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Addition of some 6-amino-4-aryl-2(1*H*)-pyridones to phenylisocyanate and related reactions

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Abstract: The Michael addition of enaminoesters to coumarins leads to the formation of the rearranged adduct **1** whose structure has been previously elucidated by X-ray crystallographic analysis. Now, *N*- and/or *O*-carbamoylation of the 6-amino-2-pyridone **1** by treatment with phenyl isocyanate in a molar ratio of 1:1 and 1:2 gave *N*-mono- (**2a**) or *N,O*-bis-(phenylcarbamoyl) (**3**) derivatives, respectively. Further transformations of the corresponding new 2-pyridone derivative **2a** into the *O*-acetyl derivative **2b** and the chromeno[3,4-*c*]pyridine **4** are reported as well.

Keywords: chromeno[3,4-*c*]pyridine; enaminoesters; phenyl isocyanate; pyridine derivatives; rearrangement; ureides.

Dedicated to: Professor Willi Kantlehner (Aalen, Germany) on the occasion of his 75th birthday.

1 Introduction

In a series of previous papers, we described the Michael addition of some enaminoesters to coumarin and to some of its 3-substituted (e.g. the coumarin-3-carboxylic acid) and 3,6-disubstituted derivatives [1–5]. The initially formed adduct spontaneously undergoes further intramolecular rearrangement to give the simplest one of the resulting stable adducts, ethyl 2-amino-4-(2-hydroxyphenyl)-6-oxo-1,4,5,6-tetrahydro-3-pyridinecarboxylate (**1**, Scheme 1). The latter compound (**1**) could also be obtained from coumarin-3-carboxylic acid and ethyl 3,3-diaminoacrylate, accompanied by decarboxylation.

Carbamoylation of enamines with heterocumulenes, leading to either *C*- or *N*-adducts, has been widely used as an initial step for the synthesis of various heterocyclic

compounds, mainly derivatives of uracil [6]. Thus, 3-aminopropenoic esters were added to organic isocyanates or isothiocyanates yielding *N*-adducts which have been readily cyclized to 6-substituted uracils, e.g. [7], in the presence of a base. Similarly, we have earlier developed the first general method for direct preparation of 3-mono-substituted 6-aminouracils [8] by the addition of the ene-diamine (ketene aminal) **2** to alkyl isocyanates. It seemed reasonable to try to exploit this approach by carbamoylation of the coumarin–enaminoester adduct, the 2-pyridone **1**, containing the same ketene aminal moiety (Scheme 1). On the other hand, as we reported earlier [2], the adduct readily underwent simple recyclization on heating to give the substituted chromeno[3,4-*c*]pyridine **4**. Conditions have also been reported [5] for consecutive acetylation of the primary amino and the phenolic group to yield the corresponding acetyl derivatives of type **2b**.

In the present paper we wish to report the *N*- and/or *O*-carbamoylation of **1** with phenyl isocyanate and the results of some trials for further transformations of the *N*-mono- (**2a**) and *N,O*-bis-(phenylcarbamoyl) (**3**) derivatives thus obtained (Scheme 1).

2 Results and discussion

In continuation of our interest in biologically active 2-pyridones [9–12], structurally related to the 1,4-dihydropyridine calcium antagonists, we first studied the reaction of **1** with phenyl isocyanates in order to achieve selective *C*(2)-*N*-carbamoylation and to avoid the competitive *O*-carbamoylation at the phenolic hydroxyl group (Scheme 2). Thus, the reaction was successfully performed in anhydrous acetonitrile at reflux to give the ureide **2a** or **3** in yields, as given in Table 1. The expected IR spectral bands could be observed for NH/OH associated groups as well as for all three different carbonyl groups (ester, lactam, urea) of **2a** at about 1670 (C=O ester), 1630 (C=O, lactam), 1601 (C=O, ureide) cm^{−1}, respectively. All relevant proton groups show the expected signals in the ¹H NMR spectra. The structure of ureides analogous to **2a** was recently confirmed by means of X-ray crystallographic analysis [13].

The successive *O*-acetylation of the phenolic hydroxyl group in **2a** was carried out in pyridine to selectively

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Scheme 1: Reactions of the coumarin-enaminoester adduct **1** with phenylisocyanate and related reactions.

Scheme 2: Alternative synthesis of the carbamoyl derivatives **2a** and **3** from coumarin-3-carboxylic acid (**6**) and the ketene aminal **7**.

afford the corresponding *O*-acetyl derivative **2b** (cf. [5]) in quantitative yield. These products have also been characterized by means of spectral and analytical methods

(see the Experimental section). Important is the characteristic presence of the acetyl CH_3 singlet in the ^1H NMR spectrum.

Table 1: Conditions and products of the reaction of **1** with phenyl isocyanate.

Trial no.	Molar ratio 1:PhNCO	React. temp. (°C in CH ₃ CN)	Reaction time (h)	Isolated products	Yield (%)
1	1:1	20–25	2	1 (recovered)	–
2	1:2	20–25	24	2a 4	37 2
3	1:1.1	Reflux	1	2a	18
4	1:2	Reflux	6	2a 3 4	– ^a – ^a 1
5	1:3	Reflux	24 ^b	2a 3 4	12 12 4

^aDetected by TLC; yield not determined; according to ¹H NMR the product mixture contains mainly **3** and traces of **4**.

^bReflux duration does not visibly affect the product ratio and the yield after the first hour of heating (TLC control).

In order to chemically prove the structure of the products **2a** and **3**, we additionally synthesized **2a** in an alternative way, starting from coumarin-3-carboxylic acid (**6**, Scheme 2) and ethyl 3-amino-3-[(phenylcarbamoyl)amino] prop-2-enoate (**7**, Scheme 2) and we obtained a product (**2a**) which was identical to that of the reaction of **1** with phenyl isocyanate. As a next step, **2a**, thus obtained, was treated with phenyl isocyanate to give product **3** again as an end result. This synthetic pathway is a chemical proof for the structures of **2a** and **3**.

The overall yield of **3** thus synthesized (Scheme 2) amounts to 60%. Its melting point, *R_f* value and IR spectrum are fully identical to the product **3** obtained according to Scheme 1. The structure of the phenylcarbamoyl *N*-mono- (**2a**) and *N,O*-bis-adducts (**3**) is in good compliance with their spectral properties. For instance, in the IR spectrum of **3**, absorption bands due to carbamate carbonyl at 1732 cm^{−1} and three amide type carbonyls at 1684, 1668 and 1637 cm^{−1} are observed. An absorption above 3300 cm^{−1} for hydroxyl group lacks in **3** in contrast to the IR spectrum of **2a**. In the ¹H NMR spectra of both ureides (in DMSO-*d*₆), the usual signals for ethyl protons of the ester group and the 4,5-dihydropyridone moiety are also in good accordance with the signals of the alkyl analogues reported earlier [13]. The integral curve of the complex multiplet for aromatic protons of compound **2a** at δ = 6.67–7.52 ppm is due to 9H. In the ¹H NMR spectrum of **3**, the multiplet due to 14H is shifted to δ = 7.15–7.58 ppm, whereas all four OH/NH protons of both products **2a** and **3** are displayed as sharp singlets. On more prolonged reflux in acetonitrile, the product **3** partially decomposes to give back **2a**, that is, the addition reaction showed reversibility.

In analogy with the published heterocyclization of other structurally similar ureide esters [6–8], we tried to perform the cyclization of **2a** under the reported conditions, i.e., in the presence of sodium ethoxide at ambient temperature [7, 14]. However, instead of the expected pyrido[2,3-*d*]pyrimidine **5**, we isolated the 2*H*-chromeno[3,4-*c*]pyridine **4**, which is actually a coumarin derivative again (Scheme 1). Its structure was confirmed by means of spectral methods (IR, NMR, MS) and elemental analyses. Thus, three different carbonyl frequencies are observed at 1726, 1691, 1660 cm^{−1} in the IR spectrum of **4** and its ¹H NMR spectrum showed a typical ABX spin system for the protons (see the Experimental section), as well as the expected D₂O-exchangeable signals due to the three NH groups at δ = 10.61, 11.26 and 11.41 ppm.

The product **3** (Scheme 1) could also be synthesized from the coumarin **6** (Scheme 2) by reflux (40 h) with 3-phenyl-6-aminouracil [2c,d] in anhydrous ethanol.

Many known approaches for the synthesis of [1]benzopyrano[3,4-*c*]pyridines or [1]benzopyrano[4,3-*b*]pyridines included coumarin derivatives as starting compounds or intermediates, e.g. [15–17]; for a review see [18]. We have also developed some new synthetic pathways leading to substituted [1]benzopyrano[4,3-*b*]pyridines via Knoevenagel condensation [19], via the Wittig reaction followed by Vilsmeier conditions [20], or even by the Erlenmeyer–Ploechl reaction [21], all of them using coumarin-3-carbaldehydes as starting material. Hence, the preparation of the 4-ureido-1,10*b*-dihydro-5*H*-[1]benzopyrano[3,4-*c*]pyridine **4**, as discussed above, is a new contribution to the synthesis of this class of heterocyclic compounds.

3 Experimental

3.1 General

The IR spectra were recorded in nujol on a Shimadzu 8001 FTIR spectrometer. ¹H and ¹³C NMR spectra were registered on a Bruker WP 100 MHz. For further information, please see the Supplementary Material for this paper. Chemical shifts are expressed in δ (ppm) downfield from hexamethyldisiloxane as an internal reference. Elemental analyses were performed by the Microanalytical Laboratory, Institute of Organic Chemistry and Biochemistry, University of Stuttgart (Head Dr. Joachim Opitz). Thin-layer chromatography (TLC) monitoring was carried out on silica gel Merck GF₂₅₄ pre-coated aluminum sheets, eluted with hexane–acetone 2:1 (v/v). Visualization of spots was done by treatment with I₂ (vapor) and under UV irradiation (λ = 254 nm).

3.1.1 Ethyl 4-(2-hydroxyphenyl)-6-oxo-2-[(phenylcarbamoyl)amino]-1,4,5,6-tetrahydropyridine-3-carboxylate (**2a**)

3.1.1.1 Method A

To a suspension of 1.38 g (5 mmol) of **1** in 20 mL of anhydrous acetonitrile was added dropwise under stirring a solution of 1.19 g (10 mmol) of phenylisocyanate in 5 mL of the same solvent. After stay at 20–25°C for 1 h, a crystalline mixture (TLC control) of approximately equal amounts of both **2a** and unreacted **1** was collected by filtration. The mother liquor was allowed to stay overnight at 20–25°C, and further crystals consisting of TLC-homogeneous **2a** were filtered afterwards (totally stay 24 h). Both isolated solids were combined and recrystallized twice from ethanol. Yield: 0.73 g (37%) of white platelets with m.p. 183–186°C. After 1 d of stay at room temperature, a TLC-homogeneous pure product (0.03 g, 2%) was isolated and identified as **4** according to TLC, m.p. and IR spectrum (see below).

3.1.1.2 Method B

To a solution of 1.5 g (6 mmol) of **7** (prepared after [8, 14]) in 50 mL of anhydrous ethanol was added portionwise under stirring to 0.95 g (5 mmol) of coumarin-3-carboxylic acid (**6**). The reaction mixture was stirred under reflux for 1 h and then allowed to stay 14 days at room temperature. The separated crystals of **2a** were filtered and washed with ice-cooled ethanol. Yield: 0.43 g (21%) of white platelets with m.p. 183–186°C. – IR (nujol, cm⁻¹): ν = 3327–3148 (OH, NH, assoc.), 1670 (C=O, ester), 1630 (C=O, lactam), 1601 (C=O, ureide). – ¹H NMR (100 MHz, DMSO-*d*₆): δ = 1.05 (t, *J* = 7 Hz, 3H, CH₃), ~2.48 (d, 1H, 5-CH^A, partially overlapped by solvent), 2.79–3.06 (dd, *J*₁ = 5.5 Hz, *J*₂ = 5.5 Hz, 1H, 5-CH^B), 4.03 (m, 2H, OCH₂), 4.41 (d, *J* = 5.5 Hz, 1H, 4-CH^X), 6.67–7.52 (m, 9H_{arom.}), 9.57 (s, 1H, OH, D₂O-exchangeable), 10.41 (s, 1H, NH, D₂O-exchangeable), 11.07 (s, 1H, NH, D₂O-exchangeable), 11.18 (s, 1H, NH, D₂O-exchangeable). – EI-MS (70 eV): *m/z* (%) = 395 (<1) [M]⁺, 276 (6) [M–C₆H₅NCO]⁺, 230 (10) [M–C₆H₅NCO–C₂H₅OH]⁺, 229 (15) [M–C₆H₅NCO–C₂H₅OH–H]⁺, 203 [M–C₆H₅NCO–COOC₂H₅]⁺, 146 (14), 119 (100). – CI-MS (gas NH₃, 100 eV): *m/z* (%) = 296 (3), 279 (100), 259 (3), 183 (6), 124 (2), 102 (56), 85 (63). – Calcd. for C₂₁H₂₁N₃O₅ (395.41) (confirmed by EI-MS isotope distribution): C 63.79, H 5.35, N 10.63; found C 63.73, H 5.32, N 10.53.

3.1.2 Ethyl 4-[2-(acetyloxy)phenyl]-6-oxo-2-[(phenylcarbamoyl)amino]-1,4,5,6-tetrahydropyridine-3-carboxylate (**2b**)

To a solution of 1.98 g (5 mmol) of **2a** in 10 mL of pyridine was added dropwise under stirring 1.02 g (10 mmol) of

acetic anhydride. The mixture was set aside and allowed to stay at 20–25°C. After exhausting of the starting compounds (14 d, TLC monitoring) the volatile components were removed in vacuo. The residue was recrystallized from ethanol. Yield 1.55 g (71%) of colorless crystals with m.p. 220–223.5°C. – IR (nujol, cm⁻¹): ν = 3349 (sh, NH), 3193 (NH_{assoc.}), 1732 (C=O, ester), 1705 (C=O, ester), 1669 (vs, C=O, amide), 1640 (vs, C=O, lactam), 1599, 1551, 1107, 758. – ¹H NMR (100 MHz, DMSO-*d*₆): δ = 1.03 (t, *J* = 7 Hz, 3H, CH₃), 2.32 (s, 3H, COCH₃), ~2.47 (part. overlapped by solvent; 1H, 5-CH^A), 2.96 (m, 1H, 5-CH^B), 3.98–4.08 (m, 2H, OCH₂), 4.27 (m, 1H, 4-CH^X), 7.18–7.52 (m, 9H_{arom.}), 10.45 (s, 1H, NH, D₂O-exchangeable), 11.11 (s, 1H, NH, D₂O-exchangeable), 11.22 (s, 1H, NH, D₂O-exchangeable). – CI-MS (gas NH₃, 100 eV): *m/z* = 438 (4) [M+1]⁺, 361 (4), 319 (100) [M–C₆H₅NCO]⁺, 229 (6), 136 (5), 80 (34); isotope distribution corresponds to C₂₃H₂₄N₃O₆ [M+1]⁺. – Calcd. for C₂₃H₂₄N₃O₆ (437.45): C 63.15, H 5.30, N 9.61; found C 62.89, H 5.41, N 9.65.

3.1.3 Ethyl 6-oxo-2-[(phenylcarbamoyl)amino]-4-{2-[(phenylcarbamoyl)oxy]phenyl}-1,4,5,6-tetrahydropyridine-3-carboxylate (**3**)

3.1.3.1 Method A (from **1**, Table 1, entry 5)

To a hot solution of 1.38 g (5 mmol) of the pyridone **1** in anhydrous acetonitrile was added dropwise under stirring 1.79 g (15 mmol) of phenyl isocyanate. The reaction mixture was refluxed for 24 h and, after cooling to 0°C, a crystalline product separated which was a mixture of several compounds according to TLC. This mixed product was filtered and recrystallized twice from anhydrous acetonitrile to give pure **3**. The small amount of crystals (0.06 g) insoluble in hot acetonitrile were identified as **4** by comparison of their *R*_F values, m.p.'s, and IR spectra. Yield of compound **3**: 0.32 g (12%) of colorless needles with m.p. 147–149°C.

The mother liquor was concentrated to 25% of its initial volume and, after staying overnight at room temperature, the separated crystals of **2a** were filtered off and recrystallized from acetonitrile. Yield of **2a**: 0.23 g (12%) of colorless crystals. – ¹H NMR (100 MHz, DMSO-*d*₆) and EI-MS of this product are fully identical to those of **2a**. – Calcd. for C₂₁H₂₁N₃O₅ (395.41): C 63.79, H 5.35, N 10.63; found C 63.87, H 5.32, N 10.63.

3.1.4 Product **3**

3.1.4.1 Method B for compound **3** (from **2a**)

A solution of 1.19 g (10 mmol) of phenyl isocyanate in 40 mL of anhydrous acetonitrile was added dropwise

under stirring to a hot solution of 2.0 g (5 mmol) **2a** in 100 mL of anhydrous acetonitrile. After reflux for 34 h the reaction mixture was cooled and allowed to stay overnight at 0–5°C. The separated crystals were filtered off, washed with cold acetonitrile and recrystallized from acetonitrile. Yield: 1.56 g (60%) of **3** as colorless crystals with m.p. 146.5–148.5°C. – IR (nujol, cm^{−1}): ν = 3277–3146 (NH_{assoc.}), 1732 (C=O, carbamate), 1684 (C=O, ester), 1668, 1637 (C=O, amide). – ¹H NMR (100 MHz, DMSO-*d*₆): δ = 0.99 (t, *J* = 7 Hz, 3H, CH₃), ~2.49 (m, partially overlapped by solvent, 1H, 5-CH^A), 3.01–3.22 (dd, 1H, 5-CH^B), 3.93–4.04 (m, 2H, OCH₂), 4.48 (d, *J* = 8 Hz, 1H, 4-CH^A), 7.15–7.58 (m, 14H_{arom.}, 2×N–C₆H₅ and 4H_{arom.}), 10.24 (s, 1H, NH, D₂O-exchangeable), 10.42 (s, 1H, NH, D₂O-exchangeable), 11.15 (s, 1H, NH, D₂O-exchangeable), 11.21 (s, 1H, NH, D₂O-exchangeable). – ¹³C NMR (25 MHz, DMSO-*d*₆): δ = 14.1 (CH₃, ester), 29.9 (C-4), 37.3 (C-5), 59.8 (OCH₂, ester), 82.9 (C-3), 118.7 (2C, *ortho*, *N*-phenyl), 119.8 (2C, *ortho*, *N*-phenyl), 123.2 (C-3'), 123.6 (2C, *para*, *N*-phenyl), 126.1 (C-5'), 127.0 (C-4'), 127.9 (C-6'), 129.0 (4C, *meta*, *N*-phenyl), 135.3 (C-1', *ipso*), 138.4 (*ipso*, *N*-phenyl), 138.9 (*ipso*, *N*-phenyl), 148.1 (C-2', *ortho*, C-O), 149.6 (C=O, carbamate), 151.8 (C=O, urea), 153.1 (C-2), 168.1 (C=O, ester), 168.7 (C-6). – MS: *m/z* (%) = 395 (<1) [O–C₆H₅NCO]⁺, 276 (2) [M–2C₆H₅NCO]⁺, 230 (8) [M–2C₆H₅NCO–C₂H₅OH]⁺, 229 (11) [M–2C₆H₅NCO–C₂H₅OH–H]⁺, 146 (9), 119 (100) [C₆H₅NCO]⁺, 118 (9). – Calcd. for C₂₈H₂₆N₄O₆ (compound **4**) (514.53): C 65.36, H 5.09, N 10.89; found C 65.54, H 5.14, N 11.00.

3.1.5 1-(2,5-Dioxo-1,3,5,10*b*-tetrahydro-2*H*-chromeno[3,4-*c*]pyridin-4-yl)-3-phenylurea (**4**)

A solution of sodium ethoxide, prepared from 0.12 g (5 mmol) of sodium and 5 mL of anhydrous ethanol, was added dropwise under stirring to a suspension of 1.98 g (5 mmol) **2a** in 20 mL of anhydrous ethanol. The reaction mixture was set aside at room temperature for 30 days. Then the separated sodium salt was filtered, mixed with some water and acidified with acetic acid to pH ≈ 5. The precipitated product **4** was filtered, washed with water and recrystallized from ethanol. Yield: 0.23 g (13%) of colorless crystals with m.p. (open tube) 353–357°C (oxidized); m.p. (sealed tube) 260–262°C. – IR (cm^{−1}): ν = 3261–3204 (NH_{assoc.}), 1726 (C=O, lactone), 1691, 1660, (C=O). – ¹H NMR (100 MHz, DMSO-*d*₆): δ = 2.72 (d, partially overlapped by solvent signal, *J* = 15 Hz, 1H, 1-H^A), 3.17 (d, partially overlapped by water signal, *J* = 4 Hz, 1H, 1-H^B), 4.20, 4.35 (dd, *J*₁ = 4 Hz, *J*₂ = 15 Hz, 1H, 10*b*-H^X), 7.07–7.54 (m, 9H_{arom.}, *N*-phenyl and 7-H, 10-H), 10.61 (s, 1H, NH, D₂O-exchangeable),

11.26 (s, 1H, NH, D₂O-exchangeable), 11.41 (s, 1H, NH, D₂O-exchangeable). – EI-MS: *m/z* = 349 (4) [M]⁺, 348 (1) [M–H]⁺, 230 (29) [M–C₆H₅NCO]⁺, 229 (46) [O–C₆H₅NCO–H]⁺, 119 (100); isotope distribution of [M+1]⁺ corresponds to C₁₉H₁₆N₃O₄ (CI-MS, gas NH₃, 100 eV). – Calcd. for C₁₉H₁₅N₃O₄ (349.34): C 65.32, H 4.33, N 12.03; found C 65.07, H 4.36, N 11.80.

Product **4** could also be directly prepared from pyridone **1** after 6 h of reflux with phenyl isocyanate (molar ratio of 1:2; see Table 1, entry 4).

References

- [1] I. C. Ivanov, L. D. Raev, *Synth. Commun.* **1986**, *16*, 1679.
- [2] I. C. Ivanov, L. D. Raev, *Eur. J. Org. Chem.* **1987**, 1107.
- [3] I. C. Ivanov, L. D. Raev, *Arch. Pharm.* **1995**, *328*, 53.
- [4] L. D. Raev, E. Voinova, I. C. Ivanov, D. Popov, *Pharmazie* **1990**, *45*, 696.
- [5] L. D. Raev, W. Frey, I. C. Ivanov, *Synlett* **2004**, *9*, 1584.
- [6] A. G. Cook, *Enamines. Synthesis, Structure and Reactions*, Marcel Dekker, New York **1969**, pp. 396–401.
- [7] Fuji Photo Film Co. (M. Sugiyama, Inv.), D.O.S. 2552364 (May 26, 1976); *Chem. Abstr.* **1976**, *85*, P 95805h; *Japan Kokai* 7762202 (May 23, 1977); *Chem. Abstr.* **1977**, *87*, P 134757g.
- [8] I. C. Ivanov, L. D. Raev, P. B. Sulay, *Farmatsiya (Sofia)* **1984**, *34*, 14.
- [9] E. V. Stoyanov, I. C. Ivanov, *Molecules* **2004**, *9*, 627.
- [10] I. C. Ivanov, E. V. Stoyanov, S. V. Alexandrova, *Farmatsiya (Sofia)* **1997**, *44*, 3; *Chem. Abstr.* **1998**, *128*, 243925w.
- [11] M. Torres, S. Gil, M. Parra, *Curr. Org. Chem.* **2005**, *9*, 1757; and references cited therein.
- [12] E. V. Stoyanov, I. C. Ivanov, D. Heber, *Molecules* **2000**, *5*, 19.
- [13] L. D. Raev, I. C. Ivanov, H. A. Astroug, W. Frey, S. G. Agontseva, *Z. Naturforsch.* **2015**, *70b*, 797.
- [14] P. B. Sulay, I. C. Ivanov, *Eur. J. Org. Chem.* **1987**, 1101.
- [15] C. N. O'Callaghan, T. B. H. McMurry, J. E. O'Brien, S. M. Draper, *J. Chem. Res. (M)* **1997**, 2101.
- [16] G. E. H. Elgemeie, A. H. H. Elghandour, *Bull. Chem. Soc. Japan* **1990**, *63*, 1230.
- [17] E. M. Beccalli, A. Contini, P. Trimarco, *Tetrahedron Lett.* **2004**, *45*, 3447; and references cited therein.
- [18] L. J. Núñez-Vergara, J. A. Squella, P. A. Navarrete-Encina, E. Vicente-García, S. Preciado, R. Lavilla, *Curr. Med. Chem.* **2011**, *18*, 4761.
- [19] I. C. Ivanov, S. K. Karagiosov, M. F. Simeonov, *Eur. J. Org. Chem.* **1992**, 203.
- [20] D. Heber, I. C. Ivanov, S. K. Karagiosov, *J. Heterocycl. Chem.* **1995**, *32*, 505.
- [21] I. C. Ivanov, T. N. Glasnov, D. Heber, *J. Heterocycl. Chem.* **2005**, *42*, 857.

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