SYNTHETIC COMMUNICATIONS®
Vol. 34, No. 15, pp. 2813–2821, 2004

N-Acyliminium Reagents of 3,4-Dihydro-β-carboline and Acyl Chlorides in the Reaction of Intermolecular α-Amidoalkylation Toward Heteroaromatics[#]

Atanaska K. Donova,[*] Stela M. Statkova-Abeghe, Atanas P. Venkov, and Iliyan I. Ivanov

Department of Organic Chemistry, University of Plovdiv, Plovdiv, Bulgaria

ABSTRACT

N-Acyliminium reagents formed from 3,4-dihydro-β-carboline and acyl chlorides were used for amidoalkylation of indole, pyrrole, and thiophene.

Key Words: *N*-Acyliminium reagents; β-Carbolines; α-Amidoalkylation reaction; Heteroaromatics; Alkaloids.

[#]This paper is dedicated to the memory of Professor Atanas Venkov.

[*]Correspondence: Atanaska K. Donova, Department of Organic Chemistry, University of Plovdiv, 24 Tsar Asen St., 4000 , Plovdiv, Bulgaria; E-mail: donova@argon.acad.bg.

DOI: 10.1081/SCC-200026238 0039-7911 (Print); 1532-2432 (Online)

INTRODUCTION

The chemistry of β-carbolines is currently of great interest due to their biological activity.[1] Besides the classical methods, the Pictet–Spengler and the Bischler–Napieralski reactions, some new synthetic routes to α-substituted β-carbolines have been developed.[2] In the last several years, *Eudistoma* alkaloids and the bengacarboline from marine organisms are objects of extensive research because of their antitumor, antiviral, and antibacterial properties.[3]

Recently, we have reported the utilization of 3,4-dihydroisoquinoline for preparation of 1-heteroaryl-2-acyl-1,2,3,4-tetrahydroisoquinolines via intermolecular α-amidoalkylation.[4] In this paper, we continue our research with another cyclic imine—3,4-dihydro-β-carboline **1**. The obtained *N*-acyliminium reagents **3** are successfully used in a reaction of intermolecular α-amidoalkylation toward heteroaromatic compounds.

There are a number of publications regarding the synthetic applications of *N*-acyliminium reagents, obtained from acid chlorides and various N-heterocycles like pyridine, quinoline, isoquinoline, and acridine.[5] So far, however, there are no reports for utilization of 3,4-β-dihydrocarbolines for the formation of *N*-acyliminium intermediates. That is why, we investigated the reaction between 3,4-dihydro-β-carboline **1** and acyl chlorides. When dichloromethane solution of imine **1** and acetyl or benzoyl chloride were mixed at room temperature, a precipitate quickly formed and in 30 min decomposed giving a complex mixture of products. Therefore, we continued our research at lower temperature, in an ice bath. To a cooled solution of 3,4-dihydro-β-carboline, equimolar amount of acyl chloride was added. All attempts for isolation, purification, and characterization of the formed *N*-acyliminium intermediates were failed, because of their high reactivity and instability. We found that after leaving the mixture at 4–5°C for about 24 hr, the *N*-acyliminium reagents converted to the corresponding 1-*oxo*-2-acyl-2,3,4,9-tetrahydro-β-carbolines. The mechanism of this process is unclear and will be subject of further studies. The presence of *N*-acyliminium intermediates could be proven only indirectly by trapping them with suitable nucleophiles.

Initially, we examined the reaction between the *N*-acyliminium intermediate **3b** (R=OEt) and the indole. To the obtained in situ reagent **3b**, an equivalent amount of an ice-cooled solution of indole was added dropwise. As a result, the expected product of α-amidoalkylation, ethyl 1-(1*H*-3-indolyl)-2,3,4,9-tetrahydro-1*H*-*b*-carboline-2-carboxylate **4b**, was isolated in 20% yield. The formation of this product is an indirect evidence for the existence of the *N*-acyliminium intermediate **3b** in the reaction mixture. We found that the product is instable in acidic media. On the other hand, nearly

20% of starting imine **1** was recovered from the reaction mixture. This led us to the assumption that under the reaction conditions a part of the 3,4-dihydro-β-carboline is blocked by the evolved HCl. Thus, the reaction was carried out in the presence of Et_3N as HCl scavenger. When indole and Et_3N were added consecutively to the reaction mixture, the product **4b** was obtained in significantly better yield − 50%. The order of addition of indole and Et_3N is of importance—if these reagents are added simultaneously to **3b**, then along with the main product **4b** (40% yield), a minor product **4d** is obtained in 10% yield. The spectral data show that **4d** is a product of second acylation in the carboline moiety.

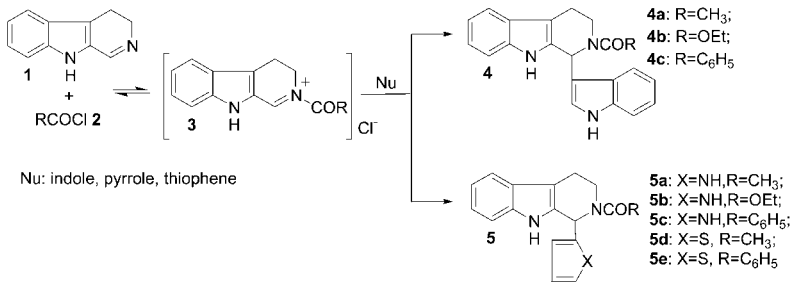
These results prompted us to broaden the studies of the reaction with the use of acetyl and benzoyl chlorides (R=CH_3, C_6H_5). In all cases, the *N*-acyliminium reagents **3** were obtained by adding the corresponding acyl chloride **2** to an ice-cooled solution of 3,4-dihydro-β-carboline **1** in dichloromethane and stirring the reaction mixture for 30 min at 0°C. The *N*-acyliminium reagents prepared in this way were successfully used for amidoalkylation of indole according to the above procedure. The only difference is that here the order of addition of Et_3N and indole does not affect the outcome of the reactions. The yields of obtained products **4a–c** and the reaction conditions are displayed in Table 1.

The studies were continued with the utilization of pyrrole and thiophene as nucleophiles. The results from these experiments are summarized in Schs. 1 and 2 and in Table 1.

Table 1. Reaction conditions, yields and melting points of the compounds **4**, **5**, and **7**.

Entry	Conditions [hr; T(°C)]	Yield (%)	Mp (°C)
4a	1.5; 0	67	238–240[a]
4b	1.5; 0	50	236–238[a]
4c	1.5; 0	70	179–181[a]
5a	1; 0	25	198–200[a,b]
5b	1; 0	43	133–134[a]
5c	1.5; 0	35	243–244[a,c]
5d	12; 5–10	27	221–222[d]
5e	2; 50	30	174–176
7	2; 50	25	170–172

[a]With decomposition.
[b]Mp 233–235°C in Ref.[6].
[c]Mp 262–263°C in Ref.[6].
[d]Mp 251–252°C in Ref.[6].

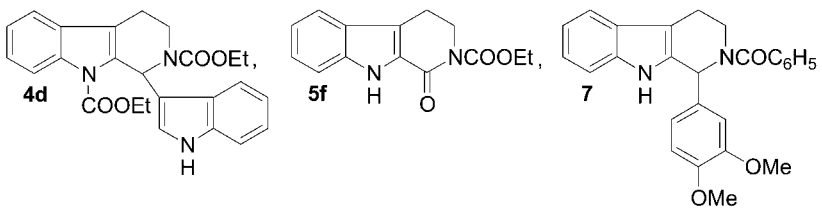


Scheme 1. Synthesis of 1,2-disubstituted tetrahydro-β-carbolines **4** and **5**.

The reactions with pyrrole were carried out under the reaction conditions shown in Table 1, in the presence of Et_3N. As a result, the corresponding products **5a–c** were obtained in good yields. The signals in ^{1}H-NMR spectra of compounds **5a–c** indicate that only mono α-substitution in the pyrrole ring takes place. Diamidoalkylation was not observed, in spite of the ratio of **3** and pyrrole.

With ethyl chloroformate, along with the main product **5b**, a minor product **5f** in 27% yield was isolated. That could be explained with oxidation of *N*-acyliminium reagent **3b** under the reaction conditions.

We continued our work with amidoalkylation of thiophene and the initial experiments were carried out in the absence of HCl scavenger. When ethyl chloroformate was used, the reaction to the corresponding product of amidoalkylation failed and only product **5f** was isolated from the reaction mixture. When acetyl or benzoyl chlorides were used, the amidoalkylation of thiophene was successful and the corresponding products **5d** and **5e** were obtained with 27% and 30% yield, respectively. Upon work-up of the reaction mixtures, 50% and 25% of the starting 3,4-dihydro-β-carboline was recovered, respectively. Most likely it had been blocked by the evolved HCl in the course of the reaction. That is why, to increase the yields, we tried



Scheme 2. Structural representation of **4d**, **5f**, and **7**.

again to carry out the reaction in the presence of Et_3N. This strategy, however, proved unsuccessful and no amidoalkylation of thiophene was observed in the presence of Et_3N, regardless of the applied various reaction conditions.

Finally, we tried to carry out the reaction of amidoalkylation with 1,2-dimethoxybenzene, as a representative of benzene aromatics. For this purpose, we used the *N*-benzoyl iminium reagent **3c** ($R=C_6H_5$), because of its relatively higher stability at elevated temperatures. As a result of the reaction, after 2 hr at 50°C, the product **7** was obtained in 25%; and once again 20% of the starting imine was blocked by the evolved HCl. All attempts to increase the yield of **7** were failed.

As the reactivity of the acyliminium reagents is often improved in the presence of the Lewis acids, we carried out some experiments with $BF_3 \cdot Et_2O$ and $AlCl_3$. The acyliminium reagents **3**, obtained from 3,4-dihydro-β-carboline, proved highly unstable and were decomposed by the Lewis acids.

As a conclusion, we report for the first time an application of *N*-acyliminium reagents of 3,4-dihydro-β-carboline. We demonstrate that the obtained in situ *N*-acyliminium intermediates are good electrophilic reagents in intermolecular α-amidoalkylation toward heteroaromatics as indole, pyrrole, and thiophene. This represents a new and a convenient route to 1-heteroaryl-2-acyl-2,3,4,9-tetrahydro-β-carbolines. Some of the synthesized products are analogs of known biologically active substances like *Eudistoma* alkaloids.

EXPERIMENTAL

Melting points were determined on a Boetius hotstage apparatus and are uncorrected. Unless otherwise noted, NMR spectra were recorded on a Bruker 250 MHz device by using [D6]DMSO as solvent. Chemical shifts (δ, ppm) are downfield from TMS as an internal standard and coupling constants are in Hz. Mass spectra were recorded on a Jeol JMS-D300 spectrometer (70 eV). All new compounds had correct parent ion peaks by mass spectrometry.

General Procedure for Preparation of Products 4, 5, and 7 (Table 1)

The starting 3,4-dihydro-β-carboline **1** was obtained by known procedure.[7]

Acyl chloride (3 mmol) was added dropwise to a stirred and an ice-cooled solution of 3,4-dihydro-β-carboline (3 mmol) in dry dichloromethane (5 mL). The mixture was stirred 30 min in order to obtain *N*-acyliminium intermediate

3. For preparation of products **4** and **5a–c**, an ice-cooled solution of indole (3 mmol) or pyrrole (3 mmol) and Et_3N (3 mmol) in dichloromethane (1 mL) was added dropwise. Similarly, ice-cooled solutions of thiophene and 1,2-dimethoxybenzene were added to the dichloroethane solution of **3** for the preparation of **5d, e** and **7**. The reaction mixtures were stirred for the time and the temperatures given in Table 1, then were treated with 6% CH_3COOH (10 mL) and rapidly extracted with CH_2Cl_2 (3×10 mL). The combined extract was washed with aq. $NaHCO_3$ (2×10 mL), dried (Na_2SO_4) and the solvent was removed by vacuum distillation. The products were separated and purified by recrystallization or column chromatography on a neutral Al_2O_3.

1-[1-(1*H*-3-Indolyl)-2,3,4,9-tetrahydro-1*H*-β-carbolin-2-yl]-1-ethanone 4a: (recrystallization: MeOH). ^{1}H-NMR: 2.13 (s, 3H), 2.76–2.96 (m, 2H), 3.87–3.93 (m, 2H), 5.76 (s, 1H), 6.80 (s, 1H), 6.92–7.12 (m, 4H), 7.24–7.60 (m, 4H), 10.95 (s, 1H), 11.01 (s, 1H); ^{13}C-NMR: 21.60, 21.80, 24.30, 42.60, 105.16, 110.18, 111.06, 112.70, 118.60, 118.80, 121.40, 123.26, 124.00, 127.18, 129.60, 135.78, 137.40, 170.06 (CO); $C_{21}H_{19}N_3O$ (329.40): calcd. C 76.57, H 5.81, N 12.76%; found C 76.63, H 5.93, N 12.84%.

Ethyl 1-(1*H*-3-indolyl)-2,3,4,9-tetrahydro-1*H*-*b*-carboline-2-carboxylate 4b: (eluent: Et_2O). ^{1}H-NMR: 1.24 (t, 3H, $J = 6$), 2.80–2.90 (m, 2H), 3.14–3.25 (m, 2H), 4.17 (q, 2H, $J = 7$), 6.72 (s, 1H), 6.90–7.14 (m, 5H), 7.28–7.60 (m, 4H), 10.95 (s, 1H), 11.09 (s, 1H); ^{13}C-NMR: 13.80, 21.30, 25.70, 43.60, 65.18, 107.30, 108.10, 110.50, 112.80, 116.70, 118.80, 119.20, 119.70, 120.00, 121.20, 128.30, 132.30, 136.20, 137.80, 154.40 (CO); $C_{22}H_{21}N_3O$ (359.43): calcd. C 73.52, H 5.89, N 11.69%; found C 73.60, H 5.97, N 11.84%.

1-(1*H*-3-Indolyl)-2,3,4,9-tetrahydro-1*H*-*b*-carbolin-2-yl-phenylmethanone 4c: (eluent: mixture p.ether/ether, 1/1). ^{1}H-NMR: 3.26–3.37 (m, 2H), 3.52-3.60 (m, 2H), 7.09 (t, 2H, $J = 2$), 7.32–7.51 (m, 7H), 7.75–7.84 (m, 5H), 8.63 (t, 1H, $J = 2$), 9.96 (s, 1H), 11.67 (s, 1H); ^{13}C-NMR: 23.80, 37.30, 57.60, 110.20, 111.20, 111.60, 114.60, 115.70, 118.60, 120.60, 121.30, 123.80, 126.40, 128.50, 129.30, 130.40, 134.60, 135.60, 136.90, 137.40, 170.90 (CO), $C_{26}H_{21}N_3O$ (391.47): calcd. C 79.77, H 5.41, N 10.73%; found C 80.06, H 5.56, N 10.83%.

Diethyl 1-(1*H*-3-indolyl)-2,3,4,9-tetrahydro-1*H*-*b*-carboline-2,9-dicarboxylate 4d: (eluent: mixture p.ether/ether, 4/1). ^{1}H-NMR ($CDCl_3$): 0.70–1.00 (m, 3H), 1.17–1.50 (m, 3H), 2.70–3.00 (m, 2H), 3.05–3.33 (m, 2H), 4.18 (q, 4H, $J = 6$), 6.58 (s, 1H), 7.15–7.50 (m, 8H), 7.55 (s, 1H), 8.13–8.45 (m, 1H); ^{13}C-NMR: 13.80, 23.55, 32.95, 41.40, 65.80, 106.70, 109.80, 112.60, 116.70, 118.40, 120.60, 121.30, 122.30, 124.10, 125.40, 126.30, 135.60, 140.50, 147.60 (CO), 150.60 (CO); $C_{25}H_{25}N_3O_4$ (431.49): calcd. C 69.59, H 5.84, N 9.74%; found C 69.80, H 5.97, N 9.92%.

1-[1-(1*H*-2-Pyrrolyl)-2,3,4,9-tetrahydro-1*H*-*b*-carbolin-2-yl]-1-ethanone 5a: (eluent: Et_2O). ^{1}H-NMR ($CDCl_3$): 2.19 (s, 3H), 3.35–3.54 (m, 2H), 3.85–3.93 (m, 2H), 5.82 (s, 1H), 6.05 (s, 1H), 6.80 (s, 2H), 7.16–7.32 (m, 4H), 8.04 (s, 1H), 9.21 (s, 1H); ^{13}C-NMR: 19.80, 20.60, 31.78, 39.50, 107.60, 108.90, 112.60, 114.60, 117.96, 119.63, 123.54, 126.30, 132.70, 134.15, 140.33, 169.80 (CO); $C_{17}H_{17}N_3O$ (279.30): calcd. C 73.10, H 6.13, N 15.04%; found C 73.23, H 6.23, N 15.25%.

Ethyl 1-(1*H*-2-pyrrolyl)-2,3,4,9-tetrahydro-1*H*-*b*-carboline-2-carboxylate 5b: (eluent: mixture p. ether/ether, 4/1). ^{1}H-NMR ($CDCl_3$): 1.33 (t, 3H, $J = 5$), 2.90 (t, 2H, $J = 5$), 3.23 (t, 2H, $J = 6$), 4.30 (q, 2H, $J = 5$), 5.95 (s, 1H), 6.15 (t, 1H, $J = 3$), 6.50 (s, 1H), 6.88 (s, 1H), 7.15–7.43 (m, 3H), 7.58–7.78 (m, 1H), 8.10 (s, 1H), 9.15 (s, 1H); ^{13}C-NMR: 13.60, 19.80, 38.34, 54.18, 62.17, 102.50, 109.70, 113.40, 116.50, 118.52, 120.63, 123.40, 125.43, 134.80, 135.70, 149.75 (CO); $C_{18}H_{19}N_3O_2$ (309.36): calcd. C 69.88, H 6.19, N 13.58%; found C 70.03, H 6.27, N 13.78%.

Phenyl-1-(1*H*-2-pyrrolyl)-2,3,4,9-tetrahydro-1*H*-*b*-carbolin-2-ylmethanone 5c: (eluent: mixture p.ether/ether, 1/1). ^{1}H-NMR: 2.70–2.90 (m, 2H), 3.36–3.45 (m, 1H), 3.64–3.68 (m, 1H), 5.77 (s, 1H), 5.95 (s, 1H), 6.71 (s, 1H), 6.83 (s, 1H), 6.95–7.11 (m, 3H), 7.30 (d, 1H, $J = 8$), 7.47 (s, 5H), 10.69 (s, 1H), 11.06 (s, 1H); ^{13}C-NMR: 20.18, 34.12, 59.17, 105.40, 112.80, 114.70, 115.35, 118.60, 120.95, 123.65, 125.18, 126.96, 129.16, 131.50, 132.63, 134.85, 140.16, 169.87 (CO); $C_{22}H_{19}N_3O$ (341.41): calcd. C 77.40, H 5.61, N 12.31%; found C 77.15, H 5.73, N 12.45%.

1-[1-(2-Thienyl)-2,3,4,9-tetrahydro-1*H*-*b*-carbolin-2-yl]-1-ethanone 5d: (eluent: $CHCl_3$). ^{1}H-NMR: 1.74 (s, 3H), 3.15 (m, 2H), 3.27–3.37 (m, 2H), 7.05–7.12 (m, 2H), 7.28–7.34 (m, 1H), 7.39 (s, 1H), 7.75 (d, 2H, $J = 8$), 7.99 (t, 2H, $J = 5$), 11.72 (s, 1H); ^{13}C-NMR: 19.18, 20.80, 34.83, 56.30, 108.30, 112.63, 116.45, 118.34, 121.34, 124.80, 126.80, 127.30, 132.64, 136.50, 139.73, 172.80 (CO); $C_{17}H_{16}N_2OS$ (296.38): calcd. C 68.89, H 5.44, N 9.45%; found C 68.95, H 5.54, N 9.53%.

Phenyl-1-(2-thienyl)-2,3,4,9-tetrahydro-1*H*-*b*-carbolin-2-ylmethanone 5e: (eluent: Et_2O). ^{1}H-NMR: 3.30–3.37 (m, 2H), 3.52–3.60 (m, 2H), 7.05–7.11 (m, 2H), 7.31–7.35 (m, 2H), 7.38–7.50 (m, 4H), 7.74–7.84 (m, 5H), 11.66 (s, 1H); ^{13}C-NMR: 20.84, 35.43, 58.40, 108.60, 110.30, 115.38, 118.63, 120.34, 123.78, 126.23, 127.10, 127.65, 129.54, 131.27, 134.37, 134.83, 139.65, 142.43, 168.89 (CO); $C_{22}H_{18}N_2OS$ (358.45): calcd. C 73.72, H 5.06, N 7.82%; found C 73.94, H 5.28, N 7.97%.

Ethyl 1-*oxo*-2,3,4,9-tetrahydro-1*H*-*b*-carboline-2-carboxylate 5f: (eluent: Et_2O). ^{1}H-NMR ($CDCl_3$): 1.25 (t, 3H, $J = 6$), 3.35–3.68 (m, 4H), 4.20 (q, 2H, $J = 6$), 7.30–7.60 (m, 2H), 8.00–8.20 (m, 2H), 9.50 (s, 1H); ^{13}C-NMR: 12.65, 19.34, 36.58, 54.15, 110.58, 118.64, 119.53, 121.80, 123.75,

124.03, 124.15, 129.65, 149.50 (CO), 158.63 (CO); $C_{14}H_{14}N_2O_3$ (258.27): calcd. C 65.11, H 5.46, N 10.85%; found C 65.23, H 5.58, N 10.94%.

1-(3,4-Dimethoxyphenyl)-2,3,4,9-tetrahydro-1*H*-*b*-carbolin-2-yl-phenylmethanone 7: (eluent: Et_2O). ^{1}H-NMR ($CDCl_3$): 3.28–3.38 (m, 2H), 3.51–3.59 (m, 8H), 5.73 (s, 1H), 7.05–7.11 (m, 1H), 7.28–7.34 (m, 2H), 7.39–7.50 (m, 4H), 7.73–7.83 (m, 5H), 11.65 (s, 1H); ^{13}C-NMR: (CO), 158.63 (CO); $C_{26}H_{24}N_2O_3$ (412.48): calcd. C 75.71, H 5.86, N 6.79%; found C 75.84, H 5.93, N 6.90%.

REFERENCES

1. (a) Dulenko, V.I.; Comissarov, I.V.; Doljenko, A.T.; Nikolukin, U.A. *β-Carbolines, Chemistry and Neurobiology*; Andronati, C.A., Ed.; Naukova Dumka: Kiev, 1992; 88–188; (b) Ho, B.T. *Current Developments in Psychopharmacology*; Essman, W.B., Valzelli, L., Eds.; Spectrum Publications: New York, 1977; Vol. 4, 151; (c) Agarwal, D.P.; Goedde, H.W. *Alcohol Metabolism, Alcohol Intolerance and Alcoholism*; Springer-Verlag: Berlin, 1990; 99.
2. (a) Rocca, P.; Marsais, F.; Godard, A.; Queguiner, G. A new convergent synthesis of α-substituted-β-carbolines. Tetrahedron **1993**, *49* (16), 3325–3342; (b) Love, B.E.; Raje, P.S. Preparation of 1-aryl-β-carbolines. J. Org. Chem. **1994**, *59* (11), 3219–3222.
3. (a) Kobayashi, J.; Nakamura, H.; Ohizumi, Y. Eudistomidin-A, a novel calmodulin antagonist from the Okinawan tunicate *Eudistoma glaucus*. Tetrahedron Lett. **1986**, *27* (10), 1191–1194; (b) Rinehart, K.L., Jr.; Kobayashi, J.; Harbour, G.C.; Gilmore, J.; Mascal, M.; Holt, T.G.; Shield, L.S.; Lafargue, F. Eudistomins, A.-Q, β-carbolines from the antiviral Caribbean tunicate *Eudistoma olivaceum*. J. Am. Chem. Soc. **1987**, *109* (11), 3378–3387; (c) Debitus, C.; Laurent, D. Alcaloides d'une ascidie neocaledonienne, *Eudistoma fragum*. J. Nat. Prod. **1988**, *51* (4), 799–801; (d) Kobayashi, J.; Cheng, J.; Ohta, T.; Nozoe, S.; Ohizumi, Y.; Sasaki, T. Eudistomidins, B, C and D: novel antileukemic alkaloids from okinawan marine tunicate *Eudistoma glaucus*. J. Org. Chem. **1990**, *55* (11), 3666–3670; (e) Badre, A.; Boulanger, A.; Abou-Mansour, E.; Banaigs, B.; Combaut, G.; Francisco, C. Eudistomin U and isoeudistomine U, new alkaloids from the Caribean ascidian *Lissoclinum fragile*. J. Nat. Prod. **1994**, *57* (4), 528–533; (f) Foderaro, T.A.; Barrows, L.R.; Lassota, P.; Ireland, C.M. Bengacarboline, a new β-carboline from a marine ascidian *Didemnum* sp. J. Org. Chem. **1997**, *62* (17), 6064–6065.

4. Venkov, A.P.; Statkova-Abeghe, S.M.; Donova, K.A. Amidoalkylation of heteroaromatic compounds with adducts of acyl chlorides and 3,4-dihydroisoquinoline and isoquinoline. Cent. Eur. J. Chem. **2004**, *2* (1), 234–246. www.cesj.com.
5. (a) Sheinkman, A.K. Heteroarylation of organic compounds. Khimia Heterocycl. Soedin. **1974**, *1*, 3–18; (b) Sheinkman, A.K.; Deikalo, A.A. Reactions of cyclammonium cations XV. Hetarylation of pyrroles by N-acyl salts of isoquinolinium and acridinium. Khimia Heterocycl. Soedin. **1971**, *7* (12), 1654–1659. (Chem. Abstr. **1972**, *77*, 5310a); (c) Dobeneck, H.; Goltzsche, W. Reactionen von *N*-Acyl-cyclimmonium-salzen mit nucleophilen verbindungen. Chem. Ber. **1962**, *95*, 1484–1492.
6. Analgesics. Brit. Patent 6,512,087, March 17, 1966, ICI Ltd. (Chem. Absrt. **1966**, *65*, 3844c).
7. Bertrand, M.; Poissonnet, G.; Theret-Bettiol, M.; Gaspard, C.; Werner, G.H.; Pfeiffer, B.; Renard, P.; Leonce, S.; Dodd, R.H. Cytotoxic activities of novel hexahydroindolizino[8,7-*b*]indole derivatives prepared by 1,3-dipolar cycloaddition reactions of 3,4-dihydro-*β*-carboline ylides. Bioorg. Med. Chem. **2001**, *9*, 2155–2164.

Received in Poland March 31, 2004