N-Acyl and *N*-Alkoxycarbonyl Derivatives of 1*H*-1,2,3-Triazolo-[4,5-*c*]pyridine; Preparation and Application

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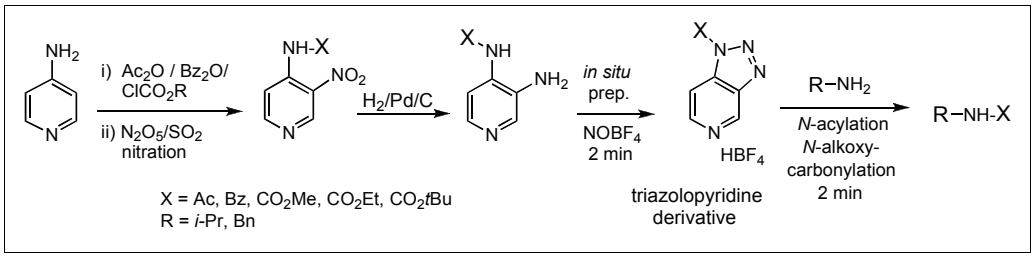

The *N*-acylating and *N*-alkoxycarbonylation ability of the *N*-substituted 1,2,3-triazolo[4,5-*c*]pyridines **1a-e** have been investigated. The alkoxycarbonyl triazolopyridine derivatives (**1c-e**) were readily prepared in 81-96 % yield (the corresponding tetrafluoroborate > 95 %). Triazolo[4,5-*c*]pyridine (**1**) has been shown to work as a good leaving group by the formation of amido- and carbamate protected derivatives of primary amines. The method was also successful for the *N*-*tert*-butoxycarbonyl (*N*-BOC) protection of the amino acid, phenylalanine. The synthetic transformations are facilitated by the one-pot preparation of **1a-e** followed by the direct reaction with the amines or amino acid. The present method thus offers an efficient and convenient protocol for the *in situ* preparation of triazolopyridine reagents to be used directly for the protection of amines and amino acids. *N*-Acyl- and *N*-alkoxycarbonyl triazolopyridines (**1a-e**) were readily prepared in 4 steps from 4-aminopyridine (**4**) by amine protection, pyridine nitration, nitro reduction and diazotizations/cyclizations. All reactions offer the advantages of rapid conversions in high yields under very mild conditions.

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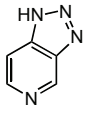
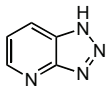
Introduction.

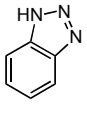
Some substituted 1,2,3-triazolopyridines (**1,2**) are analgesic, antipyretic, antiasthmatic or useful as inflammation inhibitors [1,2] while others have been patented for their anxiolytic antidepressant properties [3] and herbicidal activity [4]. The 1,2,3-triazolo[4,5-*c*]pyridine (**1**) is a commercially available fine chemical, but to our knowledge, only to a very high price. Substituted 1,2,3-triazolopyridines (**1,2**) have previously been prepared by amine substitution of a chloroaminopyridine followed by diazotization and cyclization [1,5]. Diazotization of ethyl 2-aminopyridyl-3-carbamate with isoamyl nitrite in acetic acid has been reported to give the ethyl 3-carbamate derivative of 1,2,3-triazolo[4,5-*b*]pyridine (**2**) [6] while 1,2,3-benzotriazole (**3**) has been synthesized in high yields by diazotization of *o*-phenylenediamine with sodium nitrite in acetic acid solution followed by cyclization [7-10].



1
1,2,3-triazolo[4,5-*c*]pyridine



2
1,2,3-triazolo[4,5-*b*]pyridine



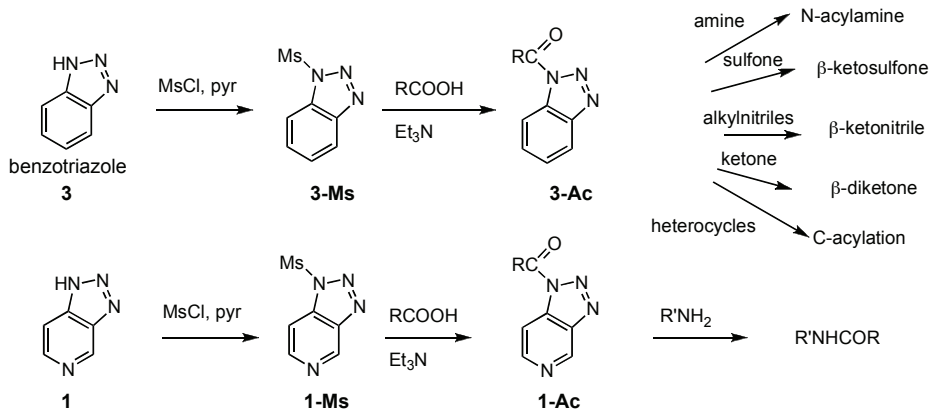
3
benzotriazole

The use of *N*-acylbenzotriazole (**3-Ac**, see Scheme 1) as an effective neutral acylating agent for the preparation of primary, secondary and tertiary amides has been reported by Katritzky *et al.* [11]. As an alternative to *N*-acylimidazole several advantages have been reported for the *N*-acylbenzotriazoles. They are stable crystalline non-volatile storable intermediates and allow the acyl group to be introduced and removed easily by simple work-up procedures.

Katritzky *et al.* have demonstrated the synthetic auxiliary properties of benzotriazole [12]. Due to the activation of the carbon to which the triazole is attached, a series of synthetic transformations can be performed. The reaction principle have been applied for the *C*-acylation of sulfones in the preparation of β-ketosulfones [13], of alkyl cyanides to α-substituted β-ketonitriles [14] and for the synthesis of β-dicarbonyl compounds [15], as well as for regiospecific *C*-acylation of heterocycles [16]. 1,2,3-Triazolo[4,5-*b*]pyridine (**2**) has also been studied for its acylation and alkoxycarbonylation abilities [6].

The high reactivity of these acylating agents is caused by the relative weakness of the "amide" bond; the aromatic character of the heterocycle makes the -:N-C=O less delocalized and therefore less stabilized compared to regular amides. Triazolopyridine (**1**) is expected to be an

Scheme 1



even better leaving group than benzotriazole **3** due to the π-electron-deficient character of the pyridine moiety.

We have investigated the corresponding *N*-acylating and *N*-alkoxycarbonylation properties of the triazolopyridine derivatives **1a-e** aiming at the formation of amido- and carbamate protected derivatives of primary amines and BOC amino acids. The method was also applied on one amino acid for the preparation of the *N-tert*-butylcarbonyl (BOC) derivative. The diazotization reactions of 3,4-diaminopyridine derivatives (**7a-e**) for the preparation of the 1,2,3-triazolopyridine derivatives (**1a-e**) have been studied. The key substrates for our syntheses of **1a-e** are 4-substituted 3-nitropyridines, which have now been readily available through an improved nitration method [17,18].

3,4-Diaminopyridine, which is a suitable substrate for the preparation of unsubstituted 1,2,3-triazolopyridine (**1**) [5], has also readily been prepared by the improved nitration method, affording higher yields [19] compared to previous methods [20].

Results and Discussion.

Preparation of Triazolopyridine Derivatives **1a-e**.

The acyl- and alkoxycarbonyl triazoles **1a-e** were readily available from 4-aminopyridine (**4**) *via* **7a-e** in four steps, as shown in Scheme 2. The nitration of 4-aminopyridine (**4**) was carried out after protection of the 4-amino group by acyl or alkoxycarbonyl groups to give **6a,b** and **6c-e**, respectively [19,21]. Methyl carbamate **6c** has also been prepared by nitration of methyl 4-pyridylcarboxylate (**5**) followed by diazotization of the hydrazide intermediate and Curtius rearrangement in methanol [22]. The amides (**7a,b**) and carbamates (**7c-e**) were obtained by selective reduction of the nitro group in quantitative yield by catalytic hydrogenation. As expected, traditional diazotization (sodium nitrite, sulfuric acid) of the methyl carbamate **7c** and cyclization of the diazonium intermediate afforded the non-derivatised triazolopyridine (**1**) in quantitative yield. However, by less vigorous diazotization conditions, using *iso*-amyl nitrite and tetrafluoroboric acid in ethanol or nitrosonium tetrafluoroborate in acetonitrile, the carbamates **7c-e** were readily converted to the alkoxycarbonyl triazolopyridines (**1c-e**) and isolated as the corresponding tetrafluoroborates in > 95 % yield. Respectively, the "free" triazolopyridine derivatives (**1c-e**) were prepared in 81-96 % yield by acetic acid and *iso*-amyl nitrite [6] for characterization. The *N*-acyltriazolopyridines (**1a,b**) were correspondingly obtained by *iso*-amyl nitrite/tetrafluoroboric acid or nitrosonium tetrafluoroborate diazotization of the amides **7a,b**. The hydrolysis product **1** was readily prepared by heating crystalline **1a** in sulfuric acid (2 %).

In general, either *iso*-amyl nitrite/tetrafluoroboric acid or nitrosonium tetrafluoroborate could be used for the diazotization and cyclization of **7a-e** to the triazolo products **1a-e**. ^{1}H nmr of the crude products showed quantitative and spontaneous formation of the cyclic products **1a-e** by both methods. The triazolopyridines **1a-e** are formed as tetrafluoroborates. Our experience was, however, that especially the amido products **1a,b** were sensitive to moisture due to water in the tetrafluoroboric acid solution. We observed that the amidotriazolo compounds **1a,b** were less stable than the carbamates **1c-e**, using the tetrafluoroboric acid/*iso*-amyl nitrite reaction conditions, since **1a,b** easily hydrolyzed to triazolopyridine **1** during work-up from the tetrafluoroboric acid solution. Nearly quantitative yields of all the crude products **1a-e** were obtained using nitrosonium tetrafluoroborate, as shown by ^{1}H nmr. To avoid hydrolysis of the triazolo derivatives **1a-e** we therefore preferred the milder nitrosonium tetrafluoroborate method.

The cyclization of **7a-e** to the triazolo compounds **1a-e** could easily be followed by ^{1}H nmr. Due to the deshielding effect of the triazolo moiety, unusual high pyridine proton frequencies were in particular observed

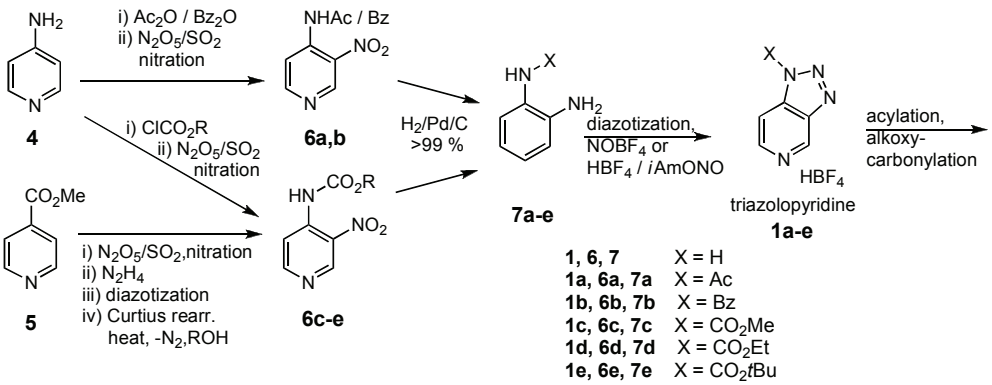
for H-2 for the tetrafluoroborates of **1a-e**. This is demonstrated by the pyridine chemical shift of H-2 of **1c** tetrafluoroborate; δ 9.89 in deuterochloroform and 10.33 in d_6-acetone, respectively. The ir spectra of the triazolo derivatives were also characteristic as shown by the high frequency strong carbonyl absorptions at approximately 1800 cm^{-1}, most predominant for the methyl carbamate (**1c**).

We experienced that the methoxy- and ethoxycarbonyl derivatives **1c,d** could be purified by flash chromatography and that the crystalline products **1c,d** could be stored at room temperature for weeks. The *tert*-butyl carbamate **1e** and the acyl compounds **1a,b** were however less stable and could neither be stored nor isolated by chromatography.

borates of the cyclic triazolopyridines **1a-e** by addition of nitrosonium tetrafluoroborate, the immediate reactions with the subsequently added *iso*-propylamine or benzylamine were complete within few minutes, as shown by ^{1}H nmr. The amine derivatives **8a-j** were isolated in 72 - 84 % yield by flash chromatography without extraction (Table 1). We observed that the *in situ* prepared triazolopyridine tetrafluoroborate reagents (**1c-e** tetrafluoroborates) were more reactive than the "free" triazolopyridine reagents (**1c-e**), due to the activation by protonation of the triazolopyridine in order to improve its leaving group ability.

Katritzky's method [11] (Scheme 1) is based on the non-derivatised benzotriazole substrate and involves an additional benzotriazole mesylation step (**3** to **3-Ms**) before acylation (**3-Ms** to **3-Ac**) and eventually the

Scheme 2



N-Acylation and *N*-Alkoxycarbonylation.

Due to their high reactivity, the prepared triazolopyridines **1a-e** were used immediately for the derivatization of amines. For synthetic use we thus developed a convenient method for the *in situ* preparation of **1a-e** followed by the direct reaction with amines (Scheme 3). After the spontaneous and complete conversion of the non-cyclic precursors **7a-e** to the corresponding tetrafluoro-

reaction with the substrate to be modified. By preparation of both the mesyltriazolopyridine **1-Ms** and benzotriazole **3-Ms** by the Katritzky method [11], the triazolopyridine **1-Ms** was, as expected, less stable than **3-Ms**. Similarly to the acyltriazolopyridines (**1a,b**) **1-Ms** had to be used for synthetic purposes immediately and could not be properly characterised or stored. Compared to the Katritzky methodology (in Scheme 1), following our protocol

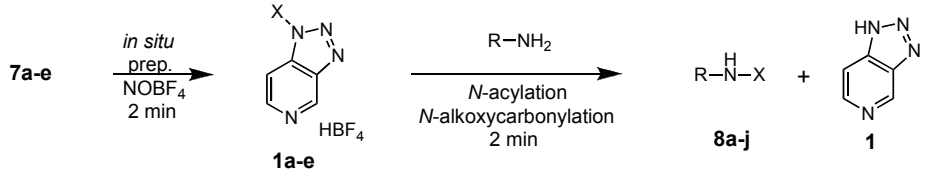
Table 1

Protection of *iso*-propyl- and benzylamine with triazolopyridine reagents **1a-e** (see Scheme 3).

Triazolopyridine	Amine	Product	Conversion/Yield [a]	[ref]
1a	*iso*-propylamine	**8a**; X = Ac, R = *i*-Pr	>99 % / 76 %	[23]
	benzylamine	**8b**; X = Ac, R = Bn	>99 % / 72 %	[24]
1b	*iso*-propylamine	**8c**; X = Bz, R = *i*-Pr	>99 % / 72 %	[25]
	benzylamine	**8d**; X = Bz, R = Bn	>99 % / 73 %	[26]
1c	*iso*-propylamine	**8e**; X = CO_2Me, R = *i*-Pr	>99 % / 76 %	[27]
	benzylamine	**8f**; X = CO_2Me, R = Bn	>99 % / 84 %	[28]
1d	*iso*-propylamine	**8g**; X = CO_2Et, R = *i*-Pr	>99 % / 73 %	[29]
	benzylamine	**8h**; X = CO_2Et, R = Bn	>99 % / 73 %	[30]
1e	*iso*-propylamine	**8i**; X =CO_2*t*-Bu, R = *i*-Pr	>99 % / 74 %	[31]
	benzylamine	**8j**; X = CO_2*t*-Bu, R = Bn	>99 % / 73 %	[32]

[a] Conversion is based on ^{1}H nmr of crude product reaction mixture. Yields are calculated after chromatography.

Scheme 3

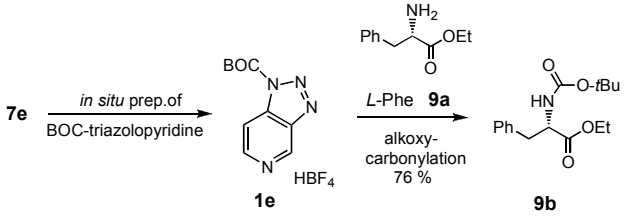


8a R = *i*-Pr, X = Ac **8b** R = Bn, X = Ac
8c R = *i*-Pr, X = Bz **8d** R = Bn, X = Bz
8e R = *i*-Pr, X = CO_2Me **8f** R = Bn, X = CO_2Me
8g R = *i*-Pr, X = CO_2Et **8h** R = Bn, X = CO_2Et
8i R = *i*-Pr, X = CO_2t-Bu **8j** R = Bn, X = CO_2t-Bu

(Scheme 2,3), the *N*-acyl or the *N*-alkoxycarbonyl groups have already been introduced, and the acyl- and alkoxycarbonyl triazoles (**1a-e**) can be made directly by diazotization and cyclization. For our purposes the mesylated intermediate (**1-Ms**) can thus be left out.

Protective groups are important in amino acid chemistry. Carbamates are in particular used as protective groups for amino acids to minimize racemization in peptide synthesis. Since the *tert*-butoxy carbamate (BOC) group, is extensively used for amino acid protection, the *tert*-butoxy carbonyl (BOC)-triazolopyridine method was applied on one amino acid to demonstrate the versatility of the method. In a similar manner as above for the primary amines, L-phenylalanine ethyl ester **9a** (Scheme 4) was reacted with BOC-triazolopyridine **1e**, prepared *in situ,* to give the BOC protected amino acid **9b**. The reaction was slower than the previous ones (**8a-j**) and full conversion to the BOC amino acid **9b**, was obtained in 4 days, as shown by ^{1}H nmr of the reaction mixture. After chromatography 76 % yield was obtained. The optical purity of the BOC protected amino acid **9b** was not lost during the reaction.

Scheme 4



Conclusion.

The *N*-acylating and *N*-alkoxycarbonylation ability of the 1,2,3-triazolopyridine derivatives **1a-e** were studied. The alkoxycarbonyl triazolopyridine derivatives (**1c-e**) were readily prepared in 81-96 % yield and the corresponding tetrafluoroborates in > 95 % yield. 1,2,3-Triazolo[4,5-*c*]pyridine (**1**) has been shown to work as a good leaving group in the acylation and alkoxycarbonylation of amines. The method was also successful for the *N*-*tert*-butyl carbamate (*N*-BOC) protection of the amino acid phenylalanine (**9a**). The protection reactions of *iso*-propyl- and benzylamines were complete within few minutes and the amides and carbamates **8a-j**, were isolated in 72 -84 % yield. Longer reaction time was needed for the amino acid since L-phenylalanine was converted to the BOC protected amino acid (76 %) in 4 days.

The synthetic transformations were facilitated by development of the *in situ* preparation method of **1a-e** to offer the advantages of a one-pot procedure. *N*-Acyl- and *N*-alkoxycarbonyl-1,2,3-triazolo[4,5-*c*]pyridine (**1a-e**) were readily prepared in 4 steps from 4-aminopyridine (**4**) by amine protection, pyridine nitration, nitro reduction and diazotization/cyclization.

Our strategy thus offers an efficient and convenient protocol for the *in situ* preparation of triazolopyridine reagents to be used directly for the protection of amines. All reactions are performed quickly in high yields under very mild conditions. The triazolopyridine method may have a synthetic potential for a series of transformations and may represent a supplement to the benzotriazole methodology.

EXPERIMENTAL

Chemicals: Nitrosonium tetrafluoroborate (Sigma), tetrafluoroboric acid and *iso*-propylamine (Acros), *iso*-amyl nitrite and benzylamine (Fluka); solvents: *pro analysi* quality. ^{1}H/^{13}C nmr: Bruker Avance DPX 300 and 400 MHz spectrometers, chemical shifts are reported in ppm downfield from tetramethyl silane. Hexafluorobenzene was correspondingly used as reference for ^{19}F nmr. J values are given in Hz. ms: Finnigan MAT 95 XL (EI / 70 eV). ir: Nicolet 20SXC FT-IR spectrophotometer. All melting points are uncorrected, measured by Griffin apparatus. Elemental analysis was measured by an Elementar Vario III instrument at the Institute of Chemical Technology, Prague. Flash chromatography: Silica (sds, 60 Å, 40-63 μm). The intermediates **6a-e** and **7a-e** were prepared by nitration and reduction according to the literature [21,33-35].

Triazolopyridine Derivatives (**1a-e**).

Tetrafluoroborates were prepared for characterization by the following general diazotization procedure: A solution of **7a-e**

(100 mg, 0.47-0.66 mmol), tetrafluoroboric acid (43-63 mg, 1.05 equivalent) and *iso*-amyl nitrite (58-81 mg, 1.05 equiv.) in ethanol (1 ml) was stirred at 0 °C for approx. 15 minutes. The product **1a-e** were afforded as tetrafluoroborates, pure by ^{1}H nmr. The acyl (**1a,b**) and the *tert*-butyl carbamate (BOC, **1e**) products easily hydrolyzed into the non-derivatised triazolopyridine 1 by extraction and isolation and were therefore prepared *in situ* (see below) and used directly in the next step without further purification. Only methoxy- and ethoxycarbonyltriazolopyridine (**1c,d**) were fully characterized as their respective tetrafluoroborates, while the "free" methoxy, ethoxy and *tert*-butoxy triazolopyridine derivatives (**1c,d,e**) were characterized after preparation by acetic acid and *iso*-amyl nitrite [6]. For synthetic use, all compounds **1a-e** were prepared *in situ* and reacted directly with the amines, see general *N*-acylation/*N*-alkoxycarbonylation procedure below.

1-Acetyl-1*H*-1,2,3-triazolo[4,5-*c*]pyridine (**1a**) Tetrafluoroborate.

This compound was prepared from **7a**, pure by ^{1}H nmr (quantitative conversion); ^{1}H nmr (300 MHz, d_6-dimethyl sulfoxide): δ 3.01 (s, 3H), 8.46 (d, J 6.2, 1H, H-5), 8.60 (d, J 6.2, 1H, H-6), 9.86 (s, 1H, H-2); ^{13}C nmr (100 MHz, d_6-dimethyl sulfoxide): δ 12.6, 111.1, 135.8, 139.7, 142.4, 143.1, 170.0. ^{19}F nmr (376 MHz, d_6-dimethyl sulfoxide) δ -148.8.

1-Benzoyl-1*H*-1,2,3-triazolo[4,5-*c*]pyridine (**1b**) Tetrafluoroborate.

This compound was prepared from **7b**, pure by ^{1}H nmr (quantitative conversion); ^{1}H nmr (400 MHz, deuteriochloroform): δ 7.38 (m, 2H, Ph-H), 7.52 (m, 1H, Ph-H), 7.86 (d, J 7.2, 2H), 8.33 (d, J 6.8, 1H, H-5), 8.60 (d, J 6.8, 1H, H-6), 9.81 (s, 1H, H-2); ^{13}C nmr (100 MHz, deuteriochloroform): δ 110.7, 128.4, 129.0, 129.3, 133.5, 135.1, 138.5, 140.0, 140.6, 169.8. ^{19}F nmr (376 MHz, d_6-dimethyl sulfoxide) δ -148.3.

1-Methoxycarbonyl-1*H*-1,2,3-triazolo[4,5-*c*]pyridine (**1c**) Tetrafluoroborate.

This compound was prepared from **7c**, pure by ^{1}H nmr (quantitative conversion). **1c** tetrafluoroborate precipitated quantitatively from the reaction solution and could be recrystallized (> 95 %); mp 156-157 °C (acetone). ir (potassium bromide) 3274s, 3147m, 3087m, 2969w, 1800s, 1644s, 1618m, 1552m, 1474s, 1437m, 1369m, 1253s, 1090s, 943m, 911s cm^{-1}; ^{1}H nmr (400 MHz, d_6-dimethyl sulfoxide): δ 4.30 (s, 3H), 8.38 (d, J 6.1, 1H, H-5), 8.89 (d, J 6.1, 1H, H-6), 9.89 (s, 1H, H-2); correspondingly in d_6-acetone: δ 4.37 (s, 3H), 8.88 (d, J 6.8, 1H, H-5), 9.25 (d, J 6.8, 1H, H-6), 10.33 (s, 1H, H-2); ^{13}C nmr (75 MHz, d_6-dimethyl sulfoxide): δ 56.0, 110.6, 135.8, 140.6, 142.4, 145.4, 148.2; ^{19}F nmr (376 MHz, d_6-dimethyl sulfoxide) δ -148.5.

Anal. Calcd. for $C_7H_7BF_4N_4O_2$: C, 31.61; H, 2.65; N, 21.07. Found: C, 31.67; H, 2.54; N, 20.85.

1-Methoxycarbonyl-1*H*-1,2,3-triazolo[4,5-*c*]pyridine (**1c**).

Free **1c** was prepared according to literature [6] to give 92 % yield, pure by ^{1}H nmr; mp 139-140 °C; ir (potassium bromide) 3106m, 3000w, 2972w, 1794s, 1626m, 1475m, 1448m, 1377s, 1330m, 1256s, 1213s, 1181s, 1062s, 922m, 844m, 759m, 587m cm^{-1}; ^{1}H nmr (300 MHz, deuteriochloroform): δ 4.28 (s, 3H), 8.03 (dd, J 1.1, 5.7, 1H, H-2), 8.78 (d, J 5.7, 1H, H-6), 9.60 (d, J 1.1, 1H, H-5); ^{13}C nmr (75 MHz, d_6-dimethyl sulfoxide): δ 56.2, 108.4, 136.5, 143.3, 145.1, 148.6, 149.3; ms: m/z 178 (M^+, 51 %), 150 (13), 135 (53), 119 (15), 107 (100), 91 (12), 80 (26); HRMS: calcd for $C_7H_6N_4O_2$; 178.04908, observed 178.04917.

1-Ethoxycarbonyl-1*H*-1,2,3-triazolo[4,5-*c*]pyridine (**1d**) Tetrafluoroborate.

This compound was prepared from **7d**, pure by ^{1}H nmr (quantitative conversion, > 95 % isolated yield); mp 143.5-144.5 °C (pentane); ir (potassium bromide) 3066w, 1771s, 1635s, 1613s, 1558m, 1498m, 1323s, 1109s, 1070s, 1018s, 958m, 838m, 786s, 713m cm^{-1}; ^{1}H nmr (300 MHz, d_6-dimethyl sulfoxide): δ 1.60 (t, J 7.1, 3H), 4.75 (q, J 7.1, 2H), 8.30 (d, J 6.1, 1H, H-2), 8.88 (d, J 6.1, 1H, H-6), 9.85 (s, 1H, H-5); ^{13}C nmr (75 MHz, d_6-dimethyl sulfoxide): δ 13.9, 65.9, 109.6, 136.8, 142.2, 143.0, 145.1, 147.5; ^{19}F nmr (376 MHz, d_6-dimethyl sulfoxide) δ -148.1.

Anal. Calcd. for $C_8H_9BF_4N_4O_2$: C, 34,32; H, 3,24; N, 20,01. Found: C, 33.98; H, 3,23; N, 19,75.

1-Ethoxycarbonyl-1*H*-1,2,3-triazolo[4,5-*c*]pyridine (**1d**).

Free **1d** was prepared according to literature [6] to give 96 % yield, pure by ^{1}H nmr; mp 170-171 °C; ir (potassium bromide) 3159m, 2989m, 1790s, 1710s, 1593m, 1514m, 1477m, 1401w, 1366m, 1319w, 1231s, 1062s, 837w, 795w, 772w cm^{-1}; ^{1}H nmr (300 MHz, deuteriochloroform): δ 1.61 (t, J 7.1, 3H), 4.74 (q, J 7.1, 2H), 8.04 (dd, J 1.0, 5.7, 1H, H-2), 8.78 (d, J 5.7, 1H, H-6), 9.56 (d, J 1.0, 1H, H-5); ^{13}C nmr (75 MHz, deuteriochloroform): δ 13.8, 65.5, 107.7, 135.6, 142.4, 144.2, 147.6, 147.9; ms: m/z 192 (M^+, 25 %), 164 (6), 136 (100), 120 (54), 105 (2), 92 (61), 80 (12); HRMS: calcd for $C_8H_8N_4O_2$; 192.0647 observed 192.06419.

1-*tert*-Butoxycarbonyl-1*H*-1,2,3-triazolo[4,5-*c*]pyridine (**1e**) Tetrafluoroborate.

This compound was prepared from **7e**, pure by ^{1}H nmr (quantitative conversion, > 95 % isolated yield); ^{1}H nmr (300 MHz, d_6-dimethyl sulfoxide): δ 1.72 (s, 9H), 8.35 (d, J 6.4, 1H, H-5), 8.84 (d, J 6.4, 1H, H-6), 9.97 (s, 1H, H-2); ^{13}C nmr (100 MHz, deuteriochloroform): δ 27.7, 89.9, 111.8, 135.9, 141.7, 142.8, 146.0, 149.4; ^{19}F nmr (376 MHz, d_6-dimethyl sulfoxide) δ -148.9.

1-*tert*-Butoxycarbonyl-1*H*-1,2,3-triazolo[4,5-*c*]pyridine (**1e**).

Free 1e was prepared from **7e** and nitrosonium tetrafluoroborate and added triethyl amine to give 81 % yield of free **1e**, pure by ^{1}H nmr; mp 87-88 °C; ir (potassium bromide) 3004m, 2989m, 1782m, 1709s, 1601w, 1364s, 1321w, 1255m, 1222m, 1152m, 1092m, 1040m, 930w, 828w cm^{-1}; ^{1}H nmr (400 MHz, deuteriochloroform): δ 1.79 (s, 9H), 7.98 (dd, J 0.8, 5.6, 1H, H-2), 8.74 (d, J 5.6, 1H, H-6), 9.52 (s, 1H, H-5); ^{13}C nmr (100 MHz, deuteriochloroform): δ 27.9, 88.0, 108.1, 135.9, 142.9, 144.5, 146.5, 147.7.

1-Methylsulfonyl-1*H*-1,2,3-triazolo[4,5-*c*]pyridine (**1-Ms**).

This compound was made according to the procedure for *N*-(1-methanesulfonyl)benzotriazole (**3-Ms**) [11] in 30 % yield. The compound was unstable and could not be isolated for full characterization; ^{1}H nmr (300 MHz, deuteriochloroform): 3.54 (s, 3H), 7.86 (dd, J 5.80, 1H), 8.69 (d, J 5.80, 1H), 9.47 (d, J 1.0, 1H); ^{13}C nmr (75 MHz, deuteriochloroform): δ 43.1, 106.6, 135.8, 141.9, 144.8, 147.9. IR (film): 3651, 3422, 2254, 1598, 1386, 1255, 1194, 1179, 967, 734 cm^{-1}; ir (potassium bromide) 1598w, 1386m, 1193s, 1179s cm^{-1};

1*H*-1,2,3-Triazolo[4,5-*c*]pyridine (**1**).

A solution of **7c** (120 mg, 0.72 mmol), in water (6 ml) was drop-wise added sulfuric acid (conc. 0.1 ml). The mixture was stirred, cooled to 0 °C and drop-wise added a solution of sodium nitrite (124 mg, 1.8 mmol, 2.5 equivalents) in water (3 ml) during 10 minutes. The reaction mixture was left stirring at 0 °C for 1 hour and refluxed for 3 hours. The pH was adjusted to 5-6 by addition of a saturated sodium carbonate solution. An off-white crystalline product, pure by ^{1}H nmr, was obtained after extraction, drying and evaporation of the solvent (85 mg, 99 %). **1** was also quantitatively prepared from triazolo carbamate **1c** by heating in 2 % sulfuric acid for 20 minutes; mp 186-187 °C; ir (potassium bromide) 3414m, 1625m, 1457w, 1323w, 1139s, 995m, 620s cm^{-1}; ^{1}H nmr (300 MHz, d_6-dimethyl sulfoxide): δ 7.89 (d, J 5.9, 1H, H-5), 8.49 (d, J 5.9, 1H, H-6), 9.47 (s, 1H, H-1); ^{13}C nmr (75 MHz, d_6-dimethyl sulfoxide): δ 107.5, 139.0, 140.0, 141.7, 142.4; ms: m/z 120 (M$^+$, 100 %), 92 (81), 65 (48), 52 (20); HRMS: calcd for $C_5H_4N_4$ 120.04360, observed 120.04329.

N-Acylation and *N*-Alkoxycarbonylation of Primary Amines by **1a-e,** Prepared *in situ*.

The amides and carbamates **8a-j** [23-32] were prepared from *iso*-propylamine or benzylamine, respectively, and **1a-e**, prepared *in situ* from **7a-e**, by the following general procedure: The appropriate 3-amino-4-pyridyl carbamate (**7a-e**, 0.5 – 1.0 mmol, 1.1 equivalents) was dissolved in dry acetonitrile (3 ml) under N_2 atmosphere. Nitrosonium tetrafluoroborate (1.1 equivalent) in dry acetonitrile (3 ml) was cooled to 0 °C under nitrogen atmosphere and the aminocarbamate (**7a-e**) solution was added drop-wise. After stirring for 20 minutes cooling was removed. *Iso*-propylamine or benzylamine (1 equivalent) was dissolved in dry acetonitrile (1 ml) and added drop-wise at room temperature. The products **8a-j** were isolated in 72 - 84 % yield (see Table 1) by flash chromatography (20 % ethyl acetate in hexane) without previous extraction and characterized in accordance with literature data [23-39].

N-iso-Propylacetamide **8a** [23]: (76 %); ^{1}H nmr (300 MHz, deuteriochloroform): δ 5.34 (br, 1H), 4.06 (hept, J 6.6, 1H), 1.95 (s, 3H), 1.15 (d, J 6.6, 6H).

N-Benzylacetamide **8b** [24]: (72 %); ^{1}H nmr (300 MHz, deuteriochloroform): δ 7.24-7.31 (m, 5H), 6.53 (br, 1H), 4.35 (d, J 5.5, 2H), 1.95 (s, 3H).

N-iso-Propylbenzamide **8c** [25, 38]: (72 %).

N-Benzylbenzamide **8d** [26, 39]: (73 %).

Methyl *N-iso*-propylcarbamate (**8e**) [27]: (76 %); ^{1}H nmr (400 MHz, deuteriochloroform): δ 1.15 (d, J 6.4, 6H), 3.65 (s, 3H), 3.80 (m, 1H), 4.49 (br., 1H).

Methyl *N*-benzylcarbamate (**8f**) [28]: (84 %); ^{1}H nmr (300 MHz, deuteriochloroform): δ 7.27 (m, 5H), 5.19 (br, 1H), 4.33 (d, J 5.8, 2H), 3.67 (s, 3H).

Ethyl *N-iso*-propylcarbamate (**8g**) [29]: (73 %); ^{1}H nmr (300 MHz, deuteriochloroform): δ 1.15 (d, J 6.5, 6H), 1.24 (t, J 7.1, 3H), 3.81 (m, 1H), 4.11 (q, J 7.1, 2H), 4.55 (br, 1H).

Ethyl *N*-benzylcarbamate (**8h**) [30]: (73 %); ^{1}H nmr (300 MHz, deuteriochloroform): δ 7.27 (m, 5H), 5.18 (br, 1H), 4.32 (d, J 5.9, 2H), 4.11 (q, J 7.1, 2H), 1.23 (t, J 7.1, 3H).

tert-Butyl *N-iso*-propylcarbamate (**8i**) [31]: (74 %); ^{1}H nmr (400 MHz, deuteriochloroform): δ 4.35 (br, 1H), 3.76 (m, 1H), 1.46 (s, 9H), 1.14 (d, J 6.4, 6H).

tert-Butyl *N*-benzylcarbamate (**8j**) [32]: (73 %); ^{1}H nmr (300 MHz, deuteriochloroform): δ 7.28 (m, 5H), 4.89 (br, 1H), 4.30 (d, J 5.7, 2H), 1.46 (s, 9H).

N-Alkoxycarbonylation of L-phenylalanine Ethyl Ester **9a**.

L-Phenylalanine ethyl ester *N-tert*-butyl carbamate (**9b**) [36] was prepared from L-phenylalanine ethyl ester hydrochloric salt **9a** and *tert*-butoxycarbonyltriazolopyridine **1e** (prepared *in situ* from **7e**) as described above for the amine derivatives **8i** and **8j**. However, larger excess of BOC-triazolopyridines **1e** (2 equivalents) was used and the reaction was performed in the presence of triethyl amine (2 equivalents). Four days reaction time was needed to obtain 76 % yield after flash chromatography (20 % ethyl acetate in hexane). The product was characterized according to literature [37].

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