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Synthesis of Biologically Relevant Compounds by Ruthenium Porphyrin Catalyzed Amination of Benzylic C−H Bonds

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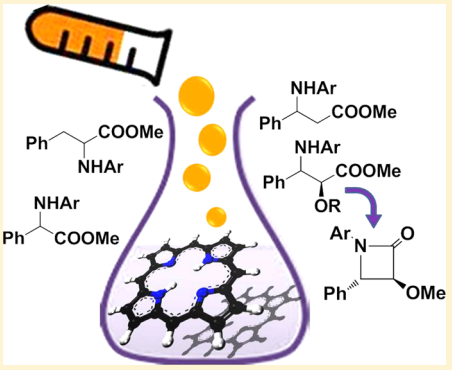
Supporting Information

ABSTRACT: Herein we report the catalytic activity of ruthenium porphyrin complexes to promote the amination of benzylic C−H bonds by aryl azides, yielding α- and β-amino esters. The catalytic methodology is also effective to synthesize two derivatives of methyl L-3-phenyllactate in order to convert one of them into the corresponding β-lactam. The catalytic experimental conditions have been optimized on the basis of a preliminary mechanistic investigation which underlines the pivotal role of the substrate concentration to maximize the reaction productivity.

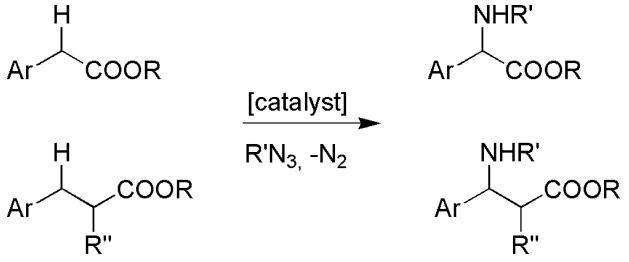


INTRODUCTION

The C−H amination of hydrocarbons catalyzed by metal complexes is an efficient tool to synthesize high-value nitrogen-containing compounds employing cheap starting materials.[1−4] In order to respond to common requests for sustainable chemistry, the scientific community is very interested in the employment of organic azides (RN_3) as nitrogen sources for the synthesis of aza-containing molecules.[5−12] The process shows good atom efficiency and ecocompatibility due to the formation of environmentally friendly molecular nitrogen as the only stoichiometric byproduct. The extensive use of organic azides as starting materials, up to now, has been largely hampered by their intrinsic danger.[7] However, among RN_3 compounds, aryl azides (ArN_3) show good chemical stability, as the azide group conjugates well with the aromatic moiety. In fact, Sigma-Aldrich has recently developed an efficient synthetic method to obtain these compounds in bulky amounts using a safe procedure.[13] This could open new doors to the extensive employment of aryl azides in different fields of synthetic chemistry.

The nitrene transfer reaction is efficiently catalyzed by metal porphyrin complexes,[14−22] and in the past decade we have extensively employed ruthenium[23−26] and cobalt porphyrins[27−29] to promote the reaction between aryl azides and activated sp^3 C−H bonds.[30] Even though metal porphyrins are efficient catalysts for benzylic C−H aminations, the direct nitrene transfer from an azide into a benzylic C−H bond placed in a position α or β to an ester group has been less explored (Scheme 1).[16,31] This is due to the poor reactivity of electron-deficient benzylic positions toward electrophilic metallonitrene intermediates.

Scheme 1. Synthesis of α- and β-Amino Esters



In view of the great importance of amino esters, not to mention their role as precursors of other biological and pharmaceutical compounds, a wide variety of catalytic methods[32−37] such as the N−H insertion of carbenes[38−42] and reduction of β-enamino esters[43−46] have been studied.

We describe herein the catalytic activity of ruthenium porphyrins to synthesize α- and β-amino esters and the conversion of the latter into β-lactams. In order to optimize the reaction efficiency, a mechanistic study was also performed.

RESULTS AND DISCUSSION

We started studying the amination of methyl phenylacetate by 3,5-bis(trifluoromethyl)phenyl azide in the presence of different metal porphyrin catalysts (Table 1).

As reported in Table 1, the aminated compound **1** was formed in higher yields when the ruthenium porphyrin **2** (Table 1, run 1) was used instead of Co(TPP) (**4**; TPP =

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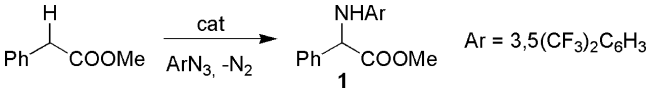
Table 1. Amination of Methyl Phenylacetate by 3,5-Bis(trifluoromethyl)phenyl Azide[a]



run	catalyst	conversion (%)[b]	t (h)	yield (%)[c]
1	Ru(TPP)CO (**2**)	100	8	64
2	Ru(TPP)CO (**2**)	100	21[d]	30
3	Ru(TPP)CO (**2**)	100	31[e]	40
4	Ru(TPP)CO (**2**)	100	3[f]	70
5	Ru(p-CF_3TPP)CO (**3**)	100	10	60
6	Co(TPP) (**4**)	100	3	51
7	Mn(TPP)Cl (**5**)	0		
8	Fe(TPP)Cl (**6**)	0		

[a]Reactions were run at 80 °C under nitrogen in 30 mL of benzene with 1/10/50 cat./ArN_3/benzylic substrate until complete aryl azide conversion. [b]The ArN_3 conversion was monitored by IR spectroscopy following the N_3 absorbance decrease at 2116 cm^{-1}. [c]Measured by NMR spectroscopy using 2,4-dinitrotoluene as the internal standard. [d]Run in 1,2-dichloroethane. [e]Run in acetonitrile. [f]Run in methyl phenylacetate.

dianion of tetraphenylporphyrin) as catalyst (Table 1, run 6). On the other hand, no azide conversion was observed in the presence of Mn(TPP)Cl (**5**) and Fe(TPP)Cl (**6**) (Table 1, runs 7 and 8, respectively). Shorter reaction times were achieved by using methyl phenylacetate as the solvent (Table 1, run 4). If the temperature of the reaction run in methyl phenylacetate was increased from 80 to 100 °C, a further decrease of the azide conversion time was observed. Methyl (3,5-bis(trifluoromethyl)phenylamino)phenylacetate (**1**) was obtained in only 1.5 h in 72% yield.

Compound **1** (Figure 1) crystallizes in space group $P\bar{1}$ with two independent molecules in the asymmetric unit and therefore four molecules in the unit cell. The packing is quite loose, in the absence of any strong intermolecular interaction, and as a result, all the CF_3 groups are rotationally disordered about their ideal 3-fold axis. The purpose of this crystal structure determination was mainly to have a reference for the ligand used in coordination to ruthenium (see below).

The TLC analyses of the crude of the reactions catalyzed by Ru(TPP)CO in benzene (Table 1, run 1) and methyl phenylacetate (Table 1, run 4) revealed the presence of different ruthenium species at the end of the catalysis according to the employed solvent. Ru(TPP)CO is the only ruthenium complex observed when methyl phenylacetate is the reaction solvent, while a new purple ruthenium species was formed in addition to Ru(TPP)CO by running the reaction in benzene. If in the latter case the catalytic azide concentration was doubled (the Ru(TPP)CO/azide/methyl phenylacetate ratio of 1/10/50 was replaced by 1/20/50), the aryl azide conversion was not complete (80%), organic compound **1** was obtained in a low yield (29%), and the new purple complex was the only ruthenium species detectable by TLC in the catalytic mixture. This last experiment indicated that the aryl azide/Ru(TPP)CO ratio is fundamental to drive the reaction toward the formation of the new complex when a low methyl phenylacetate concentration in benzene is employed. Conversely, when the reaction is performed in methyl phenylacetate as the reaction solvent, Ru(TPP)CO was the principal ruthenium species in the catalytic mixture also by using a Ru(TPP)CO/azide catalytic ratio of 1/50. The aryl azide conversion was complete

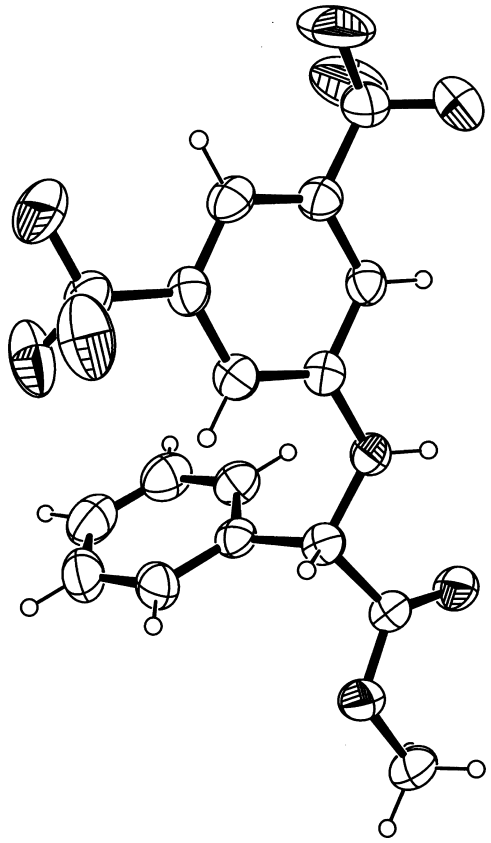


Figure 1. ORTEP plot of the molecular structure of methyl (3,5-bis(trifluoromethyl)phenylamino)phenylacetate (**1**). The disorder of the CF_3 groups has been removed for the sake of clarity.

in 6 h, and compound **1** was isolated in 80% reaction yield (see below).

Any attempt to recover this new complex in a pure form failed due to the constant presence of traces of **1**. Conversely, when the reaction was catalyzed by Ru^{II}(p-CF_3TPP)CO (**3**), the purification of the crude product by flash chromatography allowed the isolation of the bis-amido species Ru^{IV}(p-CF_3TPP)$(ArNR)_2$ (Ar = 3,5-$(CF_3)_2C_6H_3$, R = CH(Ph)-COOMe) (**7**) as purple crystals. Complex **7** was fully characterized, and its molecular structure determined by single-crystal X-ray diffraction is reported in Figure 2.

Complex **7** crystallizes in the space group $C2/c$. The unit cell contains eight molecules, although of two nonequivalent kinds. In fact, two different molecules of **7** are present, each sitting on an inversion center, coinciding of course with the ruthenium position. Therefore, the asymmetric unit contains two half-molecules. The crystal packing is not very efficient, and molecules of solvent (n-hexane and CH_2Cl_2) are cocrystallized. CH_2Cl_2 is disordered over two positions; moreover, some unexplained voids are found, compatible with additional CH_2Cl_2 molecules, although no significant residual electron density is calculated in these sites.

The geometry, the conformation, and the main bonding features of the two molecules of **7** are substantially identical. The main difference is due to the torsion of *meso*-aryl groups, which is very close to 90° (with respect to the porphyrin plane) in the molecule of Ru1, whereas it is smaller in the molecule of Ru2.

The average Ru−N bond distance of the porphyrin, 2.049(4) Å, is quite in keeping with the statistics available from the

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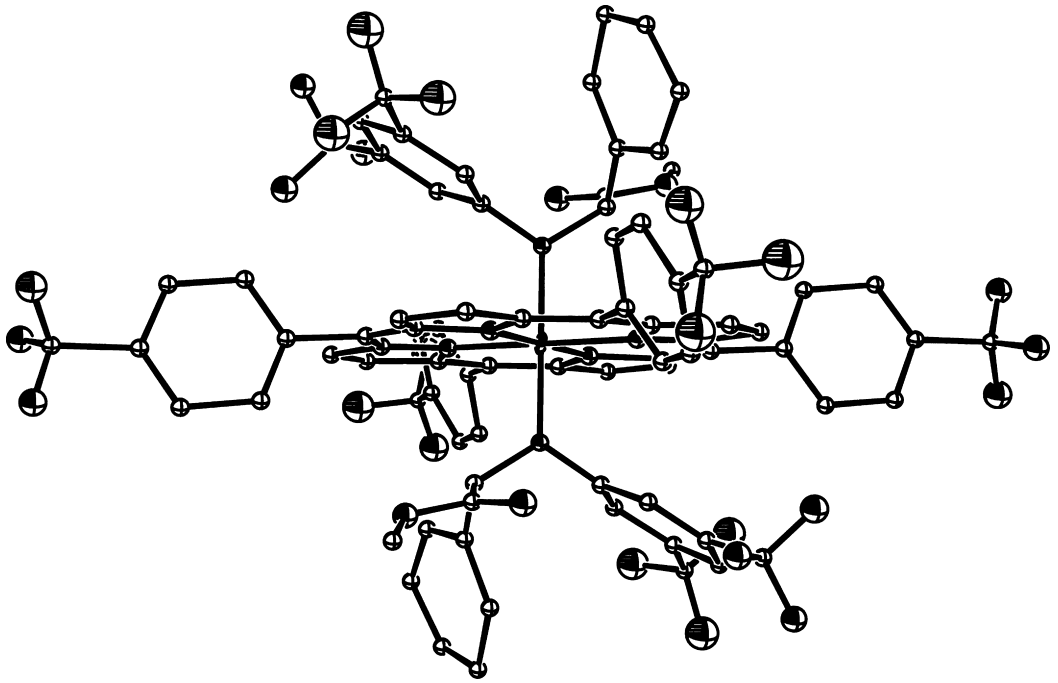
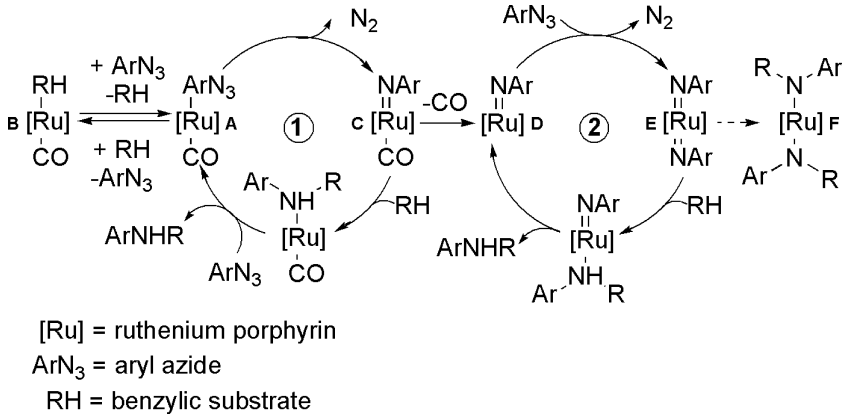


Figure 2. ORTEP plot of the molecular structure of **7**.

Scheme 2. Mechanistic Proposal for the Synthesis of 1



Cambridge Structural Database,[47] 2.052(1) Å. The coordination of the axial ligand is also quite similar to that of other hexacoordinated metals in porphyrins. In both independent molecules Ru−N is 1.944(5) Å, comparable to that of Ru^{IV}(*p*-CH_3TPP)(*p*-$ClC_6H_4NH)_2$[48] or Ru^{IV}(TPP)(3,5-$(CF_3)_2C_6H_3N$-(C_6H_9)).[24,26]

In comparison with compound **1**, the main difference is the conformation adopted by the 3,5-$(CF_3)_2C_6H_3$ moiety, which is antiperiplanar with respect to the acetate group (along the N−C_α bond) in **1**, whereas it is synclinal in **7**. Moreover in **1**, the aryl ring and the acetate group lie on the same plane, but they are ca. 48° inclined in **7**. The most important change in bond distances occurs for the N−C_{aryl} bond, which is much longer in **7** (1.462(7) and 1.470(6) Å) than in **1** (1.375(3) and 1.376(3) Å).

Complex **7** is a very air stable compound and does not show any catalytic activity in the reaction between azide and methyl phenylacetate. For this reason we hypothesize that complex **7** is a deactivated catalyst which can be obtained by the partial decomposition of the bis-imido derivatives Ru(*p*-CF_3TPP)-$(NAr)_2$ (**8**)[24,26] formed during the catalysis run at low substrate concentrations. We suggest that the formation of **7** occurs by a homolytic cleavage of the substrate benzylic C−H bond, similarly to that already described for the synthesis of an analogous bis-amido ruthenium(IV) complex.[24,26] It should be noted that complex **7** would never have formed if the concentration of methyl phenylacetate was larger than 1.0 M.

To validate the hypothesis stated above, we prepared and characterized complex **8** from the stoichiometric reaction of Ru(*p*-CF_3TPP)(CO) with ArN_3 to employ it as a catalyst for the synthesis of methyl (3,5-bis(trifluoromethyl)phenylamino)-phenylacetate (**1**) (see the Experimental Section). The *α*-amino ester **1** was obtained in 22 h at a 51% yield, indicating that Ru(*p*-CF_3TPP)$(NAr)_2$ (**8**) is a less efficient catalyst than Ru(*p*-CF_3TPP)(CO) (**3**), which produced in 10 h a 60% yield of **1** (entry 5, Table 1). The analysis of the crude reaction product revealed the presence of the inactive complex Ru^{IV}(*p*-CF_3TPP)$(ArNR)_2$ (**7**), supporting the hypothesis that the lower observed catalytic efficiency is due to the partial transformation of **8** into **7**.

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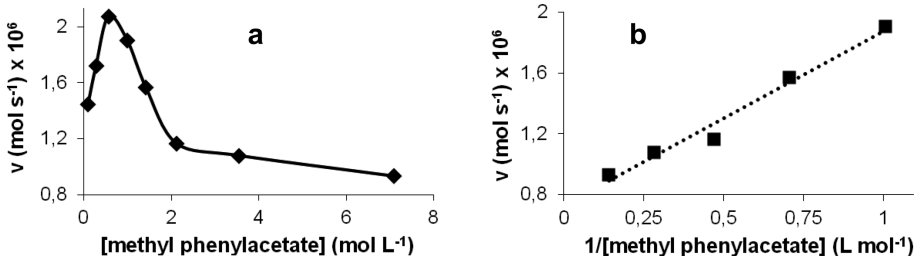

Figure 3. Dependence of the reaction rate with respect to the methyl phenylacetate concentration.

In order to study the mechanism of the formation of **7**, we reacted the bis-imido complex **8** with an excess of methyl phenylacetate (**8**/methyl phenylacetate 1/250) in benzene. We observed the formation of the aminated compound **1** in addition to the contemporary transformation of **8** into unidentified ruthenium species. On the other hand, when a benzene solution of **8** was refluxed in the presence of both the aryl azide and the substrate, a TLC analysis of the reaction mixture revealed the complete conversion of **8** into **7**. These data are in accord with those already observed for the allylic amination of cyclohexene.[24]

The formation of an inactive bis-amido complex can also explain the difference in reaction times reported in entries 1 and 4 (Table 1), respectively. The aryl azide conversion was slower in benzene than in methyl phenylacetate due to a decrease of the catalyst loading in solution as a consequence of the deactivation process.

Taking into account our recent theoretical study on the amination of allylic C−H bonds,[49] we propose a similar mechanism (Scheme 2) where a central role in the catalytic cycle is played by the monoimido ruthenium(IV) complex **C**. We suggest that complex **A** can lose molecular nitrogen, forming the monoimido species Ru(TPP)(NAr)CO (**C**), which can either be trapped by methyl phenylacetate to yield the desired amino ester or be transformed into the bis-imido derivative Ru(TPP)$(NAr)_2$ (**E**), depending on the benzylic substrate concentration.

This proposal is in accord with our experimental results which indicate that better catalytic performances are achieved by working in the presence of high benzylic substrate concentrations. In this case the formation of bis-imido complex **E** is limited, which in turn limits the decomposition of **E** into the deactivated catalyst **F** (cycle 2, Scheme 2).

In order to investigate the influence of the substrate concentration on the rate of the Ru(TPP)CO-catalyzed reaction between methyl phenylacetate and 3,5-bis-(trifluoromethyl)phenyl azide, we performed eight runs at 75 °C by employing different benzylic substrate concentrations and a catalyst/azide ratio of 1/5 (Figure 3a). The azide concentration was chosen in order to limit the formation of the bis-imido derivatives (**E**) and the occurrence of cycle 2 of Scheme 2. The measurements[50] were executed in the 0.1−7.0 mol L^{-1} methyl phenylacetate concentration range, and the azide consumption was followed by IR spectroscopy, monitoring the decrease of the N_3 absorbance at 2116 cm^{-1}.

The reaction rate increased by increasing the methyl phenylacetate concentration up to 0.6 mol L^{-1}; then a substrate inhibition was evident (Figure 3a).[51] As clearly reported in Figure 3b, the reaction rate was inversely proportional to the methyl phenylacetate concentration in the 1.0−7.0 mol L^{-1} range.

The observed inhibition process could be due to a reversible coordination of the substrate to the metal center. This hypothesis was supported by an IR analysis of the reaction between Ru(TPP)CO and an excess of methyl phenylacetate. A shift of the CO absorbance from 1956 to 1948 cm^{-1} was observed after the addition of methyl phenylacetate to a benzene solution of Ru(TPP)CO (see the Supporting Information for experimental details and IR spectra).[52]

The data reported above imply that the first step of the mechanism could be the substitution of the coordinated substrate (RH in Scheme 2) with aryl azide, yielding species **A**, which can enter into the catalytic cycle 1 reported in Scheme 2. Clearly, the rate of the whole catalytic process also depends on the substitution reaction rate, which is determined by the substrate concentration. All of these results point out that the benzylic substrate plays a double role in the mechanism: it reacts with the ruthenium monoimido complex **C** to form the desired α-amino ester, and with the catalyst Ru(TPP)CO (**A**) it yields complex **B** (Scheme 2). Although at high methyl phenylacetate concentrations the formation of **B** is favored with a resulting decrease in reaction rates, these experimental conditions are necessary to reduce the formation of the deactivated catalyst **F** by keeping active the catalytic cycle 1 of Scheme 2. It should be noted that, when the occurrence of cycle 2 is limited, the catalyst loading remains constant during the reaction with a consequential improvement in the catalytic efficiency. A more in-depth kinetic study will be performed to better clarify all the kinetic aspects of the catalytic cycle.

Taking into account all the mechanistic information, we studied the scope of the reaction by reacting methyl phenylacetate with some other aryl azides and by investigating the reactivity of methyl dihydrocinnamate as the benzylic substrate (Table 2). In order to render the methodology economically sustainable, in all runs reported in Table 2, the substrate excess was recovered at the end of the reaction by high-vacuum distillation.

Experimental results indicate that 3,5-bis(trifluoromethyl)-phenyl azide is the most effective azide for the amination of both methyl phenylacetate (Table 2, run 1) and methyl dihydrocinnamate (Table 2, run 2). To optimize the synthetic procedure, we decreased the catalyst loading from 2 to 1 mol % in the synthesis of compound **1** (run 1, Table 2). After 23 h, only 50% of the starting azide was consumed and **1** was formed in 27% yield. We suggest that the decomposition of the catalyst into the inactive species **7** is favored by employing these experimental conditions.

The amination of methyl phenylacetate by other aryl azides afforded the corresponding aminated compounds in a low yield (Table 1, run 1, products **9**−**11**). However, the reaction of the same azides with methyl dihydrocinnamate only afforded traces of the corresponding β-amino esters. As is reported in Table 2,

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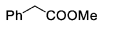
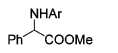
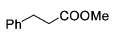
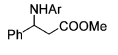
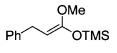
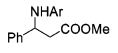
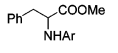
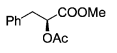
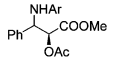
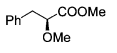
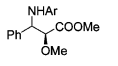
Table 2. Synthesis of α- and β-Amino Esters Catalyzed by Ru(TPP)CO (2)[a]

run	substrate	product	Ar	t[b] (h)	yield[c] %
1[d]			**1**, 3,5(CF$_3$)$_2$C$_6$H$_3$	6	80
			9, 4(CF$_3$)C$_6$H$_4$	5	26
			10, 4(NO$_2$)C$_6$H$_4$	8	32
			11, 4(^{t}Bu)C$_6$H$_4$	5	20
2			**12a**, 3,5(CF$_3$)$_2$C$_6$H$_3$	10	77
3[e]			**12a**, 3,5(CF$_3$)$_2$C$_6$H$_3$	0.3	65
			14a, 4(CF$_3$)C$_6$H$_4$	2	38
			15a, 4(NO$_2$)C$_6$H$_4$	0.7	55
			16a, 3,5(Cl)$_2$C$_6$H$_3$	1.2	65
			**12b**, 3,5(CF$_3$)$_2$C$_6$H$_3$	0.3	12
			14b, 4(CF$_3$)C$_6$H$_4$	2	14
			15b, 4(NO$_2$)C$_6$H$_4$	0.7	21
			16b, 3,5(Cl)$_2$C$_6$H$_3$	1.2	8
4			**17**, 3,5(CF$_3$)$_2$C$_6$H$_3$	23	35 *syn/anti* = 20/80
5			**18**, 3,5(CF$_3$)$_2$C$_6$H$_3$	6.5	53 *syn/anti* = 45/55

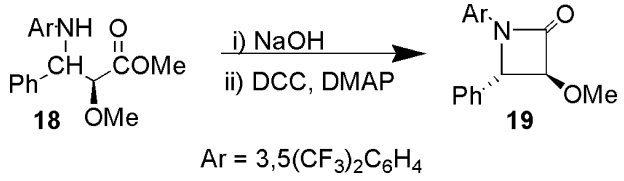
[a]Reactions were run under nitrogen in 8.0 mL of benzene at 80 °C with 1/50/1000 **2**/ArN$_3$/ester. [b]Time required to complete the ArN$_3$ conversion. [c]Isolated yields. [d]Run in methyl phenylacetate at 100 °C; [e]1/50/250 **2**/ArN$_3$/substrate.

compound **12a** was obtained in a good yield but after a long reaction time (Table 2, run 2) together with another purple porphyrin complex that was detected by TLC analysis. This new ruthenium complex **13** was isolated by performing the synthesis of **12a** using **8** as the catalyst. Analytic data for complex **13** are very similar to those reported for **7** to indicate an analogous bis-amido molecular structure (see the Supporting Information for details).

To optimize the synthesis of **12a**, the amination was performed by employing the ketene trimethylsilyl acetal of methyl dihydrocinnamate as the substrate (Table 2, run 3). The reaction time decreased from 10 h to 20 min, but in the meantime a decrease of the reaction selectivity was registered. The β-amino ester **12a** was formed along with the isomer **12b** in the ratio 85/15 **12a**/**12b**. Considering that the formation of compound **12b** could be due to the uncatalyzed reaction between the ketene trimethylsilyl acetal of methyl dihydrocinnamate and 3,5-bis(trifluoromethyl)phenyl azide,[53] we repeated the reaction in the absence of the ruthenium catalyst, but after 2 h the IR analysis did not reveal any consumption of the starting azide. The formation of the isomeric mixtures **14a**/**14b**, **15a**/**15b**, and **16a**/**16b** was also observed by running the reaction in the presence of the three other aryl azides reported in run 3 of Table 2. This experimental procedure allowed the synthesis of β-amino esters derived from aryl azides bearing EWG groups in short reaction times and without using a large excess of the substrate (Table 2, run 3). Even if the employment of the ketene silyl acetal decreased the reaction selectivity, it is important to underline that the two obtained isomers can easily be separated by flash chromatography. Compounds **12**−**16** were obtained after desilylation with TBAF; any attempt to isolate compounds derived from the direct amination of the ketene trimethylsilyl acetal failed.

The reaction between methyl L-3-phenyllactate, where the hydroxy moiety is protected as acetoxy (Table 2, run 4) or methoxy (Table 2, run 5) groups, and 3,5-bis(trifluoromethyl)-phenyl azide yielded the corresponding aminated compounds in moderate yields. The interest in these last two reactions comes from the use of compounds **17** and **18** as precursors of biologically relevant compounds such as β-lactams[36] and 2-oxazolidinones.[54] Then we studied the conversion of compound **18** into the corresponding β-lactam, which was obtained as a single diasteroisomer in 30% yield (Scheme 3). The stereochemistry of compound **19** was assigned by comparing its NMR data with those reported in the literature for a similar compound.[55]

Scheme 3. Conversion of β-Amino Ester 18 into the Corresponding β-Lactam 19



It should be noted that **19**, formed by a ring closure reaction of the anti stereoisomer of **18**, is the only recovered compound; the β-lactam corresponding to the syn isomer was not detected in the reaction mixture. Note that the syn/anti ratio of 1/1 implies that a maximum yield of 50% can be obtained with respect to the anti isomer when **19** is the product. It is worth noting that compound **19** was obtained in only four steps, starting from the low-priced L-phenylalanine through to the formation of methyl L-3-phenyllactate,[56] which was protected as the methoxy derivative[56] and then transformed into **18** (see the Supporting Information).

CONCLUSION

We have reported herein the ruthenium porphyrin catalyzed synthesis of α- and β-amino esters starting from the appropriate benzylic substrate and aryl azide. A preliminary mechanistic investigation, performed to optimize catalytic experimental conditions, revealed the presence of at least two interconnected catalytic cycles. The predominance of one over the other depends on the benzylic substrate (RH) concentration. When the reaction is run at high RH concentrations (7.0 mol L^{-1}), a Ru^{II}(porphyrin)CO complex is the active catalyst (cycle 1 of Scheme 2); conversely, by using low RH concentrations a bis-imido Ru^{VI}(porphyrin)(NAr)$_2$ complex is the active species (cycle 2 of Scheme 2). This second cycle showed a minor catalytic efficiency because Ru(porphyrin)(NAr)$_2$ can be transformed into the catalytically inactive bis-amido Ru^{IV}(porphyrin)(ArNR)$_2$ complex.

Mechanistic data indicated that the reaction productivity is strongly related to the benzylic substrate concentration and, to achieve satisfactory product yields, a high benzylic substrate concentration is required. The benzylic substrate excess was always recovered at the end of the reactions by high-vacuum distillation to increase the sustainability of the methodology. The reported catalytic method was also employed to synthesize two derivatives of methyl L-3-phenyllactate in order to convert them into the corresponding β-lactam.

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EXPERIMENTAL SECTION

General Conditions. All reactions were carried out under a nitrogen atmosphere employing standard Schlenk techniques and vacuum-line manipulations. Benzene was dried with an M. Braun SPS-800 solvent purification system, while 1,2-dichloroethane and acetonitrile were purified by distillation under nitrogen over CaH_2.

Reagents. Organic azides,[57] ketene silyl acetal,[58] methyl L-3-phenyllactate derivatives,[56] $TPPH_2$,[59] p-CF_3TPPH_2,[59] Ru(TPP)CO (**2**),[60] Ru(p-CF_3TPP)CO) (**3**),[60] and Co(TPP) (**4**)[61] were synthesized by methods reported in the literature or using minor modifications of them.[52] Methyl phenylacetate was distilled prior to use under nitrogen. Complexes **5** and **6** together with all the other starting materials are commercial products and were used as received.

Instruments. NMR spectra were recorded at 300 K (unless otherwise specified) operating either at 300 MHz for ^{1}H, 75 MHz for ^{13}C and 282 MHz for ^{19}F or at 400 MHz for ^{1}H and 100 MHz for ^{13}C. Chemical shifts (ppm) are reported relative to TMS. The ^{1}H NMR signals of the compounds described in the following have been assigned by COSY and NOESY techniques. Assignments of resonances in ^{13}C NMR were made by using the APT pulse sequence and HSQC and HMBC techniques. GC-MS analyses were performed on an instrument equipped with a capillary column (30 m × 0.25 mm × 0.25 μm film thickness). Infrared spectra, UV/vis spectra, and mass spectra were recorded in the analytical laboratories of Milan University.

General Procedures for Catalytic Reactions. The catalytic reactions were monitored by IR spectroscopy by measuring the characteristic N_3 absorbance in the range 2095−2130 cm^{-1}. The reaction was considered complete when the absorbance value of the azide was below 0.01 (by using a 0.1 mm thick cell). ^{1}H NMR analysis was performed using 2,4-dinitrotoluene as the internal standard.

Method A. Aryl azide (6.1×10^{-1} mmol) was added to a suspension of the catalyst (6.0×10^{-2} mmol) and substrate (3.0 mmol) in the desired solvent (30.0 mL). The resulting mixture was heated to 80 °C by using a preheated oil bath until the complete consumption of the azide. The solvent was evaporated to dryness and the residue analyzed by ^{1}H NMR spectroscopy.

Method B. Aryl azide (5.0×10^{-1} mmol) was added to a methyl phenylacetate (10.0 mL) suspension of Ru(TPP)CO (7.4 mg, 1.0×10^{-2} mmol). The resulting mixture was heated to 100 °C using a preheated oil bath until the complete consumption of the azide. The solvent was evaporated to dryness and purified by flash chromatography (silica gel, gradient elution with *n*-hexane/ethyl acetate).

Method C. Aryl azide (1.0×10^{-1} mmol) was added to a benzene (7.0 mL) suspension of Ru(TPP)CO (7.4 mg, 1.0×10^{-2} mmol) and substrate (10.0 mmol). The resulting mixture was refluxed using a preheated oil bath until the complete consumption of the azide. Benzene was evaporated to dryness, and the benzylic substrate excess was recovered by high-vacuum distillation (0.035 mmHg at 80 °C). The crude was purified by flash chromatography (silica gel, gradient elution with *n*-hexane/ethyl acetate).

Method D. The experimental procedure was identical to that described in method C except for the azide amount (5.0×10^{-1} mmol).

Method E. Aryl azide (5.0×10^{-1} mmol) was added to a benzene (10.0 mL) suspension of Ru(TPP)CO (7.4 mg, 1.0×10^{-2} mmol) and ketene silyl acetal (591.0 mg, 2.5 mmol). The resulting mixture was refluxed using a preheated oil bath until the complete consumption of the azide, and then the solvent was evaporated to dryness. THF (25.0 mL) was added to the residue, and the resulting solution was placed in an ice bath before adding a THF solution of tetra-*n*-butylammonium fluoride (TBAF) (1.0 mol L^{-1}, 3.0 mL). The solution was stirred for 15 min at 0 °C, poured into a saturated aqueous NH_4Cl solution (200.0 mL), and extracted with AcOEt (50.0 mL × 3), the extracts were dried with Na_2SO_4, and the solvent was evaporated to dryness. The crude product was then purified by flash chromatography (silica gel, gradient elution with *n*-hexane/ethyl acetate).

Synthesis of Methyl (3,5-Bis(trifluoromethyl)phenylamino)-phenylacetate (1). For complex **2** as the catalyst and benzene as the reaction solvent: 64% yield, method A; 80% yield, method B. For complex **3** as the catalyst and benzene as the reaction solvent: 60% yield, method A. For complex **4** as the catalyst and benzene as the reaction solvent: 51% yield, method A. For complex **8** as the catalyst: 51% yield, method A. δ_H (300 MHz; $CDCl_3$): 7.48−7.34 (5H, m, H Ar), 7.15 (1H, s, H Ar), 6.90 (2H, s, H Ar), 5.48 (1H, br, NH), 5.09 (1H, s, C*H*(NHAr)), 3.76 (3H, s, OCH_3). δ_C (75 MHz; $CDCl_3$): 171.5 (C═O), 146.5 (C Ar), 136.2 (C Ar), 132.6 (CF_3, q, J = 32.7 Hz), 129.4 (CH Ar), 129.0 (CH Ar), 127.3 (CH Ar), 125.3 (C Ar), 121.7 (C Ar), 112.8 (CH Ar), 111.3 (CH Ar), 60.3 (CH), 53.3 (OCH_3). δ_F (282 MHz; $CDCl_3$): −63.62 (CF_3). HRMS ESI: (M + H)$^+$ calcd for $C_{17}H_{14}NO_2F_6$ 378.0923, found 378.0927. IR (ATR): 3377 (ν_{N-H}), 1733 cm^{-1} ($\nu_{C=O}$). X-ray-quality crystals were obtained by slow evaporation of a pentane solution of compound **1** at room temperature.

Synthesis of Complex 7. A benzene (30.0 mL) solution of Ru(p-CF_3TPP)CO (**3**; 45.8 mg, 5.2×10^{-2} mmol), 3,5-bis(trifluoromethyl)-phenyl azide (141.1 mg, 5.5×10^{-1} mmol), and methyl phenylacetate (384.0 mg, 2.6 mmol) was refluxed until the aryl azide was completely consumed (the reaction was monitored by IR spectroscopy, $\nu_{N=N}$ 2116 cm^{-1}). The solvent was evaporated to dryness and the residue purified by flash chromatography (silica gel, *n*-hexane/dichloromethane 7/3) in 75% yield. The solid was dissolved in pentane, and the solution was to slowly concentrate dat room temperature to give X-ray-quality crystals. δ_H (300 MHz, C_6D_6, 338 K): 8.40 (8H, s, H_β), 8.04 (8H, br, H_1), 7.75 (8H, d, J = 7.7 Hz, H_2), 6.93 (2H, s, H_3), 6.30 (2H, m, H_4), 6.11 (4H, m, H_5), 4.18 (4H, m, H_6), 4.11 (2H, s, H_7), 2.58 (3H, s, OCH_3), 2.52 (3H, s, OCH_3), 1.88 (2H, m, H_8), −0.88 (s, 2H, H_9). δ_C (75 MHz, C_6D_6, 338 K): 162.9 (C═O), 158.6 (C), 145.5 (C), 144.0 (C), 134.1 (CH Ar), 132.9 (CH_β), 131.9 (C), 131.1 (CF_3 porphyrin), 127.4 (CH Ar), 124.1 (CH Ar), 121.9 (CH Ar), 117.3 (CH Ar), 80.2 (CH), 51.07 (OCH_3), 51.98 (OCH_3), the aryl CF_3 signals and three quaternary carbon signals were not detected. δ_F (282 MHz, C_6D_6, 338 K): −62.01 (12F, CF_3 porphyrin), −62.49 (6F, CF_3 Ar), −63.07 (6F, CF_3 Ar). UV−vis (CH_2Cl_2): λ_{max} (log ε) 419 (5.20), 524 (4.53), 553 nm (4.36) sh. IR (ATR): 1744 ($\nu_{C=O}$), 1014 cm^{-1} (oxidation marker band). MS (FAB$^+$): m/z 1362 [M − 376(R-N-Ar)]$^+$.

Synthesis of Complex 8. 3,5-Bis(trifluoromethyl)phenyl azide (42.0 mg, 0.165 mmol) was added to a benzene (30 mL) suspension of Ru(p-CF_3TPP)CO (**3**; 41.0 mg, 4.0×10^{-2} mmol). The resulting dark mixture was refluxed for 5 h until the complete consumption of **3** (TLC, *n*-hexane/CH_2Cl_2 7/3). The solvent was evaporated to dryness, and *n*-hexane (20 mL) was added. The dark violet solid that precipitated was collected by filtration and dried under vacuum (29.2 mg, 50%). δ_H (300 MHz, C_6D_6): 8.70 (8H, s, H_β), 7.98 (8H, d, J = 7.8 Hz, H Ar porphyrin), 7.76 (8H, d, J = 8.0 Hz, H Ar porphyrin), 6.50 (2H, s, H Ar), 2.76 (4H, s, H Ar). δ_C (75 MHz, C_6D_6): 151.6 (C), 144.9 (C), 142.4 (C), 134.4 (CH Ar), 132.2 (CH_β), 131.7 (CF_3), 129.9 (CF_3), 124.4 (C), 122.6 (C), 118.3 (CH), 117.8 (CH). δ_F (282 MHz, C_6D_6): −61.67 (12F, s, CF_3 porphyrin), −63.46 (12F, s, CF_3 Ar). UV−vis (CH_2Cl_2): λ_{max} (log ε) 359 (4.63), 419 (5.24), 524 (3.97), 590 nm (3.75). IR (ATR): 1014 cm^{-1} (oxidation marker band), 884 cm^{-1} (imido band). MS (FAB$^+$): m/z 1440 [M]$^+$.

Synthesis of Methyl (4-(Trifluoromethyl)phenylamino)-phenylacetate (9).[62] Yield: 26% (method B). Analytical data are in accord with those reported in the literature.

Synthesis of Methyl (4-Nitrophenylamino)phenylacetate (10).[63] Yield: 32% (method B). Analytical data are in accord with those reported in the literature.

Synthesis of Methyl (4-*tert*-Butylphenylamino)phenyl-acetate (11).[64] Yield: 20% (method B). Analytical data are in accord with those reported in the literature.

Synthesis of Methyl 3-(3,5-Bis(trifluoromethyl)phenyl-amino)-3-phenylpropanoate (12a). Yield: 85% (method C, methyl dihydrocinnamate was employed as the substrate), 77% (method D, methyl dihydrocinnamate was employed as the substrate), 65% (method E). δ_H (300 MHz, $CDCl_3$): 7.38−7.27 (5H, m, H Ar), 7.12 (1H, s, H Ar), 6.90 (2H, s, H Ar), 5.17 (1H, br, NH), 4.85 (1H, dd, J = 7.7 Hz, J = 5.3 Hz, C*H*(NHAr)), 3.67 (3H, s, OCH_3), 2.90 (1H, dd,

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J = 15.2, 5.2 Hz, C*H*H), 2.82 (1H, dd, J = 15.2, 7.8 Hz, CH*H*). δ_C (75 MHz, $CDCl_3$): 171.4 (C═O), 147.5 (C Ar), 140.6 (C Ar), 132.5 (CF_3, q, J = 32.9 Hz), 129.3 (CH Ar), 128.2 (CH Ar), 126.2 (CH Ar), 125.4 (C Ar), 121.8 (C Ar), 113.0 (CH Ar), 111.0 (CH Ar), 54.9 (CH), 52.2 (OCH_3), 42.3 (CH_2). δ_F (282 MHz, $CDCl_3$): −63.58 (CF_3). IR (ATR): 3396 (ν_{N-H}), 1727 cm^{-1} ($\nu_{C=O}$). HRMS ESI: $(M + H)^+$ calcd for $C_{18}H_{16}NO_2F_6$ 392.1080, found 392.1074.

Synthesis of Methyl 2-(3,5-Bis(trifluoromethyl)phenylamino)-3-phenylpropanoate (12b). Yield: 12% (method E). δ_H (300 MHz, $CDCl_3$): 7.35−7.23 (3H, m, H Ar), 7.20−7.12 (3H, m, H Ar), 6.88 (2H, s, H Ar), 4.63 (1H, br, NH), 4.40 (1H, t, J = 5.3 Hz, C*H*(NHAr)), 3.74 (3H, s, OCH_3), 3.21 (1H, dd, J = 13.7, 5.6 Hz, C*H*H), 3.11 (1H, dd, J = 13.7, 5.6 Hz, CH*H*. δ_C (75 MHz, $CDCl_3$): 172.7 (C═O), 147.3 (C Ar), 135.7 (C Ar), 132.7 (CF_3, q, J = 32.8 Hz), 129.4 (CH Ar), 128.9 (CH Ar), 127.6 (CH Ar), 125.4 (C Ar), 121.7 (C Ar), 112.7 (CH Ar), 111.5 (CH Ar), 57.4 (CH), 52.6 (OCH_3), 38.7 (CH_2). δ_F (282 MHz, $CDCl_3$): −63.54 (CF_3). HRMS ESI: $(M + H)^+$ calcd for $C_{18}H_{16}NO_2F_6$ 392.1080, found 392.1074.

Synthesis of Complex 13. 3,5-Bis(trifluoromethyl)phenyl azide (814.0 mg, 3.2 mmol) was added to a benzene (30 mL) solution of **8** (90.7 mg, 6.3×10^{-2} mmol) and methyl dihydrocinnamate (2.12 g, 13 mmol). The resulting solution was refluxed until the aryl azide was completely consumed (the reaction was monitored by IR spectroscopy, $\nu_{N=N}$ 2116 cm^{-1}). The mixture was concentrated, and methyl dihydrocinnamate was removed by high-vacuum distillation. The residue was purified by flash chromatography (silica gel, *n*-hexane/AcOEt 50/1) (30% yield). δ_H (400 MHz, C_6D_6, 343 K): 8.43 (8H, m, H_β), 8.07 (8H, m, H_1), 7.75 (8H, d, J = 7.8 Hz, H_2), 6.97 (2H, s, H_3), 6.43 (2H, m, H_4), 6.20 (4H, m, H_5), 4.07 (4H, t, J = 7.6 Hz, H_6), 3.00 (1H, s, H_7), 2.95 (1H, s, H_7), 2.69 (1H, s, OCH_3), 1.89 (1H, s, H_8), 1.86 (1H, s, H_8), 0.49 (2H, m, H_9), −0.64 (2H, m, H_{10}), −1.72 (2H, d, J = 15.0 Hz, H_{11}). δ_C (75 MHz, C_6D_6, 343 K): 167.7 (C═O), 157.5 (C Ar), 157.3 (C Ar), 145.1 (C Ar), 144.0 (C Ar), 134.4 (CH Ar), 133.3 (CH Ar), 133.0 (C Ar), 131.1 (CF_3), 127.3 (CH Ar), 126.8 (CH Ar), 124.2 (CH Ar), 122.1 (CH Ar), 119.2 (CH Ar), 117.6 (CH Ar), 75.2 (CH), 50.8 (OCH_3), 31.7 (CH_2), one CF_3 signal and three quaternary carbon signals were not detected. δ_F (282 MHz, C_6D_6, 343 K): −62.31 (12F, s, $CF_{3\ porphyrin}$), −62.81 (12F, s, CF_3 Ar), −63.53 (12F, s, CF_3 Ar). UV−vis (CH_2Cl_2): λ_{max} (log ε) 419 (5.11), 521 (4.32), 551 nm (4.20) sh. IR (ATR): 1740 ($\nu_{C=O}$), 1012 cm^{-1} (oxidation marker band). MS (FAB^+): m/z 1376 [M − 390 (R-N-Ar)]$^+$.

Synthesis of Methyl 3-(4-(Trifluoromethyl)phenylamino)-3-phenylpropanoate (14a). Yield: 38% (method E). δ_H (400 MHz, $CDCl_3$): 7.39−7.24 (7H, m, H Ar), 6.58 (2H, d, J = 8.4 Hz, H Ar), 4.86 (1H, m, C*H*(NHAr)), 3.66 (3H, s, OCH_3), 2.85 (2H, m, CH_2), NH signal not detected. δ_C (100 MHz, $CDCl_3$): 171.5 (C═O), 149.3 (C Ar), 141.3 (C Ar), 129.1 (CH Ar), 128.0 (CH Ar), 126.7 (CH Ar), 126.3 (CH Ar), 123.6 (C Ar), 119.7 (CF_3, q, J = 32.0 Hz), 113.1 (CH Ar), 54.8 (CH), 52.1 (OCH_3), 42.5 (CH_2). δ_F (282 MHz, $CDCl_3$): −61.48 (CF_3). HRMS ESI: $(M + H)^+$ calcd for $C_{17}H_{17}NO_2F_3$ 324.1206, found 324.1210..

Synthesis of Methyl 3-(4-(Trifluoromethyl)phenylamino)-3-phenylpropanoate (14b). Yield: 14% (method E). δ_H (300 MHz, $CDCl_3$): 7.40 (2H, d, J = 8.5 Hz, H Ar), 7.29 (3H, m, H Ar), 7.14 (2H, m, H Ar), 6.60 (2H, d, J = 8.5 Hz, H Ar), 4.41 (1H, t, J = 6.1 Hz, CH), 3.71 (3H, s, OCH_3), 3.11 (1H, dd, J = 13.7, 6.3 Hz, C*H*H), (1H, dd, J = 13.7, 5.9 Hz, CH*H*), NH signal was not detected. δ_C (75 MHz, $CDCl_3$): 173.0 (C═O), 149.0 (C Ar), 136.0 (C Ar), 129.4 (CH Ar), 128.8 (CH Ar), 127.4 (CH Ar), 126.9 (CH Ar), 123.1 (C Ar), 120.1 (CF_3, q, J = 32.7 Hz), 112.8 (CH Ar), 57.2 (CH), 52.4 (OCH_3), 38.5 (CH_2). δ_F (282 MHz, $CDCl_3$): −61.53 (CF_3). HRMS ESI: $(M + H)^+$ calcd for $C_{17}H_{17}NO_2F_3$ 324.1206, found 324.1211.

Synthesis of Methyl 3-(4-Nitrophenylamino)-3-phenylpropanoate (15a). Yield: 55% (method E). δ_H (300 MHz, $CDCl_3$): 8.00 (2H, d, J = 9.1 Hz, H Ar), 7.38−7.24 (5H, m, H Ar), 6.51 (2H, d, J = 9.1 Hz, H Ar), 5.63 (1H, d, J = 6.5 Hz, NH), 4.92 (1H, dd, J = 12.7, 6.7 Hz, C*H*(NHAr)), 3.65 (3H, s, OCH_3), 2.98−2.79 (2H, m, CH_2). δ_C (75 MHz, $CDCl_3$): 171.3 (C═O), 152.2 (C Ar), 140.5 (C Ar), 138.6 (C Ar), 129.2 (CH Ar), 128.2 (CH Ar), 126.3 (CH Ar), 126.1 (CH Ar), 112.3 (CH Ar), 54.5 (CH), 52.2 (OCH_3), 42.1 (CH_2). HRMS ESI: $(M + H)^+$ calcd for $C_{16}H_{17}N_2O_4$ 301.1183, found 301.1187.

Synthesis of Methyl 2-(4-Nitrophenylamino)-3-phenylpropanoate (15b). Yield: 21% (method E). δ_H (300 MHz, $CDCl_3$): 8.07 (2H, d, J = 9.2 Hz, H Ar), 7.33−7.22 (3H, m, H Ar), 7.16−7.09 (2H, m, H Ar), 6.52 (2H, d, J = 9.2 Hz, H Ar), 4.97 (1H, d, J = 8.0 Hz, NH), 4.47 (1H, dt, J = 8.0, 6.0 Hz, C*H*(NHAr)), 3.74 (3H, s, OCH_3), 3.23 (1H, dd, J = 13.8, 6.0 Hz, C*H*H), 3.14 (1H, dd, J = 13.8, 6.2 Hz, CH*H*). δ_C (75 MHz, $CDCl_3$): 172.2 (C═O), 151.6 (C Ar), 139.1 (C Ar), 135.4 (C Ar), 129.3 (CH Ar), 128.9 (CH Ar), 127.6 (CH Ar), 126.5 (CH Ar), 112.0 (CH Ar), 56.9 (CH), 52.7 (OCH_3), 38.3 (CH_2). HRMS ESI: $(M + H)^+$ calcd for $C_{16}H_{17}N_2O_4$ 301.1183, found 301.1182.

Synthesis of Methyl 3-(3,5-Dichlorophenylamino)-3-phenylpropanoate (16a). Yield: 65% (method E). δ_H (400 MHz, $CDCl_3$) 7.45−7.22 (5H, m, H Ar), 6.64 (1H, br s, H Ar), 6.43 (2H, d, J = 1.6 Hz, H Ar), 4.78 (2H, m, C*H*(NHAr) and NH), 3.66 (3H, s, OCH_3), 2.85 (1H, dd, J = 15.1, 5.3 Hz, C*H*H), 2.85 (1H, dd, J = 15.1, 5.3 Hz, C*H*H), 2.78 (1H, dd, J = 15.1, 7.8 Hz, C*H*H). δ_C (100 MHz, $CDCl_3$) 171.4 (C═O), 148.5 (C Ar), 141.0 (C Ar), 135.5 (C Ar), 129.1 (CH Ar), 128.0 (CH Ar), 126.2 (CH Ar), 117.7 (CH Ar), 112.0 (CH Ar), 54.7 (CH), 52.1 (OCH_3), 42.4 (CH_2). HRMS ESI: $(M + H)^+$ calcd for $C_{16}H_{16}NO_2Cl_2$ 324.0553, found 324.0549.

Synthesis of Methyl 2-(3,5-Dichlorophenylamino)-3-phenylpropanoate (16b). Yield: 8% (method E). δ_H (400 MHz, $CDCl_3$): 7.34−7.23 (3H, m, H Ar), 7.13 (2H, d, J = 6.8 Hz, H Ar), 6.70 (1H, pst, H Ar), 6.43 (2H, d, J = 1.6 Hz, H Ar), 4.30 (2H, m, C*H*(NHAr) and NH), 3.72 (3H, s, OCH_3), 3.17 (1H, dd, J = 13.7, 5.4 Hz, C*H*H), 3.08 (1H, dd, J = 13.7, 5.9 Hz, CH*H*). δ_C (75 MHz, $CDCl_3$): 172.8 (C═O), 148.1 (C Ar), 135.82 (C Ar), 135.76 (C Ar), 129.4 (CH Ar), 128.8 (CH Ar), 127.4 (CH Ar), 118.3 (CH Ar), 111.8 (CH Ar), 57.3 (CH), 52.5 (OCH_3), 38.5 (CH_2). HRMS ESI: $(M + H)^+$ calcd for $C_{16}H_{16}NO_2Cl_2$ 324.0553, found 324.0555.

Synthesis of (2*S*)-Methyl 2-Acetoxy-3-(3,5-bis(trifluoromethyl)phenylamino)-3-phenylpropanoate (17). Combined yield of both syn and anti isomers: 35% (syn/anti 20/80, method D, (2*S*)-methyl 2-acetoxy-3-phenylpropanoate employed as the substrate). Syn/anti assignment was performed on the basis of chemical shifts and coupling constant trends reported in the literature.[62] δ_H (400 MHz; $CDCl_3$): major isomer (anti) 7.38−7.30 (5H, m, H Ar), 7.15 (1H, s, H Ar), 6.91 (2H, s, H Ar), 5.35 (1H, d, J = 4.9 Hz, C*H*(OAc)), 5.20 (1H, m, NH), 4.95 (1H, br, C*H*(NHAr)), 3.64 (3H, s, OCH_3), 2.15 (3H, s, CH_3 acetoxy); minor isomer (syn) 7.38−7.30 (5H, m, H Ar), 7.15 (1H, s, H Ar), 6.91 (2H, s, H Ar), 5.41 (1H, d, J = 2.6 Hz, C*H*(OAc)), 5.16−5.05 (2H, m, NH and C*H*(NHAr)), 3.75 (3H, s, OCH_3), 2.11 (3H, s, CH_3 acetoxy). δ_C (100 MHz, $CDCl_3$): major isomer (anti) 170.2 (C═O acetoxy), 168.4 (C═O methyl ester), 147.1 (C Ar), 136.8 (C Ar), 136.1 (C Ar), 132.6 (CF_3, q, J = 33.1 Hz), 129.1 (CH Ar), 127.2 (CH Ar), 126.8 (CH Ar), 124.9 (C Ar), 122.2 (C Ar), 113.0 (CH Ar), 111.4 (CH Ar), 74.7 (*C*H(OAc)), 58.4 (*C*H(NHAr)), 52.6 (OCH_3 methoxy), 20.7 (CH_3 acetoxy); minor isomer (syn) 169.7 (C═O acetoxy), 168.4 (C═O methyl ester), 147.0 (C Ar), 136.8 (C Ar), 136.1 (C Ar), 132.6 (CF_3, q, J = 33.1 Hz), 129.2 (CH Ar), 128.9 (CH Ar), 128.7 (CH Ar), 124.9 (C Ar), 122.2 (C Ar), 113.0 (CH Ar), 111.4 (CH Ar), 75.3 (*C*H(OAc)), 58.0 (*C*H(NHAr)), 53.1 (OCH_3 methoxy), 20.5 (CH_3 acetoxy). δ_F (282 MHz, $CDCl_3$): −63.24 (CF_3 minor isomer), −63.25 (CF_3 major isomer). HRMS ESI: $(M + H)^+$ calcd for $C_{20}H_{18}NO_4F_6$ 450.1135, found 450.1137.

Synthesis of (2*S*)-Methyl 2-Methoxy-3-(3,5-bis(trifluoromethyl)phenylamino)-3-phenylpropanoate (18). Combined yield of both syn and anti isomers 53% (syn/anti = 45:55, method D, (2*S*)-methyl 2-methoxy-3-phenylpropanoate employed as the substrate). Syn/anti assignment was done on the basis of chemical shift and coupling constants trends reported in the literature.[62] δ_H (300 MHz; $CDCl_3$): major isomer (anti) 7.37−7.27 (5H, m, H Ar), 7.11 (1H, s, H Ar), 6.91 (2H, s, H Ar), 5.37 (1H, d, J = 7.3 Hz, NH), 4.85 (1H, m, C*H*(NHAr)), 4.20 (1H, d, J = 4.7 Hz, C*H*(OMe)), 3.62 (3H, s, OCH_3 ester), 3.48 (3H, s, OCH_3 ether); minor isomer (syn)

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7.37−7.27 (5H, m, H Ar), 7.09 (1H, s, H Ar), 6.87 (2H, s, H Ar), 5.27 (1H, d, J = 7.6 Hz, NH), 4.85 (1H, m, C*H*(NHAr)), 4.05 (1H, d, J = 3.0 Hz, C*H*(OMe)), 3.75 (3H, s, OCH_3 ester), 3.36 (3H, s, OCH_3 ether). δ_C (75 MHz, $CDCl_3$): major isomer (anti) 170.8 (C═O), 147.4 (C Ar), 136.6 (C Ar), 132.4 (CF_3, q, J = 32.7 Hz), 128.9 (CH Ar), 128.6 (CH Ar), 127.3 (CH Ar), 125.4 (C Ar), 121.8 (C Ar), 113.0 (CH Ar), 110.9 (CH Ar), 83.2 (*C*H(OMe)), 59.3 (OCH_3 ether), 59.1 (*C*H(NHAr)), 52.1 (OCH_3 ester); minor isomer (syn) 170.2 (C═O), 147.5 (C Ar), 138.2 (C Ar), 132.4 (CF_3, q, J = 32.7 Hz), 129.0 (CH Ar), 128.3 (CH Ar), 127.1 (CH Ar), 125.4 (C Ar), 121.8 (C Ar), 113.0 (CH Ar), 110.9 (CH Ar), 83.7 (*C*H(OMe), 59.6 (OCH_3 ether), 59.1 (*C*H(NHAr)), 52.5 (OCH_3 ester). δ_F (282 MHz, $CDCl_3$): −63.59 (CF_3). HRMS ESI: $(M + H)^+$ calcd for $C_{19}H_{18}NO_3F_6$ 422.1185, found 422.1181.

Synthesis of (3*S*)-3-Methoxy-4-phenyl-1-(3,5-bis(trifluoromethyl))phenylazetidin-2-one (19). Compound **19** was obtained from compound **18** (189 mg, 4.5×10^{-1} mmol) by using a reported procedure (30% yield).[36] Only one diastereoisomer was formed. δ_H (300 MHz; $CDCl_3$): 7.70 (2H, s, H Ar), 7.55 (1H, s, H Ar), 7.44−7.30 (5H, m, H Ar), 4.99 (1H, d, J = 1.9 Hz, C*H*(Ph)), 4.53 (1H, d, J = 1.9 Hz, C*H*(OMe)), 3.60 (3H, s, OCH_3 methoxy). δ_C (75 MHz, $CDCl_3$): 164.8 (C═O), 138.5 (C Ar), 135.0 (C Ar), 132.8 (CF_3, q, J = 33.7 Hz), 129.8 (CH Ar), 129.6 (CH Ar), 126.1 (CH Ar), 124.8 (C Ar), 121.1 (C Ar), 117.7 (CH Ar), 117.3 (CH Ar), 91.8 (*C*H(OMe)), 64.1 (CH(Ph)), 58.6 (OCH_3 methoxy). δ_F (282 MHz, $CDCl_3$): −63.53 (CF_3). HRMS ESI: $(M + H)^+$ calcd for $C_{18}H_{14}NO_2F_6$ 390.0923, found 390.0926.

■ ASSOCIATED CONTENT

Supporting Information

Figures giving NMR, UV−vis, IR, and GC-MS spectra of isolated compounds and CIF files and tables giving crystallographic data for **1** and **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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