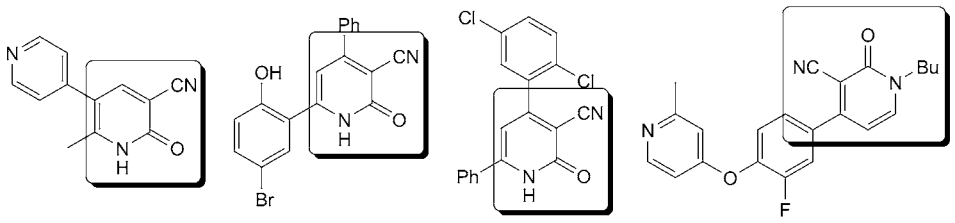
First Synthesis of Ferrocenyl-Substituted 1,2-Dihydro-2-oxopyridine-3-carbonitriles

by **Hong Zhang**, **Yang Li**, and **Wentao Gao***

Institute of Superfine Chemicals, Bohai University, Jinzhou 121000, P. R. China
(phone/fax: +86-416-3400266; e-mail: bhuzh@163.com)

In the present investigation, the first incorporation of both ferrocene scaffold and 1,2-dihydro-2-oxopyridine-3-carbonitrile pharmacophore leading to a series of structurally novel ferrocene-based hybrids has been achieved, involving the condensation reaction of ferrocenyl substituted chalcones with 2-cyanoacetamide in a freshly prepared EtONa solution at 70°. The molecular structures of these newly synthesized products were confirmed by IR, and ^{1}H- and ^{13}C-NMR analyses.

Introduction. – Molecules containing the 2-oxopyridine-3-carbonitrile moiety have received considerable interest from the medicinal community due to their potent biological properties, particularly anticancer, antimicrobial, antidepressant, and cardiotonic activities [1–4]. Among the successful examples as drug candidates possessing the 1,2-dihydro-2-oxopyridine-3-carbonitrile nucleus are milrinone (**1**), which has been introduced to the clinic for the treatment of congestive heart failure [5]. The recently reported oncogenic serine/threonine kinase PIM-1 inhibitor **2** and survivin inhibitor **3** also contain this carbonitrile [6][7]. Compound **4** with this ring system was also reported to display robust *in vivo* activity in a sleep–wake electroencephalogram (sw-EEG) [8].



1 **2** **3** **4**

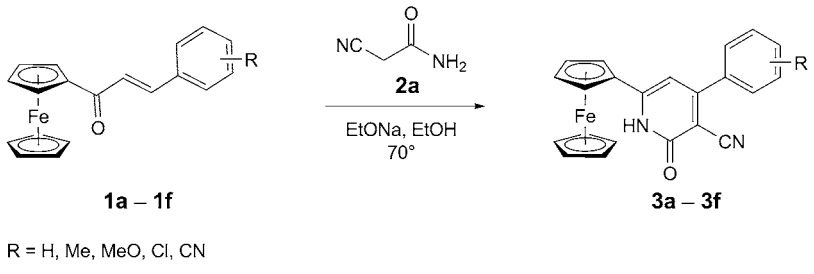
These examples emphasize the importance of 1,2-dihydro-2-oxopyridine-3-carbonitrile as key pharmacophores in bioactive small molecules. Apart from these, 2-oxopyridine-3-carbonitrile derivatives also serve as important intermediates in the synthesis of many biologically active compounds such as pyridone-containing farnesyltransferase inhibitors [9]. Not surprisingly, the mentioned framework has been an attractive synthetic target, and strategies for accessing new scaffolds of 2-oxopyridine-3-carbonitrile are of great interest to synthetic chemists [10–13].

On the other hand, it is well-established that the interchange of an aromatic or heterocyclic ring with the ferrocene nucleus in some organic compounds possessing a certain property (*e.g.*, biological activity) might lead to products with enhanced or unexpected chemical and pharmacological properties compared to that of the parent compound. This fact could be rationalized as being due to the unique properties of the ferrocene nucleus such as membrane permeation, aqueous stability, anomalous metabolism, and redox behavior [14–16]. The incorporation of the ferrocene unit into a heterocyclic molecule according to classical methods of organic chemistry has been recognized as an attractive way to endow a novel molecule functionally [17][18]. For example, *Zhao* and *Liu* demonstrated that the modification of ailanthoidol by a ferrocenyl group enhanced its ability to quench radicals and to protect DNA against radical-induced oxidation [19]. Thus, introduction of the ferrocene unit into bioactive heterocyclic skeletons would be a challenge for medicinal applications. Therefore, it is of high interest to synthesize ferrocene–heterocycle hybrids to expand the structure diversity for current medicinal chemistry needs.

Considering the above mentioned findings, we conceived that the incorporation of the ferrocene scaffold into the 2-oxopyridine-3-carbonitrile pharmacophore, leading to a series of structurally novel compounds as possible drug-like candidates, would be of synthetic importance. A literature survey revealed that there are a number of reports for the synthesis of 1,2-dihydro-2-oxopyridine-3-carbonitrile derivatives, and considerable attention has been focused on the synthesis of aryl or hetaryl substituted 2-oxopyridine-3-carbonitrile. Although the importance of both 2-oxopyridine-3-carbonitrile and ferrocene core compounds is undisputed, surprisingly, the synthesis of ferrocenyl-substituted 2-oxopyridine-3-carbonitrile has not been achieved so far. Thus, in continuation of our efforts to synthesize highly interesting types of heterocycles [20–23], herein report the synthesis of a system, which combines these two important components *via* the condensation of a ferrocenyl substituted chalcone with 2-cyanoacetamide.

Results and Discussion. – The synthetic sequence employed in our laboratories for preparation of 6-ferrocenyl-1,2-dihydro-2-oxo-4-phenylpyridine-3-carbonitriles, **3a**–**3f**, is outlined in *Scheme 1*. The starting compounds, ferrocenyl chalcones, were prepared as previously described in [24][25].

Scheme 1



The condensation of a chalcone or enone with 2-cyanoacetamide for the synthesis of 1,2-dihydro-2-oxopyridine-3-carbonitrile derivatives is a well-known reaction. Prior to the current investigation, a number of examples involving this reaction have been reported [26–32]. For example, it has been reported that the condensation reaction of chalcones with 2-cyanoacetamide using a catalytic amount of piperidine in EtOH [27] or BuOH [29] yielded the 1,2-dihydro-2-oxopyridine-3-carbonitrile. However, in our attempts to follow the method, we did not observe any trace of the expected product, but only undefined mixtures. Further investigation towards the cyclocondensation reaction was conducted according to reported methods using DMSO/^{t}BuOK system under an O_2 atmosphere [28][31]. Unfortunately, the attempts in our case were also unfruitful, and no promising result was obtained even after refluxing for a prolonged period (24 h). Recently, *Ji* and co-workers described the synthesis of ferrocenyl substituted pyridine-3-carbonitriles *via* the condensation of ferrocenyl substituted chalcones with malononitrile [33]. On this basis, we presumed that this approach can be extended for our synthesis. Thus, we first investigated the reaction of ferrocenylchalcone **1a** with 1.1 equiv. of 2-cyanoacetamide (**2a**) using EtONa/EtOH at 50°, but this led to a modest yield of 31% of **3a**. Interestingly, a further increase of the reaction temperature led to a significant increase in the yield of **3a**, reaching 62% at a temperature of 70°. However, at temperatures $>70°$, by-products were formed as observed on TLC, which reduced the yield of the desired products. After complete formation of the product as monitored by TLC, H_2O was added, the mixture was acidified with 10% AcOH, and the precipitate, which separated on standing, was collected. Recrystallization from EtOH gave the product in 62% yield. In addition, in our case, the use of microwave irradiation did not further improve the yield, in contrast to the literature results. To retain the simplicity of the procedure, no further changes in reaction conditions were tested and the above mentioned condition was chosen for the following work.

To further investigate the viability of the transformation, the reaction was tested with other substituted ferrocenylchalcones **1b**–**1f** in a similar fashion. This reaction invariably led to the formation of the corresponding 6-ferrocenyl-1,2-dihydro-2-oxopyridine-3-carbonitriles **3b**–**3f** in acceptable yields, and the results of this series of experiments are compiled in the *Table*.

Table. *Cyclocondensation Reaction of Ferrocenylchalcones with 2-Cyanoacetamide*

Entry	**3a**–**3f**	R	Time [h]	Yield [%][a])
1	**3a**	H	5	62
2	**3b**	4-Me	8	59
3	**3c**	4-MeO	8	61
4	**3d**	4-Cl	4	67
5	**3e**	4-CN	4	70
6	**3f**	2,6-Cl_2	4	65

[a]) Yields of the isolated products.

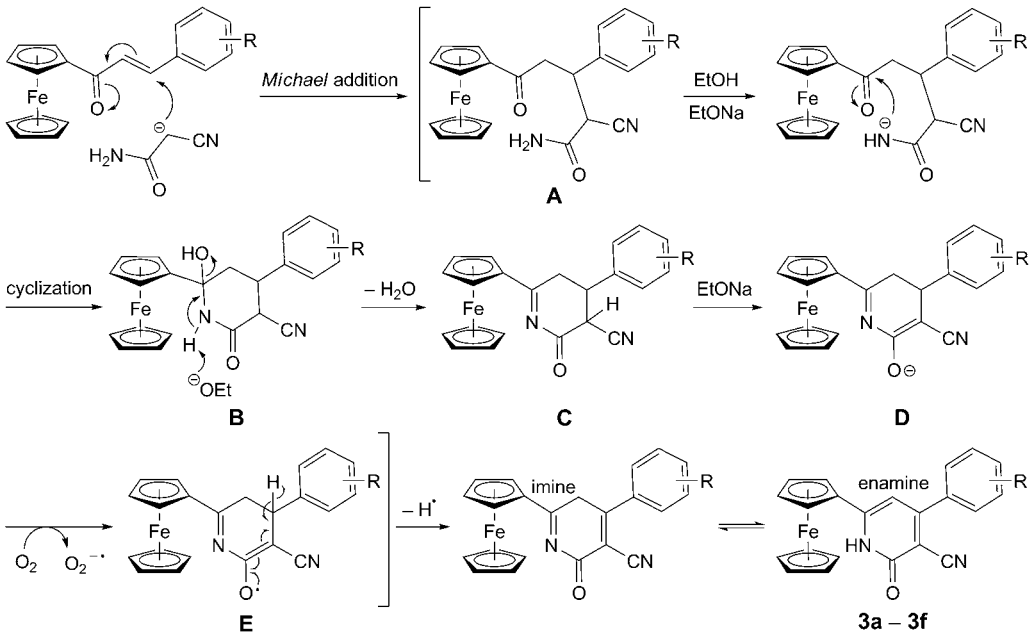
Both electron-donating (Me and MeO) and electron-withdrawing (Cl and CN) substituents of **1b**–**1f** were all well-tolerated when reacting with **2a**, providing the

corresponding **3b**–**3f** in acceptable yields. But it is noteworthy that **1b** and **1c** with electron-donating substituents required slightly longer reaction times for complete conversion (*Entries 2* and *3*).

To the best of our knowledge, ferrocene substitution at C(6) of 1,2-dihydro-2-oxopyridine-3-carbonitrile has not previously been reported. The structures of the compounds **3a**–**3f** were confirmed *via* spectroscopic methods and elemental analyses, with the results being in good agreement with the expected compounds. For instance, the IR spectrum of compound **3b** clearly exhibited the absorption bands characteristic of the 2-oxopyridine C=O group at 1629 cm^{-1}, of the CN group at 2216 cm^{-1}, and of the NH group at 3455 cm^{-1}. The main features of its ^{1}H-NMR spectrum were the presence of the signals corresponding to H–C(5) and NH of the 2-oxopyridine ring at 6.49 and 13.18 ppm, respectively, which is consistent with the assigned structure of **3b**. In the ^{1}H-decoupled ^{13}C-NMR spectrum, the signal for the C=O group appeared at 164.28 ppm, while the CN signal was detected at 116.65 ppm. All these observations are consistent with the chemical shifts of similar types of 2-oxopyridine-3-carbonitrile [13][27][31], and thus, clearly indicated the formation of the desired product. Finally, the obtained elemental analysis values are also in agreement with calculated data.

On the basis of these experiments, a mechanistic proposal portraying the probable sequence of events for the formation of the title compounds is outlined in *Scheme 2*. Condensation of the two fragments involves in the first step the formation of the *Michael* adduct **A**, which undergoes subsequent intramolecular nucleophilic cyclization with participation of the amide N-atom and the chalcone C=O group to form the

Scheme 2



dihydro-2-oxopyridine-3-carbonitrile **C** *via* **B** by elimination of H_2O. Subsequently, the species would be converted to an anion of the type **D** in the presence of excess EtONa, which, in the presence of an oxidant such as O_2, is further converted to radical anion **E** *via* single-electron transfer [31][34]. Finally, aromatization of **E** by loss of an H-atom results in the formation of product **3**.

^{1}H-NMR Spectroscopy was used to monitor the reaction. However, neither the *Michael* adduct **A** nor the cyclized intermediate **C** was detected. The result indicated that the generated intermediate **A** was highly reactive and underwent spontaneous cyclization with the subsequent dehydration and aromatization to provide the final 1,2-dihydro-2-oxopyridine-3-carbonitrile. It is worthy to mention that *Carles et al.* [34] observed that the condensation of an enone with 2-cyanoacetamide derivatives in the presence of ^{t}BuOK yielded 'descyano pyridine-2-ones' in the absence of an O_2 atmosphere *via* 'decyanidative aromatization'. However, under our reaction conditions, the transformation leading to 'descyano pyridin-2ones' was not observed, probably because the O_2 concentration in solution was sufficient to promote rapid oxidation of **C**. An example that is particularly relevant to the present discussion is described in [29], where 1,2-dihydro-2-oxopyridine-3-carbonitrile derivatives could also be obtained in refluxing BuOH in the absence of O_2.

Conclusions. – We have described a facile synthesis of a new series of ferrocenyl-substituted 1,2-dihydro-2-oxopyridine-3-carbonitrile derivatives. In view of the synergism of both the ferrocene ring system and pyridine-3-carbonitrile moiety in a single molecule, the newly synthesized compounds would likely possess significant biological activities and could be employed in the developement of lead compounds. The biological activities of the synthesized compounds are under investigation. Additionally, it should be emphasized that these compounds belong to a new class of 1,2-dihydro-2-oxopyridine-3-carbonitrile systems, and thus, a further investigation of the synthetic potential of these scaffolds should provide access to significant chemical diversity *via* further derivatization reactions.

Experimental Part

General. M.p.: *WRS-1B* melting-point apparatus; uncorrected. IR Spectra: *Shimadzu FT-IR-8400S* (*Shimadzu*, Japan) spectrophotometer; KBr pellets; $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR spectra: *Bruker Avance* spectrometer, at 400 and 100 Mhz, resp., with $CDCl_3$ or (D_6)DMSO as solvent; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. Elemental analyses: *EL-III* element analyzer.

General Procedure for the Preparation of 4-Aryl-6-ferrocenyl-1,2-dihydro-2-oxopyridine-3-carbonitriles **3a**–**3f**. A mixture of one of the selected ferrocenyl chalcones **1a**–**1f** (1.0 mmol) [24][25] and 2-cyanoacetamide (**2a**; 92.4 mg, 1.1 mmol) in 8 ml of a freshly prepared EtONa (68.0 mg, 1 mmol) soln. in EtOH was stirred at 70°. After the completion of the reaction (TLC), the mixture was acidified with 10% AcOH, and the resulting solid, which precipitated on standing, was collected. Recrystallization from EtOH gave the corresponding product (59–70% yields).

6-Ferrocenyl-1,2-dihydro-2-oxo-4-phenylpyridine-3-carbonitrile (**3a**). Yield: 235 mg (62%). Purple needles. M.p. 246–248°. IR (KBr): 3449 (NH), 3103, 2217 (CN), 1633 (C=O), 1588, 1535, 1491, 1444, 1378. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.30 (*s*, 5 H, ferrocenyl (Fc)); 4.67 (*s*, 2 H, Fc); 5.11 (*s*, 2 H, Fc); 6.48 (*s*, C_5NH); 7.55–7.58 (*m*, 3 H, Ph); 7.69–7.71 (*m*, 2 arom. H); 12.50 (*s*, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): 67.0; 68.0; 70.3; 70.9; 95.5; 102.8; 113.9; 127.2; 129.2; 129.7; 138.6; 147.9; 153.9; 165.2. Anal. calc. for $C_{22}H_{16}FeN_2O$ (380.22): C 69.50, H 4.24, N 7.37; found: C 65.62, H 4.13, N 7.56.

6-Ferrocenyl-1,2-dihydro-4-(4-methylphenyl)-2-oxopyridine-3-carbonitrile (**3b**). Yield: 232 mg (59%). Purple needles. M.p. 256–258°. IR (KBr): 3455 (NH), 3101, 2916, 2848, 2216 (CN), 1629 (C=O), 1590, 1528, 1487, 1447, 1381. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.44 (*s*, Me); 4.27 (*s*, 5 H, Fc); 4.64 (*s*, 2 H, Fc); 5.17 (*s*, 2 H, Fc); 6.49 (*s*, C_5NH); 7.42 (*d*, J = 8.4, 2 arom. H); 7.61 (*d*, J = 8.4, 2 arom. H); 13.18 (*s*, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): 21.5; 29.7; 68.0; 70.7; 72.4; 74.5; 92.7; 104.7; 116.7; 128.0; 129.6; 131.5; 140.9; 154.5; 160.1; 164.3. Anal. calc. for $C_{23}H_{18}FeN_2O$ (394.25): C 70.07, H 4.60, N 7.11; found: C 69.84, H 4.42, N 7.27.

6-Ferrocenyl-1,2-dihydro-4-(4-methoxyphenyl)-2-oxopyridine-3-carbonitrile (**3c**). Yield: 250 mg (61%). Purple needles. M.p. 240–241°. IR (KBr): 3440 (NH), 3104, 2918, 2850, 2217 (CN), 1632 (C=O), 1598, 1528, 1489, 1447, 1386. ^{1}H-NMR (400 MHz, (D_6)DMSO): 3.86 (*s*, MeO); 4.21 (*s*, 5 H, Fc); 4.62 (*s*, 2 H, Fc); 5.30 (*s*, 2 H, Fc); 6.65 (*s*, C_5NH); 7.13 (*d*, J = 8.4, 2 arom. H); 7.69 (*d*, J = 8.4, 2 arom. H); 12.21 (*s*, NH). ^{13}C-NMR (100 MHz, (D_6)DMSO): 55.9; 68.4; 70.7; 72.2; 75.1; 95.5; 103.7; 114.5; 118.0; 128.7; 130.3; 154.3; 159.1; 161.4; 162.5. Anal. calc. for $C_{23}H_{18}FeN_2O_2$ (410.25): C 67.34, H 4.42, N 6.83; found: C 67.14, H 4.29, N 6.67.

4-(4-Chlorophenyl)-6-ferrocenyl-1,2-dihydro-2-oxopyridine-3-carbonitrile (**3d**). Yield: 277 mg (67%). Purple needles. M.p. 262–264°. IR (KBr): 3459 (NH), 3105, 2213 (CN), 1629 (C=O), 1595, 1527, 1487, 1445, 1422, 1383. ^{1}H-NMR (400 MHz, (D_6)DMSO): 4.22 (*s*, 5 H, Fc); 4.64 (*s*, 2 H, Fc); 5.31 (*s*, 2 H, Fc); 6.48 (*s*, C_5NH); 7.66 (*d*, J = 8.4, 2 arom. H); 7.71 (*d*, J = 8.4, 2 arom. H); 12.36 (*s*, NH). ^{13}C-NMR (100 MHz, (D_6)DMSO): 68.4; 70.7; 72.5; 74.3; 96.2; 103.7; 117.5; 129.1; 129.2; 130.6; 132.3; 135.5; 158.4; 162.3. Anal. calc. for $C_{22}H_{15}ClFeN_2O$ (414.67): C 63.72, H 3.65, N 6.76; found: C 63.81, H 3.50, N 6.62.

4-(4-Cyanophenyl)-6-ferrocenyl-1,2-dihydro-2-oxopyridine-3-carbonitrile (**3e**). Yield: 283 mg (70%). Orange needlels. M.p. 243–245°. IR (KBr): 3436 (NH), 3101, 2212 (CN), 2220 (CN), 1622 (C=O), 1589, 1516, 1483, 1443, 1417, 1379. ^{1}H-NMR (400 MHz, (D_6)DMSO): 4.17 (*s*, 5 H, Fc); 4.48 (*s*, 2 H, Fc); 5.15 (*s*, 2 H, Fc); 6.41 (*s*, C_5NH); 7.75 (*d*, J = 8.8, 2 arom. H); 7.98 (*d*, J = 8.8, 2 arom. H); 11.74 (*s*, NH). ^{13}C-NMR (100 MHz, (D_6)DMSO): 67.4; 68.1; 70.3; 70.9; 111.6; 119.1; 128.3; 129.8; 132.6; 133.2; 143.6; 152.6; 162.8; 163.7. Anal. calc. for $C_{23}H_{15}FeN_3O$ (405.23): C 68.17, H 3.73, N 10.37; found: C 68.39, H 3.55, N 10.20.

4-(2,6-Dichlorophenyl)-6-ferrocenyl-1,2-dihydro-2-oxopyridine-3-carbonitrile (**3f**). Yield: 292 mg (65%). Purple needles. M.p. 249–251°. IR (KBr): 3457 (NH), 3102, 2221 (CN), 1640 (C=O), 1597, 1532, 1489, 1459, 1429, 1382. ^{1}H-NMR (400 MHz, (D_6)DMSO): 4.19 (*s*, 5 H, Fc); 4.66 (*s*, 2 H, Fc); 5.35 (*s*, 2 H, Fc); 6.72 (*s*, C_5NH); 7.58 (*d*, J = 8.4, 2 arom. H); 7.71 (*t*, J = 8.4, 1 arom. H); 12.57 (*s*, NH). ^{13}C-NMR (100 MHz, (D_6)DMSO): 68.7; 70.9; 72.9; 74.1; 97.7; 104.3; 116.1; 129.1; 132.3; 132.7; 155.5; 156.8; 161.8. Anal. calc. for $C_{22}H_{14}Cl_2FeN_2O$ (449.11): C 58.84, H 3.14, N 6.24; found: C 58.97, H 3.32, N 6.10.

We would like to acknowledge the financial support from the *Natural Science Foundation of Liaoning Province* (Grant No. 201202001).

REFERENCES

[1] P. Thompson, V. C. Manganiello, E. Degerman, *Curr. Topic Med. Chem.* **2007**, *7*, 421.
[2] A. H. Abadi, D. A. Abouel-Ella, J. Lehmann, H. N. Tinsley, B. D. Gary, G. A. Piazza, M. A. O. Abdel-Fattah, *Eur. J. Med. Chem.* **2010**, *45*, 90.
[3] A. H. Abadi, T. M. Ibrahim, K. M. Abouzid, J. Lehmann, H. N. Tinsley, B. D. Gary, G. A. Piazza, *Bioorg. Med. Chem.* **2009**, *17*, 5974.
[4] M. Panunzio, M. A. Lentini, E. Campana, G. Martelli, E. Tamanini, P. Vicennati, *Synth. Commun.* **2004**, *34*, 345.
[5] G. Pastelin, R. Mendez, E. Kabela, A. Farah, *Life Sci.* **1983**, *33*, 1787.
[6] I. W. Cheney, S. Yan, T. Appleby, H. Walker, T. Vo, N. Yao, R. Hamatake, Z. Hong, J. Z. Wu, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1679.
[7] M. D. Wendt, C. Sun, A. Kunzer, D. Sauer, K. Sarris, E. Hoff, L. Yu, D. G. Nettesheim, J. Chen, S. Jin, K. M. Comess, Y. Fan, S. N. Anderson, B. Isaac, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 3122.

[8] J. M. Cid, G. Duvey, G. Tresadern, V. Nhem, R. Furnari, P. Cluzeau, J. A. Vega, A. I. de Lucas, E. Matesanz, J. M. Alonso, M. L. Linares, J. I. Andrés, S. M. Poli, R. Lutjens, H. Himogai, J. P. Rocher, G. J. Macdonald, D. Oehlrich, H. Lavreysen, A. Ahnaou, W. Drinkenburg, C. Mackie, A. A. Trabanco, *J. Med. Chem.* **2012**, *55*, 2388.
[9] L. A. Hasvold, W. Wang, S. L. Gwaltney, T. W. Rockway, L. T. J. Nelson, R. A. Mantei, S. A. Fakhoury, G. M. Sullivan, Q. Li, N. H. Lin, L. Wang, H. Zhang, J. Cohen, W. Z. Gu, K. Marsh, J. Bauch, S. Rosenberg, H. L. Sham, *Bioorg. Med. Chem. Lett.* **2003**, *13*, 4001.
[10] L. Öhberg, J. Westman, *Synlett* **2001**, 1296.
[11] K. Pradhan, P. Bhattacharyya, S. Paul, A. R. Das, *Tetrahedron Lett.* **2012**, *53*, 5840.
[12] A. M. Serry, S. Luik, S. Laufer, A. H. Abadi, *J. Comb. Chem.* **2010**, *12*, 559.
[13] S. S. Bisht, N. Jaiswal, A. Sharma, S. Fatima, R. Sharma, N. Rahuja, A. K. Srivastava, V. Bajpai, B. Kumar, R. P. Tripathi, *Carbohydr. Res.* **2011**, *346*, 1191.
[14] R. P. Hanzlik, P. Soine, W. H. Soine, *J. Med. Chem.* **1979**, *22*, 424.
[15] G. Tabbì, C. Cassino, G. Cavigiolio, D. Colangelo, A. Ghiglia, I. Viano, D. Osella, *J. Med. Chem.* **2002**, *45*, 5786.
[16] A. Pejovic, I. Damljanovic, D. Stevanovic, M. Vukicevic, S. B. Novakovic, G. A. Bogdanovic, N. Radulovic, R. D. Vukicevic, *Polyhedron* **2012**, *31*, 789.
[17] J. Quirante, F. Dubar, A. González, C. Lopez, M. Cascante, R. Cortés, I. Forfar, B. Pradines, C. Biot, *J. Organomet. Chem.* **2011**, *696*, 1011.
[18] Y.-S. Xie, X.-H. Pan, B.-X. Zhao, J.-T. Liu, D.-S. Shin, J.-H. Zhang, L.-W. Zheng, J. Zhao, J.-Y. Miao, *J. Organomet. Chem.* **2008**, *693*, 1367.
[19] C. Zhao, Z.-Q. Liu, *Biochimie* **2012**, *94*, 1805.
[20] W.-T. Gao, Y. Yan, Y. Li, *Chem. Pap.* **2012**, *66*, 691.
[21] W.-T. Gao, X.-P. Cheng, Y. Li, *Heterocycles* **2010**, *81*, 1923.
[22] W.-T. Gao, X.-P. Cheng, Y. Li, *Chin. J. Org. Chem.* **2010**, *30*, 456.
[23] Y. Li, W.-T. Gao, *Beilstein J. Org. Chem.* **2010**, *6*, 966.
[24] C. R. Hauser, J. K. Lindsay, *J. Org. Chem.* **1957**, *22*, 482.
[25] S.-J. Ji, Z.-L. Shen, S.-Y. Wang, *Chin. Chem. Lett.* **2003**, *14*, 663.
[26] J. L. Soto, C. Seoane, A. M. Mansilla, *Org. Prep. Proc. Int.* **1981**, *13*, 331.
[27] C. N. O'Callaghan, T. B. H. McMurry, C. J. Cardin, D. J. Wilcock, *J. Chem. Soc., Perkin Tans. 1* **1993**, 2479.
[28] R. Jain, F. Roschangar; M. A.Ciufolini, *Tetrahedron Lett.* **1995**, *36*, 3307.
[29] H. I. El-Subbagh, S. M. Abu-Zaid, M. A. Mahran, F. A. Badria, A. M. Al-Obaid, *J. Med. Chem.* **2000**, *43*, 2915.
[30] C. G. Dave, D. A. Shah, Y. K. Agrawal, *Indian J. Chem., Sect. B* **2004**, *43*, 885.
[31] M. Nitta, T. Sakakida, H. Miyabara, H.Yamamoto, S. Naya, *Org. Biomol. Chem.* **2005**, *3*, 638.
[32] S. S. Chavan, M. S. Degani, *Catal. Lett.* **2011**, *141*, 1693.
[33] W.-J. Zhou, S.-J. Ji, Z.-L. Shen, *J. Organomet. Chem.* **2006**, *691*, 1356.
[34] L. Carles, K. Narkunan, S. Penlou, L. Rousset, D. Bouchu, M. A. Ciufolini, *J. Org. Chem.* **2002**, *67*, 4304.

Received January 10, 2013