DOI: 10.1002/adsc.200505268

A General and Efficient Method for the Preparation of β-Enamino Ketones and Esters Catalyzed by Indium Tribromide

Zhan-Hui Zhang, Liang Yin, Yong-Mei Wang*

Department of Chemistry and the State Key Laboratory of Elemento-Organic Chemistry, Nankai University,
Tianjin 300071, People's Republic of China
Fax: (+86)-22-2350-2654, e-mail: zhanhui@mail.nankai.edu.cn

Received: July 7, 2005; Accepted: November 24, 2005

Supporting Information for this article is available on the WWW under http://asc.wiley-vch.de/home/.

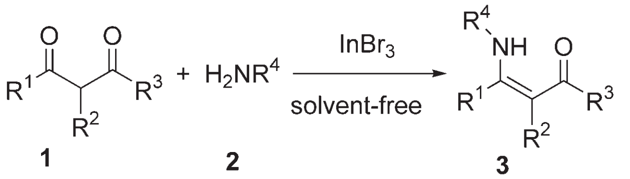
Abstract: A variety of β-enamino ketones and esters have been synthesized in high to exellent yields by reacting β-dicarbonyl compounds with amines in the presence of a catalytic amount of indium tribromide. The reaction proceeds smoothly at room temperature in a short reaction time under solvent-free conditions.

Keywords: amines; β-dicarbonyl compounds; enaminones; indium tribromide; solvent-free

Introduction

Enamination of β-dicarbonyl compounds forming β-enamino ketones and esters, is an important and widely used transformation.[1] The latter compounds are a highly versatile class of intermediates for the synthesis of heterocycles and biologically active compounds.[2] In particular, the enamino ketone moiety has attracted much interest because it is a basic and versatile structure for the synthesis of natural therapeutic and biologically active analogues including taxo,[3] anticonvulsivant,[4] anti-inflammatory,[5] and antitumor agents,[6] as well as quinolone antibacterials[7] and quinoline antimalarials.[6] Pyrroles, oxazoles, pyridinones, quinolines, dibenzodiazepines, tetrahydrobenzoxazines, tetronic acids, aza steroids, (1*H*)-pyridin-2-one, pyrazolo[1,5-*a*]pyrimidine and isoxazole derivatives have also been prepared from enaminones.[8] In addition, chiral enaminones obtained from optically active compounds are useful ligands for diastereoselective synthesis.[9] β-Enamino esters are useful precursors for the preparation of biologically active compounds such as β-enamino acids, γ-enamino alcohols or β-enamino esters.[10] A number of reviews have been published about the chemistry of β-enamino ketones and esters, their hydrolysis under a variety of conditions, their physicochemical properties and uses.[11] It is therefore not surprising that many synthetic methods have been developed for the preparation of these compounds. These compounds can be synthesized *via* addition of metallic ester or amide enolates to nitriles,[12] tosylimines[13] and imidoyl halides,[14] *via* addition of enamines[15] or ketimines[16] to activated carboxylic acid derivatives and the reaction of β-enamino esters with organolithium reagents.[17] Moreover, β-enamino ketones or esters can also be successfully obtained from the direct condensation of 1,3-dicarbonyl compounds with amines. This is the most simple and straightforward procedure for their synthesis, in which the azeotropic removal of water is usually required under reflux using a Dean–Stark trap in an aromatic solvent.[18] A variety of catalysts such as HCl,[19] H_2SO_4,[20] *p*-TSA,[21] HOAc,[22] trimethylsilyl trifluoromethanesulfonate (TMSTf),[23] montmorillonite K10 under microwave irradiation[24] or ultrasound,[25] I_2,[19b] $BF_3 \cdot OEt_2$,[26] Al_2O_3,[27] silica gel,[28] $Zn(ClO_4)_2 \cdot 6\,H_2O$,[29] $CeCl_3 \cdot 7\,H_2O$,[30] $NaAuCl_4$,[31] and natural clays[32] have been employed to effect this transformation. Recently, this condensation reaction has also been performed in water[33,34] or in ionic liquid medium.[30,35] Although these methods are suitable for certain synthetic conditions, sometimes, however, many of these procedures are associated with one or more disadvantages such as long reaction time, low yield, use of volatile organic solvents, requirement of excess of reagents or catalysts, special apparatus and harsh reaction conditions. Due to the importance of these compounds as intermediates in organic synthesis, the development of convenient, environmentally benign, high-yielding and clean approaches is highly desirable.

In recent years, indium tribromide has received increasing attention as a novel type of water-tolerant green Lewis acid catalyst for organic synthesis with highly chemo-, regio- and stereoselective results. Compared to conventional Lewis acids, it has advantages of water stability, recyclability, operational simplicity, strong tolerance to oxygen and nitrogen-containing reaction substrates and functional groups.[36] As a part of our program aiming at developing selective and environmental friendly methodologies for the preparation of fine chemicals and in continuation of our interest in Lewis acid-catalyzed organic reactions,[37] we herein report a green, mild and efficient method for the regio- and chemoselective enamination of β-dicarbonyl compounds using a catalytic amount of $InBr_3$ under solvent-free conditions (Scheme 1).



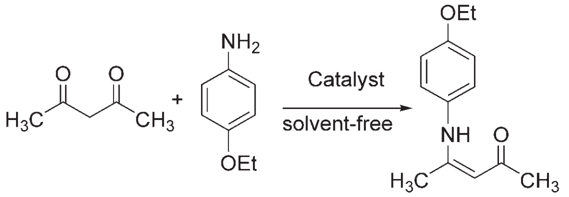
Scheme 1.

Results and Discussion

Firstly, the efficacy of various Lewis acids was investigated in the model reaction using acetylacetone with 4-ethoxyaniline under solvent-free condition at room temperature and the results are summarized in Table 1. The results established that $InBr_3$ was superior with respect to amount of catalysts, reaction times and product yields. Entry 1 shows the blank reaction without addition of any catalyst, in this case only 48% product was reached after 24 h. Although the reactions also proceeded with $InCl_3$, long reaction times are typical to achieve comparable yields to those obtained with $InBr_3$. Lower catalyst loading can be used with only a decline in reaction rate (Table 1, entry 21). We next planned to determine the influence of solvent on the catalytic property of the reaction of acetylacetone with 4-ethoxyaniline. Obviously, the presence of additional solvents makes the reaction rate lower (Table 1, entries 22, 23 and 24). So we choose to perform this reaction under solvent-free conditions.

To evaluate the scope and limitations of this catalyst's application, various cyclic and acyclic β-keto esters such as methyl acetoacetate, ethyl acetoacetate, 2-acetybutyrolactone, and ethyl 2-oxocyclopentanecarboxylate were treated with a range of primary, secondary, benzylic and aromatic amines in the presence of catalytic amounts (1 mol %) of $InBr_3$ under solvent-free conditions and the results are summarized in Table 2. The reaction was clean and highly diastereoselective and proceeded smoothly to give the corresponding β-enamino esters in good to excellent yields. In all reactions, the products were obtained with the *Z*-geometry stabilized by an intramolecular hydrogen bonding and their structures were confirmed by detailed ^1H NMR.[38,39]

Table 1. Condensation of acetylacetone with 4-ethoxyaniline in the presence of various Lewis acids under various reaction conditions.[a]

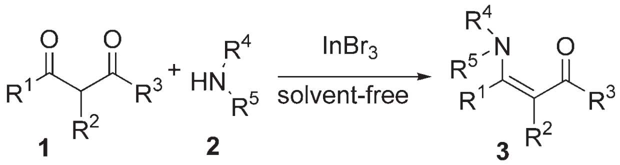


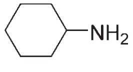
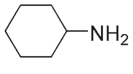
Entry	Catalyst	Time [h]	Yield [%][b]
1	none	24	48
2	$Mg(ClO_4)_2$	4	92
3	$BiCl_3$	0.8	90
4	$CuCl_2$	2	89
5	$FeCl_3$	5	90
6	$ZnCl_2$	5	87
7	$AlCl_3$	5	82
8	$LiClO_4 \cdot 3\,H_2O$	8	85
9	$NiCl_2 \cdot 6\,H_2O$	3.5	89
10	$Zn(OTf)_2$	1	92
11	$LaCl_3$	4	90
12	$LiBr \cdot H_2O$	10	62
13	$Ti(SO_4)_2$	1	81
14	LiCl	15	58
15	$ZnBr_2$	4	89
16	$SrCl_2 \cdot 6\,H_2O$	15	56
17	$CdCl_2 \cdot 2.5\,H_2O$	16	76
18	I_2	1.5	93
19	$InCl_3$	1	90
20	$InBr_3$	0.3	96
21	$InBr_3$	8	94[c]
22	$InBr_3$	3	91[d]
23	$InBr_3$	3	89[e]
24	$InBr_3$	4	86[f]

[a] *General reaction conditions:* acetylacetone (5 mmol), 4-ethoxyaniline (5 mmol), catalyst (1.0 mol %).
[b] Yields are given for isolated products.
[c] 50 mmol of substrates and 0.1 mol % catalyst were used.
[d] 5 mL of CH_2Cl_2 were added.
[e] 5 mL of H_2O were added.
[f] 5 mL of EtOAc were used.

The nucleophilic addition of amines to carbonyl compounds, catalyzed by $InBr_3$, was found to be dependent on steric and electronic factors of β-keto esters and amines. The reaction of aniline with cyclic β-keto esters with carrying a substituent different than hydrogen in the α-position (Table 2, entries 41 and 47) took longer compared to the corresponding reaction with ethyl acetoacetate (Table 2, entry 18) under similar conditions. The different reactivities of the anilines were dependent on the substituents on the benzene ring. The presence of an electron-withdrawing group on the benzene ring decreased the reactivity of the substrate (Table 2, entries 29 and 30). Anilines containing strongly electron-withdrawing groups, such as 3-nitroaniline and 4-nitroaniline

Table 2. Synthesis of β-enamino esters **3** *via* condensation of β-keto ester **1** with amine **2** catalyzed by $InBr_3$.



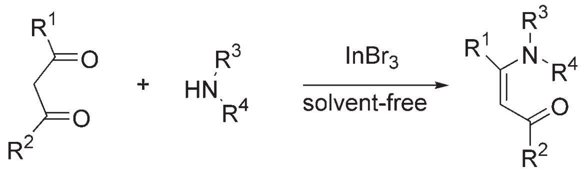
Entry	R^1	R^2	R^3	Amines	Time [min]	Yield [%][a]
1	Me	H	OEt	$CH_3(CH_2)_3NH_2$	15	92
2	Me	H	OMe	$(CH_3)_2CHNH_2$	90	94
3	Me	H	OEt	$(CH_3)_2CHNH_2$	90	92
4	Me	H	OMe	$CH_2{=}CHCH_2NH_2$	15	93
5	Me	H	OEt	$CH_2{=}CHCH_2NH_2$	20	96
6	Me	H	OMe		15	95
7	Me	H	OEt		15	95
8	Me	H	OMe	$H_2NCH_2CH_2CH_2NH_2$	10	95
9	Me	H	OEt	$H_2NCH_2CH_2CH_2NH_2$	15	96
10	Me	H	OMe	$PhCH_2CH_2NH_2$	10	95
11	Me	H	OMe	$PhCH_2NH_2$	10	92
12	Me	H	OEt	$PhCH_2NH_2$	10	94
13	Me	H	OMe	(*R*)-$PhCH(CH_3)NH_2$	15	95
14	Me	H	OEt	(*R*)-$PhCH(CH_3)NH_2$	15	94
15	Me	H	OMe	*p*-MeO-$C_6H_4CH_2CH(CH_3)NH_2$	25	91
16	Me	H	OEt	*p*-MeO-$C_6H_4CH_2CH(CH_3)NH_2$	20	96
17	Me	H	OMe	$PhNH_2$	60	91
18	Me	H	OEt	$PhNH_2$	50	98
19	Me	H	OMe	4-Me-$C_6H_4NH_2$	50	95
20	Me	H	OEt	4-Me-$C_6H_4NH_2$	40	95
21	Me	H	OMe	2-Me-$C_6H_4NH_2$	90	93
22	Me	H	OEt	2-Me-$C_6H_4NH_2$	90	92
23	Me	H	OMe	4-MeO-$C_6H_4NH_2$	50	92
24	Me	H	OEt	4-MeO-$C_6H_4NH_2$	45	93
25	Me	H	OMe	4-EtO-$C_6H_4NH_2$	60	92
26	Me	H	OEt	4-EtO-$C_6H_4NH_2$	60	95
27	Me	H	OMe	2-EtO-$C_6H_4NH_2$	90	92
28	Me	H	OEt	2-EtO-$C_6H_4NH_2$	90	86
29	Me	H	OMe	4-Cl-$C_6H_4NH_2$	8 h	76
30	Me	H	OEt	4-Cl-$C_6H_4NH_2$	8 h	80
31	Me	H	OMe	2,6-Et_2-$C_6H_3NH_2$	6 h	85
32	Me	H	OMe	2,6-*i*-Pr_2-$C_6H_3NH_2$	6 h	81
33	Me	H	OEt	2,6-*i*-Pr_2-$C_6H_3NH_2$	6 h	80
34	Me	H	OEt	3-NO_2-$C_6H_4NH_2$	8 h	36[b]
35	Me	H	OEt	4-NO_2-$C_6H_4NH_2$	8 h	28[b]
36	Ph	H	OEt	$PhNH_2$	24 h	23
37	Ph	H	OEt	(*R*)-$PhCH(CH_3)NH_2$	24 h	28
38	Me	$(CH_2)_2O$		$CH_2{=}CHCH_2NH_2$	20	95
39	Me	$(CH_2)_2O$		$PhCH_2NH_2$	30	93
40	Me	$(CH_2)_2O$		(*R*)-$PhCH(CH_3)NH_2$	40	95
41	Me	$(CH_2)_2O$		$PhNH_2$	70	95
42	Me	$(CH_2)_2O$		4-Me-$C_6H_4NH_2$	30	86
43	Me	$(CH_2)_2O$		2-Me-$C_6H_4NH_2$	120	84
44	Me	$(CH_2)_2O$		2-EtO-$C_6H_4NH_2$	70	82
45	Me	$(CH_2)_2O$		4-EtO-$C_6H_4NH_2$	60	89
46	Me	$CH_2)_2O$		4-MeO-$C_6H_4NH_2$	30	85
47	$(CH_2)_3$	OEt		$PhNH_2$	90	92
48	$(CH_2)_3$	OEt		2-EtO-$C_6H_4NH_2$	120	90
49	$(CH_2)_3$	OEt		4-EtO-$C_6H_4NH_2$	100	93
50	$(CH_2)_3$	OEt		4-MeO-$C_6H_4NH_2$	100	94

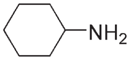
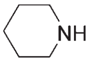
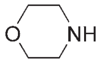
[a] Yields are given for isolated products.

[b] The reactions were performed at 50 °C.

afforded the corresponding β-enamino esters in only 36% and 28% yield at 50 °C, respectively (Table 2, entries 34 and 35), which showed an obvious electronic effect. *ortho*-Substituted anilines whatever the character of the substituent groups required longer reaction times. It was revealed that yields were significantly decreased when the sizes of the *ortho*-substituent groups were large. For example, 2,6-diethylaniline (Table 2, entry 31) and 2,6-diisopropylaniline (Table 2, entries 32 and 33) were found to be less active and gave the corresponding β-keto esters in 80–85% yields even after 6 h. This may due to the steric hindrance exhibited by the 2,6-diethyl and 2,6-diisopropyl groups of the aniline towards the approaching β-keto esters. Aliphatic amines reacted efficiently to produce the corresponding β-enamino esters. In the case of 1,3-diaminopropane, 2 equivs. of β-keto ester were used giving products with two enamino ester groups (Table 2, entries 8 and 9). It is noteworthy that optically active amines were converted into the corresponding β-keto esters without any racemization or inversion (Table 2, entries 13, 14, 37 and 40). The less reactive aryl-substituted β-keto esters such as ethyl benzoylacetate generated the desired products in only 23% and 28%, respectively, even on longer reaction times (24 h) (Table 2, entries 36 and 37).

Table 3. Synthesis of β-enamino ketones *via* condensation of β-diketones **4** with aniline **2** catalyzed by $InBr_3$.

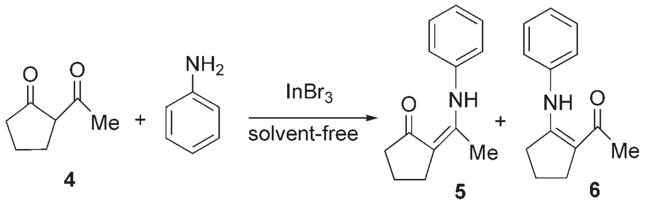


Entry	R^1	R^2	Amines	Time [min]	Yield [%][a]
1	Me	Me	$CH_3(CH_2)_3NH_2$	20	93
2	Me	Me	$(CH_3)_2CHNH_2$	90	96[b]
3	Me	Me	$H_2C{=}CHCH_2NH_2$	15	98
4	Me	Me	$H_2NCH_2CH_2NH_2$	10	93[b]
5	Me	Me	$H_2NCH_2CH_2CH_2NH_2$	12	95
6	Me	Me		10	96[b]
7	Me	Me		5 h	76[b]
8	Me	Me		10 h	72
9	Me	Me	$PhCH_2NH_2$	5	95[b]
10	Me	Me	(*R*)-$PhCHCH_3NH_2$	8	93[b]
11	Me	Me	*p*-MeO-$C_6H_4CH_2CHCH_3NH_2$	20	92
12	Me	Me	$PhNH_2$	10	94
13	Me	Me	4-Me-$C_6H_4NH_2$	10	97
14	Me	Me	2-Me-$C_6H_4NH_2$	12	95
15	Me	Me	4-MeO-$C_6H_4NH_2$	10	96
16	Me	Me	4-EtO-$C_6H_4NH_2$	18	96
17	Me	Me	2-EtO-$C_6H_4NH_2$	40	94
18	Me	Me	4-Cl-$C_6H_4NH_2$	5 h	84
19	Me	Me	3-Cl-$C_6H_4NH_2$	5 h	86
20	Me	Me	2-Br-$C_6H_4NH_2$	8 h	85
21	Me	Me	4-NO_2-$C_6H_4NH_2$	8 h	65[b]
22	Me	Ph	$PhNH_2$	50	85
23	Me	Ph	3-Me-$C_6H_4NH_2$	50	81
24	Me	Ph	4-EtO-$C_6H_4NH_2$	60	78
25	Me	Ph	2-EtO-$C_6H_4NH_2$	80	72
26	Me	Ph	2-MeO-$C_6H_4NH_2$	80	83
27	Ph	Ph	$PhCH_2NH_2$	6 h	75[b]
28	Ph	Ph	$PhNH_2$	6 h	68[b]
29	Ph	Ph	4-EtO-$C_6H_4NH_2$	6 h	72[b]
30	Ph	Ph	2-MeO-$C_6H_4NH_2$	8 h	63[b]

[a] Yields are given for isolated products.

[b] The reactions were performed at 50 °C.

As shown in Table 3, the condensation reaction between β-diketones like acetylacetone and 1-benzoylacetone and amines was explored in order to extend the present method to the synthesis of β-enamino ketones. For most of the amines tested, good yields were obtained when the reaction was carried out at room temperature. However, a long reaction time was needed when an arylamine with an electron-withdrawing group on the benzene ring was used, which is consistent with the observation for the reaction of β-keto esters. In addition, secondary amines also gave low conversion as evidenced by the fact that the reaction of acetylacetone with morpholine provided the product in 72% yield and required a long reaction time (Table 3, entry 8). In some cases, acetylacetone gave a precipitate with aliphatic amines (Table 3, entries 2, 4, 6, 9 and 10) because of the formation of a carbinolamine derivative.[38] These compounds were relatively unstable and they were dehydrated by heating to give β-enamino ketones. In the case of 1,2-diaminoethane and 1,3-diaminopropane, 2 equivs. of β-keto ester was used giving products with two enaminone groups (Table 3, entries 4 and 5). In the case of unsymmetrical β-diketones the regiochemistry is controlled by the more reactive carbonyl group, which undergoes the attack by the amine. 1-Benzoylacetone reacted with aniline to obtain exclusively a single regioisomer (Table 3, entries 22–26). Reactions involving deactivated dibenzoylmethane afforded good isolated yields, but longer reaction times and higher temperatures were required (Table 3, entries 27–30). However, in the case of 2-acetylcyclopentanone (**4**), the condensation reaction between the cyclic β-diketone and aniline under our experiment conditions occurred on both the side-chain and ring carbonyls to furnish a mixture of **5** and **6** (Scheme 2).



Scheme 2.

In order to evaluate the possibility of applying this methodology in a large-scale reaction, we carried out the reaction of equimolar amounts of acetylacetone with 4-ethoxyaniline starting from 13.7 g (100 mmol) of amine. The yield in the β-enamino ketone (94%) was almost the same as that of the small-scale (5 mmol) run.

Conclusion

In conclusion, indium tribromide was found to be a highly efficient and convenient catalyst for the preparation of β-enamino ketones and esters in good to excellent yields under solvent-free conditions. This method offers several advantages including mild reaction conditions, enhanced reaction rates, clean reaction profiles, small quantity of catalyst, operational and experimental simplicity. With increasing environmental concerns the solvent-free reaction conditions[40] make this process environmentally friendly and applicable for the large-scale synthesis of β-enamino ketones and esters.

Experimental Section

Melting points were measured using an X-4 apparatus and are uncorrected. NMR spectra were taken with a Bruker 300 spectrometer in $CDCl_3$ solution with tetramethylsilane as an internal standard. IR spectra were obtained using a Bruker-TENSOR 27 spectrometer. Mass spectra were performed on a ThermoFinnigan LCQ Advantage instrument with an ESI source (4.5 keV). Elemental analyses were carried out on an MT-3 analyzer.

General Procedure for the Preparation of β-Enamino Ketones or Esters

A mixture of the β-dicarbonyl compound (5 mmol), the amine (5 mmol) and $InBr_3$ (0.05 mmol) was stirred at room temperature for the appropriate time (Table 1). After completion of the reaction as indicated by GLC or TLC, the reaction mixture was diluted with H_2O (10 mL) and extracted with EtOAc (2 × 10 mL). The combined organic layers were dried over $MgSO_4$, concentrated, and the resulting product was purified by column chromatography on SiO_2 with EtOAc-cyclohexane (2:8) to afford pure β-enamino ketones or esters in good yields.

Most of the products are known, except for entries 8, 15, 16, 19, 25, 27, 28, 29, 31, 33, 44, 45, 46, 49 in Table 2 and entries 11, 14, 17, 24, 25, 29, 30 in Table 3. All new compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR, MS and elemental analysis.

Supporting Information Available

The details of the characterization of products and references to known compounds can be found in the Supporting Information.

Acknowledgements

The authors thank National Natural Science Foundation of China (20472032) and the State Key Laboratory of Elemento-Organic Chemistry for financial support.

References and Notes

[1] a) Z. Rappoport, *The Chemistry of Enamines*, *Part 1*; John Wiley & Sons: New York, **1994**; b) C. M. Kascheres, *J. Braz. Chem. Soc.* **2003**, *41*, 945–969.

[2] a) G. J. Reddy, D. Latha, C. Thirupathaiah, K. S. Rao, *Tetrahedron Lett.* **2005**, *46*, 301–302; b) G. Negri, C. Kascheres, A. J. Kascheres, *J. Heterocycl. Chem.* **2004**, *41*, 461–491; c) M. M. Abdelkhalik, A. M. Eltoukhy, S. M. Agamy, M. H. Elnagdi, *J. Heterocycl. Chem.* **2004**, *41*, 431–434; d) B. Al-Saleh, M. M. Abdelkhalik, A. M. Eltoukhy, M. H. Elnagdi, *J. Heterocycl. Chem.* **2002**, *39*, 1035–1038.

[3] a) A. Dondoni, D. Perrone, *Synthesis* **1993**, 1162–1176; b) H. M. C. Ferraz, E. O. Oliveira, M. E. Payret-Arrua, C. A. Brandt, *J. Org. Chem.* **1995**, *60*, 7357–7359; c) J. P. Michael, C. B. Koning, G. D. Hosken, T. V. Stanbury, *Tetrahedron* **2001**, *57*, 9635–9648; d) T. Tatee, K. Narita, S. Kurashige, S. Ito, H. Miyazaki, H. Yamanaka, M. Mizugaki, T. Sakamoto, H. Fukuda, *Chem. Pharm. Bull.* **1986**, *34,* 1643–1655.

[4] M. Azzaro, S. Geribaldi, B. Videau, *Synthesis* **1981**, 880–881.

[5] G. Dannhardt, A. Bauer, U. Nowe, *J. Prakt. Chem.* **1998**, *340*, 256–263.

[6] D. L. Boger, T. Ishizaki, J. R. J. Wysocki, S. A. Munk, P. A. Kitos, O. Suntornwat, *J. Am. Chem. Soc.* **1989**, *111*, 6461–6463.

[7] Y. F. Wang, T. Izawa, S. Kobayashi, M. Ohno, *J. Am. Chem. Soc.* **1982**, *104*, 6465–6466.

[8] a) A. Alberola, L. A. Calvo, A. G. Ortega, M. C. S. Ruiz, P. Yustos, *J. Org. Chem.* **1999**, 64, 9493–9498; b) I. Chaaban, J. V. Greenhill, P. Akhtar, *J. Chem. Soc. Perkin Trans. 1* **1979**, 1593–1596; c) R. Augusti, C. Kascheres, *J. Org. Chem.* **1993**, *58*, 7079–7083; d) A. Müller, A. Maier, R. Neumann, G. Maas, *Eur. J. Org. Chem.* **1998**, 1177–1187; e) E. Bejan, H. Aït-Haddou, J. C. Daran, G. G. A. Balavoine, *Eur. J. Org. Chem.* **1998**, 2907–2912; f) M. N. Eberlin, C. Kascheres, *J. Org. Chem.* **1988**, *53*, 2084–2086; g) F. Al-Omran, A. A. El-Khair, *J. Heterocycl. Chem.* **2005**, *45*, 307–312.

[9] a) S. A. Popov, Y. V. Gatilov, T. V. Rybalova, A. V. Tkachev, *Tetrahedron: Asymmetry* **2003**, *14*, 233–238; b) S. A. Popov, A. V. Tkachev, *Synth. Commun.* **2001**, *31*, 233–243; c) S. A. Popov, A. V. Tkachev, *Tetrahedron: Asymmetry* **1995**, *6*, 1013–1018.

[10] a) W. D. Lubell, M. Kitamura, R. Noyori, *Tetrahedron: Asymmetry* **1991**, *2*, 543–554; b) G. Bartoli, C. Cimarelli, E. Marcantoni, G. Palmieri, M. Petrini, *J. Org. Chem.* **1994**, *59*, 5328–5335; c) C. Cimarelli, G. Palmieri, G. Bartoli, *Tetrahedron: Asymmetry* **1994**, *5*, 1455–1458; d) C. Cimarelli, G. Palmieri, *J. Org. Chem.* **1996**, *61*, 5557–5563.

[11] a) P. Lue, J. V. Greenhill, in: *Advances in Heterocyclic Chemistry*, vol. 67, (Eds.: A. R. Katritzky), Academic Press, New York, **1997**, pp. 207–343; b) J. V. Greenhill, *Chem. Soc. Rev.* **1977**, *6*, 277–294; c) A.-Z. A. Elassar, A. A. El-Khair, *Tetrahedron* **2003**, *59*, 8463–8480; d) J. P. Michael, C. B. De Koning, D. Gravestock, G. D. Hosken, A. S. Howard, C. M. Jungmann, R. W. M. Krause, A. S. Parsons, S. C. Pelly, T. V. Stanbury, *Pure Appl. Chem.* **1999**, *71*, 979–988; e) H. M. C. Ferraz, F. L. C. Pereira, *Quimica Nova* **2004**, *27*, 89–95.

[12] a) S. M. Hannick, Y. Kishi, *J. Org. Chem.* **1983**, *48*, 3833–3835; b) A. S.-Y. Lee, R.-Y. Cheng, *Tetrahedron Lett.* **1997**, *38*, 443–446; c) T. G. C. Bird, A. Olivier, *Bioorg. Med. Chem. Lett.* **1996**, *6*, 515–520.

[13] a) T. Fukuyama, Y. M. Yung, *Tetrahedron Lett.* **1981**, *22*, 3759–3760; b) N. Jiang, Z. Qu, J. Wang, *Org. Lett.* **2001**, *3*, 2989–2992.

[14] a) K. Uneyama, O. Morimoto, F. Yamashita, *Tetrahedron Lett.* **1989**, *30*, 4821–4824; b) S. Fustero, B. Pina, A. Simón Fuentes, *Tetrahedron Lett.* **1997**, *38*, 6771–6774; c) S. Fustero, B. Pina, E. Salavert, A. Navarro, C. Ramírez de Arellano, A. Simón, *J. Org. Chem.* **2002**, *67*, 4667–4679; d) S. Fustero, B. Pina, M. García de la Torre, Navarro, C. Ramirez de Arellano, A. Simón, *Org. Lett.* **1999**, *1*, 977–980.

[15] a) G. Bartoli, C. Cimarelli, R. Dalpozzo, G. Palmieri, *Tetrahedron* **1995**, *51*, 8613–8622; b) A. R. Katritzky, Y. Fang, A. Donkor, J. Xu, *Synthesis* **2000**, 2029–2032.

[16] S. Fustero, M. García de la Torre, V. Jofrè, R. Pérez Carlon, A. Navarro, A. Simón Fuentes, *J. Org. Chem.* **1998**, *63*, 8825–8836.

[17] G. Cimarelli, G. Palmieri, E. Volpini, *Tetrahedron Lett.* **2004**, *45*, 6629–6631.

[18] a) P. G. Baraldi, D. Simoni, S. Manfredini, *Synthesis* **1983**, 902–903; b) T. Potešil, *J. Chromatogr.* **1984**, *312*, 387–393; c) E. J. Cone, R. H. Garner, A. W. Hayes, *J. Org. Chem.* **1972**, #37#*26*, 4436–4439.

[19] a) A. A. H. Saeed, *J. Chem. Eng. Data* **1984**, *29*, 358–361; b) C. R. Hauser, G. A. Reynolds, *J. Am. Chem. Soc.* **1948**, *70*, 2402–2404; c) S. Coffey, J. K. Thomson, F. J. Wilson, *J. Chem. Soc.* **1936**, 856–859.

[20] D. F. Martin, G. A. Janusonis, B. B. Martin, *J. Am. Chem. Soc.* **1961**, *83*, 73–75.

[21] a) P. W. Hickmott, G. Sheppard, *J. Chem. Soc. Perkin Trans. 1* **1972**, 1038–1041; b) H. Bieräugel, J. M. Akkerman, J. C. Lapierre Armande, U. K. Pandit, *Recl. Trav. Chim. Pays-Bas* **1976**, *95*, 266–269; c) D. Gravel, M. Labelle, *Can. J. Chem.* **1985**, *63*, 1874–1882; d) A. D. Yapi, M. Mustofa, A. Valentin, O. Chavignon, J.-C. Teulade, M. Mallie, J.-P. Chapat, Y. Blache, *Chem. Pharm. Bull.* **2000**, *48*, 1886–1889.

[22] a) V. H. Naringrekar, V. J. Stella, *J. Pharm. Sci.* **1990**, *79*, 138–146; b) R. J. Brown, F. W. S. Carver, B. L. Hollingsworth, *J. Org. Chem.* **1967**, *32*, 2624–2626; c) C. A. Brandt, A. C. M. P. Da Silva, C. G. Pancote, C. L. Brito, M. A. B. Da Silveira, *Synthesis* **2004**, 1557–1559.

[23] C. P. Cartaya-Marin, D. G. Henderson, R. W. Soeder, *Synth. Commun.* **1997**, *27*, 4275–4283.

[24] a) B. Rechsteimer, F. Texier-Boullet, J. Hamelin, *Tetrahedron Lett.* **1993**, *34*, 5071–5074; b) H. T. S. Braibante, M. E. F. Braibante, G. B. Rosso, D. A. Oriques, *J. Braz. Chem. Soc.* **2003**, *14*, 994–997.

[25] C. J. Valduga, A. Squizani, H. S. Braibante, M. E. F. Braibante, *Synthesis* **1998**, 1019–1022.

[26] B. Stefane, S. Polanc, *Synlett* **2004**, 698–702.

[27] F. Texier-Bouliet, *Synthesis* **1985**, 679–681.

[28] Y.-H. Gao, Q.-H. Zhang, J.-X. Xu, *Synth. Commun.* **2004**, *34*, 909–916.

[29] G. Bartoli, M. Bosco, M. Locatelli, E. Marcantoni, P. Melchiorre, L. Sambri, *Synlett* **2004**, 239–242.

[30] M. M. Khodaei, A. R. Khosropour, M. Kookhazadeh, *Synlett* **2004**, 1980–1984.

[31] A. Arcadi, G. Bianchi, S. Di Giuseppe, F. Marinelli, *Green Chem.* **2003**, *5*, 64–67.

[32] F. C. Silva, M. C. B. V. De Souza, V. F. Ferreira, S. J. Sabino, O. A. C. Antunes, *Catal. Commun.* **2004**, *5*, 151–155.

[33] H. A. Stefani, I. M. Costa, D. De O. Silva, *Synthesis* **2000**, 1526–1528.

[34] A. R. Khosropour, M. M. Khodaei, M. Kookhazadeh, *Tetrahedron Lett.* **2004**, *45*, 1725–1728.

[35] M. M. Khodaei, A. R. Khosropour, M. Kookhazadeh, *Can. J. Chem.* **2005**, *83*, 209–212.

[36] Z.-H. Zhang, *Synlett* **2005**, 711–712.

[37] a) L. Yin, Z.-H. Zhang, Y.-M. Wang, M.-L. Pang, *Synlett* **2004**, 1727–1730; b) Z.-H. Zhang, L. Yin, Y.-M. Wang, J.-Y. Liu, Y. Li, *Green Chem.* **2004**, *6*, 563–565; c) Z.-H. Zhang, L. Yin, Y. Li, Y.-M. Wang, *Tetrahedron Lett.* **2005**, *46*, 889–893; d) Z.-H. Zhang, L. Yin, Y.-M. Wang, *Synthesis* **2005**, 1949–1954.

[38] F. C. Pennington, W. D. Kehret, *J. Org. Chem.* **1967**, *32*, 2034–2036.

[39] C. Kashima, H. Aoyama, Y. Yamamoto, T. Nishi, K. Yamada, *J. Chem. Soc. Perkin Trans. 2* **1975**, 665–670.

[40] J. M. Desimone, *Science* **2002**, *297*, 799–803.