Tetrahedron 74 (2018) 2030–2040

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Aminothiazoles and aminothiadiazoles as nucleophiles in aminocarbonylation of iodobenzene derivatives

Máté Gergely [a], László Kollár [a, b, *]

[a] Department of Inorganic Chemistry, University of Pécs and Szentágothai Research Centre, H-7624 Pécs, P.O. Box 266, Hungary
[b] MTA-PTE Research Group for Selective Chemical Syntheses, H-7624 Pécs, Ifjúság u. 6, Hungary

ARTICLE INFO

Article history:
Received 15 January 2018
Received in revised form
1 March 2018
Accepted 4 March 2018
Available online 6 March 2018

Keywords:
Palladium
Iodoarene
Thiazole
Carbonylation
Carbon monoxide
Carboxamide

ABSTRACT

Various 2-, 3- and 4-substituted iodobenzenes were aminocarbonylated using aminothiazole and aminothiadiazole derivatives in palladium-catalysed reaction. The reaction is chemospecific toward the corresponding carboxamides. Consequently, the application of the above *N*-nucleophiles provided the *N*-1,3-thiazol-2-yl- and *N*-1,3,4-thiadiazol-2-ylcarboxamides in moderate to high yields. Due to the facile work-up of the reaction mixture isolated yields of 90% or higher were obtained in most cases.

© 2018 Elsevier Ltd. All rights reserved.

1. Introduction

Among heterocycles, thiazoles and especially 1,3,4-thiadiazoles represent families of biological importance.[1] Functionalized 1,3,4-thiadiazole derivatives provided pharmacological effect in a wide spectrum, and several compounds have found applications in material science.[2]

Therefore, the facile synthetic procedures targeting these heterocycles are still in the focus. The synthetic approaches and medical significance of 1,3,4-thiadizoles were reviewed recently.[3]

One of the most efficient homogeneous catalytic reactions of practical importance is the palladium-catalysed aminocarbonylation, *i.e.*, the carbonylation of iodo- or bromoarenes (or their synthetic surrogates, aryl triflates) in the presence of *N*-nucleophiles ('Heck-carbonylation').[4] During the past three decades the efficiency and applicability of this reaction have been proved for the wide variety of compounds including the structure of both the substrates and nucleophiles. The influence of the reaction conditions (CO pressure, temperature, base added) on the chemoselectivity, *i.e.*, the ratio of carboxamides and 2-ketocarboxamides formed in single and double CO insertion, respectively, was also investigated in detail.[5] It has to be added that the analogous substrates, iodoalkenes (or their synthetic surrogates, enol triflates) can be aminocarbonylated mainly with high chemoselectivity toward the corresponding carboxamides.[6]

The synthesis of several thiadiazole-based carboxamides, as well as their biological investigations were published. The introduction of carboxamide functionality into the thiazole and thiadiazole ring is of practical importance because there are several families of compounds possessing pharmacological effect. For instance, carboxamides of aminothiadiazole derivatives have shown good antagonist activity for human EP_3.[7] Among other substituents, the introduction of amide-functionalities into various positions of benzothiazoles and benzothiadiazoles leads to compounds of antioxidant and radioprotective effects.[8] The antiproliferative activity of N-substituted 2-amino-1,3,4-thiadiazoles,[9] as well as their cytotoxicity were studied.[10] Starting from 4-hydroxy-3-methoxybenzaldehyde novel thiadiazole-based TRPV1 antagonists were synthesised.[11]

To the best of our knowledge, there are only sporadic results for the application of homogeneous catalytic approaches for the functionalization of thiadiazole nucleus. As an example of synthetic interest, C–H arylation in Pd/Cu-catalysed reaction should be mentioned.[12]

* Corresponding author. Department of Inorganic Chemistry, University of Pécs and Szentágothai Research Centre, H-7624 Pécs, P.O. Box 266, Hungary.
E-mail address: kollar@gamma.ttk.pte.hu (L. Kollár).

https://doi.org/10.1016/j.tet.2018.03.007
0040-4020/© 2018 Elsevier Ltd. All rights reserved.

Since the above functionalizations of thiazole and thiadiazole nuclei were carried out mainly by using conventional synthetic methodologies, we were prompted to investigate some catalytic approaches. In this way, the high-yielding catalytic aminocarbonylation of various iodoaromatics with aminothiazole and aminothadiazole nucleophiles was carried out.

2. Results and discussion

2.1. Aminocarbonylation of 4-substituted iodobenzenes with 2-amino-1,3,4-thiadiazole derivatives (*a-c*) under atmospheric carbon monoxide pressure

Iodobenzene (**1**) and 4-substituted iodobenzenes (**2**–**13**) were aminocarbonylated using 2-amino-1,3,4-thiadiazole derivatives (**a-c**), *i.e.*, the parent 2-amino-1,3,4-thiadiazole (**a**) and the *tert*-butyl- (**b**) and trifluoromethyl-substituted (**c**) *N*-nucleophiles (Scheme 1). The aminocarbonylation was carried out at low (atmospheric) and high (40 bar) pressure of carbon monoxide at various temperatures (30, 50 and 70 °C) (Table 1). A well-known, widely applied palladium(0) catalyst, formed *in situ* from palladium(II) acetate and triphenylphosphine, was used. Both the mechanistic details including the catalytic cycles[5] and the formation of palladium(0) species were discussed.[13]

The aminocarbonylation is highly chemoselective toward carboxamides. No other products, for instance 2-ketocarboxamide type derivatives, were detected. These compounds are typically formed in the aminocarbonylation of aromatic iodides using primary and secondary amines as nucleophiles.[14] The aminothiadiazole nucleophiles (**a-c**) gave the characteristic carboxamide-specific reaction of aryl amines. Similarly to those reactions carried out with aniline derivatives[15] no 2-ketocarboxamide formation due to double CO insertion was observed with **a-c** even under 40 bar CO pressure.

It was revealed by detailed analysis of the samples taken after 2, 6, 12 and 24 h reaction time, that the increase in the temperature, while the CO pressure was kept at 1 bar, resulted in increased reactivity (Table 1, *entries 1–3*, Fig. 1 *(upper)*). Similar tendencies were observed with nucleophiles **b** and **c** (*entries 7,8 and 9, 10*, respectively). Carrying out the aminocarbonylation with **a**n under 40 bar CO pressure, no increased activity was observed (*entries 4–6*, Fig. 1 *(bottom)*). In turn, negligible activity was observed at 30 °C.

The aminocarbonylation of the *t*Bu- and CN-substituted iodobenzenes (**2** and **13**, respectively) showed similar features (*entries 11–16 and 17–20*, Fig. 2). The only exception was the aminocarbonylation of **13** (possessing an electron-withdrawing group, CN) with nucleophile **c** (possessing an electron-withdrawing group, CF_3) where the desired product **13c** was formed in traces only even at 50 and 70 °C, therefore its full characterization was failed. Comparing the amine nucleophiles (**a-c**), similar reactivities were obtained in the aminocarbonylation of **1** (Fig. 3).

Under optimized conditions all carboxamides (**1a-13a**, **1b**, **2b**, **13b**, **1c**, **2c**) were obtained with practically full conversion and isolated in good to excellent yields (Fig. 4). Not only 4-substituted iodoarenes but 2-iodoanisole (**14**) and 2-iodothiophene (**15**), as well as selected 3-substituted iodobenzenes (**16** and **17**) were aminocarbonylated efficiently.

Table 1
Aminocarbonylation of 4-substituted iodobenzenes (**1**, **2**, **13**) and 3-substituted iodobenzenes (**16**, **17**) in the presence of $Pd(OAc)_2$/2 PPh_3 *'in situ'* catalyst using 2-amino-1,3,4-thiadiazol derivatives (**a-c**)[a].

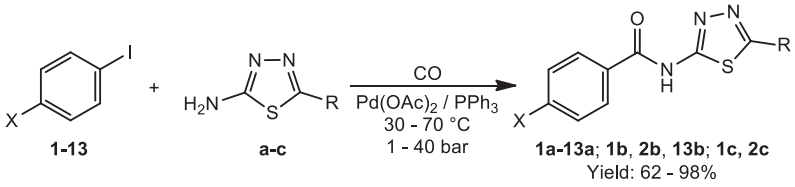
Entry	Substrate	Amine	Time [h]	p(CO) [bar]	Temp. [°C]	Conv.[b] [%]
1	**1**	**a**	24	1	30	51
2	**1**	**a**	24	1	50	87
3	**1**	**a**	6	1	70	>98
4	**1**	**a**	24	40	30	<1
5	**1**	**a**	24	40	50	82
6	**1**	**a**	12	40	70	>98
7	**1**	**b**	24	1	50	88
8	**1**	**b**	6	1	70	>98
9	**1**	**c**	24	1	50	81
10	**1**	**c**	24	1	70	98
11	**2**	**a**	24	1	50	68
12	**2**	**a**	6	1	70	>98
13	**2**	**b**	24	1	50	82
14	**2**	**b**	6	1	70	>98
15	**2**	**c**	24	1	50	69
16	**2**	**c**	24	1	70	84
17	**13**	**a**	6	1	50	34
18	**13**	**a**	6	1	70	>98
19	**13**	**b**	6	1	50	19
20	**13**	**b**	6	1	70	>98
21	**13**	**c**	24	1	50	<1
22	**13**	**c**	24	1	70	<1
23	**16**	**a**	2	1	70	>98
24	**17**	**a**	2	1	70	>98

[a] Reaction conditions: 1 mmol substrate (**1**, **2**, **13**, **16** or **17**), 1.2 mmol 2-amino-1,3-thiazole nucleophile (**a**, **b** or **c**); 0.025 mmol of $Pd(OAc)_2$, 0.05 mmol of PPh_3, 0.5 mL of Et_3N, 10 mL of DMF.
[b] Determined by GC and GC–MS.

2.2. Aminocarbonylation of 4-substituted iodobenzenes (*1–13*) with 2-amino-1,3-thiazole (*d*)

The set of 4-substituted iodobenzenes were aminocarbonylated using 2-amino-1,3-thiazol (**d**) under various conditions (Scheme 2). As above, the reaction was found perfectly chemoselective and the corresponding carboxamides (**1d-13d**) were isolated in 75–94% yields. In addition, four further substrates (**14**, **15**, **16** and **17**) were aminocarbonylated and the isolated carboxamides (**14d**, **15d**, **16d** and **17d**) were fully characterized (Fig. 7).

By the variation of the reaction conditions, similar features as in case of nucleophile **a-c** were observed. The use of higher reaction temperature (70 °C) resulted in increase in conversion (Table 2, *entries 1–3;* Fig. 5 *(upper diagram)*). A specially high reactivity was observed with **13** (*entries 6,7*), The application of high pressure



X = H (**1**), *t*Bu (**2**), CH_3 (**3**), OCH_3 (**4**), Ph (**5**), F (**6**), Cl (**7**), Br (**8**), COOH (**9**), $COOCH_3$ (**10**), $C(O)CH_3$ (**11**), CF_3 (**12**), CN (**13**)
R = H (**a**), *t*Bu (**b**), CF_3 (**c**)

Scheme 1. Aminocarbonylation of 4-substituted iodobenzenes (**1**–**13**) with 2-amino-1,3,4-thiadiazol derivatives (**a-c**).

Download English Version:

https://daneshyari.com/en/article/7827310

Download Persian Version:

https://daneshyari.com/article/7827310

Daneshyari.com