[^{11}C]Carbon Monoxide in Selenium-Mediated Synthesis of ^{11}C-Carbamoyl Compounds

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Using either amines, amino alcohols, or alcohols in selenium-mediated synthesis with [^{11}C]carbon monoxide, 3 ureas, 6 carbamates, and 1 carbonate were labeled. Tetrabutylammonium fluoride ((TBA)F) was discovered to form a soluble and reactive complex with selenium and drastically increase the radiochemical yields. Of the selected carbamoyl compounds, one was a receptor ligand, one was an enzyme inhibitor, and one was a muscular relaxant pharmaceutical. The ^{11}C-target compounds were obtained in radiochemical yields ranging from low to almost quantitative and with specific radioactivity up to 1300 GBq/μmol. The radiochemical purity of the final products exceeded 98%. In one case, the corresponding ^{13}C-substituted compound was produced to verify the position of the ^{11}C-label. In a typical experiment starting with 16.4 GBq [^{11}C]carbon monoxide, 7.0 GBq of LC-purified 5-phenyl-1,3-oxazolidin-[2-^{11}C]-2-one was obtained within 20 min from start of the carbonylation reaction (84% decay-corrected radiochemical yield). The presented approach is an interesting alternative to the use of [^{11}C]phosgene in labeling chemistry.

Introduction

In positron emission tomography (PET) tracers labeled with short-lived positron emitting radionuclides (e.g. ^{11}C, $t_{1/2} = 20.3$ min) are used for noninvasive in vivo studies.[1] Special synthetic methods are required for the production of PET tracers because of the short half-lives and the submicromole quantities involved.[2] Development of new ^{11}C-labeled precursors and new synthetic labeling strategies is important not only to increase the number of compounds that can be labeled but also to give the option to label a given compound in selected positions.[3] Throughout the development of a synthetic labeling method using short-lived radionuclides, the recognition of time as a parameter in the same category as chemical yield is important.[4]

Carbamoyl groups are common in biologically active compounds such as pharmaceuticals and are thus an important target for ^{11}C-labeling. The use of [^{11}C]phosgene has been the most common approach for ^{11}C-labeling of carbamoyl compounds. Phosgene is highly reactive, which means that good yields can be obtained at short reaction times with a broad range of substrates. However, the methods for [^{11}C]phosgene production have had some disadvantages. The systems used for [^{11}C]phosgene production need careful maintenance, such as a frequent change of catalysts, and if systems are used occasionally, the reliability is poor. The decay corrected radiochemical yield of [^{11}C]phosgene is usually in the range 30−50%, and the specific radioactivity (i.e. the ratio of radioactivity to mass) of labeled tracer is in the range 20−30 GBq/μmol. This is significantly lower than the corresponding value for tracers labeled with [^{11}C]methyl iodide.[5] In another method [^{11}C]carbon dioxide has been utilized for labeling of ureas in a three-step reaction, via dehydration of intermediately formed carbamate salts.[6] The scope of this method has not been fully investigated, but the use of phosphoryl chloride is likely to limit the range of functional groups that can be present. The specific radioactivity obtained using the [^{11}C]carbon dioxide method was also low (i.e., 25 GBq/μmol), probably due to isotopic dilution from atmospheric carbon dioxide.

During the last 6 years we have been investigating the scope and limitation of labeling methods using [^{11}C]carbon monoxide, primarily in palladium-mediated reactions.[7] A crucial step in this work was the advent of a method that made it possible to efficiently use [^{11}C]carbon monoxide in labeling synthesis.[8] The low solubility and reactivity[9] makes it difficult or impossible to trap [^{11}C]car-

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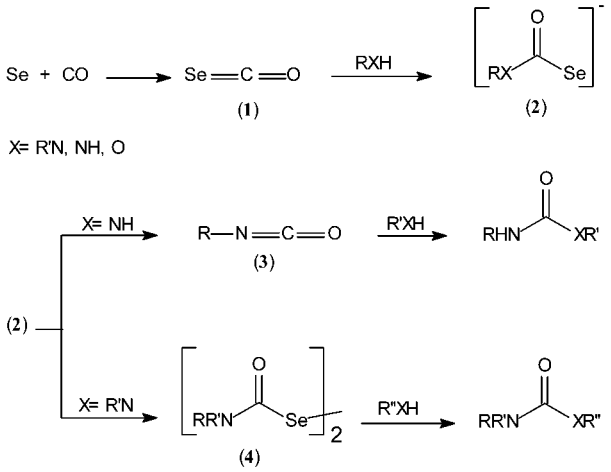
Scheme 1

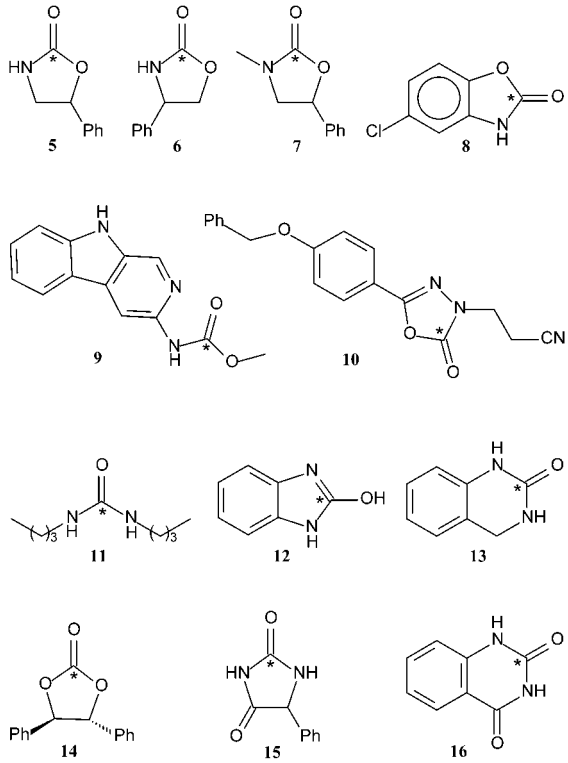


bon monoxide in a reaction mixture using conventional methods, i.e., by leading the radioactive precursor in a carrier gas into a solvent or solution. In our fully automated method,[10] [^{11}C]carbon monoxide is concentrated to a volume on the order of 10−50 μL, transferred to a microautoclave, and pressurized with the reaction mixture at 30−40 kPa.

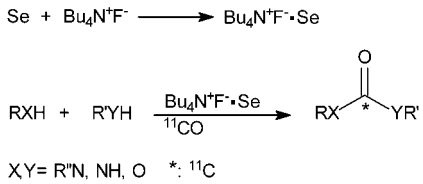
The first investigation of selenium-mediated carbonylation reactions with carbon monoxide was performed by Sonoda and co-workers almost 30 years ago.[11] The reaction has been postulated to proceed via a carbonyl selenide (**1**), which can react with an amine or an alcohol to form the next intermediate a carbamoselenoate (**2**) (Scheme 1).[11] With primary amines, the products are probably formed by nucleophilic attack on isocyanates (**3**) generated by the elimination of hydrogen selenide from the carbamoselenoate.[12] The carbonylation of secondary amines has been suggested to proceed via nucleophilic attack on bis(carbamoyl) diselenides (**4**) formed by oxidation of the carbamoselenoate.[13] Carbonates were synthesized in like manner using alkoxides.[14] The procedure was straightforward, and the reactions proceeded under mild conditions. Especially in the synthesis of carbamoyl heterocycles the reaction had a wide applicability and was highly selective.[15]

In this paper, the selenium-mediated reaction has been adopted to the labeling of carbamoyl compounds with [^{11}C]carbon monoxide at concentrations below 10^{-4} M, to produce ^{11}C-labeled products with very high specific radioactivity. Three of the carbamoyl compounds selected for this study (**8**,[16] **9**,[17] and **10**[18]; Chart 1) possess known biological activity and could be of interest as PET tracers.

Chart 1. Target Compounds (* = ^{11}C)



Scheme 2



Results and Discussion

The ^{11}C-labeled carbamoyl compounds (Chart 1) were synthesized in a microautoclave (200 μL) at pressures exceeding 35 MPa using [^{11}C]carbon monoxide with selenium(0) and either an amine, amino alcohol, or alcohol (Scheme 2). The results are presented in Table 1, and the corresponding substrates are shown in Chart 2. The specific radioactivity of the [^{11}C]carbon monoxide using a 20−30 μAh bombardment was, at the start of synthesis, in the range 800−2200 GBq/μmol that corresponds to a mass range of 0.3−0.8 μg. In the syntheses, the [^{11}C]carbon monoxide and the reaction mixture were transferred to the microautoclave at ambient temperature and the microautoclave was then placed in a heated oil bath for 5 min. According to measurements, the microautoclave reached the set temperature minus approximately 10 °C in 5 min.

Selenium has a very low solubility in most common solvents. However, in the procedures described in the

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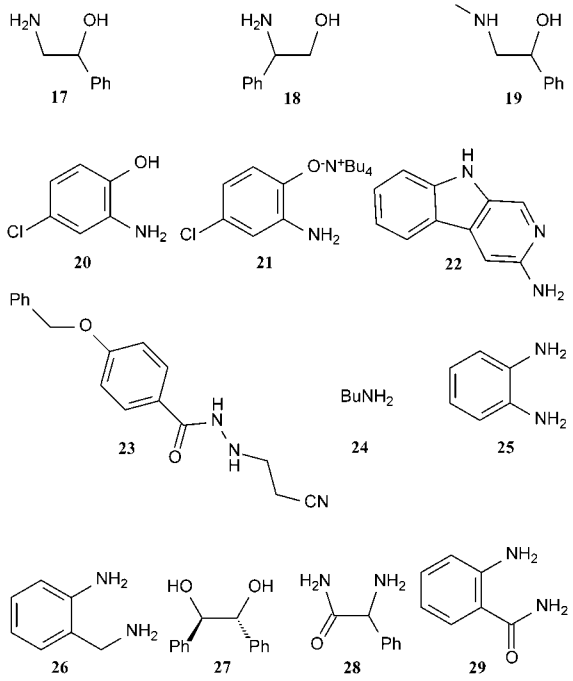
Table 1. Radiochemical Yields and Synthesis Parameters for the ^{11}C-Labeled Carbamoyl Compounds Presented

entry	substrate	product	solvent/ method	amt of substrate (μmol)	trapping efficiency[a] (%)	isolated rcy[b] (%)
1	**17**	**5**	DMSO/A	73	95 ± 1 (3)[c]	84 ± 2 (3)
2	**17**	**5**	DMSO/C	35	95 ± 1 (3)	84 ± 2 (3)
3	**17**	**5**	THF/C	7	92 ± 3 (3)	75 ± 3 (3)
4	**18**	**6**	THF/C	35	95 ± 1 (2)	83 ± 3 (2)
5	**19**	**7**	DMSO/C	33	93 ± 2 (3)	70 ± 2 (2)
6	**20**	**8**	DMSO/C	21	19 ± 2 (2)	16 ± 3 (2)
7	**21**	**8**	DMSO/A	21	80 ± 4 (3)	50 ± 10 (3)
8	**22**	**9**	DMSO/C	55	59 ± 10 (2)	22 ± 2 (2)
9	**23**	**10**	DMSO/A	34	17	5
10	**23**	**10**	DMSO/B	34	79 ± 3 (2)	25 ±2 (2)
11	**23**	**10**	THF/C	17	94 ± 1 (2)	44 ±3 (2)
12	**24**	**11**	DMSO/A	49	98 ± 1 (2)	88 ± 2 (2)
13	**25**	**12**	DMSO/C	157	98 ± 1 (2)	72 ± 4 (2)
14	**26**	**13**	THF/C	41	19	17
15	**26**	**13**	DMSO/C	41	95 ± 1 (2)	78 ± 5 (2)
16	**27**	**14**	DMSO/C	93	52	38
17	**28**	**15**	DMSO/C	27	94 ± 1 (2)	<1
18	**29**	**16**	DMSO/C	162	51 ± 4 (3)	<0.1

[a] Decay-corrected, the fraction of radioactivity left in the crude product after purge with nitrogen. [b] Rcy = radiochemical yield; decay-corrected, calculated from the amount of radioactivity in the crude product before nitrogen purge and the radioactivity of the LC purified product. [c] Values in parentheses show the number of runs.

Chart 2. Substrates Used in the ^{11}C-Labeling Reactions



literature where carbon monoxide is used in large excess and at pressures ranging from ambient up to 3 MPa, the selenium rapidly dissolves as it reacts.[11] In contrast, the employment of nanomole quantities of [^{11}C]carbon monoxide in an apparatus where the reagents are transferred through capillaries required a soluble form of selenium. It was found that when a mixture of a primary alkylamine such as **17** or **24**, DMSO, and selenium was heated, a brown colored solution resulted. This solution gave excellent radiochemical yields of labeled ureas upon reaction with [^{11}C]carbon monoxide (entries 1 and 12). The disadvantages of this method were that relative high concentrations of the amines were needed and that the yields were low unless primary alkylamines were employed. For example, when **23** was heated together with selenium and DMSO, there was no significant coloring of the solution and the radiochemical yield of compound **10** was only 5% (entry 9).

The radiochemical yield of **10** was increased 5-fold when a high concentration of imidazole (1.7 M) was used (entry 10). The reason for the increased yield was probably not due to an increased concentration of selenium, since the reaction mixture only became slightly colored when heated with selenium. A plausible explanation is instead that the reaction proceeded via a ^{11}C-labeled imidazole compound such as the phosgene-substitute 1,1′-carbonyldiimidazole.[19]

The scope of the labeling method was further increased when we discovered that tetrabutylammonium fluoride ((TBA)F) formed a soluble complex with selenium (Scheme 2). When a solution of (TBA)F was mixed with selenium, the solution rapidly turned dark green. With this approach other solvents, such as THF, could be used, but DMSO gave the highest concentration of the complex, resulting in an almost black solution. In the synthesis of compound **10**, the use of THF gave higher radiochemical yields than with DMSO, while the opposite was true in most other cases (e.g., **13**, entry 14 and 15). Unfortunately, the combination of imidazole and (TBA)F was not useful since selenium was precipitated when imidazole was added to a (TBA)F−selenium complex. It should be noted that the use of (TBA)F, to form a soluble and reactive complex with selenium, should be generally beneficial in syntheses where the reaction with solid selenium is slow or inconvenient.

Ring closure reactions were much more favorable than the corresponding syntheses of open compounds. The alkyl amino alcohols gave good to nearly quantitative radiochemical yields (entries 1−5), even with substrate concentrations below 30 mM and with THF as solvent. The high radiochemical yield of compound **7** (entry 5) is especially noteworthy since the ^{11}C-labeling of open carbamoyl compounds failed when secondary amines were employed. This result is in accordance with the pathways shown in Scheme 1, where the carbonylation of secondary amines proceeds via bis(carbamoyl) diselenides (**4**). Due to the low concentration ($<10^{-4}$ M) of [^{11}C]carbon monoxide, the formation of **4** should be negligible.

In the synthesis of compound **8**, the use of tetrabutylammonium fluoride gave a low radiochemical yield. Instead, the tetrabutylammonium ion was used to ion pair the phenolate to obtain substrate **21**. With this approach the radiochemical yield was increased nearly 4-fold compared to the experiments when TBAF was used (entries 6 and 7).

In the synthesis of compound **9**, better results were obtained when the diacetate salt of substrate **22** was used with imidazole than when the free base **22** was used with (TBA)F.

In attempts to synthesize the carbonate **14** using the corresponding alkoxide of the diol **27**, the trapping efficiency was nearly quantitative but the decay-corrected radiochemical yield was less than 4%. The main product was [^{11}C]carbonate. When compound **27** was used, the

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trapping efficiency was much lower but the decay-corrected radiochemical yield of **14** was 52%. (entry 16).

The failure in the synthesis of **15** and **16** was not expected. Nonradioactive **16** has previously been synthesized by selenium-mediated carbonylation in 23% yield. A general explanation is the relative weak nucleophilicity of both the aniline-amine and the amide nitrogen of substrate **29**. In the synthesis of **16**, the trapping efficiency was low and the main radioactive product was [^{11}C]carbonate. Due to the similarities between substrates **18** and **28** and the almost quantitative yield of **6,** a successful synthesis of **15** was expected. However, despite a good trapping efficiency only trace amounts of **15** were observed. Acidification of the crude product and purge with nitrogen resulted in a 75% loss of radioactivity, presumably in the form of [^{11}C]carbon dioxide or [^{11}C]carbamoyl selenide.[20]

Compounds **5**−**14** where purified with semipreparative LC and obtained with radiochemical purity exceeding 98%.

The specific radioactivity for compounds **5** and **12** was 1300 and 500 GBq/μmol, respectively, at 25 min after the end of 25 μAh bombardments, which indicates that there was no significant isotopic dilution during the handling and synthesis after the nuclide production. The difference probably reflects variations in the specific radioactivity of the [^{11}C]carbon dioxide rather than variations in the carbonylation reactions.

Introductory identifications were performed using analytical LC with co-injection of nonradioactive reference material. The additional confirmation of the identities of compounds **5**−**14** was made using LC-MS. The identity of compound **5** was further confirmed by ^{13}C NMR analysis of 5-phenyl-(2-^{13}C)-2-oxazolidone synthesized as **5**. The ^{13}C NMR signal at 160.0 ppm corresponded to the ^{13}C signal from the carbonyl carbon of authentic 5-phenyl-2-oxazolidone.

In comparison with the labeling reactions using [^{11}C]phosgene, the scope of the selenium-mediated carbonylation with [^{11}C]carbon monoxide is limited. However, there are several advantages with the latter, namely higher specific radioactivity and higher radiochemical yields in reactions with alkylamines plus it is a more reliable technique that is easy to automate. Another important aspect is that this system can be also used for a broad range of other carbonylation reactions, which has given completely new possibilities for ^{11}C-labeling.[8,21] This aspect is important since synthetic methods in general, and apparatus in particular, should be of the multitask type to meet the logistic and space demands of a PET laboratory.

Conclusions

The use of [^{11}C]carbon monoxide at concentrations below 10^{-4} M in selenium-promoted carbonylations of amines, alcohols, and amino alcohols has been shown to be a viable method for the production of ^{11}C-labeled carbamoyl compounds. Using this approach 10 different carbamoyl compounds were synthesized in low to quantitative radiochemical yields with high specific radioactivity. The presented method is rapid, mild, and conducted in a one-pot procedure using an automated apparatus. This apparatus has become commercially available and is also useful for a range of other carbonylation reactions. The method holds promise for routine production of ^{11}C-labeled carbamoyl compounds. The use of (^{13}C)carbon monoxide in a similar method enables the synthesis of different carbonyl ^{13}C-substituted carbamoyl compounds.

The use of (TBA)F, to form a soluble and reactive complex with selenium, should be generally beneficial in syntheses where the reaction with solid selenium is slow or inconvenient due to solubility problems.

Experimental Section

General Methods. [^{11}C]Carbon dioxide production was performed using a Scanditronix MC-17 cyclotron at the Uppsala University PET Centre. The ^{14}N(p,α)^{11}C reaction was employed in a gas target containing nitrogen (AGA, Nitrogen 6.0) and 0.1% oxygen (AGA, Oxygen 4.8) which was bombarded with 17 MeV protons.

[^{11}C]Carbon monoxide was produced as described previously.[7b] The production of [^{11}C]carbon monoxide and the labeling syntheses were performed using an automated, commercially available apparatus.[10,22]

Liquid chromatographic analysis (LC) was performed with a gradient pump and a variable-wavelength UV detector in series with a β^+-flow detector. The following mobile phases were used: 0.05 M ammonium formate, pH 3.5 (A); acetonitrile/H_2O 50/7 (B); 0.01 M trifluoroacetic acid, pH 3.5 (C); acetonitrile (D); 0.01 M formic acid (E). For analytical LC, a C_{18}, 4 μm, 250 × 4.6 mm (i.d.) column was used at a flow of 1.5 mL/min. For semipreparative LC, a C_{18}, 4 μm, 250 × 10 mm (i.d.) column was used at a flow of 4 mL/min. An automated synthesis system[10,22] was used for LC injection and fraction collection.

Radioactivity was measured in an ion chamber. For coarse estimations of radioactivity during production, a portable dose-rate meter was used.

In the analysis of the ^{11}C-labeled compounds, unlabeled reference substances were used for comparison in all LC runs. Identities of precursors and reference compounds were determined using ^{1}H and ^{13}C NMR and GC-MS and LC-MS. The data were compared with the corresponding found in the literature. NMR spectra were recorded on a 300 MHz instrument with tetramethylsilane or chloroform-d_1 as an internal standard. LC-MS was performed using an instrument with electrospray ionization. An autosampler and an ODS C_{18} (5 μm, 100 × 4.6 mm i.d.) column were used. The mobile phases were A and B.

THF was distilled under nitrogen from sodium/benzophenone.

The reference compounds for **5**,[23] **6**,[24] **7**,[25] and **11**[26] were synthesized using phosgene.[27] Compounds **22**[17] and **23**[18] and the reference compounds for **9**,[17] **10**,[18] and **13**[15b] were synthesized according to the literature. All other chemicals were purchased.

Preparation of Reagents and Reference Compounds. (4*R*,5*R*)-4,5-Diphenyl-1,3-dioxolan-2-one (Reference for 14).[28] To an ice-cooled solution of (1*R*,2*R*)-hydrobenzoin (**27**) (2.14 g, 10 mmol) in dry THF (5 mL) under argon was added

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butyllithium (8 mL, 2.5 M in hexane, 20 mmol.). The mixture was stirred at room temperature for 15 min and was then concentrated under reduced pressure. The residue was dissolved in dry toluene (10 mL), and phosgene (1.9 M in toluene, 10.5 mL, 2 equiv) was added at 0 °C. The reaction mixture was stirred for 2 h at room temperature and was then concentrated under reduced pressure. Purification using flash column chromatography, with silica gel and ethyl acetate/hexane (1:2) as eluent, yielded a white crystalline product (1.75 g, 95%). LC-MS (ESI$^+$), solvent C/D: *m*/*z* 242 [M + H]$^+$.

Methyl Aminophenylacetate, HCl Salt.[29] To an ice-cooled solution of aminophenylacetic acid (3.77 g, 24.9 mmol) in dry methanol (25 mL) was added thionyl chloride (25 mL, 343 mmol) during 15 min. The reaction mixture was refluxed for 2.5 h and was then concentrated under reduced pressure. The residue was recrystalized from methanol/ether to give the title compound (4.82 g, 96%) as white crystals. LC-MS (ESI$^+$), solvent D/E: *m*/*z* 166 [M + H]$^+$.

2-Amino-2-phenylacetamide (28).[29] Methyl aminophenylacetate, HCl salt (1.47 g, 7.3 mmol), was dissolved in ammonium hydroxide (30 mL, 28% in water) and stirred at room temperature for 92 h. The mixture was extracted with methylene chloride (3 × 100 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was recrystallized from ethanol to obtain **28** (0.43 g, 86%) as a white solid. LC-MS (ESI$^+$), solvent D/E: *m*/*z* 152 [M + H]$^+$.

5-Phenylimidazolidine-2,4-dione (Reference for 15).[30] An ice-cooled solution of the acetamide **28** (160 mg, 1.06 mmol) in dry THF (5 mL) was treated with butyllithium (1.6 M in hexane, 1.33 mL, 2.13 mmol) under a nitrogen atmosphere. The resulting mixture was stirred at room temperature for 20 min and then concentrated under reduced pressure. The residue was dissolved in dry toluene (5 mL), and phosgene (20% in toluene, 1.93 M, 0.72 mL, 1.38 mmol) was added at 0 °C. The reaction mixture was stirred overnight, poured into saturated $NaHCO_3$(aq), and extracted with methylene chloride (3 × 25 mL). The combined organic phases were dried and concentrated under reduced pressure. Purification using flash column chromatography with silica gel and diethyl ether as eluent yielded the desired compound (88 mg, 47%). LC-MS (ESI$^+$), solvent D/E: *m*/*z* 178 [M + H]$^+$.

Tetrabutylammonium 2-Amino-4-chlorophenolate (21). 2-Amino-4-chlorophenol (144 mg, 1 mmol) was dissolved in THF (1 mL), tetrabutylammonium hydroxide (650 μL 1.54 M_{aq}, 1 mmol) was added, and the resulting solution was stirred for 30 min. The solution was concentrated under reduced pressure, dried in a vacuum at 60 °C for 1 h, and dissolved in DMSO (1 mL).

5-Phenyl-(2-^{13}C)-2-oxazolidone (^{13}C-5). A vial (5 mL) was charged with selenium (20 mg, 250 μmol), DMSO (2 mL), and 2-amino-1-phenylethanol (**17**) (30 mg, 210 μmol) and flushed with nitrogen. Tetrabutylammonium fluoride (50 μL, 1 M in THF, 50 μmol) was added, and the vial was shaken until the solution was dark green. The vial was evacuated and charged with (^{13}C)carbon monoxide (10 mL). The mixture was heated at 110 °C and stirred vigorously for 1 h. Water (3 mL) and a sufficient amount of **5** were added, and the resulting solution was injected on the semipreparative LC. The chromatography was performed as described for **5**. The radioactive fraction was collected and evaporated under reduced pressure to yield the desired compound (25 mg, 70% calculated from 2-amino-1-phenylethanol (**17**)). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.52 (1H, dt), 3.98 (1H, dt), 5.62 (1H, t), 6.30 (1H, br), 7.41 (5H, s). ^{13}C NMR($CDCl_3$, 300 MHz): δ 160 (major signal), 128.9, 125.7, 77.9, 48.3.

Synthesis of Carbonyl-^{11}C-Labeled Carbamoyl Compounds. General Procedure A: Amine Complex. A vial (1 mL) was charged with selenium (10 mg, 126 μmol), DMSO (250 μL), and the amine. The vial was capped, flushed with nitrogen, shaken, and heated at 130 °C until the solution was brown. The resulting mixture was filtered and transferred with pressure (35 MPa) to the microautoclave (200 μL), precharged with [^{11}C]carbon monoxide at ambient temperature. The microautoclave was then put into an oil bath at 150−200 °C for 5 min. The crude product was transferred to a preevacuated septum-fitted vial (5 mL). The microautoclave was filled with solvent (250 μL) and again emptied in to the collection vial containing the reaction mixture. The radioactivity was measured before and after the vial was purged with nitrogen. Water (1.5 mL) was added, and the resulting solution was injected on the semipreparative LC. The identity and radiochemical purity of the collected fraction were assessed by analytical LC and LC-MS.

General Procedure B: Imidazole Mediated. A vial (1 mL) was charged with selenium (10 mg, 126 μmol), DMSO (250 μL), imidazole (30 mg, 440 μmol), and the amine. The vial was capped, flushed with nitrogen, shaken, and heated at 130 °C until the solution was weak brown. The resulting mixture was used as described above.

General Procedure C: Tetrabutylammonium Fluoride Complex. A vial (1 mL) was charged with selenium (10 mg, 126 μmol), DMSO or THF (250 μL), and tetrabutylammonium fluoride (10 μL, 2 M in THF, 20 μmol). The vial was capped, flushed with nitrogen, and shaken until the solution was dark green. The amine (5−50 μmol) was added, and the resulting mixture was used as described above. When THF was used, the solvent volume was reduced to less than 0.2 mL by heating at 130 °C and purging with nitrogen. Acetonitrile/water, 1/1 (2 mL), was added, and the resulting solution was injected on the semipreparative LC.

5-Phenyl-1,3-oxazolidin-[2-^{11}C]-2-one (5). The synthesis was performed using procedure A or C and 2-amino-1-phenylethanol (**17**) at 170 °C. Semipreparative LC: Solvent A/B (70/30) linear gradient to 30/70 in 8 min, flow 4 mL/min, t_R = 8.3 min. Analytical LC: solvent A/B (70/30) linear gradient to 0:100 in 8 min, flow 1.5 mL/min, wavelength 254 nm, t_R = 4.1 min. LC-MS (ESI$^+$), solvent C/D: *m*/*z* 164 [M + H]$^+$.

4-Phenyl-1,3-oxazolidin-[2-^{11}C]-2-one (6). The synthesis was performed using procedure C and 2-amino-2-phenylethanol (**18**) at 170 °C. Semipreparative LC: t_R = 8.2 min. Analytical LC: t_R = 4.3 min. LC-MS: *m*/*z* 164 (M$^+$ + 1).

3-Methyl-5-phenyl-1,3-oxazolidin-[2-^{11}C]-2-one (7). The synthesis was performed using procedure C and *N*-methyl-2-amino-1-phenylethanol (**19**) at 170 °C. Semipreparative LC: t_R = 9.1 min. Analytical LC: t_R = 4.8 min. LC-MS (ESI$^+$), solvent D/E: *m*/*z* 178 [M + H]$^+$.

5-Chloro-1,3-benzoxazol-[2-^{11}C]-2(3*H*)-one (8). The synthesis was performed using procedure A with the following specifications. A vial (1 mL) was charged with selenium (10 mg, 126 μmol), DMSO (250 μL), and tetrabutylammonium 2-amino-4-chlorophenolate (**21**) (10 μL, 1 M in DMSO, 10 μmol). The vial was capped, flushed with nitrogen, and shaken at ambient temperature until the solution became dark colored. Reaction temperature: 170 °C. Semipreparative LC as for **5**: t_R = 10.9 min. Analytical LC LC as for **5**: t_R = 6.4 min. LC-MS: *m*/*z* 170 (M$^+$ + 1).

Methyl 9*H*-β-carbolin-3-yl-[^{11}C]carbonylcarbamate (9). The synthesis was performed using procedure C and 9*H*-β-carbolin-3-amine (**22**) with methanol (20 μL, 494 μmol) at 170 °C. Semipreparative LC as for **5**: t_R = 9.9 min. Analytical LC as for **5**: t_R = 5.6 min. LC-MS (ESI$^+$), solvent D/E: *m*/*z* 242 [M + H]$^+$.

3-[5-[4-(Benzyloxy)phenyl]-2-[^{11}C]oxo-1,3,4-oxadiazol-3(2*H*)-yl]propanenitrile (10). The synthesis was performed using procedure A (150 °C), B (190 °C), or C (150 °C) and 4-(benzyloxy)benzoic acid *N*′-(2-cyanoethyl)hydrazide (**23**). Semipreparative LC as for **5**: t_R = 11.8 min. Analytical LC as for **5**: t_R = 7.3 min. LC-MS (ESI$^+$), solvent C/D: *m*/*z* 322 [M + H]$^+$.

***N*,*N*′-Dibutyl-[^{11}C]urea (11).** The synthesis was performed using procedure A or C and butylamine (**24**) at 150 °C.

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Semipreparative LC as for **1**: t_R = 15.6 min. Analytical LC as for **5**: t_R = 7.5 min. LC-MS (ESI^+), solvent C/D: *m*/*z* 173 $[M + H]^+$.

2-Hydroxy[2-^{11}C]benzimidazole (12). The synthesis was performed using procedure C and *o*-phenylenediamine (**25**) at 190 °C. Semipreparative LC: solvent A/B (80/20) linear gradient to 0/100 in 14 min, flow 4 mL/min, t_R = 8.3 min. Analytical LC as for **5**: t_R = 3.1 min. LC-MS (ESI^+), solvent C/D: *m*/*z* 135 $[M + H]^+$.

3,4-Dihydroquinazolin-[2-^{11}C]-2(1*H*)-one (13). The synthesis was performed using procedure C and 2-aminobenzylamine (**26**) at 150 °C. Semipreparative LC: solvent A/B (85/15) linear gradient to 40/60 (9 min), linear gradient to 0/100 in 0.5 min, flow 4 mL/min, t_R = 11.1 min. Analytical LC as for **5**: t_R = 3.8 min. LC-MS (ESI^+), solvent D/E: *m*/*z* 149 $[M + H]^+$.

(4*R*,5*R*)-4,5-Diphenyl-1,3-dioxolan-[2-^{11}C]-2-one (14). The synthesis was performed using procedure C and (1*R*,2*R*)-hydrobenzoin (**27**) at 150 °C. Semipreparative LC: solvent A/B (70/30) linear gradient to 0/100 in 8 min, flow 4 mL/min, t_R = 11.1 min. Analytical LC as for **5**: t_R = 6.7 min. LC-MS (ESI^+), solvent C/D: *m*/*z* 242 $[M + H]^+$.

5-Phenylimidazolidine-[2-^{11}C]-2,4-dione (15). The synthesis was attempted using procedure C and 2-amino-2-phenylacetamide (**28**) at 150 °C. Analytical LC as for **1**: t_R= 4.1 min.

Quinazoline-[2-^{11}C]-2,4(1*H*,3*H*)-dione (16). The synthesis was attempted using procedure C and 2-aminobensoylamide (**29**) at 180 °C. Analytical LC as for **5**: t_R = 6.2 min.

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