NOVEL ASPECTS OF THE SILVER CARBONATE PROMOTED REACTION OF HYDRAZONYL CHLORIDES WITH HOMOALLYLIC AND HOMOPROPARGYLIC ALCOHOLS

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

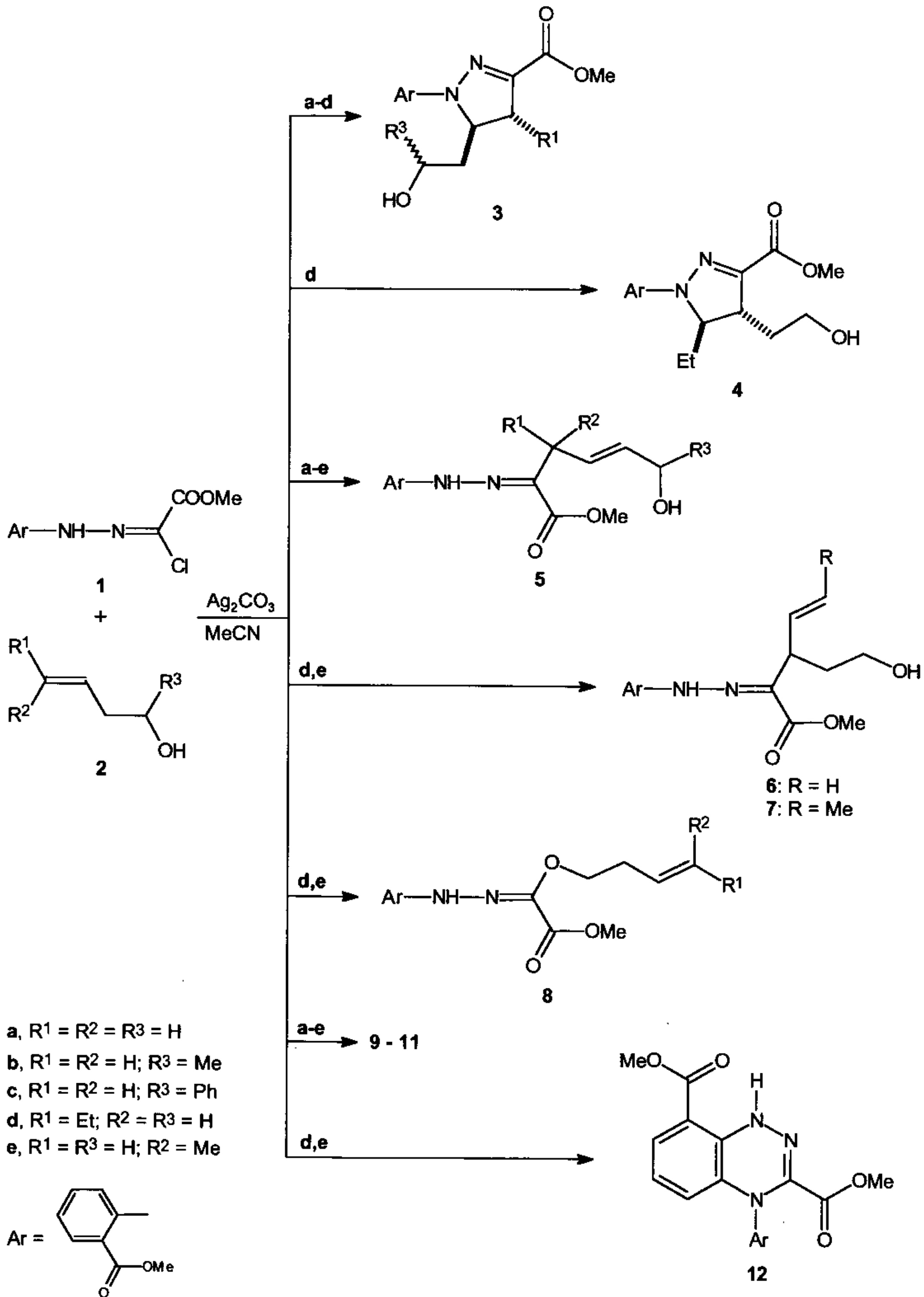
Dipartimento di Chimica Organica e Industriale dell'Università, via Golgi 19, 20133 Milano, Italy

Abstract - The title reaction gives, in addition to trivial side-products, both ring-closed products (**3**, **4**, **14**, and **15**) and open-chain products (**5**-**8**, and **16**). The role of the silver ion and the mechanistic possibilities for the formation of the various kinds of products are discussed.

Silver carbonate has been used to promote the *in situ* generation of nitrile oxides[1,2] and imines[3-8] from hydroximoyl and hydrazonoyl halides, respectively. In certain cases, this species has been proven more fruitful than conventional bases such as tertiary amines. Furthermore, we have recently found that the reaction between hydrazonoyl chlorides and allylic alcohols in the presence of silver carbonate exhibits some features which have not been observed in the presence of triethylamine.[9] Aiming at a better understanding of this difference, we have turned our attention to the silver carbonate promoted behaviour of hydrazonyl chloride (**1**) towards homoallylic and homopropargylic alcohols (**2**) and (**13**), respectively (see Schemes 1 and 2).

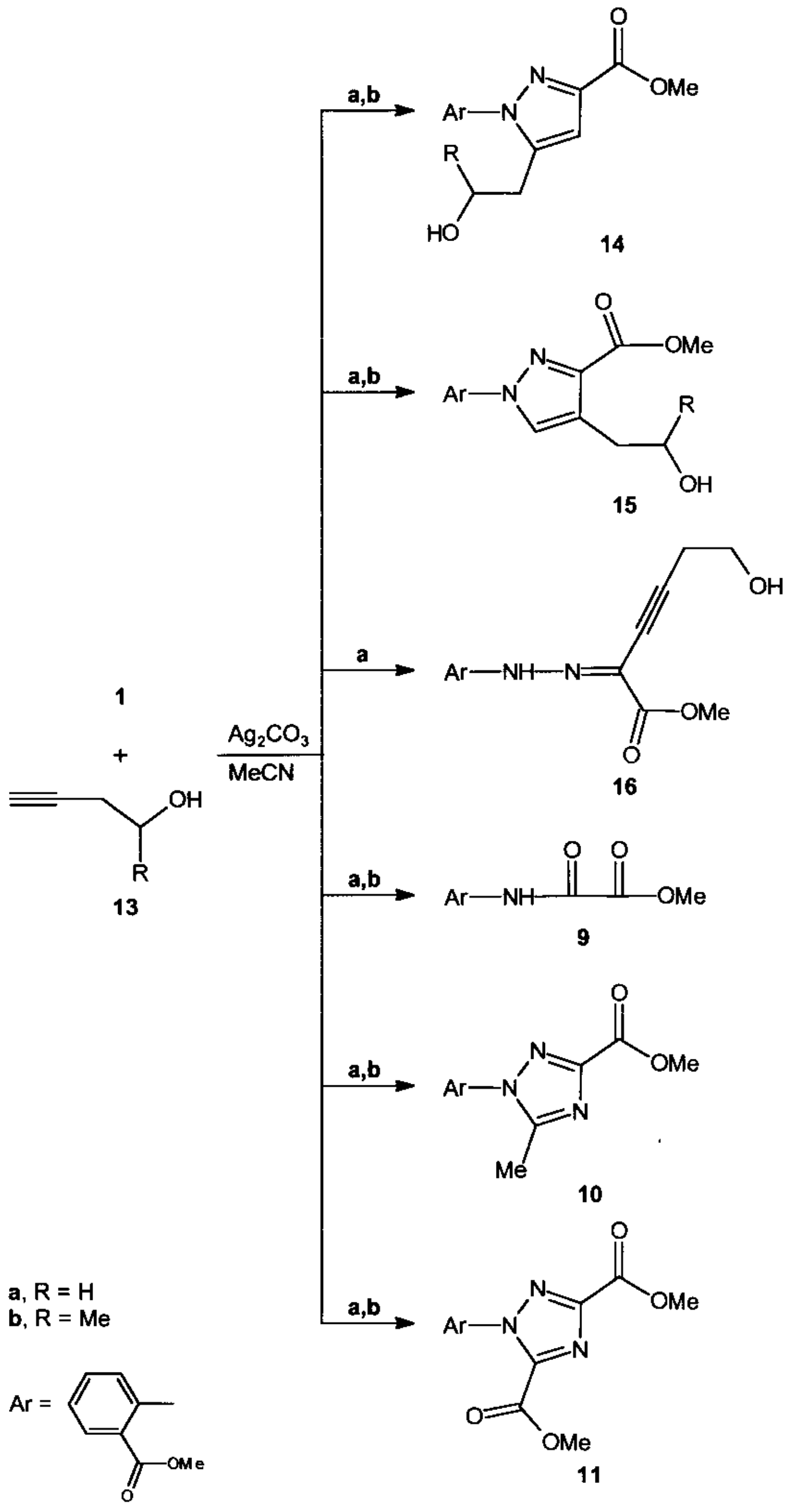
RESULTS AND DISCUSSION

Compound (**1**) reacted with an excess of alcohol (**2**) or (**13**) as well as of silver carbonate in acetonitrile. In all cases, the reaction led to a complex mixture, whose chromatographic treatment allowed isolation of the products indicated in Table 1. Structural assignement followed from analytical and spectral data (see Tables 2 and 3). In particular, the regiochemistry of the cycloaddition products was easily established by NMR spectra, which are known to be markedly different for 4-unsubstituted and 5-unsubstituted dihydropyrazoles.[10] In the case of the 4,5-disubstituted regioisomers **3d** and **4**, the distinction required decoupling NMR experiments, which showed that the 4-pyrazolinic hydrogen of **3d** lies neighbouring to an ethyl group. The *trans*-stereochemistry of both **3d** and **4** was indicated unequivocally by the vicinal



a-d
3
d
4
a-e
5
1
Ag_2CO_3
MeCN
2
d,e
6: R = H
7: R = Me
d,e
8
a-e
9 - 11
d,e
12
a, R1 = R2 = R3 = H
b, R1 = R2 = H; R3 = Me
c, R1 = R2 = H; R3 = Ph
d, R1 = Et; R2 = R3 = H
e, R1 = R3 = H; R2 = Me
Ar =

Scheme 1



a,b
Ar
N
OMe
R
HO
14
a,b
15
OH
a
NH
16
Ag$_2$CO$_3$
MeCN
1
+
13
9
10
Me
11
a, R = H
b, R = Me
Ar =

Scheme 2

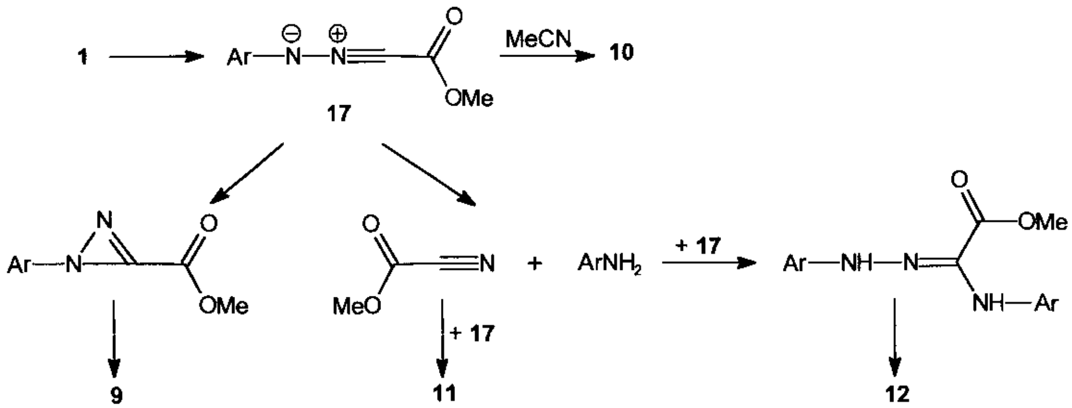
coupling constants of the pyrazolinic hydrogens,[10] while in the case of **3b** and **3c** the relative configuration of the two stereocentres remains undetermined.

Table 1 Reaction of **1** with alcohols (**2a-e**) and (**13a,b**) in the presence of silver carbonate in acetonitrile.

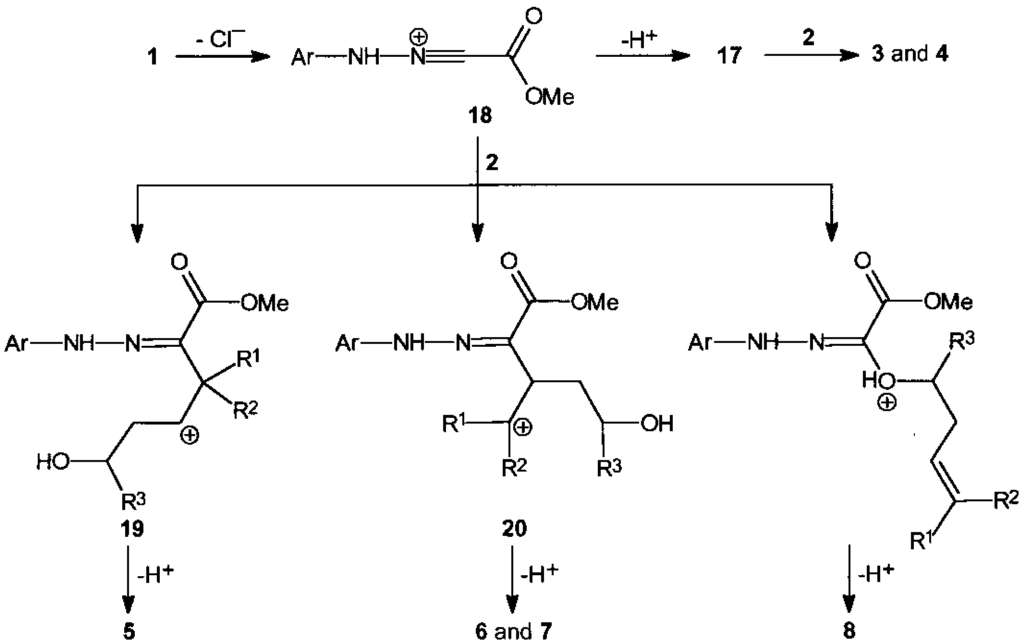
Alcohol	Temp.	Time (h)	Product distribution (% yield)[a,b]										Eluent
			3	**4**	**5**	**6**	**7**	**8**	**12**	**14**	**15**	**16**	
2a	rt	16	33	–	7	–	–	–	–	–	–	–	CH_2Cl_2-AcOEt (8:1)
2b	rt	16	38[c]	–	5	–	–	–	–	–	–	–	Et_2O
2c	rt	24	24[d]	–	4	–	–	–	–	–	–	–	Et_2O-LP[e] (1:1)
2d	rt	24	13	13	2	–	2	4	6	–	–	–	Et_2O-LP[e] (1:1)
2e	rt	24	–	–	3	2	–	3	7	–	–	–	Et_2O
13a	reflux	4	–	–	–	–	–	–	–	17	2	3	Et_2O
13b	reflux	2	–	–	–	–	–	–	–	25	2	–	CH_2Cl_2

[a]Isolation yield of pure product. [b]Side-products **9** (2-3%) (ref. 9), **10** (2-5%) (ref. 9), and **11** (2-4%) were usually isolated. [c]Only one diastereoisomer. [d]Overall yield of two isolated diastereoisomers. [e]LP= light petroleum bp 45-60°C.

Some comments on the above results are needed. First of all, compounds (**9-12**) represent trivial side-products, being the consequence of decomposition reactions of the intermediate nitrile imine (**17**) or of its cycloaddition onto the solvent (Scheme 3). Precedents of such behaviour patterns are available in the literature.[5,9,11-14] As the cycloaddition pyrazolic products are concerned, one can note that the extent of their formation spreads over a wide range, going from good to null as a function of the substitution degree of the dipolarophile. However, the most striking feature of the above results is the formation of compounds (**5-7**) and (**16**), which possess open-chain structures due to carbon-carbon bonding. A plausible sequence leading to them involves (*i*) silver ion promoted heterolysis of the carbon-halogen bond, (*ii*) capture of the derived carbocation-like species (**18**) by the π bond of the unsaturated alcohol, and (*iii*) proton loss to restore the unsaturation. Scheme 4 illustrates the situation in the case of homoallylic alcohols (**2**). The regioselectivity of step (*ii*), which is total in the case of **2a-c** and modest in the case **2d,e**, reflects the general trend of electrophilic additions to alkenes.[15,16] Conversely, the observed site preference of step (*iii*) is rather surprising and may perhaps be due to some kind of intramolecular basic catalysis by the sp^2 hybridised nitrogen. Of course, particularly when the double bond of **2** is sterically hindered, the hydroxy group can intervene as a competitive nucleophile, so leading to **9**.



Scheme 3



Scheme 4

If species (**19**) and (**20**) are real intermediates, one can devise them as precursors of the final pyrazoles (**3**, **4**, **14**, and **15**) in the place of the nitrile imine cycloaddition pathway. However, the retention of stereochemistry in the formation of **3d** and **4** as well as the lack of cycloadducts deriving from **2e** are better explicable in terms of the classical pericyclic mechanism rather than of the multi-step ionic one.

Table 2. Characterisation of new compounds.[a]

Compd (Formula)	mp[b] (°C)	IR (nujol) ν(cm^{-1})	Microanalyses C found (calcd)	H found (calcd)	N found (calcd)	MS m/z (M$^+$)
3a ($C_{15}H_{18}N_2O_5$)	59	3430, 1730, 1710	58.9 (58.8)	5.9 (5.9)	9.25 (9.15)	306
3b ($C_{16}H_{20}N_2O_5$)	76	3450, 1730, 1710	60.15 (60.09	6.2 (6.3)	8.75 (8.7)	320
3c[c] ($C_{21}H_{22}N_2O_5$)	89	3390, 1740, 1725	66.1 (66.0)	5.8 (5.8)	7.4 (7.3)	382
3c[d] ($C_{21}H_{22}N_2O_5$)	65	3465, 1730, 1715	66.15 (66.0)	5.85 (5.8)	7.25 (7.3)	382
3d ($C_{17}H_{22}N_2O_5$)	63	3450, 1730, 1710	61.25 (61.1)	6.7 (6.6)	8.5 (8.4)	334
4 ($C_{17}H_{22}N_2O_5$)	56	3390, 1730, 1710	61.0 (61.1)	6.7 (6.6)	8.4 (8.4)	334
5a ($C_{15}H_{18}N_2O_5$)	55	3430, 3240, 1705	58.9 (58.8)	5.9 (5.9)	9.3 (9.15)	306
5b ($C_{16}H_{20}N_2O_5$)	69	3440, 3240, 1720, 1700	59.8 (60.0)	6.35 (6.3)	8.8 (8.7)	320
5c ($C_{21}H_{22}N_2O_5$)	113	3450, 3250, 1725, 1690	65.9 (66.0)	5.8 (5.8)	7.45 (7.3)	382
5d ($C_{17}H_{22}N_2O_5$)	72	3440, 3230, 1725, 1700	61.25 (61.1)	6.6 (6.6)	8.5 (8.4)	334
5e ($C_{16}H_{20}N_2O_5$)	104	3480, 3270, 1750, 1680	59.85 (60.0)	6.35 (6.3)	8.8 (8.7)	320
6 ($C_{16}H_{20}N_2O_5$)	102	3380, 3250, 1720, 1700	60.15 (60.0)	6.2 (6.3)	8.8 (8.7)	320
7 ($C_{17}H_{22}N_2O_5$)	70	3270, 1730, 1700	61.2 (61.1)	6.5 (6.6)	8.85 (8.7)	334
8d ($C_{17}H_{22}N_2O_5$)	38	3270, 1725, 1695	61.0 (61.1)	6.7 (6.6)	8.5 (8.4)	334
8e ($C_{16}H_{20}N_2O_5$)	40	3270, 1730, 1690	60.15 (60.0)	6.4 (6.3)	8.9 (8.7)	320
11 ($C_{14}H_{13}N_3O_6$)	114	1745, 1725	52.7 (52.65)	4.0 (4.1)	13.3 (13.2)	319
12 ($C_{19}H_{17}N_3O_6$)	139	1735, 1725, 1700	59.65 (59.5)	4.5 (4.47)	11.1 (11.0)	383
14a ($C_{15}H_{16}N_2O_5$)	107	3380, 1730, 1725	59.3 (59.2)	5.2 (5.3)	9.1 (9.2)	304
14b ($C_{16}H_{18}N_2O_5$)	102	3380, 1735, 1720	60.5 (60.4)	5.7 (5.7)	8.8 (8.8)	318
15a ($C_{15}H_{16}N_2O_5$)	96	3400, 1730, 1725	59.3 (59.2)	5.2 (5.3)	9.35 (9.2)	304
15b ($C_{16}H_{18}N_2O_5$)	92	3370, 1720, 1700	60.2 (60.4)	5.6 (5.7)	8.85 (8.8)	318
16 ($C_{15}H_{16}N_2O_5$)	116	3470, 3390, 2210, 1720, 1715	59.2 (59.2)	5.35 (5.3)	9.3 (9.2)	304

[a]NMR data are given in Table 3. [b]From diisopropyl ether. [c]First pure diastereoisomer. [d]Second pure diastereoisomer.

Table 3. ^{1}H-NMR data of new compounds.

Compd	^{1}H-NMR ($CDCl_3$)[a] δ, J (Hz)
3a	1.72-2.00 (3H, m), 3.02 (1H, dd, J=18, 7), 3.31 (1H, dd, J=18, 12), 3.60-3.76 (2H, m), 3.83 (3H, s), 3.87 (3H, s), 4.77-4.84 (1H, m), 7.06-7.72 (4H, m)
3b	1.19 (3H, d, J=7), 1.50-1.80 (3H, m), 2.96 (1H, dd, J=18, 7), 3.32 (1H, dd, J=18, 12), 3.78 (3H, s), 3.86 (3H, s), 3.75-3.90 (1H, m), 4.80-4.93 (1H, m), 6.96-7.48 (4H, m)
3c[b]	1.70 (1H, ddd, J=13, 11, 4), 2.12 (1H, ddd, J=13, 11, 3), 2.70 (1H, br s), 3.11 (1H, dd, J=18, 7), 3.33 (1H, dd, J=18, 12), 3.75 (3H, s), 3.80 (3H, s), 4.64 (1H, dd, J=11, 3), 4.78-4.82 (1H, m), 6.98-7.71 (9H, m)
3c[c]	1.85-2.15 (2H, m), 2.56 (1H, br s), 2.93 (1H, dd, J=18, 8), 3.21 (1H, dd, J=18, 11), 3.70 (3H, s), 3.76 (3H, s), 4.42-4.73 (2H, m), 6.90-7.50 (9H, m)
3d	0.93 (3H, t, J =7.3), 1.53-1.82 (4H, m), 2.07 (1H, br s), 3.16 (1H, ddd, J=8.6, 8.5, 3.6)[d], 3.52-3.63 (2H, m), 3.80 (3H, s), 3.85 (3H, s), 4.48 (1H, ddd, J=8.6, 8.5, 3.3)[e], 7.01-7.48 (4H, m)
4	0.80 (3H, t, J=7.3), 1.50 (2H, qd, J=7.4, 7.3), 1.80-1.92 (2H, m), 2.56 (1H, br s), 3.32 (1H, ddd, J=6.6, 6.4, 2.1), 3.64-3.73 (2H, m), 3.81 (3H, s), 3.84 (3H, s), 4.30 (1H, ddd, J=6.6, 6.3, 3.0), 7.00-7.52 (4H, m)
5a	1.80 (1H, br t, J=4), 3.47 (2H, d, J=6), 3.87 (3H, s), 3.90 (3H, s), 4.11 (2H, dd, J=6, 4), 5.67-6.03 (2H, m), 6.94-7.92 (4H, m), 11.36 (1H, br s)
5b	1.18 (3H, d, J=6.4), 2.10 (1H, br s), 3.40 (1H, dd, J=16.1, 6.4), 3.47 (1H, dd, J=16.1, 5.1), 3.86 (3H, s), 3.88 (3H, s), 4.24-4.31 (1H, m), 5.60 (1H, td, J=15, 6), 5.70 (1H, dd, J=15, 6.4), 6.90-7.93 (4H, m), 11.30 (1H, br s)
5c	2.70 (1H, br s), 3.44 (1H, dd, J=16.4, 6.7), 3.58 (1H, dd, J=16.4, 5.4), 3.87 (3H, s), 3.89 (3H, s), 5.20 (1H, d, J=7), 5.72 (1H, td, J=15.4, 6.1), 6.00 (1H, dd, J=15.4, 7), 6.92-7.93 (9H, m), 11.33 (1H, br s)
5d	0.92 (3H, t, J=7), 1.7-2.2 (2H, m), 2.35 (1H, br s), 3.80 (3H, s), 3.85 (3H, s), 4.00-4.10 (3H, m), 5.60-5.70 (2H, m), 6.80-7.90 (4H, m), 11.35 (1H, br s)
5e	1.39 (3H, d, J=7), 2.49 (1H, br s), 3.83 (3H, s), 3.87 (3H, s), 4.05-4.15 (3H, m), 5.90-5.95 (2H, m), 6.85-7.95 (4H, m), 11.35 (1H, br s)
6	1.60 (1H, br s), 1.93 (1H, ddd, J=14, 13.6, 8), 2.08 (1H, ddd, J=14, 13.6, 7), 3.65-3.72 (3H, m), 3.86 (3H, s), 3.93 (3H, s), 5.03-5.15 (2H, m), 5.82-5.92 (1H, m), 6.90-7.95 (4H, m), 13.80 (1H, br s)
7	1.60 (1H, br s), 1.67 (3H, d, J=8), 1.90-2.10 (2H, m), 3.62 (2H, t, J=7), 3.80 (3H, s), 3.90 (3H, s), 3.95-4.00 (1H, m), 5.80-5.90 (2H, m), 6.00-8.00 (4H, m), 13.40 (1H, br s)
8d	0.92 (3H, t, J=7.5), 1.97 (2H, dq, J= 7.5, 7.3), 2.50 (2H, dt, J=6.8, 6.6), 3.88 (3H, s), 3.89 (3H, s), 4.32 (2H, t, J=6.8), 5.42-5.66 (2H, m), 6.85-7.91 (4H, m), 11.40 (1H, br s)
8e	1.61 (3H, d, J=6.4), 2.56 (2H, dt, J=7.0, 6.9), 3.87 (3H, s), 3.90 (3H, s), 4.32 (2H, t, J=7), 5.40-5.60 (2H, m), 6.85-7.90 (4H, m), 11.45 (1H, br s)
11	3.70 (3H, s), 3.88 (3H, s), 4.00 (3H, s), 7.00-8.20 (4H, m)
12	3.82 (3H, s), 3.85 (3H, s), 3.87 (3H, s), 5.90-7.80 (7H, m), 9.30 (1H, br s)
14a	2.45 (1H, br s), 2.72 (2H, t, J=6), 3.67 (3H, s), 3.69 (2H, t, J=6), 3.84 (3H, s), 6.80 (1H, s), 7.21-8.08 (4H, m)
14b	1.24 (3H, d, J=7), 2.48 (1H, br d, J=4), 2.62 (1H, dd, J=15, 9), 2.72 (1H, dd, J=15, 4), 3.75 (3H, s), 3.88-4.00 (1H, m), 3.90 (3H, s), 6.87 (1H, s), 7.35-8.05 (4H, m)
15a	1.80 (1H, br s), 3.08 (2H, t, J=6), 3.75 (3H, s), 3.87 (2H, t, J=6), 3.92 (3H, s), 7.49-7.56 (3H, m), 7.60 (1H, s), 7.92 (1H, dd, J=8, 1.6)
15b	1.22 (3H, d, J=6.4), 2.20 (1H, br s), 2.83 (1H, dd, J=14.7, 7,5), 3.08 (1H, dd, J=14.7, 11.6), 3.72 (3H, s), 3.90 (3H, s), 4.02-4.10 (1H, m), 7.48-7.62 (3H, m), 7.60 (1H, s), 7.89 (1H, dd, J=8.2, 1.6),
16	2.91 (2H, t, J=5.3), 3.70 (1H, br t, J=6), 3.87 (3H, s), 3.94 (3H, s), 3.90-4.00 (2H, m), 7.00-7.93 (4H, m), 12.20 (1H, br s)

[a]Coupling constants are given in Hz. [b]First pure diastereoisomer. [c]Second pure diastereoisomer. [d]After irradiation of the signal at δ 3.16: 1.71 (2H, q, J=7.3) and 4.48 (1H, dd, J=8.6, 3.3). [e]After irradiation of the signal at δ 4.48: 3.16 (1H, dd, J=8.6, 3.6).

EXPERIMENTAL

Melting points were determined with a Büchi apparatus and are uncorrected. IR spectra were recorded on a FT IR Perkin-Elmer 1725 X spectrophotometer. MS spectra were determined with a VG-70EQ apparatus. ^1H NMR spectra were taken with a Bruker AC-300 instrument in $CDCl_3$ solutions; chemical shifts are given as ppm from Me_4Si.

Compounds (**2**) and (**13**) are commercially available products. Hydrazonoyl chloride (**1**) was prepared as previuosly reported.[9]

General Procedure for the Treatment of Hydrazonoyl Chloride (1) with Alkenols (2) in the Presence of Silver Carbonate. A solution of **1** (2.7 g, 10 mmol) and the proper alkenol (15 mmol) in dry acetonitrile (65 mL) was treated with silver carbonate (5.5 g, 20 mmol) and stirred at rt in the dark for the time indicated in Table 1. The undissolved material was filtered off, the solvent was removed under reduced pressure and then the residue was chromatographed on a silica gel column. Eluents, products and yields are given in Table 1. Physical and spectral data of the new products are collected in Table 2.

General Procedure for the Treatment of Hydrazonoyl Chloride (1) with Alkynols (13) in the Presence of Silver Carbonate. A solution of **1** (2.7 g, 10 mmol) and the proper alkynol (15 mmol) in dry acetonitrile (150 mL) was treated with silver carbonate (5.5 g, 20 mmol) and refluxed in the dark for the time indicated in Table 1. The undissolved material was filtered off, the solvent was removed under reduced pressure and then the residue was chromatographed on a silica gel column. Eluents, products and yields are reported in Table 1. Physical and spectral data of the new products are collected in Table 2.

ACKNOWLEDGEMENTS

We thank MURST and CNR for financial support.

REFERENCES

1. L. Beltrame, C. Veglio, and M. Simonetta, *J. Chem. Soc. B*, 1967, 867.
2. Y. Tokunaga, M. Ihara, and K. Fukumoto, *Heterocycles*, 1996, **43**, 1771.
3. A. Padwa and S. Nahm, *J. Org. Chem.*, 1979, **44**, 4746.
4. A. Padwa and S. Naham, *J. Org. Chem.*, 1981, **46**, 1402.
5. G. Broggini, L. Bruché, L. Garanti, and G. Zecchi, *J. Chem. Soc., Perkin Trans. 1*, 1994, 433.
6. G. Broggini, L. Garanti, G. Molteni, and G. Zecchi, *Heterocycles*, 1994, **38**, 1601
7. G. Broggini, L. Garanti, G. Molteni, and G. Zecchi, *J. Chem. Res.*, 1995, 385(*S*), 2389(*M*).
8. G. Broggini, L. Garanti, G. Molteni, and G. Zecchi, *Org. Proc. Prep. Int.*, 1996, **28**, 699.

9. L. Garanti, G. Molteni, and G. Zecchi, *Heterocycles*, 1995, **40**, 777.

10. T. J. Batterham, '*NMR Spectra of Simple Heterocycles,*' Wiley, New York, 1973.

11. C. Wentrup, *Adv. Heterocycl. Chem.*, 1981, **28**, 231.

12. P. Caramella and P. Grünanger, '*1,3-Dipolar Cycloaddition Chemistry,*' ed. by A. Padwa, Wiley-Interscience, New York, 1984, Vol. 1, Ch. 3.

13. R. Huisgen and J. Wulff, *Chem. Ber.*, 1969, **102**, 1848.

14. F. A. Neugebauer and I. Umminger, *Chem. Ber.*, 1980, **113**, 1205.

15. S. P. McManus and C. U. Pittman, Jr., '*Organic Reactive Intermediates*,' ed. by S. P. McManus, Academic Press, 1973, ch. 4.

16. G. H. Schmid and D. G. Garratt, '*The Chemistry of Double-bonded Functional Groups*,' ed. by S. Patai, Wiley, 1977, part 2, Ch. 9.

Received, 17th July, 1997