Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 2183–2186

TETRAHEDRON LETTERS

Oxidation of aldimines to amides by *m*-CPBA and $BF_3{\cdot}OEt_2$

Gwang-il An,[a] Misoo Kim,[b] Jin Yeon Kim[c] and Hakjune Rhee[a,*]

[a]*Department of Chemistry, Hanyang University, Ansan, Kyunggi-Do 425-791, Republic of Korea*
[b]*Department of Basic Science, Hankyong National University, Ansung, Kyunggi-Do 456-749, Republic of Korea*
[c]*Department of Chemistry, Seonam University, Namweon, Chunrabuk-Do 590-170, Republic of Korea*

Received 20 September 2002; revised 27 December 2002; accepted 10 January 2003

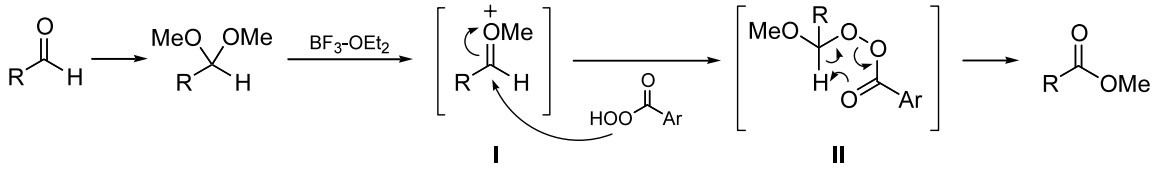
Abstract—Several amides were obtained in high yields by an efficient method from the corresponding imines which are readily prepared from aldehydes. This procedure involves the oxidation of aldimines with *m*-CPBA and $BF_3{\cdot}OEt_2$. In this reaction, the product is strongly influenced by the electron releasing capacity of the aromatic substituent.

Numerous methods for the oxidation of aldehydes have been reported over the years.[1] We developed a simple one-pot procedure for the conversion of aldehydes to methyl esters via dimethyl acetal formation from aldehydes and subsequent oxidation.[2] The proposed oxidation mechanism involves the formation and rapid fragmentation of the peroxy intermediate **II**, as shown below (Scheme 1). Other alkyl acetals and cyclic acetals were also readily converted to the corresponding esters by the same methodology.[3]

Although a number of oxidation methods for the conversion of aldehydes to amides have been reported, a few of these proceed through imines.[4] Since imines are readily prepared from the corresponding aldehydes,[5] it would be expected that the imine carbon could likewise be activated via the coordination of the Lewis acid, $BF_3{\cdot}OEt_2$ on the lone pair of nitrogen atom as occurs on the oxygen atom in the acetal oxidation. Another possible reaction pathway could be through an oxaziridine intermediate since there is literature precedent for the formation of oxaziridines from the corresponding imines with peroxyacid.[6] Thus, Scheme 2 shows a plausible competitive reaction mechanism for the oxidation of imines to amides by *m*-CPBA with $BF_3{\cdot}OEt_2$.

If the reaction proceeds as in the acetal oxidation, the amide would be the only product formed via an internal hydrogen abstraction. If the reaction proceeds via the formation of an oxaziridine, one might expect the selective rearrangement of the aryl group or the hydrogen atom as in the Beckmann rearrangement and the Baeyer–Villiger oxidation. We now wish to report an oxidation of aldimines to amides by *m*-CPBA and $BF_3{\cdot}OEt_2$. The results are summarized in Table 1.[7]

The results in Table 1 would indicate that the reaction product is strongly influenced by the electron releasing capacity of the aromatic substituent. With the electron-releasing substituent on the aryl group (entries 1–3 and 9–10), the oxidation of imines afforded formamides in which aryl group migration occurred. However, an electron-withdrawing substituent on the aryl group provided the amide formed from hydride migration (entries 5–8). In the case of the chloro substituent (entry 4), the



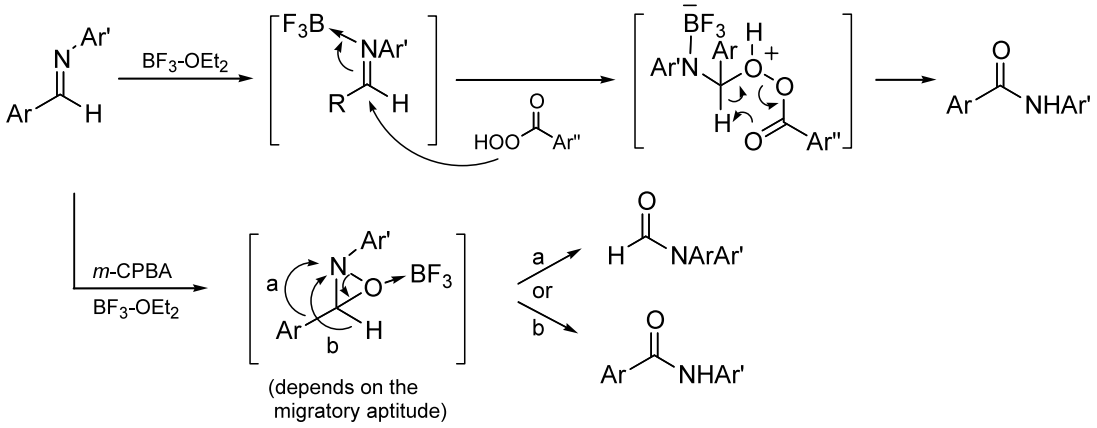
Scheme 1.

Keywords: oxidative rearrangement; aldimines; migratory aptitude; formamides; amides.
* Corresponding author. E-mail: hrhee@hanyang.ac.kr

0040-4039/03/$ - see front matter
doi:10.1016/S0040-4039(03)00156-4

formamide was obtained as the major product (83% yield) along with 5.6% of the amide. These results suggest that the reaction mechanism can be tentatively rationalized by the oxaziridine ring formation and Lewis acid mediated ring opening with subsequent migration of the aryl group or the hydrogen atom, depending on the difference in the migratory aptitude of those groups to an electron deficient nitrogen atom (Scheme 2, bottom). Thermal reaction studies of the oxaziridines by Splitter and Calvin[8] and the oxidative rearrangement of aldimines with sodium perborate by Ramsden and co-worker[4b,c] support the reaction mechanism shown in the bottom of Scheme 2. Contrary to our results, however, their procedures gave very poor selectivity and yield in the oxidative rearrangement of aldimines.

In contrast to entries 1–10, when *p*-anisidine is used for the oxidation of aldimine (entries 11–14), the oxidation affords only the *N*-(*p*-methoxyphenyl)-*p*-substituted-benzamide along with a considerable amount of the recovered arylaldehyde. It is presumed that the reaction follows an internal hydrogen abstraction (Scheme 2, top) and decomposition to the corresponding aldehyde. The electron releasing group, i.e. the methoxy group of *p*-anisidine, increases the electron density on the nitrogen atom and helps the coordination of the Lewis acid on the lone pair of the nitrogen atom. After the formation of the peroxy intermediate by the attack of *m*-CPBA on the iminium carbon, rapid fragmentation of the peroxy intermediate presumably occurs to provide the amide (Scheme 2).



Scheme 2.

Table 1. Oxidation of aldimines to amides by *m*-CPBA and $BF_3{\cdot}OEt_2$

Entry	Imine	Product	Yield (%)[a]
1	$C_6H_5CH{=}NC_6H_5$	$HCON(C_6H_5)_2$	82
2	*p*-Me-$C_6H_4CH{=}NC_6H_5$	$HCONC_6H_5$ *p*-Me-C_6H_4	90
3	*p*-MeO-$C_6H_4CH{=}NC_6H_5$	$HCONC_6H_5$ *p*-MeO-C_6H_4	91
4	*p*-Cl-$C_6H_4CH{=}NC_6H_5$	$HCONC_6H_5$ *p*-Cl-C_6H_4	89[b]
5	*p*-NO_2-$C_6H_4CH{=}NC_6H_5$	*p*-NO_2-$C_6H_4CONHC_6H_5$	71
6	*p*-NC-$C_6H_4CH{=}NC_6H_5$	*p*-NC-$C_6H_4CONHC_6H_5$	79
7	*p*-F_3C-$C_6H_4CH{=}NC_6H_5$	*p*-F_3C-$C_6H_4CONHC_6H_5$	75
8	$C_6F_5CH{=}NC_6H_5$	$C_6F_5CONHC_6H_5$	71
9	*trans*-$C_6H_5CH{=}CH{-}CH{=}NC_6H_5$	$HCONC_6H_5$ *trans*-$C_6H_5CH{=}CH$	80
10	*trans*-$C_6H_5CH{=}CMe{-}CH{=}NC_6H_5$	$HCONC_6H_5$ *trans*-$C_6H_5CH{=}CMe$	82
11	$C_6H_5CH{=}N$ *p*-MeO-C_6H_4	C_6H_5CONH *p*-MeO-C_6H_4	42[c]
12	*p*-Me-$C_6H_4CH{=}N$ *p*-MeO-C_6H_4	*p*-Me-C_6H_4CONH *p*-MeO-C_6H_4	45[d]
13	*p*-MeO-$C_6H_4CH{=}N$ *p*-MeO-C_6H_4	*p*-MeO-C_6H_4CONH *p*-MeO-C_6H_4	52[e]
14	*p*-Cl-$C_6H_4CH{=}N$ *p*-MeO-C_6H_4	*p*-Cl-C_6H_4CONH *p*-MeO-C_6H_4	39[f]
15	$C_6H_5CH{=}N$ *p*-Cl-C_6H_4	$HCONC_6H_5$ *p*-Cl-C_6H_4	84
16	*p*-Me-$C_6H_4CH{=}N$ *p*-Cl-C_6H_4	HCON *p*-Me-C_6H_4 *p*-Cl-C_6H_4	84
17	*p*-MeO-$C_6H_4CH{=}N$ *p*-Cl-C_6H_4	HCON *p*-MeO-C_6H_4 *p*-Cl-C_6H_4	86
18	*p*-Cl-$C_6H_4CH{=}N$ *p*-Cl-C_6H_4	$HCON(p\text{-Cl-}C_6H_4)_2$	82[g]

[a] Yields refer to isolated products.
[b] Formamide and amide were obtained in a 14.8: 1 ratio.
[c] Benzaldehyde was also isolated in 51% yield.
[d] *p*-Tolualdehyde was also isolated in 50% yield.
[e] *p*-Anisaldehyde was also isolated in 43% yield.
[f] *p*-Chlorobenzaldehyde was also isolated in 51% yield.
[g] *N*-(*p*-Chlorophenyl)-*p*-chlorobenzamide was also isolated in 7% yield.

However, with an electron withdrawing group, i.e. the chloro group of *p*-chloroaniline (entries 15–18), the reaction products were the same as in the aniline cases and also follow the oxaziridine ring formation and Lewis acid mediated ring opening with the subsequent migration of the aryl group or the hydrogen atom to the electron deficient nitrogen atom.

The products of this oxidation were identified by a ^{1}H NMR comparison with that of known compounds (entries 1–8, 11–16, 18).[4b,c,9] Otherwise, these were fully characterized by IR, ^{1}H and ^{13}C NMR, and HRMS analysis (entries 9, 10, 17).[10–12] In the case of the electron-withdrawing substituent on the aryl group (entries 5–8) and in *p*-anisidine (entries 11–14), a deuterium exchange of the amide NH was observed in the ^{1}H NMR spectra.

In summary, we have developed an efficient method for the conversion of various aldimines to their corresponding *N*,*N*-diarylformamides or amides by *m*-CPBA and $BF_3{\cdot}OEt_2$. The hydrolysis of *N*,*N*-diarylformamides will provide diarylamines and this method could be a valuable alternative to the Chapman rearrangement[13] and the Ullmann–Goldberg condensation.[14]

Acknowledgements

This work, carried out in 2001, was supported by Hanyang University, Korea. M.K. would also like to thank the Hankyong National University Research Fund for providing partial support in 2001.

References

1. For a list of methods, see: Larock, R. C. *Comprehensive Organic Transformations*: *A Guide to Functional Group Preparations*; 2nd ed.; John Wiley & Sons: New York, 1999; pp. 1653–1661 and references cited therein.
2. Rhee, H.; Kim, J. Y. *Tetrahedron Lett*. **1998**, *39*, 1365.
3. Kim, J. Y.; Rhee, H. *Bull Korean Chem. Soc*. **2000**, *21*, 355.
4. (a) Enders, D.; Amaya, A. S.; Pierre, F. *New J. Chem*. **1999**, *23*, 261; (b) Nongkunsarn, P.; Ramsden, C. A. *Tetrahedron* **1997**, *53*, 3805; (c) Nongkunsarn, P.; Ramsden, C. A. *Tetrahedron Lett*. **1993**, *34*, 6773; (d) Larsen, J.; Jorgensen, K. A.; Christensen, D. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1187; (e) Aitken, R. A.; Raut, S. V. *Synlett* **1991**, 189; (f) Chuang, T. H.; Yang, C. C.; Chang, C. J.; Fang, J. M. *Synlett* **1990**, 733; (g) De Kimpe, N.; Verhe, R.; De Buyck, L.; Chys, J.; Schamp, N. *Org. Prep. Proced. Int*. **1978**, *10*, 149; (h) Sandhu, J. S.; Mohan, S.; Sethi, P. S. *Chem. Ind*. **1970**, 1297.
5. (a) MacPherson, D. T.; Rami, H. K. In *Comprehensive Organic Functional Group Transformations*; Katritzky, A. R.; Otto, M.; Rees, C. W., Eds.; Elsevier: Amsterdam, 1995; Vol. 3, pp. 405–406 and references cited therein; (b) Smith, M. B.; March, J. In *March's Advanced Organic Chemistry*: *Reactions, Mechanisms, and Structure*; 5th ed.; John Wiley & Sons: New York, 2001; pp. 1185–1187 and references cited therein.
6. (a) Kitagawa, O.; Velde, D. V.; Dutta, D.; Morton, M.; Takusagawa, F.; Aubé, J. *J. Am. Chem. Soc*. **1995**, *117*, 5169; (b) Davis, F. A.; Weismiller, M. C.; Murphy, C. K.; Reddy, R. T.; Chen, B. C. *J. Org. Chem*. **1992**, *57*, 7274; (c) Aubé, J.; Hammond, M.; Gherardini, E.; Takusagawa, F. *J. Am. Chem. Soc*. **1991**, *113*, 499; (d) Duhamel, P.; Bénard, D.; Plaquevent, J.-C. *Tetrahedron Lett*. **1985**, *26*, 6065; (e) Emmons, W. D.; Pagano, A. S. In *Organic Syntheses*; Baumgarten, H. E., Ed.; John Wiley & Sons: New York, 1973; Coll. Vol. 5, pp. 191–193; (f) Emmons, W. D. *J. Am. Chem. Soc*. **1957**, *79*, 5739.
7. **General procedure for the preparation of aldimines**: To a solution of aryl carboxaldehyde, *trans*-cinnamaldehyde, or *trans*-α-methylcinnamaldehyde (5 mmol) in $CHCl_3$ (20 mL) were added aniline, *p*-anisidine, or *p*-chloroaniline (10 mmol) and molecular sieves (1.0 g) at ambient temperature. After stirring for a certain period of time, the crude mixture was rinsed with K_2CO_3–brine solution (3×20 mL) and the crude product was concentrated by rotary-evaporation. The purity of the crude products was checked by ^{1}H NMR spectroscopy. The products were sufficiently pure to use for next reaction.
   General procedure for the preparation of amides: To a solution of aldimine (5 mmol) in anhydrous $CHCl_3$ (15 mL) were added *m*-CPBA (72%, 5.0 mmol) in anhydrous $CHCl_3$ (15 mL) and $BF_3{\cdot}OEt_2$ (1.5 mmol) at 0°C. The resulting reaction mixture was stirred for 6 h at ambient temperature. The reaction mixture was diluted with $CHCl_3$ (15 mL) and washed with saturated Na_2CO_3 solution (3×20 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated by rotary-evaporation. The residue was purified by flash column chromatography (EtOAc/*n*-hexane).
8. Splitter, J. S.; Calvin, M. *J. Org. Chem*. **1965**, *30*, 3427.
9. (a) Chakraborti, A. K.; Sharma, L.; Nayak, M. K. *J. Org. Chem*. **2002**, *67*, 6406; (b) Arisawa, M.; Yamaguchi, M. *Org. Lett*. **2001**, *3*, 311; (c) Thakur, A. J.; Boruah, A.; Prajapati, D.; Sandhu, J. S. *Synth. Commun*. **2000**, *30*, 2105; (d) Stauffer, S. R.; Sun, J.; Katzenellenbogen, B. S.; Katzenellenbogen, J. A. *Bioorg. Med. Chem*. **2000**, *8*, 1293; (e) Anilkumar, R.; Chandrasekhar, S. *Tetrahedron Lett*. **2000**, *41*, 5427; (f) Kunishima, M.; Kawachi, C.; Morita, J.; Terao, K.; Iwasaki, F.; Tani, S. *Tetrahedron* **1999**, *55*, 13159; (g) Meshram, H. M.; Reddy, G. S.; Reddy, M. M.; Yadav, J. S. *Tetrahedron Lett*. **1998**, *39*, 4103; (h) Barton, D. H. R.; Ferreira, J. A. *Tetrahedron* **1996**, *52*, 9347; (i) Perry, R. J.; Wilson, B. D. *J. Org. Chem*. **1996**, *61*, 7482; (j) Yuzuri, T.; Suezawa, H.; Hirota, M. *Bull. Chem. Soc. Jpn*. **1994**, *67*, 1664; (k) Marovec, F.; Peris, W.; Revel, L.; Giovanetti, R.; Redaelli, D.; Rovati, L. C. *J. Med. Chem*. **1992**, *35*, 3633; (l) Hishmat, O. H.; Magd El Din, A. A.; Ismail, N. A. *Org. Prep. Proc. Int*. **1992**, *24*, 33; (m) Suezawa, H.; Yuzuri, T.; Hirota, M.; Ito, Y.; Hamada, Y. *Bull. Chem. Soc. Jpn*. **1990**, *63*, 328; (n) Yoshino, K.; Kohno, T.; Uno, T.; Morita, T.; Tsukamoto, G. *J. Med. Chem*. **1986**, *29*, 820; (o) Petrenko, N. I.; Gerasimova, T. N.; Fokin, E. P. *Izv. Akad. Nauk SSSR, Ser. Khim*. **1984**, 1378; (p) Ito, S.; Tanaka, Y.; Kakehi, A. *Bull. Chem. Soc. Jpn*. **1982**, *55*, 859; (q) Orlova, N. A.; Gerasimova, T. N.; Fokin, E. P. *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk* **1980**, 131; (r) Gerasimova, T. N.; Simikolenova, N. V.;

Orlova, N. A.; Fomenko, T. V.; Fokin, E. P. *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk* **1975**, 54; (s) DoAmaral, J. R.; Blanz, E. J., Jr.; French, F. A. *J. Med. Chem.* **1969**, *12*, 21; (t) Mandyuk, V. F.; Lushina, N. P. *USSR. Zh. Prikl. Spektrosk.* **1968**, *9*, 670; (u) Brown, R. F. C.; Radom, L.; Sternhell, S.; Rae, I. D. *Can. J. Chem.* **1968**, *46*, 2577.

10. The characterization of *N*-phenyl-*N*-*trans*-styrylformamide: IR (thin film) 3060, 2879, 1685, 1643, 1495, 1228, 950, 693, 585 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.27 (s, 1H, CHO), 7.99 (d, $J=15.0$ Hz, 1H, CH=C), 7.18–7.56 (m, 10H, ArH), 5.85 (d, $J=14.7$ Hz, 1H, CH=C); ^{13}C NMR ($CDCl_3$) δ 161.0, 138.0, 136.0, 130.2, 129.1, 128.8, 128.2, 127.2, 126.1, 125.3, 115.7; HRMS (EI) m/z: calcd for ($C_{15}H_{13}NO$): 223.0997, found 223.0986 [M^+].
11. The characterization of *N*-phenyl-*N*-α-methyl-*trans*-styrylformamide: IR (thin film) 3061, 3028, 2918, 2877, 1685, 1595, 1493, 1301, 1270, 1246, 745 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.65 and 8.55 (pair of s, 1H, CHO), 7.24–7.46 (m, 10H, ArH), 6.56 and 6.54 (pair of br s, 1H, CH=C), 2.14 and 1.97 (pair of d, J = 1.5 and 1.2 Hz, 3H, MeC=C); ^{13}C NMR ($CDCl_3$) δ 161.5, 161.0, 137.3, 136.6, 135.6, 135.4, 129.7, 129.5, 129.3, 129.0, 128.8, 128.6, 128.4, 127.5, 127.3, 127.2, 126.9, 126.3, 125.8, 123.9, 17.9, 17.3; HRMS (EI) m/z: calcd for ($C_{16}H_{15}NO$): 237.1154, found 237.1144 [M^+].
12. The characterization of *N*-(*p*-chlorophenyl)-*N*-(*p*-methoxyphenyl)formamide: IR (thin film) 3069, 3004, 2934, 2908, 1688, 1592, 1511, 1492, 1327, 1276, 1247, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.63 and 8.52 (pair of s, 1H, CHO), 6.90–7.35 (m, 8H, ArH), 3.81 and 3.79 (pair of s, 3H, OMe); ^{13}C NMR ($CDCl_3$) δ 161.6, 161.3, 158.9, 158.4, 140.6, 138.6, 133.8, 132.2, 131.8, 131.5, 129.6, 129.0, 127.6, 127.3, 126.2, 125.3, 114.9, 114.5, 55.4, 55.3; HRMS (EI) m/z: calcd for ($C_{14}H_{12}ClNO_2$): 261.0557, found 261.0553 [M^+].
13. (a) Marsh, A.; Nolen, E. G.; Gardinier, K. M.; Lehn, J. M. *Tetrahedron Lett.* **1994**, *35*, 397; (b) Kuroda, T.; Suzuki, F. *Tetrahedron Lett.* **1992**, *33*, 2027; (c) Dessolin, M.; Eisenstein, O.; Golfier, M.; Prange, T.; Sautet, P. *J. Chem. Soc., Chem. Commun.* **1992**, 132; (d) Esser, F.; Brandt, K.; Pook, K. H.; Foerster, H. J.; Koeppen, H.; Leger, J. M.; Carpy, A. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3311; (e) Kimura, M.; Okabayashi, I.; Isogai, K. *J. Heterocyclic Chem.* **1988**, *25*, 315; (f) Suttle, N. A.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1983**, 1369; (g) Peterson, L. H.; Douglas, A. W.; Tolman, R. L. *J. Heterocyclic Chem.* **1981**, *18*, 659; (h) Ramirez, F.; Telefus, C. D.; Prasad, V. A. V. *Tetrahedron* **1975**, *31*, 2007; (i) Goldberg, V. D.; Harris, M. M. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1303; (j) Shawali, A. S.; Hassaneen, H. M. *Tetrahedron* **1972**, *28*, 5903; (k) McCullough, J. D., Jr.; Curtin, D. Y.; Paul, I. C. *J. Am. Chem. Soc.* **1972**, *94*, 874; (l) Fischer, H. P.; Funk-Kretschmar, F. *Helv. Chim. Acta* **1969**, *52*, 913; (m) Wheeler, O. H.; Roman, F.; Santiago, M. V.; Quiles, F. *Can. J. Chem.* **1969**, *47*, 503; (n) Relles, H. M. *J. Org. Chem.* **1968**, *33*, 2245; (o) Bock, G. *Chem. Ber.* **1967**, *100*, 2870; (p) Schulenberg, J. W.; Archer, S. In *Organic Reactions*; Cope, A. C.; Adams, R.; Boekelheide, V.; Blatt, A. H.; Cairns, T. L.; Niemann, C., Eds.; John Wiley: New York, 1965; Vol. 14, p. 1.
14. (a) Pellon, R. F.; Carrasco, R.; Marquez, T.; Mamposo, T. *Tetrahedron Lett.* **1997**, *38*, 5107; (b) Pellon, R. F.; Mamposo, T.; Carrasco, R.; Rodes, L. *Synth. Commun.* **1996**, *26*, 3877; (c) Pellon, R. F.; Carrasco, R.; Rodes, L. *Synth. Commun.* **1996**, *26*, 3869; (d) Hanoun, J.-P.; Galy, J.-P.; Tenaglia, A. *Synth. Commun.* **1995**, *25*, 2443; (e) Pellon, R. F.; Carrasco, R.; Millian, V.; Rodes, L. *Synth. Commun.* **1995**, *25*, 1077; (f) Pellon, R. F.; Carrasco, R.; Rodes, L. *Synth. Commun.* **1993**, *23*, 1447; (g) Lindley, J. *Tetrahedron* **1984**, *40*, 1433; (h) Kalten-bronn, J. S.; Scherrer, R. A.; Short, F. W.; Jones, E. M.; Beatty, H. R.; Saka, M. M.; Winder, C. V.; Wax, J.; Williamson, W. R. N. *Arzneim. Forsch.* **1983**, *33*, 621; (i) Hebky, J.; Radek, O.; Kejha, J. *Collect. Czech. Chem. Commun.* **1958**, 3988.