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Nucleophilic addition of potassium organotrifluoroborates to chiral cyclic *N*-acyliminium ions: stereoselective synthesis of functionalized *N*-heterocycles

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Abstract

The stereoselective nucleophilic addition of potassium aryl- and alkynyltrifluoroborates to cyclic *N*-acyliminium ion derivatives from *N*-benzyl-3,4,5-triacetoxy-2-pyrrolidinone, affording the respective 5-substituted 2-pyrrolidinone is described. The products were obtained in moderate to good yields and with preference for the *syn* diastereomer.

1. Introduction

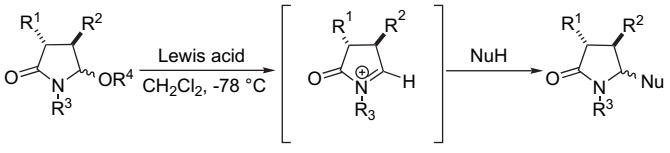
N-Acyliminium ions[1] are very important in organic synthesis since they are reactive intermediates involved in the synthesis of many compounds with interesting biological properties. Nucleophilic additions to *N*-acyliminium ions constitute an important method to provide α-functionalized amino compounds and for the preparation of alkaloids and many other biologically active nitrogen heterocycles.[2] Of particular interest are the intermolecular nucleophilic substitution reactions of cyclic *N*-acyliminium ions precursors (*N*,*O*-acetal derivatives) with carbon-based nucleophiles through activation by a Lewis acid (α-amidoalkylation reaction) (Scheme 1).

The activation of the *N*,*O*-acetal derivatives in order to perform α-amidoalkylations[3] can be carried out under mild conditions with catalytic amounts of acid to access sensitive target molecules. α-Amidoalkylation has been extensively investigated[3a] and the intermediates thereof have been employed in polar cycloadditions.[3b,c]

Different classes of carbon nucleophiles can react with *N*-acyliminium ions, including allylsilanes,[4] allyl-,[5] alkyl- and aryl-[4e,6] and alkynylmetal,[7] TMSCN,[4d,8] isonitriles,[8c] enol derivatives,[2b,4d,i,j,8c,9] and aromatics.[2e,10]

While a wide variety of nucleophiles are known to attack *N*-acyliminium ions, there are few reactions with alkenyl-, alkynyl- or arylmetal derivatives.[4e,11] Batey et al.[12a] and Pyne et al.[12b] reported the stereoselective addition reaction of alkenyl- and arylboronates to activated *N*-acyliminium ion precursor under Lewis acidic catalysis.[12]

In the recent years, organoboron compounds have become one of the most popular organometallic reagents into the car-



Scheme 1. Nucleophilic additions to the *N*-acyliminium ions.

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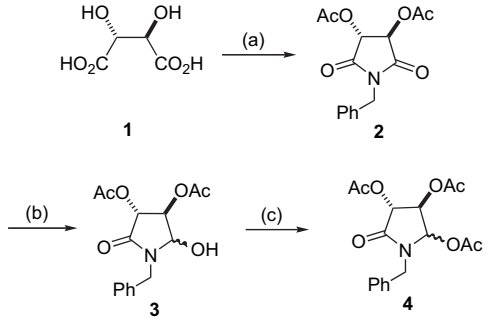
bon–carbon bond formation chemistry.[13] The organoboron compounds most used are boronic acids and boronate esters, but these compounds have some drawbacks, among them we can mention the low stability, very high price of some reagents and high sensitivity to air and moisture. To solve the problems those organoboron have been replaced by potassium organotrifluoroborate salts. These latter reagents are very stable to air and moisture, crystalline solids, easily prepared from inexpensive materials and show a greater nucleophilicity compared with their boronic acids or boronate esters analogues.[14a] Petasis et al. developed a three-component coupling reaction of alkenyl- and arylboronic acids with aldehydes and amines, for the synthesis of allylamines and α-amino acids.[15] Similar reactions were performed with potassium organotrifluoroborates in the synthesis of allylic-,[16] homoallylic-,[17] propargyl-,[18] tertiary-[19] and α-(fluoroalkyl)amines.[20] These reactions were demonstrated not to occur via direct addition to free iminium ions. However, we considered that the greater reactivity of *N*-acyliminium ions could enable reaction with potassium organotrifluoroborates.

2. Results and discussion

In connection with our research interest on the preparation and reactivity of potassium organotrifluoroborates, and their use as intermediates in organic synthesis,[14] we wish to report here the stereoselective addition reactions of aryl- and alkynyltrifluoroborates to the endocyclic *N*-acyliminium ion derivative from L-tartaric acid 3,4,5-triacetoxy-2-pyrrolidinone **4**.

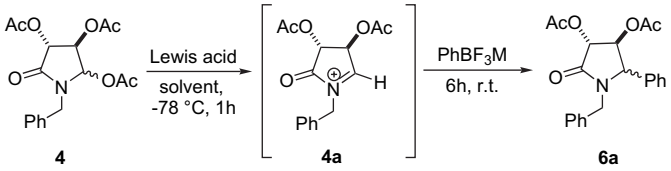
L-Tartaric and L-malic acids have proven to be useful precursors for *N*-acyliminium ion reactions leading to enantiopure pyrrolidine derivatives.[1] The *N*-benzyl imide **2** was prepared from inexpensive L-tartaric acid **1**, according to literature procedure[9c] (Scheme 2).



Scheme 2. Reagents and conditions: (a) (i) CH_3COCl, reflux, 24 h; (ii) benzyl amine, THF, rt, 4 h; (iii) CH_3COCl, reflux, 5 h (**2**, 78%); (b) $NaBH_4$, EtOH, THF, −30 °C, 30 min (**3**, 83%); (c) Ac_2O, Et_3N, 4-DMAP, CH_2Cl_2, rt, 3 h (**4**, 88%).

Acid **1** was successively treated with acetyl chloride, benzyl amine and acetyl chloride to afford the respective imide **2**. Regio- and stereoselective reduction of the imide **2** was accomplished by the reaction with excess sodium borohydride in ethanol/THF at −30 °C for 30 min to give the 5-hydroxy-2-pyrrolidinone derivative **3** as a 95:5 mixture of *syn*/*anti* diastereoisomers.[9c] After acylation of the alcohol with acetic anhydride, the desired *N*-acyliminium ion precursor **4** was obtained in good yield. The stereochemistry of the major *syn*-isomer was determined on the basis of the $J_{(H4-H5)}$ coupling constant of 2.0 Hz.

Our initial studies were focused on the development of an optimum set of reaction conditions. For initial screening experiments *N*-benzyl-3,4,5-triacetoxy-2-pyrrolidinone **4** and potassium phenyltrifluoroborate **5a** were selected as starting materials and dichloromethane as solvent. Reaction of **4** with potassium phenyltrifluoroborate in the absence of a Lewis acid did not lead to the desired adducts and the starting material **4** was recovered unchanged. The requirement for Lewis acidic activation strongly implies the intermediacy of *N*-acyliminium ions in this kind of reaction. In view of this result, we initially evaluated the influence of the Lewis acid on the stereoselective addition of potassium phenyltrifluoroborate. For this purpose, the *N*-benzyl-3,4,5-triacetoxy-2-pyrrolidinone **4** was treated with $BF_3 \cdot Et_2O$ (1.0 equiv) at −78 °C to ensure in situ formation of the corresponding *N*-acyliminium ion **4a**, which was formed in 30 min (Scheme 3), as evidenced by the consumption of **4** by TLC analysis.



Scheme 3. Lewis acid-mediated nucleophilic addition of phenyltrifluoroborate to the substrate **4**.

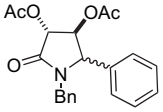
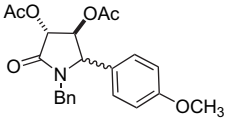
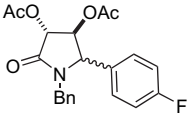
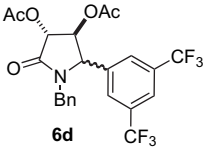
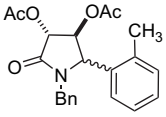
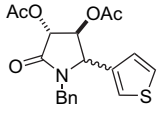
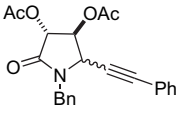
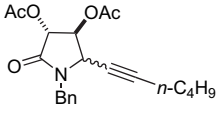
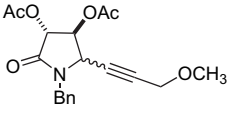
Next, potassium phenyltrifluoroborate **5a** (1.2 equiv) was added and the reaction was allowed to warm to room temperature and stirred for 6 h. The desired product **6a** was obtained in only 21% isolated yield as a mixture in 75:25 ratio of the *syn* and *anti* diastereoisomers, respectively (Table 1, entry 2).

Table 1
Conditions and results for the synthesis of compound **6a** according to Scheme 3

Entry	Lewis acid (equiv)	Solvent	M	*syn*/*anti* Ratio[a]	Yield[b] (%)
1	—	CH_2Cl_2	K	—	—
2	$BF_3 \cdot Et_2O$ (1.0)	CH_2Cl_2	K	75:25	21
3	$BF_3 \cdot Et_2O$ (2.0)	CH_2Cl_2	K	75:25	23
4	$BF_3 \cdot Et_2O$ (3.0)	CH_2Cl_2	K	80:20	46
5	$BF_3 \cdot Et_2O$ (4.0)	CH_2Cl_2	K	90:10	85
6[c]	$BF_3 \cdot Et_2O$ (5.0)	CH_2Cl_2	K	90:10	84
7	$BF_3 \cdot Et_2O$ (4.0)	CH_2Cl_2	n-Bu_4N^+	90:10	81
8	$BF_3 \cdot Et_2O$ (4.0)	CH_3CN	K	65:35	67
9	$BF_3 \cdot Et_2O$ (4.0)	Toluene	K	60:40	54
10	$BF_3 \cdot Et_2O$ (4.0)	Toluene	n-Bu_4N^+	60:40	51
11	$BF_3 \cdot Et_2O$ (4.0)	$Cl(CH_2)_2Cl$	K	90:10	82
12	$TiCl_4$ (4.0)	CH_2Cl_2	K	50:50	13
13	$SnCl_4$ (4.0)	CH_2Cl_2	K	—	—
14	$ZnBr_2$ (4.0)	CH_2Cl_2	K	—	—

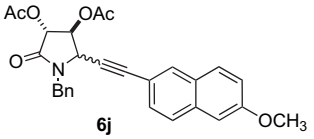
[a] Ratios determined by ^1H NMR (300 MHz) integration of the hydrogen attached to the α-nitrogen carbon on the crude reaction mixture.
[b] Isolated yields of the pure product after flash chromatography.
[c] The reaction was performed at room temperature for 24 h.

Table 2
5-Substituted 2-pyrrolidinones **6a–j**

Entry	Nucleophile (**5**)	Product (**6**)	*syn*/*anti* Ratio[a]	Yield[b] (%)
1	$C_6H_5BF_3K$ (**5a**)	 **6a**	90:10	84
2	4-$CH_3OC_6H_4$-BF_3K (**5b**)	 **6b**	90:10	87
3	4-$FC_6H_4BF_3K$ (**5c**)	 **6c**	90:10	68
4	3,5$(CF_3)_2C_6H_3$-BF_3K (**5d**)	 **6d**	70:30	65
5	2-$CH_3C_6H_4$-BF_3K (**5e**)	 **6e**	90:10	76
6	3-$C_4H_3SBF_3K$ (**5f**)	 **6f**	85:15	71
7	$C_6H_5C{\equiv}CBF_3K$ (**5g**)	 **6g**	90:10	73
8	*n*-$C_4H_9C{\equiv}C$-BF_3K (**5h**)	 **6h**	70:30	83
9	$CH_3OCH_2C{\equiv}C$-BF_3K (**5i**)	 **6i**	80:20	78

(*continued*)

Table 2 (*continued*)

Entry	Nucleophile (**5**)	Product (**6**)	*syn*/*anti* Ratio[a]	Yield[b] (%)
10	6-CH_3O–$C_{10}H_6C{\equiv}C$ (**5j**)	 **6j**	70:30	71

[a] Ratios determined by ^{1}H NMR (300 MHz) integration of the hydrogen attached to the α-nitrogen carbon on the crude reaction mixture.
[b] Isolated yields of the pure product after flash chromatography.

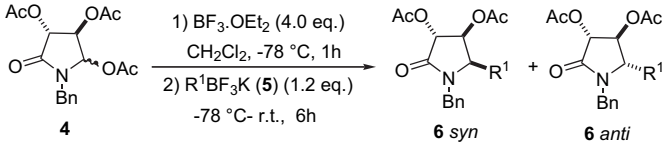
Surprisingly, potassium phenyltrifluoroborate did not react when $SnCl_4$ and $ZnBr_2$ were used as Lewis acids and the use of $TiCl_4$ led to very low yields and diastereoselectivity (Table 1, entries 12–14). However, with 4.0 equiv of $BF_3{\cdot}Et_2O$ the reaction proceeded to completion in 6 h, affording the product **6a** in very good yield and diastereomeric ratio (Table 1, entry 5). When higher amounts of $BF_3{\cdot}Et_2O$ were employed, no improvement on the yield and selectivity was observed, even when the reaction was performed at room temperature for 24 h (Table 1, entry 6).

The use of smaller amounts of $BF_3{\cdot}Et_2O$ resulted in very low yields (Table 1, entries 2–4). Next, we evaluated the influence of the organotrifluoroborate counter ion and found no significant influence on the reaction behaviour in respect to yield and diastereoisomeric ratio by using the tetra-*n*-butylammonium derivative (Table 1, entries 7 and 10). The use of other solvents such as acetonitrile and toluene afforded low isolated yields, and 1,2-dichloroethane produces similar results to CH_2Cl_2 (Table 1, entry 8–11).

Among the several reaction conditions tested the use of 4.0 equiv of $BF_3{\cdot}Et_2O$ as Lewis acid and 1.2 equiv of the potassium organotrifluoroborate in CH_2Cl_2 at −78 °C, under anhydrous and inert atmosphere for 1 h and room temperature for 6 h afforded the 5-substituted-2-pyrrolidinone **6a** in 84% yield in a 90:10 diastereomeric ratio in favour to the *syn*-isomer (determined by ^{1}H NMR analysis).

These optimised conditions were subsequently applied to the different potassium aryl- and alkynyltrifluoroborates **5b–j** as outlined in Table 2. The reaction proceeded with satisfactory to good yields and in good levels of diastereoselection in most cases. The scope of the reaction has been demonstrated by the evaluation of an array of donor–acceptor nucleophiles alkynyl-, aryl- and heteroaryltrifluoroborate combinations (Scheme 4).

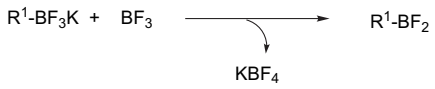
Reaction of *N*-acyliminium ion precursor **4** with electron-rich potassium aryltrifluoroborate **5b** led to 5-aryl-2-pyrrolidinone in a very good yield and diastereoselectivity (Table 2,



Scheme 4. Stereoselective addition of potassium organotrifluoroborates to *N*-acyliminium ion.

entry 2). Even with electron-poor potassium aryltrifluoroborates as nucleophiles the reaction proceeded in satisfactory yield (Table 2, entries 3 and 4). Similar level of diastereoselectivity and yields were also obtained by employing potassium alkynyltrifluoroborates **5g–j**.

Concerning the mechanism of this reaction, $BF_3 \cdot Et_2O$ reacts with potassium organotrifluoroborate to provide, as described by Kaufmann et al.,[21] organoboron difluoride, which was detected by ^{11}B NMR[20,21] (Scheme 5). The organoboron difluoride is also a Lewis acid able to activate the hemiaminal and generate iminium and nucleophilic species. Thus, the active nucleophile may be the R^1BF_2 species in this kind of reaction.[20]



Scheme 5. Generation of R^1BF_2 species.

The stereochemistry of the newly created stereogenic centre of **6b** was determined by ^1H NMR analysis of the crude mixture. The cis relative stereochemistry of the major product was established after analysis of the multiplicity and vicinal coupling constant of the hydrogen attached to the α-nitrogen (H-5) and then was extended to the other related compounds. In this way, the relative stereochemistry of compounds **6a–j** was assigned by the correlation of the chemical shifts and coupling constant data with similar compounds already described in the literature.[2e,22]

For the analogous 2-pyrrolidinones the vicinal coupling constant $^3J_{(H5-H4)}$ for the *syn*-isomer shows smaller value than the *anti*-isomer. These chemical correlations are in agreement with the major isomer obtained by us and the relative stereochemistry of the major isomer was assigned as being *syn*.[23] This result is unexpected, since neighbouring group participation of the 4-*O*-acetyl group in the stereocontrol does not seem to be affective; but it is rather the 3-*O*-acetyl group that provides anchimeric assistance, which leads to preferential formation of the *syn*-isomer (Scheme 6).

Several studies in the literature report on the preferential cis addition of nucleophiles to *N*-acyliminium ions, revealing that the stereochemical outcome is not ruled by steric effects. The *syn* preference indicate favourable orbital interaction[24] over steric interaction experienced during *syn* approach of the boron nucleophile to the resident OAc group of *N*-acyliminium intermediate **4a** in the presence of $BF_3 \cdot Et_2O$. Danishefsky et al.[25] hypothesised that in the Lewis acid catalysed processes the stabilisation of the emerging σ* orbital interaction with the adjacent σ bonds becomes critical factors for the *syn* additions.

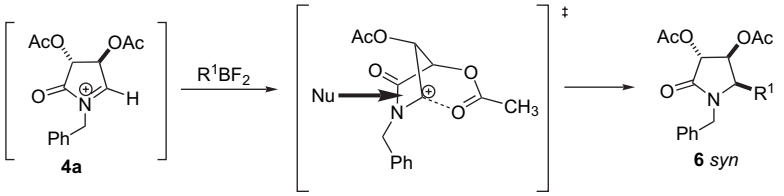
3. Conclusion

In summary, functionalized *N*-heterocycles are efficiently formed by the reaction of potassium aryl- and alkynyltrifluoroborates with activated *N*-acyliminium ion precursor under Lewis acidic conditions, affording preferentially the *syn*-5-substituted-2-pyrrolidinones in good diastereoselectivity. This methodology is advantageous relative to many *N*-acyliminium ion based strategies, because of the ready availability, high stability, low toxicity and mild nucleophilic character of the potassium organotrifluoroborate salts. Studies towards the employing of this methodology in the synthesis of indolizidine ring system are under investigation and will be reported in due course.

4. Experimental

4.1. General

All air-sensitive and/or water-sensitive reactions were carried out under nitrogen atmosphere with dry solvents under anhydrous conditions. Standard syringe techniques were applied for transfer of dry solvents and some air-sensitive reagents. The reactions were monitored by TLC carried out on Merck silica gel (60 F_{254}) by using UV light as visualising agent and 5% vanillin in 10% H_2SO_4 and heat as developing agents. Merck silica gel (particle size 0.040–0.063 mm) was used for flash chromatography. CH_2Cl_2 and CH_3CN were distilled from P_2O_5 and stored over MS 4 Å under atmosphere of dry nitrogen. Toluene was distilled from CaH_2 and stored over sodium-wire. Dry THF was distilled from sodium benzophenone ketyl prior to use. EtOH was dried, distilled from CaH_2 and stored over MS 4 Å. Et_3N was distilled from KOH pellets. Acetic anhydride was distilled from P_2O_5 and stored under atmosphere of dry nitrogen. NMR spectra were recorded with Bruker DPX 300 (300 MHz) instrument using $CDCl_3$ as solvent and calibrated using tetramethylsilane as internal standard. Chemical shifts are reported in δ parts per million relative to $(CH_3)_4Si$ for ^1H and $CDCl_3$ for ^{13}C NMR. Coupling constants (*J*) are reported in hertz. Diastereomeric ratios were determined by peak integration in the ^1H NMR spectra of the crude product. Infrared (IR) spectra were obtained from $CHCl_3$ solutions, using a Varian 3100 FT-IR spectrophotometer and wavelengths are reported in cm^{-1}. Mass spectra (MS) were measured on a Shimadzu GCMS-QP5050A mass spectrometer. The HRMS spectra



Scheme 6. Stereoselective addition of the R^1BF_2 to *N*-acyliminium ions.

were measured on a Bruker Daltonics Micro TOF (direct inlet probe).

4.2. Synthesis of *N*-acyliminium ion precursor **4**

The *N*-acyliminium ion precursor was prepared starting from L-tartaric acid using standard procedures.[9c]

4.2.1. (3R,4R)-3,4-Bis-(acetoxy)-1-benzyl-2,5-dioxopyrrolidin-3-yl acetate (**2**)

A mixture of L-tartaric acid (15.0 g, 100 mmol) and acetyl chloride (70 mL, 1.0 mol) was stirred under reflux for 24 h under nitrogen atmosphere, during which the solution became homogeneous. Excess acetyl chloride was removed by distillation at 1 atm and trace amounts were removed under vacuum. The crude anhydride resulting was dissolved in dry THF (120 mL) and benzyl amine (10.7 g, 100 mmol) was slowly added. After the solution was stirred for 4 h, it was concentrated in vacuum and the residue was refluxed with acetyl chloride (70 mL, 1.0 mol) for another 5 h. After concentration of the reaction mixture in vacuum, the residue was purified by using column chromatography (*n*-hexane/ethyl acetate, 2:1) to give **2** (23.8 g, 78%) as a white solid, mp=120–121 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.18 (s, 6H), 4.72 (s, 2H), 5.53 (s, 2H), 7.29–7.35 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.3, 43.0, 72.7, 128.2, 128.3, 129.1, 136.2. IR cm^{-1} ($CHCl_3$ solution): 3007, 2970, 1739, 1689.

4.2.2. (3R,4R,5R)-3,4-Bis-(acetoxy)-5-hydroxy-1-benzyl-2-pyrrolidinone (**3**)

To a solution of the imide **2** (21.3 g, 70 mmol) in a mixture of 300 mL of EtOH and 100 mL of THF was added at −30 °C $NaBH_4$ (13.3 g, 350 mmol) portion wise under nitrogen atmosphere. After the addition was completed (5 min), the reaction was stirred at −30 °C for 1 h, and was acidified with 10% HCl until pH 2–3, followed by neutralisation with saturated $NaHCO_3$. The reaction mixture was partitioned between 300 mL of CH_2Cl_2 and 100 mL of water. The layers were separated and the aqueous phase was extracted with three 150 mL portions of CH_2Cl_2. The combined organic phases were dried over $MgSO_4$, filtered, and concentrated in vacuum to give the crude 5-hydroxy-2-pyrrolidinone **3** in a 95:5 mixture of *syn*/*anti* diastereoisomers (17.8 g, 83%) as a white solid. Recrystallisation (EtOAc) gave white crystals, mp=91–92 °C. *syn*-Isomer: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.10 (s, 3H), 2.15 (s, 3H), 4.23 (d, J=15.0 Hz, 1H), 4.50 (d, J=15.0 Hz, 1H), 5.13 (dd, J=4.2, 2.1 Hz, 1H), 5.37 (d, J=4.2 Hz, 1H), 6.11 (d, J=2.1 Hz, 1H), 7.23–7.35 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.6, 20.7, 43.2, 74.3, 79.2, 83.1, 127.9, 128.5, 128.8, 135.2, 166.8, 170.5, 170.6. IR cm^{-1} ($CHCl_3$ solution): 3259, 2987, 1751, 1671.

4.2.3. (3R,4R,5R)-3,4,5-Tris-(acetoxy)-1-benzyl-2-oxopyrrolidin-3-yl acetate (**4**)

To a solution of the 5-hydroxy-2-pyrrolidinone **3** (15.3 g, 50 mmol) in CH_2Cl_2 (150 mL) under nitrogen atmosphere, cooled to 0 °C were added Et_3N (7.0 mL, 50 mmol), acetic anhydride (8.8 mL, 70 mmol) and 4-(*N*,*N*-dimethylamino)pyridine (430 mg, 5 mmol). The reaction was allowed to warm up to room temperature, and stirred for 3 h. The mixture was diluted with CH_2Cl_2 (100 mL) and washed with 10% HCl (40 mL), saturated $NaHCO_3$ (40 mL) and water (2×60 mL). The organic phase was dried over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel (230–400 mesh, 30% ethyl acetate in hexanes) to afford **4** (14.3 g, 44 mmol) in 88% yield in a 96:4 mixture of *syn*/*anti* diastereoisomers and as a pale yellow oil. *Syn*-Isomer: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.89 (s, 3H), 2.07 (s, 3H), 2.18 (s, 3H), 4.35 (d, J=15.0 Hz, 1H), 4.65 (d, J=15.0 Hz, 1H), 5.21 (dd, J=4.0, 2.0 Hz, 1H), 5.36 (d, J=4.0 Hz, 1H), 6.05 (d, J=2.0 Hz, 1H), 7.23–7.36 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.4, 20.5 (2C), 44.9, 73.1, 75.9, 83.4, 127.9, 128.5, 128.8, 135.2, 167.8, 169.5, 169.6, 170.0. IR cm^{-1} ($CHCl_3$ solution): 2970, 1743, 1695. GC/MS: *m*/*z* (relative intensity) 289 (9%), 188 (10%), 124 (9%), 91 (45%), 43 (100%).

4.3. Synthesis of potassium aryl- and alkynyltrifluoroborates (**5a–j**)

The organotrifluoroborates were prepared according literature procedures.[26]

4.3.1. General procedure for the synthesis of the potassium aryltrifluoroborates (**5a–f**)[26a]

A solution of the arylmagnesium bromide (10 mmol, 1.0 equiv) in 20 mL of dry THF was cooled to −78 °C under nitrogen atmosphere, trimethylborate (1.56 g, 15 mmol, 1.5 equiv) was then added dropwise at −78 °C. The solution was stirred at this temperature for 1 h after which it was allowed to warm to −20 °C for 1 h. A saturated aqueous solution of potassium hydrogen difluoride (4.7 g, 60 mmol, 6.0 equiv) was added to the vigorously stirred solution. The resulting mixture was allowed to stir for 1 h at −20 °C after which it was allowed to warm to room temperature for 1 h. The solvent was removed under reduced pressure, and the resulting white solid was dried under high vacuum for 2 h to remove all water. The solid was then washed with acetone and hot acetone. The resulting organic solution was filtered, and the solvent was removed to afford a fluffy white solid. This solid was then dissolved in hot acetone and precipitated with diethyl ether, after which the solution was cooled to −20 °C to complete precipitation of the solid. The product **5a** was collected as a white crystalline solid (1.52 g, 83%).

4.3.2. General procedure for the synthesis of the potassium alkynyltrifluoroborates (**5g–j**)[26b]

A solution of 1-hexyne (0.82 g, 10 mmol, 1.0 equiv) in 20 mL of dry THF was cooled to −78 °C under nitrogen atmosphere, *n*-BuLi (6.25 mL, 1.6 M in hexane, 10 mmol, 1.0 equiv) was added dropwise, and the solution was stirred for 1 h at this temperature. Trimethylborate (1.56 g, 15 mmol, 1.5 equiv) was then added dropwise at −78 °C. The solution was stirred at this temperature for 1 h after which it was allowed to warm to

−20 °C for 1 h. A saturated aqueous solution of potassium hydrogen difluoride (4.7 g, 60 mmol, 6.0 equiv) was added to the vigorously stirred solution. The resulting mixture was allowed to stir for 1 h at −20 °C after which it was allowed to warm to room temperature for 1 h. The solvent was removed under reduced pressure, and the resulting white solid was dried under high vacuum for 2 h to remove all water. The solid was washed first with acetone and then with hot acetone. The resulting organic solution was filtered, and the solvent was removed to afford a fluffy white solid. This solid was then dissolved in hot acetone and precipitated with diethyl ether, after which the solution was cooled to −20 °C to complete precipitation of the solid. The product **5h** was collected as a white crystalline solid (1.66 g, 78%). Mp=256 °C (decomp.).[26b]

*4.4. General procedure for the synthesis of 5-aryl and 5-alkynyl-2-pyrrolidinones (**6a–j**)*

*4.4.1. (3R,4R)-3,4-Diacetoxy-5-phenyl-1-benzyl-2-pyrrolidinone (**6a**)*

To a solution of the 5-acetoxy-2-pyrrolidinone **4** (349 mg, 1.0 mmol) in CH_2Cl_2 (4.0 mL) at −78 °C under nitrogen atmosphere was added dropwise the $BF_3\cdot Et_2O$ (0.50 mL, 4.0 mmol, 4.0 equiv). The reaction was kept for 1 h at −78 °C when potassium phenyltrifluoroborate (220 mg, 1.2 mmol, 1.2 equiv) was added in one portion. After 1 h at −78 °C the reaction mixture was stirred for 6 h at room temperature when it was quenched with saturated $NaHCO_3$ (10 mL). The mixture was diluted with CH_2Cl_2 (20 mL), and the organic phase was washed with 10% HCl (10 mL), saturated $NaHCO_3$ (10 mL) and dried over $MgSO_4$. Evaporation under reduced pressure, followed by column chromatography on silica gel (20% ethyl acetate in hexanes) afforded **6a** in a 90:10 *syn/anti* mixture as a colourless oil, in 84% yield (312 mg). Both isomers have nearly the same R_f values and they could not be separated by column chromatography. The *syn/anti* ratio was determined to be 90:10 by the ^1H NMR (300 MHz) analysis of the crude product. Major isomer: *syn*-**6a**. ^1H NMR (300 MHz, $CDCl_3$) δ 2.06 (s, 3H), 2.21 (s, 3H), 4.22 (d, J=15.0 Hz, 1H), 4.89 (dd, J=6.2, 2.0 Hz, 1H), 5.05 (d, J=15.0 Hz, 1H), 5.10 (d, J=2.0 Hz, 1H), 5.71 (d, J=6.2 Hz, 1H), 7.28−7.40 (m, 7H), 7.50 (t, J=7.4 Hz, 1H), 7.78 (d, J=7.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 20.6, 43.1, 61.5, 73.9, 78.7, 127.1, 128.0, 128.5, 128.8, 129.0, 132.3, 134.5, 135.5, 166.8, 167.6, 170.2. GC/MS: *m/z* (%)=367 (5) [M^+], 291 (70), 262 (3), 187 (28), 117 (100), 105 (57), 91 (84), 77 (8), 43 (94). HRMS (ESI, positive) *m/z* calcd for $C_{21}H_{21}NO_5$ 368.1419 ([M+H]$^+$); found 368.1408 ([M+H]$^+$). IR cm^{-1} ($CHCl_3$ solution): 3023, 2938, 1755, 1721, 1451. Minor isomer: *anti*-**6a**. ^1H NMR (300 MHz, $CDCl_3$) δ 2.08 (s, 3H), 2.22 (s, 3H), 4.05 (d, J=15.0 Hz, 1H), 4.58 (dd, J=8.2, 5.4 Hz, 1H), 5.01 (d, J=15.0 Hz, 1H), 5.08 (d, J=5.4 Hz, 1H), 5.36 (d, J=8.2 Hz, 1H), 7.28−7.40 (m, 7H), 7.50 (t, J=7.4 Hz, 1H), 7.78 (d, J=7.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.3, 20.5, 43.0, 61.3, 73.7, 78.6, 127.0, 128.0, 128.5, 128.8, 129.0, 132.3, 134.5, 135.5, 166.7, 167.5, 170.2.

*4.4.2. (3R,4R)-3,4-Diacetoxy-5-(4-methoxyphenyl)-1-benzyl-2-pyrrolidinone (**6b**)*

The product **6b** was prepared as described in the general procedure and was obtained in a 90:10 *syn/anti* mixture as a colourless oil in 87% yield (345 mg). Major isomer: *syn*-**6b**. ^1H NMR (300 MHz, $CDCl_3$) δ 2.08 (s, 3H), 2.12 (s, 3H), 3.72 (s, 3H), 3.97 (d, J=15.0 Hz, 1H), 4.08 (dd, J=5.0, 5.2 Hz, 1H), 4.52 (d, J=5.0 Hz, 1H), 5.01 (d, J=15.0 Hz, 1H), 5.27 (d, J=5.2 Hz, 1H), 6.82 (d, J=8.3 Hz, 2H), 6.88 (d, J=8.3 Hz, 2H), 7.18−7.24 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.6, 20.7, 45.0, 55.3, 60.2, 74.7, 76.6, 111.1, 114.5, 120.7, 123.2, 128.5, 128.8, 129.3, 130.5, 135.4, 167.8, 169.8, 170.0. GC/MS: *m/z* (%)=397 (3) [M^+], 337 (39), 295 (33), 278 (17), 204 (56), 91 (100), 43 (63). HRMS (ESI, positive) *m/z* calcd for $C_{22}H_{23}NO_6$ 398.1579 ([M+H]$^+$); found 398.1563 ([M+H]$^+$). IR cm^{-1} ($CHCl_3$ solution): 3027, 2936, 1752, 1719, 1229. Minor isomer: *anti*-**6b**. ^1H NMR (300 MHz, $CDCl_3$) δ 2.09 (s, 3H), 2.14 (s, 3H), 3.75 (s, 3H), 3.98 (d, J=15.0 Hz, 1H), 4.33 (dd, J=8.0, 8.0 Hz, 1H), 4.45 (d, J=8.0 Hz, 1H), 4.90 (d, J=15.0 Hz, 1H), 5.37 (d, J=8.0 Hz, 1H), 6.85 (d, J=8.3 Hz, 2H), 6.88 (d, J=8.3 Hz, 2H), 7.18−7.24 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 20.5, 45.2, 55.4, 60.3, 74.6, 76.9, 111.2, 114.7, 120.8, 123.3, 128.6, 128.8, 129.3, 130.6, 135.6, 167.7, 169.9, 170.2.

*4.4.3. (3R,4R)-3,4-Diacetoxy-5-(4-fluorophenyl)-1-benzyl-2-pyrrolidinone (**6c**)*

The product **6c** was prepared as described in the general procedure and was obtained in a 90:10 *syn/anti* mixture as a colourless oil in 68% yield (261 mg). Major isomer: *syn*-**6c**. ^1H NMR (300 MHz, $CDCl_3$) δ 2.19 (s, 3H), 2.25 (s, 3H), 4.28 (d, J=14.6 Hz, 1H), 4.94 (dd, J=6.2, 2.0 Hz, 1H), 5.08 (d, J=14.6 Hz, 1H), 5.15 (d, J=2.0 Hz, 1H), 5.76 (d, J=6.2 Hz, 1H), 7.12 (t, J=8.8 Hz, 2H), 7.31−7.42 (m, 5H), 7.83 (dd, J=8.3, 2.1 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 20.7, 45.0, 63.2, 75.0, 77.5, 115.1, 127.7, 128.1, 128.4, 128.7, 134.6, 137.4, 167.6, 169.9, 170.2. GC/MS: *m/z* (%)=385 (3) [M^+], 309 (64), 187 (29), 177 (12), 117 (100), 105 (53), 91 (80), 43 (98). HRMS (ESI, positive) *m/z* calcd for $C_{21}H_{20}FNO_5$ 385.1325 ([M+H]$^+$); found 385.1332 ([M+H]$^+$). IR cm^{-1} ($CHCl_3$, solution): 3021, 2937, 1750, 1724. Minor isomer: *anti*-**6c**. ^1H NMR (300 MHz, $CDCl_3$) δ 2.07 (s, 3H), 2.21 (s, 3H), 4.25 (d, J=14.5 Hz, 1H), 4.62 (dd, J=7.8, 7.8 Hz, 1H), 5.01 (d, J=14.5 Hz, 1H), 5.13 (d, J=7.8 Hz, 1H), 5.71 (d, J=7.8 Hz, 1H), 7.12 (t, J=8.8 Hz, 2H), 7.31−7.42 (m, 5H), 7.83 (dd, J=8.3, 2.1 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.3, 20.5, 44.6, 63.1, 74.8, 76.8, 115.0, 127.6, 128.1, 128.4, 128.6, 134.5, 137.3, 167.5, 169.8, 170.0.

*4.4.4. (3R,4R)-3,4-Diacetoxy-5-[3,5-bis-(trifluoromethyl)-phenyl]-1-benzyl-2-pyrrolidinone (**6d**)*

The product **6d** was prepared as described in the general procedure and was obtained in a 70:30 *syn/anti* mixture as a colourless oil in 65% yield (326 mg). Major isomer: *syn*-**6d**. ^1H NMR (300 MHz, $CDCl_3$) δ 2.13 (s, 3H), 2.27 (s, 3H), 4.21 (dd, J=6.1, 6.1 Hz, 1H), 4.37 (d, J=14.6 Hz, 1H), 4.67 (d, J=6.1 Hz, 1H), 5.05 (d, J=14.6 Hz, 1H), 5.87 (d, J=6.1 Hz, 1H), 7.30−7.42

(m, 5H), 8.05 (s, 1H), 8.32 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.2, 20.4, 45.3, 69.5, 72.0, 75.0, 125.0, 128.2, 128.4, 128.8, 128.9, 129.0, 131.0, 134.2, 134.9, 168.2, 170.2, 170.4. GC/MS: *m/z* (%)=503 (1) [M^+], 427 (34), 310 (5), 295 (8), 117 (100), 106 (15), 91 (66), 43 (65). HRMS (ESI, positive) *m/z* calcd for $C_{23}H_{19}F_6NO_5$ 504.1246 ([M+H]$^+$); found 504.1230 ([M+H]$^+$). IR cm^{-1} ($CHCl_3$ solution): 3036, 2939, 1750, 1707. Minor isomer: *anti*-**6d**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.12 (s, 3H), 2.24 (s, 3H), 4.11 (d, *J*=14.6 Hz, 1H), 4.49 (dd, *J*=7.3, 7.3 Hz, 1H), 4.96 (d, *J*=7.3 Hz, 1H), 5.03 (d, *J*=14.6 Hz, 1H), 5.43 (d, *J*=7.4 Hz, 1H), 7.30–7.42 (m, 5H), 7.97 (s, 1H), 8.24 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1, 20.3, 45.1, 69.4, 71.8, 74.9, 125.1, 128.1, 128.4, 128.7, 128.9, 129.0, 130.8, 134.1, 134.8, 168.1, 170.2, 170.3.

*4.4.5. (3R,4R)-3,4-Diacetoxy-5-(2-methylphenyl)-1-benzyl-2-pyrrolidinone (**6e**)*

The product **6e** was prepared as described in the general procedure and was obtained in a 90:10 *syn/anti* mixture as a colourless oil in 76% yield (289 mg). Major isomer: *syn*-**6e**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.18 (s, 3H), 2.21 (s, 3H), 2.52 (s, 3H), 4.08 (d, *J*=14.6 Hz, 1H), 4.19 (dd, *J*=5.1, 5.1 Hz, 1H), 4.64 (d, *J*=5.1 Hz, 1H), 5.08 (d, *J*=14.6 Hz, 1H), 5.39 (d, *J*=5.1 Hz, 1H), 7.23 (d, *J*=8.2 Hz, 1H), 7.30–7.51 (m, 7H), 7.81 (d, *J*=8.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 20.6, 22.1, 44.5, 60.3, 72.0, 74.9, 124.9, 127.8, 128.3, 128.6, 128.7, 128.8, 130.1, 132.0, 134.5, 136.5, 167.6, 169.8, 170.1. GC/MS: *m/z* (%)=381 (5) [M^+], 305 (48), 261 (20), 233 (19), 187 (12), 159 (10), 128 (21), 117 (80), 91 (100), 43 (80). HRMS (ESI, positive) *m/z* calcd for $C_{22}H_{23}NO_5$ 382.1655 ([M+H]$^+$); found 382.1671([M+H]$^+$). IR cm^{-1} ($CHCl_3$ solution): 3029, 2933, 1753, 1723, 1451, 1225. Minor isomer: *anti*-**6e**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.16 (s, 3H), 2.20 (s, 3H), 2.49 (s, 3H), 4.13 (dd, *J*=6.3, 6.3 Hz, 1H), 4.30 (d, *J*=14.6 Hz, 1H), 4.94 (d, *J*=6.3 Hz, 1H), 5.02 (d, *J*=14.6 Hz, 1H), 5.76 (d, *J*=6.3 Hz, 1H), 7.21 (d, *J*=8.2 Hz, 1H), 7.30–7.51 (m, 7H), 7.81 (d, *J*=8.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.3, 20.5, 22.0, 45.0, 60.4, 71.9, 74.8, 124.8, 127.7, 128.3, 128.5, 128.7, 128.8, 130.0, 131.8, 134.4, 136.4, 167.5, 169.7, 170.0.

*4.4.6. (3R,4R)-3,4-Diacetoxy-5-(thiophen-3-yl)-1-benzyl-2-pyrrolidinone (**6f**)*

The product **6f** was prepared as described in the general procedure and was obtained in a 85:15 *syn/anti* mixture as a colourless oil in 71% yield (264 mg). Major isomer: *syn*-**6f**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.10 (s, 3H), 2.24 (s, 3H), 3.72 (d, *J*=14.0 Hz, 1H), 4.85 (dd, *J*=5.7, 5.7 Hz, 1H), 5.12 (d, *J*=14.0 Hz, 1H), 5.19 (d, *J*=5.7 Hz, 1H), 5.51 (d, *J*=5.7 Hz, 1H), 6.85 (dd, *J*=6.3, 3.5 Hz, 1H), 6.99 (d, *J*=4.0 Hz, 1H), 7.02 (d, *J*=4.0 Hz, 1H), 7.20–7.34 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.3, 20.5, 45.2, 56.4, 72.1, 75.7, 127.1, 128.3, 128.5, 128.7, 128.8, 128.9, 134.5, 137.0, 166.5, 169.8, 170.6. GC/MS: *m/z* (%)=373 (3) [M^+], 313 (9), 282 (5), 271 (39), 254 (17), 200 (19), 180 (22), 139 (40), 91 (100), 43 (83). HRMS (ESI, positive) *m/z* calcd for $C_{19}H_{19}NO_5S$ 374.1062 ([M+H]$^+$); found 374.1083 ([M+H]$^+$). IR cm^{-1} ($CHCl_3$ solution): 3032, 2934, 1749, 1706. Minor isomer: *anti*-**6f**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.07 (s, 3H), 2.21 (s, 3H), 3.69 (d, *J*=14.5 Hz, 1H), 4.76 (dd, *J*=8.1, 8.1 Hz, 1H), 5.09 (d, *J*=14.5 Hz, 1H), 5.34 (d, *J*=8.1 Hz, 1H), 5.84 (d, *J*=8.1 Hz, 1H), 6.86 (dd, *J*=6.3, 3.5 Hz, 1H), 6.98 (d, *J*=4.0 Hz, 1H), 7.03 (d, *J*=4.0 Hz, 1H), 7.20–7.34 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1, 20.4, 44.9, 56.2, 71.3, 74.8, 127.0, 128.2, 128.4, 128.6, 128.7, 128.9, 134.4, 136.8, 166.4, 167.8, 170.3.

*4.4.7. (3R,4R)-3,4-Diacetoxy-5-(2-phenyl-1-ethynyl)-1-benzyl-2-pyrrolidinone (**6g**)*

The product **6g** was prepared as described in the general procedure and was obtained in a 90:10 *syn/anti* mixture as a colourless oil in 73% yield (285 mg). Major isomer: *syn*-**6g**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.09 (s, 3H), 2.19 (s, 3H), 4.23 (d, *J*=15.0 Hz, 1H), 4.28 (d, *J*=5.7 Hz, 1H), 5.18 (d, *J*=15.0 Hz, 1H), 5.50 (d, *J*=5.7 Hz, 1H), 5.56 (dd, *J*=5.7, 5.7 Hz, 1H), 7.30–7.46 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.7, 20.9, 45.0, 51.5, 73.7, 76.2, 82.3, 88.0, 128.3, 128.6, 128.8, 129.0, 129.3, 129.4, 132.1, 135.2, 166.4, 169.9, 170.5. GC/MS: *m/z* (%)=391 (4) [M^+], 331 (15), 289 (54), 220 (9), 198 (17), 157 (13), 115 (11), 91 (84), 43 (100). HRMS (ESI, positive) *m/z* calcd for $C_{23}H_{21}NO_5$ 392.1498 ([M+H]$^+$); found 392.1485 ([M+H]$^+$). IR cm^{-1} ($CHCl_3$ solution): 3066, 2932, 2231, 1754, 1724. Minor isomer: *anti*-**6g**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.14 (s, 3H), 2.22 (s, 3H), 4.14 (d, *J*=15.0 Hz, 1H), 4.79 (d, *J*=7.8 Hz, 1H), 5.11 (d, *J*=15.0 Hz, 1H), 5.23 (dd, *J*=7.8 Hz, 1H), 5.75 (d, *J*=7.8 Hz, 1H), 7.30–7.46 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.8, 21.0, 45.6, 51.8, 73.9, 76.5, 82.4, 88.2, 128.3, 128.7, 128.9, 129.1, 129.3, 129.5, 132.0, 134.7, 166.4, 169.8, 170.1.

*4.4.8. (3R,4R)-3,4-Diacetoxy-5-(1-hexynyl)-1-benzyl-2-pyrrolidinone (**6h**)*

The product **6h** was prepared as described in the general procedure and was obtained in a 70:30 *syn/anti* mixture as a colourless oil in 83% yield (308 mg). Major isomer: *syn*-**6h**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (t, *J*=7.0 Hz, 3H), 1.21–1.45 (m, 4H), 2.08 (s, 3H), 2.16 (s, 3H), 2.23 (t, *J*=7.0 Hz, 2H), 4.15 (d, *J*=14.8 Hz, 1H), 4.71 (dd, *J*=6.2, 2.0 Hz, 1H), 4.93 (d, *J*=2.0 Hz, 1H), 5.08 (d, *J*=14.8 Hz, 1H), 5.53 (d, *J*=6.2 Hz, 1H), 7.28–7.34 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.3, 18.6, 20.4, 20.5, 25.3, 30.2, 44.6, 48.9, 71.1, 73.2, 87.3, 89.1, 127.8, 128.3, 128.5, 134.5, 166.1, 169.6, 170.1. GC/MS: *m/z* (%)=371 (3) [M^+], 311 (16), 269 (72), 252 (20), 200 (17), 178 (18), 137 (14), 91 (100), 43 (90). HRMS (ESI, positive) *m/z* calcd for $C_{21}H_{25}NO_5$ 372.1811 ([M+H]$^+$); found 372.1853 ([M+H]$^+$). IR cm^{-1} ($CHCl_3$ solution): 3032, 2957, 2239, 1754, 1723. Minor isomer: *anti*-**6h**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, *J*=7.0 Hz, 3H), 1.21–1.45 (m, 4H), 2.07 (s, 3H), 2.15 (s, 3H), 2.23 (t, *J*=7.0 Hz, 2H), 4.01 (d, *J*=14.8 Hz, 1H), 4.60 (d, *J*=7.6 Hz, 1H), 5.01 (dd, *J*=7.6, 7.6 Hz, 1H), 5.11 (d, *J*=14.8 Hz, 1H), 5.68 (d, *J*=7.6 Hz, 1H), 7.28–7.34 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.2, 18.7, 20.3, 20.4, 25.3, 30.0, 44.9, 50.6, 71.0, 73.1, 87.2, 89.0, 127.7, 128.2, 128.3, 134.5, 166.0, 169.5, 170.1.

*4.4.9. (3R,4R)-3,4-Diacetoxy-5-(3-methoxy-1-propynyl)-1-benzyl-2-pyrrolidinone (**6i**)*

The product **6i** was prepared as described in the general procedure and was obtained in a 80:20 *syn*/*anti* mixture as a colourless oil in 78% yield (280 mg). Major isomer: *syn*-**6i**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.10 (s, 3H), 2.16 (s, 3H), 3.32 (s, 3H), 4.00 (d, J=14.8 Hz, 1H), 4.08 (s, 2H), 4.56 (d, J=6.1 Hz, 1H), 5.04 (d, J=14.8 Hz, 1H), 5.12 (dd, J=6.1, 6.1 Hz, 1H), 5.64 (d, J=6.1 Hz, 1H), 7.24–7.30 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.6, 20.7, 45.4, 49.1, 57.6, 59.6, 71.4, 72.5, 77.9, 84.5, 128.2, 128.5, 128.9, 134.3, 166.2, 169.8, 170.3. GC/MS: *m*/*z* (%)=359 (3) [M^+], 299 (11), 267 (13), 257 (19), 240 (18), 225 (14), 197 (13), 187 (13), 106 (16), 91 (100), 43 (91). HRMS (ESI, positive) *m*/*z* calcd for $C_{19}H_{21}NO_6$ 360.1447 ([M+H]$^+$); found 360.1459 ([M+H]$^+$). IR cm^{-1} ($CHCl_3$ solution) 3032, 2937, 2238, 1750, 1715, 1452, 1230. Minor isomer: *anti*-**6i**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.14 (s, 3H), 2.19 (s, 3H), 3.35 (s, 3H), 3.76 (d, J=14.8 Hz, 1H), 4.12 (s, 2H), 4.30 (d, J=8.7 Hz, 1H), 5.38 (dd, J=8.7, 8.7 Hz, 1H), 5.49 (d, J=8.7 Hz, 1H), 7.24–7.30 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.5, 20.6, 45.3, 49.1, 57.4, 59.5, 71.4, 72.3, 77.8, 84.6, 128.1, 128.5, 128.9, 134.2, 166.1, 169.7, 170.3.

*4.4.10. (3R,4R)-3,4-Diacetoxy-5-[(6-methoxynaphthalen-2-yl)-ethynyl]-1-benzyl-2-pyrrolidinone (**6j**)*

The product **6j** was prepared as described in the general procedure and was obtained in a 70:30 *syn*/*anti* mixture as a colourless oil in 71% yield (334 mg). Major isomer: *syn*-**6j**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.08 (s, 3H), 2.18 (s, 3H), 3.91 (s, 3H), 4.16 (d, J=14.7 Hz, 1H), 4.31 (d, J=5.8 Hz, 1H), 5.10 (d, J=14.7 Hz, 1H), 5.50 (d, J=5.8 Hz, 1H), 5.58 (dd, J=5.6, 5.6 Hz, 1H), 7.11 (s, 1H), 7.17 (dd, J=8.5, 2.2 Hz, 1H), 7.34–7.42 (m, 6H), 7.62 (d, J=8.5 Hz, 1H), 7.70 (d, J=8.3 Hz, 1H), 7.85 (d, J=8.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.7, 44.9, 51.5, 55.3, 71.8, 73.6, 81.7, 89.0, 105.8, 116.2, 119.7, 127.0, 128.1, 128.2, 128.7, 128.9, 129.4, 131.9, 132.0, 134.6, 135.1, 158.7, 166.3, 170.0, 170.4. GC/MS: *m*/*z* (%)=471 (7) [M^+], 411 (15), 369 (36), 352 (20), 300 (11), 278 (17), 185 (8), 91 (98), 43 (100). HRMS (ESI, positive) *m*/*z* calcd for $C_{28}H_{25}NO_6$ 472.1695 ([M+H]$^+$); found 472.1682 ([M+H]$^+$). IR cm^{-1} ($CHCl_3$ solution): 3059, 2932, 2228, 1753, 1719, 1231. Minor isomer: *anti*-**6j**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.11 (s, 3H), 2.20 (s, 3H), 3.89 (s, 3H), 4.11 (d, J=14.7 Hz, 1H), 4.81 (d, J=7.5 Hz, 1H), 5.08 (d, J=14.7 Hz, 1H), 5.23 (dd, J=7.5, 7.5 Hz, 1H), 5.78 (d, J=7.5 Hz, 1H), 7.11 (s, 1H), 7.17 (dd, J=8.5, 2.2 Hz, 1H), 7.34–7.42 (m, 6H), 7.62 (d, J=8.5 Hz, 1H), 7.70 (d, J=8.3 Hz, 1H), 7.85 (d, J=8.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.8, 45.1, 51.4, 55.2, 71.6, 73.5, 81.5, 88.9, 105.8, 116.1, 119.7, 127.1, 128.1, 128.2, 128.7, 128.9, 129.4, 131.9, 132.0, 134.6, 135.1, 158.7, 166.2, 170.1, 170.3.

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