mmol) in anhydrous benzene (160mL) was treated with 50% aqueous sodium hydroxide (27.0 g) and benzyl triethylammoniumchloride (520 mg, 2.3 mmol). The mixture was refluxed under vigorous stirring for 1 h. Benzene (50 mL) was added, the organic layer was washed with water and dried over sodium sulfate. Evaporation of the solvent gave **7**.

7a (6.58 g, 65% yield) thick oil; ^{1}H-NMR: δ 3.83 (2H, t, J=6.1), 4.09 (2H, dt, J=5.5, 1.2), 4.27 (2H, t, J=6.1), 5.10-5.40 (2H, m), 5.70-6.15 (1H, m), 6.90-7.38 (4H, m); MS: m/z 223 (M$^+$). Anal. Calcd for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.27. Found: C, 59.32; H, 5.74; N, 5.83.

7b (7.52 g, 62% yield) thick oil; ^{1}H-NMR: δ 3.52-3.68 (4H, m), 3.87 (2H, t, J=4.8), 4.00 (2H, d, J=5.7), 4.24 (2H, t, J=4.8), 5.03-5.39 (2H, m), 5.65-6.10 (1H, m), 6.85-7.86 (4H, m); MS: m/z 267

(M^+). Anal. Calcd for $C_{13}H_{17}NO_5$: C, 58.42; H, 6.41; N, 5.24. Found: C, 58.54; H, 6.50; N, 5.13.

7c (10.95 g, 89% yield) thick oil; ^{1}H-NMR: δ 4.46 (2H, dt, *J*=5.1, 1.3), 4.94-5.13 (2H, m), 5.53-6.07 (1H, m), 6.70-7.97 (8H, m); MS: *m/z* 271 (M^+). Anal. Calcd for $C_{15}H_{13}NO_4$: C, 66.41; H, 4.83; N, 5.16. Found: C, 66.30; H, 4.73; N, 5.23.

General procedure for the preparation of aminoderivatives 8. A solution of **7** (20.0 mmol) in acetic acid (90 mL) was treated with $SnCl_2 \cdot 2H_2O$ (5.47 g, 24.2 mmol) in hydrochloric acid (12M, 6.4 mL). Zinc dust (1.58 g, 24.2 mmol) was added portionwise and the mixture was reacted at room temperature for 4 h. The mixture was adjusted to pH 10 with 30% aqueous sodium hydroxide and extracted with dichloromethane. The organic layer was washed with water and dried over sodium sulfate. Evaporation of the solvent gave **8**.

8a (3.82 g, 98% yield) thick oil; IR (neat): 3466, 3366 (cm^{-1}); ^{1}H-NMR: δ 3.88 (2H, t, *J*=4.9), 3.98 (2H, br s), 4.15 (2H, dt, *J*=5.6, 1.2), 4.19 (2H, t, *J*=4.9), 5.06-5.38 (2H, m), 5.70-6.15 (1H, m), 6.65-6.90 (4H, m); MS: *m/z* 193 (M^+). Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.43; H, 7.89; N, 7.21.

8b (4.22 g, 89% yield) thick oil; IR (neat): 3465, 3364 (cm^{-1}); ^{1}H-NMR: δ 3.50-4.15 (12H, m), 5.15-5.35 (2H, m), 5.70-6.15 (1H, m), 6.65-6.90 (4H, m); MS: *m/z* 237 (M^+). Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.73; H, 8.01; N, 5.95.

8c (4.58 g, 95% yield) thick oil; IR (neat): 3468, 3376 (cm^{-1}); ^{1}H-NMR: δ 3.88 (2H, br s), 4.58 (2H, dt, *J*=5.0, 1.4), 5.11-5.45 (2H, m), 5.77-6.24 (1H, m), 6.50-7.50 (8H, m); MS: *m/z* 241 (M^+). Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.53; H, 6.19; N, 5.66.

General procedure for the preparation of hydrazonyl chlorides 3 and 9. A solution of **2** or **8** (10.0 mmol) in water (35 mL) and methanol (5.0 mL) was treated with hydrochloric acid (12M, 3.3 mL) and then cooled to 0°C. Sodium nitrite (1.01 g, 14.6 mmol) was added portionwise whilst it was cooled and stirred. After 30 min, the cold mixture was adjusted to pH 5 with sodium acetate and then methyl 2-chloroacetoacetate (1.50 g, 10.0 mmol) in methanol (10 mL) was added whilst it was cooled and vigorously stirred for 6 h. After stirring at room temperature for 15 h, the mixture was extracted with diethylether. The organic solution was washed with aqueous sodium hydrogen carbonate, dried over sodium sulfate and evaporated. Recrystallisation with diisopropylether gave the pure hydrazonyl chloride **3** or **9**.

3a (2.54 g, 78% yield) m.p. 73°C; IR: 3326, 1750, 1690 (cm^{-1}); ^{1}H-NMR: δ 3.75 (2H, t, *J*=5.5), 3.90 (3H, s), 4.05 (2H, dt, *J*=5.5, 1.1), 4.51 (2H, t, *J*=5.5), 5.10-5.41 (2H, m), 5.65-6.20 (1H, m), 6.85-8.10 (4H, m), 11.70 (1H, br s); MS: *m/z* 340 (M^+). Anal. Calcd for $C_{15}H_{17}ClN_2O_5$: C, 52.87; H, 5.03; Cl, 10.40; N, 8.22. Found: C, 52.95; H, 5.10; Cl, 10.48; N, 8.30.

3b (3.03 g, 79% yield) m.p. 98°C; IR: 3330, 1720, 1690 (cm^{-1}); ^{1}H-NMR: δ 3.50-3.68 (4H, m), 3.82 (2H, t, *J*=4.8), 3.94 (3H, s), 4.03 (2H, dt, *J*=5.5, 1.2), 4.49 (2H, t, *J*=4.8), 5.03-5.25 (2H, m), 5.68-6.15 (1H, m), 6.89-8.08 (4H, m), 11.75 (1H, br s); MS: *m/z* 384 (M^+). Anal. Calcd for $C_{17}H_{21}ClN_2O_6$: C, 53.06; H, 5.50; Cl, 9.21; N, 7.28. Found: C, 53.13; H, 5.56; Cl, 9.30; N, 7.37.

3c (1.47 g, 38% yield) m.p. 96°C; IR: 3330, 1750, 1690 (cm^{-1}); ^{1}H-NMR: δ 3.95 (3H, s), 4.55 (2H, dt, *J*=4.8, 1.3), 5.06-5.30 (2H, m), 5.70-6.18 (1H, m), 6.87-8.30 (8H, m), 11.60 (1H, br s); MS: *m/z* 388 (M^+). Anal. Calcd for $C_{19}H_{17}ClN_2O_5$: C, 58.69; H, 4.41; Cl, 9.12; N, 7.20. Found: C, 58.58; H, 4.49; Cl, 9.04; N, 7.14.

9a (870 mg, 28% yield) m.p. 74°C; IR: 3330, 1730 (cm^{-1}); ^{1}H-NMR: δ 3.80 (2H, t, *J*=4.5), 3.91 (3H, s), 4.08 (2H, d, *J*=5.7), 4.21 (2H, t, *J*=4.5), 5.15-5.32 (2H, m), 5.80-5.96 (1H, m), 6.88-7.56 (4H, m), 8.95 (1H, br s); MS: *m/z* 312 (M^+). Anal. Calcd for $C_{14}H_{17}ClN_2O_4$: C, 53.77; H, 5.48; Cl, 11.34; N, 8.96. Found: C, 53.90; H, 5.50; Cl, 11.46; N, 9.00.

9b (2.21 g, 62% yield) m.p. 102°C; IR: 3330, 1730 (cm^{-1}); ^{1}H-NMR: δ 3.49-3.71 (4H, m), 3.82 (2H, t, *J*=4.8), 3.91 (3H, s), 3.95 (2H, dt, *J*=5.8, 1.1), 4.23 (2H, t, *J*=4.8), 5.05-5.36 (2H, m), 5.64-6.12 (1H, m), 6.82-7.52 (4H, m), 8.90 (1H, br s); MS: *m/z* 356 (M^+). Anal. Calcd for $C_{16}H_{21}ClN_2O_5$: C, 53.86; H, 5.93; Cl, 9.94; N, 7.85. Found: C, 53.80; H, 5.86; Cl, 9.80; N, 7.77.

9c (1.62 g, 45% yield) m.p. 61°C; IR: 3330, 1730 (cm^{-1}); ^{1}H-NMR: δ 3.90 (3H, s), 4.52 (2H, dt, *J*=5.2, 1.3), 5.04-5.28 (2H, m), 5.60-6.12 (1H, m), 6.68-7.63 (8H, m), 9.02 (1H, br s); MS: *m/z* 360 (M^+). Anal. Calcd for $C_{18}H_{17}ClN_2O_4$: C, 59.92; H, 4.75; Cl, 9.83; N, 7.76. Found: C, 60.02; H, 4.82; Cl, 9.98; N, 7.84.

General procedure for the reaction of hydrazonyl chlorides 3 and 9 with silver carbonate in dioxane. A solution of hydrazonyl chloride **3** or **9** (5 mmol) in dry dioxane (100 mL) was treated with silver carbonate (5.51 g, 20 mmol) and the mixture was stirred at room temperature in the dark for the time indicated in Table 1. The undissolved material was filtered off, the solvent was evaporated, and then the residue was chromatographed on a silica gel column. Eluents, products and isolation yields are collected in Table 1. All compounds were obtained in analytically pure state by recrystallisation from diisopropylether.

5a (167 mg, 11% yield) m.p. 108°C; IR: 1720, 1710 (cm^{-1}); ^{1}H-NMR: δ 3.15 (1H, dd, *J*=16.9, 11.6), 3.30 (1H, dd, *J*=16.9, 12.4), 3.71 (1H, dd, *J*=11.9, 1.9), 3.81 (1H, dt, *J*=11.0, 4.0), 3.83 (3H, s), 3.90-3.99 (3H, m), 4.41-4.49 (1H, m), 4.53 (1H, dt, *J*=11.0, 4.0), 7.33-7.62 (4H, m); MS: *m/z* 304 (M^+). Anal. calcd for $C_{15}H_{16}N_2O_5$: C, 59.21; H, 5.30; N, 9.21. Found: C, 59.13; H, 5.24; N, 9.08.

5b (296 mg, 17% yield) m.p. 153°C; IR: 1720, 1710 (cm^{-1}); ^{1}H-NMR: δ 3.26 (1H, dd, *J*=17.5, 12.2), 3.36 (1H, dd, *J*=17.5, 6.0), 3.45-3.79 (8H, m), 3.81 (3H, s), 4.29-4.33 (2H, m), 4.87-4.93 (1H, m), 7.00-7.60 (4H, m); MS: *m/z* 348 (M^+). Anal. calcd for $C_{17}H_{20}N_2O_6$: C, 58.61; H, 5.79; N, 8.04. Found: C, 58.53; H, 5.73; N, 8.08.

5c (480 mg, 28% yield) m.p. 160°C; IR: 1730, 1700 (cm^{-1}); ^{1}H-NMR: δ 3.41 (2H, d, *J*=11.6), 3.87 (3H, s), 4.16 (1H, tt, J=11.6, 2.5), 4.21 (2H, d, J=2.5), 7.10-7.90 (8H, m); MS: *m/z* 352 (M^+). Anal. calcd for $C_{19}H_{16}N_2O_5$: C, 64.77; H, 4.58; N, 7.95. Found: C, 64.86; H, 4.62; N, 8.08.

6 (96 mg, 8% yield) m.p. 70°C; IR: 3215, 1740, 1730 (cm^{-1}); ^{1}H-NMR: δ 3.89 (2H, t, J=4.6), 3.94 (3H, s), 4.52 (2H, t, J=4.6), 6.90-7.85 (4H, m), 11.64 (1H, br s); MS: *m/z* 264 (M^+). Anal. calcd for $C_{12}H_{12}N_2O_5$: C, 54.55; H, 4.58; N, 10.60. Found: C, 54.43; H, 4.54; N, 10.49.

11a (635 mg, 46% yield) m.p. 147°C; IR: 1720 (cm^{-1}); ^{1}H-NMR: δ 2.67 (1H, dd, J=17.8, 6.2), 3.32 (1H, dd, J=17.8, 12.8), 3.47 (1H, dd, J=12.9, 2.3), 3.75-3.94 (3H, m), 3.85 (3H, s), 4.16 (1H, dt, J=12.3, 3.4), 4.39 (1H, dt, J=12.3, 2.9), 5.46-5.58 (1H, m), 6.92-7.65 (4H, m); MS: *m/z* 276 (M^+). Anal. calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.91; H, 5.84; N, 10.22.

11b (624 mg, 39% yield) m.p. 208°C; IR: 1720 (cm^{-1}); ^{1}H-NMR: δ 3.15, 3.29 (2H, AB part of ABX system, J=17.8, 11.3, 6.7), 3.39-3.80 (8H, m), 3.85 (3H, s), 4.28-4.30 (2H, m), 5.10-5.20 (1H, m), 6.82-7.50 (4H, m); MS: *m/z* 320 (M^+). Anal. calcd for $C_{16}H_{20}N_2O_5$: C, 59.99; H, 6.29; N, 8.74. Found: C, 60.11; H, 6.33; N, 8.78.

11c (907 mg, 56% yield) m.p. 150°C; IR: 1710 (cm^{-1}); ^{1}H-NMR: δ 2.56 (1H, dd, J=17.6, 7.0), 3.21 (1H, dd, J=17.6, 11.9), 3.84 (1H, dd, J=10.6, 3.1), 3.86 (3H, s), 4.23 (1H, dd, J=12.0, 10.6), 5.10-5.14 (1H, m), 6.82-7.63 (8H, m); MS: *m/z* 324 (M^+). Anal. calcd for $C_{18}H_{16}N_2O_4$: C, 66.66; H, 4.97; N, 8.64. Found: C, 66.54; H, 5.02; N, 8.71.

13 (583 mg, 18% yield) m.p. 220°C; IR: 1730, 1710 (cm^{-1}); ^{1}H-NMR: δ 3.22 (2H, dd, J=17.8, 5.5), 3.23 (2H, dd, J=17.8, 11.1), 3.81 (2H, dd, J=9.0, 6.4), 3.87 (6H, s), 4.08 (2H, dd, J=9.0, 6.0), 5.27-5.37 (2H, m), 6.48-7.56 (16H, m); MS: *m/z* 648 (M^+). Anal. calcd for $C_{36}H_{32}N_4O_8$: C, 66.66; H, 4.97; N, 8.64. Found: C, 66.59; H, 5.03; N, 8.69.

Preparation of 15. A solution of **14** (10.0 g ,0.10 mol) in anhydrous benzene (80 mL) was treated with sodium hydride (2.64 g, 0.11 mol) and then refluxed for 1 h. Isatoic anhydride (16.3 g, 0.10 mol) in pyridine (60 mL) was added and the solution was refluxed for 3 h. The mixture was poured into ice-water (500 mL) and extracted with diethylether. The organic layer was dried over sodium sulfate and evaporated to give **15** (8.76 g, 40% yield) thick oil; IR (neat): 3480, 3290, 2117, 1690 (cm^{-1}); ^{1}H-NMR: δ 2.45 (1H, t, J=2.2), 3.81 (2H, t, J=4.3), 4.20 (2H, d, J=2.2), 4.42 (2H, t, J=4.3), 5.70 (2H, br s), 6.47-7.95 (4H, m); MS: *m/z* 219 (M^+). Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.73; H, 5.98; N, 6.39. Found: C, 65.83; H, 6.04; N, 6.44.

Preparation of 16. A solution of **15** (2.19 g, 10.0 mmol) in water (30 mL) and methanol (5.0 mL) was treated whith hydrochloric acid (10M, 3.5 mL) and then cooled to 0°C. Sodium nitrite (1.04 g, 1.50 mmol) in water (7 mL) was added dropwise whilst it was cooled and stirred. After 15 min, the cold mixture was adjusted to pH 5 with sodium acetate and then methyl 2-chloroacetoacetate (1.50 g, 10.0 mmol) in methanol (10 mL) was added whilst it was cooled and vigorously stirred for 4 h. After stirring at room temperature for 1 h, the mixture was extracted with diethylether. The organic solution was washed with aqueous sodium hydrogen carbonate, dried over sodium sulfate and evaporated. Recrystallisation with diisopropylether gave **16** (2.29 g, 76% yield) m.p. 109°C; IR: 3240, 2120, 1720 (cm^{-1}); ^{1}H-NMR: δ 2.45 (1H, t, J=2.3), 3.89 (2H, t, J=4.5), 3.93 (3H, s), 4.23 (2H, d, J=2.3), 4.51 (2H, t, J=4.5), 6.95-8.05 (4H, m), 11.72 (1H, br s); MS: *m/z* 338 (M^+). Anal. Calcd for $C_{15}H_{15}ClN_2O_5$: C, 53.24; H, 4.47; Cl, 10.34; N, 8.28. Found: C, 53.20; H, 4.41; Cl, 10.40; N, 8.31.

Reaction of hydrazonyl chloride 16 with silver carbonate in dioxane. A solution of **16** (5 mmol) in dry dioxane (100 mL) was treated with silver carbonate (5.51 g, 20 mmol) and the mixture was refluxed in the dark for 4 h. The undissolved material was filtered off, the solvent was evaporated, and then the residue was chromatographed on a silica gel column with diethyl ether-light petroleum 2:1 as eluant to give **18** (390 mg, 26% yield) m.p. 124°C; IR: 1720 (cm^{-1}); ^{1}H-NMR: δ 3.81-3.87 (3H, m), 3.94 (3H, s), 4.21-4.80 (2H, AB, J=14.0), 4.89-4.94 (1H, m), 7.03 (1H, s), 7.53-8.19 (4H, m); MS: *m/z* 302 (M^+). Anal. calcd for $C_{15}H_{14}N_2O_5$: C, 59.58; H, 4.67; N, 9.27. Found: C, 59.63; H, 4.70; N, 9.33.

Acknowledgements: We thank MURST and CNR for financial support.

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(*Received in UK* 6 *November* 1996; *revised* 7 *January* 1997; *accepted* 16 *January* 1997)