

SUPPORTING INFORMATION

Gold Catalyzed Stereoselective Tandem Hydroamination-Formal Aza-Diels Alder Reaction of Fluorinated Propargylic Amino Esters

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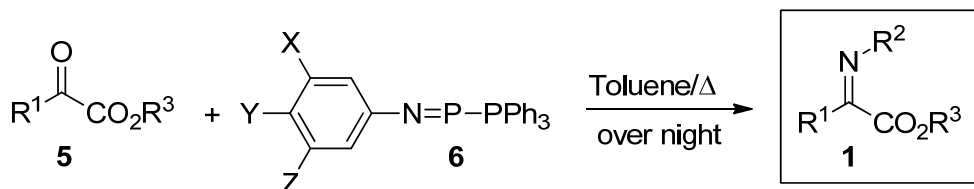
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General Remarks

Reactions were carried out under argon atmosphere unless otherwise indicated. The solvents were purified prior to use: THF, diethyl ether and toluene were distilled from sodium/benzophenone, dichloromethane and acetonitrile were distilled from calcium hydride. The reactions were monitored with the aid of thin-layer chromatography (TLC) on 0.25 mm precoated silica gel plates. Visualization was carried out with UV light and aqueous ceric ammonium molybdate solution or potassium permanganate stain. Flash column chromatography was performed with the indicated solvents on silica gel 60 (particle size 0.040-0.063 mm). ^1H and ^{13}C NMR spectra were recorded on a 300 or 400 MHz spectrometers. Chemical shifts are given in ppm (δ), with reference to the residual proton resonances of the solvents. Coupling constants (J) are given in Hertz (Hz). The letters m, s, d, t, and q stand for multiplet, singlet, doublet, triplet and quartet, respectively. The letters br indicate that the signal is broad. Imino esters **1b**¹ and **1e**² were prepared following previously described methodologies.

Preparation of starting imino esters 1a-m.

Method A: Aza-Wittig reaction.



This methodology was employed when starting ketoesters **5** were commercially available. To a solution of the corresponding iminophosphorane **6**³ (4 mmol) in dry toluene (20 ml) was added dropwise the corresponding ketoester (4 mmol, neat) and the resulting solution was refluxed over night. Then, the mixture was cooled to rt, and

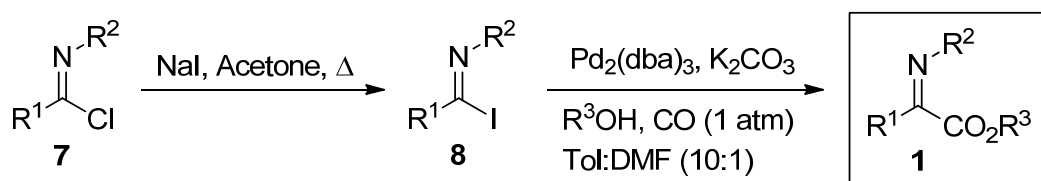
(1) S. Fustero, S. Flores, A. C. Cuñat, D. Jiménez, C. del Pozo, J. Bueno, J. F. Sanz, *J. Fluorine Chem.* 2007, **128**, 1248.

(2) S. Fustero, M. Sánchez-Roselló, V. Rodrigo, C. del Pozo, J. F. Sanz-Cervera, A. Simón, *Org. Lett.* 2006, **8**, 4129.

(3) For the preparation of iminophosphoranes, see: a) M. Alajarin, C. López-Leonardo, J. Berna, *Science of Synthesis* 2007, **31b**, 1539; b) S. R. Stauffer, Y. Sun, B. S. Katzenellenbogen, J. A. Katzenellenbogen, *Bioorg. Med. Chem.* 2000, **8**, 1293; c) L. Horner, H. Oediger, *Justus Liebig Ann. Chem.* 1959, **627**, 142.

solvents evaporated under vacuo. Diethyl ether was then added (20 mL) and a white precipitated of triphenyl phosphine oxide was formed. The solid was filtrated and washed with diethyl ether (3 x 10 mL) and after removal of the solvents, the crude was subjected to flash column chromatography with 10:1 hexanes:ethyl acetate.

Method B: Alcoxycarbonylation protocol.⁴

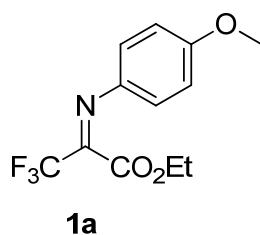


NaI (11.6 mmol) was added to a solution of the corresponding imidoyl chloride **7**⁵ (7.1 mmol) in dry acetone (20 mL) and the mixture was stirred at room temperature protected from light until the total disappearance of the starting imidoyl chloride (as confirmed by means of GC-MS). The reaction mixture was then quenched with a saturated aqueous solution of Na₂S₂O₃ and the aqueous layer was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were washed with brine (3 x 15 mL) and dried over anhydrous Na₂SO₄. Filtration and evaporation of solvents quantitatively gave the corresponding crude imidoyl iodides **8** as yellow oils; these were subsequently used in the next step of the synthesis with no further purification.

Under CO atmosphere (1 atm), a solution of the previously obtained imidoyl iodide **8** in a toluene/DMF mixture (10 mL:1 mL) and the corresponding alcohol (8.5 mmol) were both added to a two-necked flask containing K₂CO₃ (14.2 mmol) and palladium catalyst Pd₂(dba)₃·CHCl₃ (0.28 mmol). The reaction mixture was stirred at room temperature until the starting material was totally consumed, as confirmed by means of TLC. The crude reaction mixture was then filtered through a silica pad and washed with CH₂Cl₂. The solvents were eliminated under reduced pressure and the mixture was purified by means of flash column chromatography [n-hexane-AcOEt (10:1)].

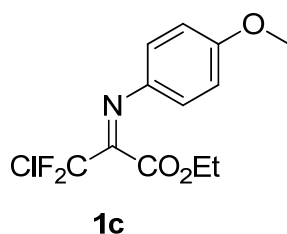
(4) (a) S. Fustero, A. Navarro, B. Pina, J. García Soler, A. Bartolomé, A. Asensio, A. Simón, P. Bravo, G. Fronza, A. Volonterio, M. Zanda, *Org. Lett.* **2001**, 3, 2621; (b) H. Amii, Y. Kishikawa, K. Kageyama, K. Uneyama, *J. Org. Chem.* 2000, **65**, 3404.

(5) (a) K. Uneyama, *J. Fluorine Chem.* 1999, **97**, 11; (b) K. Tamura, H. Mizukami, K. Maeda, H. Watanabe, K. Uneyama, *K. J. Org. Chem.* 1993, **58**, 32.



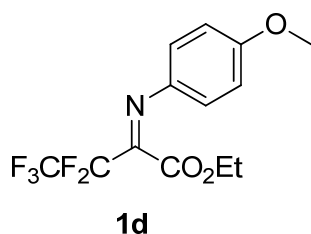
(E)- Ethyl 3,3,3-trifluoro-2-[(4-methoxyphenyl)imino]propanoate 1a.^{2b}

Following the general procedure described above (Method A), 946 mg of **1a** (yellow oil) were obtained from 680 mg ethyl trifluoropyruvate and 1.53 g of 4-methoxy-*N*-(triphenylphosphoranilidene)aniline in 86% yield. The spectroscopic data are in agreement with those previously reported in the literature.



(E)- Ethyl 3-chloro-3,3-difluoro-2-[(4-methoxyphenyl)imino]propanoate 1c.

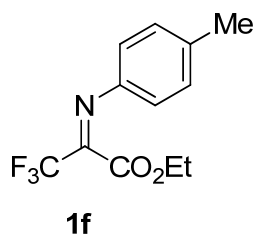
Following the general procedure described above (Method B), 2.02 g of **1c** (yellow oil) were obtained from 1.8 g of the corresponding imidoyl chloride in 98% yield. ¹H-NMR (CDCl₃, 300 MHz): δ = 1.17 (t, *J* = 7.2 Hz, 3H), 3.82 (s, 3H), 4.25 (q, *J* = 7.2 Hz, 2H), 6.89 (d, *J* = 9.0 Hz, 2H), 7.02 (d, *J* = 9.0 Hz, 2H); ¹³C-NMR (CDCl₃, 75.5 MHz): δ = 13.7, 55.4, 62.7, 114.3, 121.6 (t, ¹*J*_{CF} = 293.8 Hz), 122.2, 138.9, 150.1 (t, ²*J*_{CF} = 30.9 Hz), 159.3, 160.6; ¹⁹F-NMR (CDCl₃, 282 MHz): δ = -67.7 (s, 2F); HRMS (ES) calc. for (M+H)⁺ C₁₂H₁₃ClF₂NO₃: 292.0552; found: 292.0546.



(E)- Ethyl 3,3,4,4,4-pentafluoro-2-[(4-methoxyphenyl)imino]butanoate 1d.

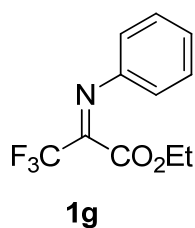
Following the general procedure described above (Method B), 1.36 g of **1d** (yellow oil) were obtained from 2.04 g of the corresponding imidoyl chloride in 59% yield. ¹H-

NMR (CDCl₃, 300 MHz): δ = 1.17 (t, J = 7.2 Hz, 3H), 3.81 (s, 3H), 4.24 (q, J = 7.2 Hz, 1H), 6.88 (d, J = 9.3 Hz, 2H), 7.03 (d, J = 9.3 Hz, 2H); ¹³C-NMR (CDCl₃, 75.5 MHz): δ = 13.6, 55.4, 62.7, 109.2 (tq, ¹ J_{CF} = 258.4 Hz; ² J_{CF} = 38.2 Hz), 114.3, 118.3 (qt, ¹ J_{CF} = 287.1 Hz; ² J_{CF} = 35.8 Hz), 122.4, 139.1, 147.7 (t, ¹ J_{CF} = 29.5 Hz), 159.6, 160.5; ¹⁹F-NMR (CDCl₃, 282 MHz): δ = -92.3 (s, 3F), -126.3 (s, 2F); HRMS (ES) calc. for (M+H)⁺ C₁₃H₁₃F₅NO₃: 326.0816; found: 326.0823.



(E)- Ethyl 3,3,3-trifluoro-2-(p-tolylimino)propanoate 1f.⁶

Following the general procedure described above (Method A), 912 mg of **1f** (yellow oil) were obtained from 680 mg of ethyl trifluoropyruvate and 1.47 g of 4-methyl-*N*-(triphenylphosphoranilidene)aniline in 88% yield. ¹H-NMR (CDCl₃, 300 MHz): δ = 1.12 (t, J = 7.2 Hz, 3H), 2.35 (s, 3H), 4.21 (q, J = 7.2 Hz, 2H), 6.89 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 8.1 Hz, 2H); ¹³C-NMR (CDCl₃, 75.5 MHz): δ = 13.5, 20.9, 62.7, 119.6, 118.2 (q, ¹ J_{CF} = 278.4 Hz), 129.6, 137.4, 143.8, 148.1 (q, ² J_{CF} = 36.8 Hz), 159.8; ¹⁹F-NMR (CDCl₃, 282 MHz): δ = -70.2 (s, 3F); HRMS (ES) calc. for (M+H)⁺ C₁₂H₁₃F₃NO₂: 260.0898; found: 260.0894.

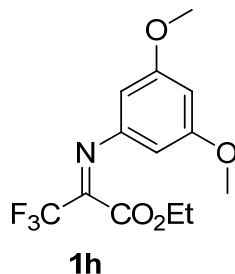


(E)- Ethyl 3,3,3-trifluoro-2-(phenylimino)propanoate 1g.⁶

Following the general procedure described above (Method A), 735 mg of **1g** (yellow solid) were obtained from 680 mg of ethyl trifluoropyruvate and 1.41 g of *N*-(triphenylphosphoranilidene)aniline in 75% yield. m. p. = 80-82 °C. ¹H-NMR (CDCl₃, 300 MHz): δ = 0.97 (t, J = 7.2 Hz, 3H), 4.08 (q, J = 7.2 Hz, 2H), 6.83-6.89 (m, 2H), 7.02-7.09 (m, 1H), 7.10-7.20 (m, 1H), 7.24-7.31 (m, 1H); ¹³C-NMR (CDCl₃, 75.5

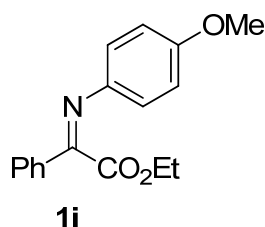
(6) T. Sakai, F. Yan, S. Kashino, K. Uneyama, *Tetrahedron* 1996, **52**, 233.

MHz): δ = 13.5, 62.7, 117.2, 118.2 (q, $^1J_{\text{CF}}$ = 278.6 Hz), 119.1, 127.0, 129.0, 149.0 (q, $^2J_{\text{CF}}$ = 36.8 Hz), 159.4; ^{19}F -NMR (CDCl_3 , 282 MHz): δ = -80.3 (s, 3F); HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{11}\text{H}_{11}\text{F}_3\text{NO}_2$: 246.0742; found: 246.0741.



(E)- Ethyl 3,3,3-trifluoro-2-[(3,5-dimethoxyphenyl)imino]propanoate 1h.

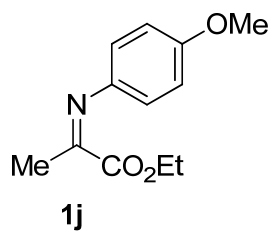
Following the general procedure described above (Method A), 659 mg of **1h** (yellow oil) were obtained from 680 mg of ethyl trifluoropyruvate and 1.65 g of 3,5-dimethoxy-*N*-(triphenylphosphoranilidene)aniline in 54% yield. ^1H -NMR (CDCl_3 , 300 MHz): δ = 1.11 (t, J = 7.2 Hz, 3H), 3.75 (s, 6H), 4.20 (q, J = 7.2 Hz, 2H), 6.09 (d, J_{m} = 2.1 Hz, 2H), 6.33 (t, J_{m} = 2.1 Hz, 1H); ^{13}C -NMR (CDCl_3 , 75.5 MHz): δ = 13.5, 55.4, 62.8, 97.4, 99.0, 118.1 (q, $^1J_{\text{CF}}$ = 278.7 Hz), 148.2, 149.3 (q, $^2J_{\text{CF}}$ = 37.1 Hz), 159.4, 161.1; ^{19}F -NMR (CDCl_3 , 282 MHz): δ = -80.4 (s, 3F); HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{13}\text{H}_{15}\text{F}_3\text{NO}_4$: 306.0953; found: 306.0954.



(Z)- Ethyl 2-[(4-methoxyphenyl)imino]-2-phenyl acetate 1i.⁷

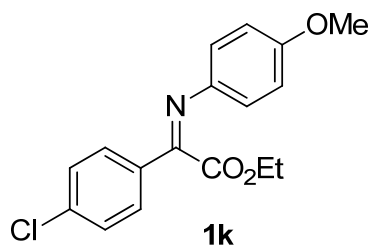
Following the general procedure described above (Method A), 1.13 g of **1i** (yellow oil) were obtained from 712 mg of ethyl benzoylformate and 1.53 g of 4-methoxy-*N*-(triphenylphosphoranilidene)aniline in 99% yield. The spectroscopic data are in agreement with those previously reported in the literature.

(7) Y. Niwa, M. Shimizu, M. *J. Am. Chem. Soc.* 2003, **125**, 3720.



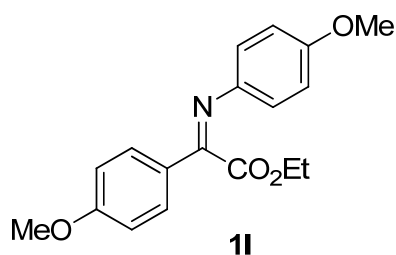
(Z)- Ethyl 2-[(4-methoxyphenyl)imino]-2-methyl acetate 1j.⁸

Following the general procedure described above (Method A), 636 mg of **1j** (yellow oil) were obtained from 464 mg of methyl pyruvate and 1.53 g of 4-methoxy-*N*-(triphenylphosphoranilidene)aniline in 72% yield. The spectroscopic data are in agreement with those previously reported in the literature.



(Z)- Ethyl 2-[(4-methoxyphenyl)imino]-2-(4-chlorophenyl) acetate 1k.⁸

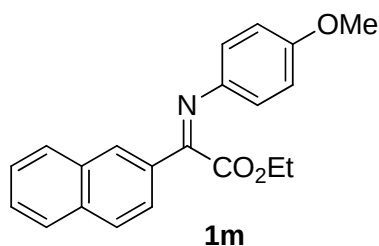
Following the general procedure described above (Method A), 1.07 g of **1k** (yellow oil) were obtained from 848 mg of ethyl 4-chlorobenzoylformate and 1.53 g of 4-methoxy-*N*-(triphenylphosphoranilidene)aniline in 84% yield. The spectroscopic data are in agreement with those previously reported in the literature.



(Z)- Ethyl 2-[(4-methoxyphenyl)imino]-2-(4-methoxyphenyl) acetate 1l.⁸

Following the general procedure described above (Method A), 851 mg of **1l** (yellow oil) were obtained from 832 mg of ethyl 4-methoxybenzoylformate and 1.53 g of 4-methoxy-*N*-(triphenylphosphoranilidene)aniline in 68% yield. The spectroscopic data are in agreement with those previously reported in the literature.

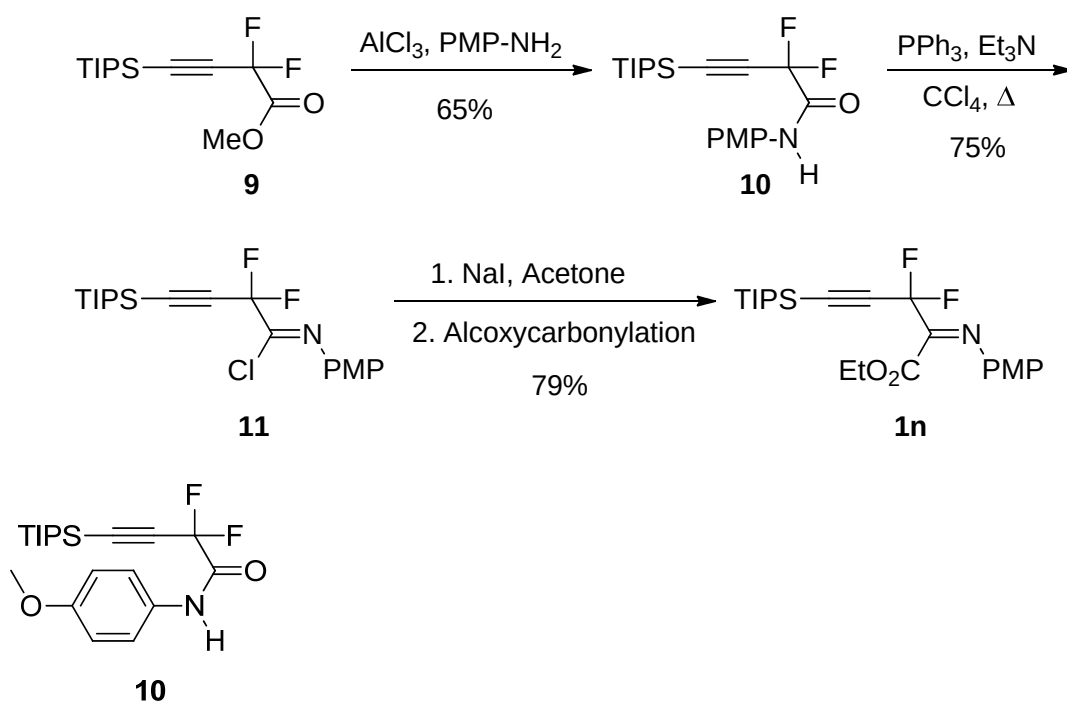
(8) G. Li, Y. Liang, J. C. Antilla, *J. Am. Chem. Soc.* 2007, **129**, 5830.



(Z)- Ethyl 2-[(4-methoxyphenyl)imino]-2-(4-methoxyphenyl) acetate 1m.

Following the general procedure described above (Method A), 1.17 g of **1m** (yellow oil) were obtained from 912 mg ethyl of ethyl 2-naphthylformate⁹ and 1.53 g of 4-methoxy-*N*-(triphenylphosphoranilidene)aniline in 88% yield. After treatment with diethyl ether and filtration of the phosphine oxide, the crude was used in the next step without further purification.

Preparation of imino ester 1n.



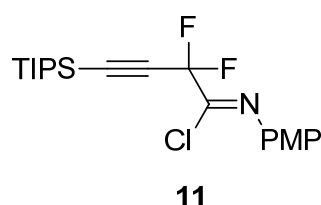
2,2-Difluoro-*N*-(4-methoxyphenyl)-4-(triisopropylsilyl)-3-butynamide 10.

To a solution of *p*-anisidine (23.3 mmol) in CH₂Cl₂ (20 mL) at 0 °C was added AlMe₃ (11 mL, 2.0 M solution in hexanes) and the reaction mixture was stirred at room temperature for 20 min. Then a solution of the fluorinated ester **9**¹⁰ (2.7 g, 7 mmol) in dry CH₂Cl₂ (20 mL) was added dropwise at 0 °C. The reaction mixture was stirred at

(9) R. Infante, J. Nieto, C. Andrés, *Chem. Eur. J.* 2012, **18**, 4375.

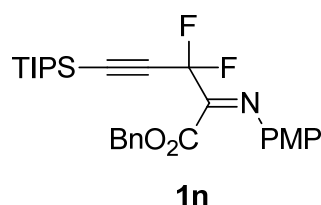
(10) S. Fustero, B. Fernández, P. Bello, C. del Pozo, S. Arimitsu, G. B. Hammond, *Org. Lett.* 2007, **9**, 4251.

this temperature until TLC showed consumption of the starting material, then quenched with 1 M aqueous HCl solution and extracted with CH₂Cl₂ (3x30 mL). The combined organic layers were washed with brine (30 mL) and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the crude mixture was purified by means of flash column chromatography [n-hexane-AcOEt (40:1)] to afford 2.3 g of **10** as a brown oil (65% yield). ¹H-NMR (CDCl₃, 300 MHz): δ = 1.09-1.13 (m, 21H), 3.80 (s, 3H), 6.90 (d, *J* = 9.0 Hz, 2H), 7.47 (d, *J* = 9.0 Hz, 2H), 7.89 (br s, 1H); ¹³C-NMR (CDCl₃, 75.5 MHz): δ = 18.5, 19.4, 65.5, 95.4 (t, ²*J*_{CF} = 37.1 Hz), 95.6 (t, ³*J*_{CF} = 5.2 Hz), 105.3 (t, ¹*J*_{CF} = 244.2 Hz), 114.4, 121.9, 128.9, 157.4, 158.8 (t, ²*J*_{CF} = 30.5 Hz); ¹⁹F-NMR (CDCl₃, 282 MHz): δ = -90.1 (s, 2F); HRMS (ES) calc. for (M+H)⁺ C₂₀H₃₀F₂NO₂Si: 382.2014; found: 382.2019.



(Z)-2,2-Difluoro-N-(4-methoxyphenyl)-4-(triisopropylsilyl)-3-butyrimidoyl

chloride 11. A 50 mL two-necked flask equipped with a septum cap, a condenser, and a Teflon-coated magnetic stirring bar was filled with Ph₃P (12 mmol), Et₃N (4.8 mmol), CCl₄ (20 mL) and amide **10** (4 mmol). The mixture was then refluxed under constant stirring (3 h). Solvents were removed under reduced pressure, and the residue was diluted with hexane and filtered. The filtrate was concentrated under reduced pressure and purified by flash column chromatography to afford 1.2 g of **11** as a yellow oil in 75% yield. ¹H-NMR (CDCl₃, 300 MHz): δ = 1.12-1.16 (m, 21H), 6.95 (d, *J* = 9 Hz, 2H), 7.22 (d, *J* = 9 Hz, 2H); ¹³C-NMR (CDCl₃, 75.5 MHz): δ = 10.9, 18.4, 55.4, 95.2 (t, ³*J*_{CF} = 4.8 Hz), 95.6 (t, ²*J*_{CF} = 37.6 Hz), 106.6 (t, ¹*J*_{CF} = 238.8 Hz), 114.1, 123.7, 134.6 (t, ²*J*_{CF} = 36.9 Hz), 136.6, 158.9; ¹⁹F-NMR (CDCl₃, 282 MHz): δ = -93.7 (s, 2F); HRMS (ES) calc. for (M+H)⁺ C₂₀H₂₉ClF₂NOSi: 400.1675; found: 400.1668.

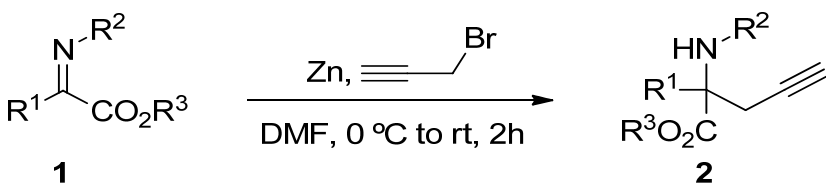


(E)-Benzyl 3,3-Difluoro-2-[(3-methoxyphenyl)imino]-5-(triisopropylsilyl)-4-pentynoate 1n. Following the general procedure described above (Method B), 988 mg of **1n** (yellow oil) were obtained from 1.0 g of the imidoyl chloride **11** in 79% yield. ¹H-NMR (CDCl₃, 300 MHz): δ = 1.02-1.11 (m, 21H), 3.73 (s, 3H), 5.12 (s, 3H), 6.68 (d, *J* = 9 Hz, 2H), 6.83 (d, *J* = 9 Hz, 2H), 7.06-7.32 (m, 5H); ¹³C-NMR (CDCl₃, 75.5 MHz): δ = 10.9, 18.4, 55.3, 67.7, 95.5 (t, ³*J*_{CF} = 4.8 Hz), 95.8 (t, ²*J*_{CF} = 37.4 Hz), 107.8 (t, ¹*J*_{CF} = 236.8 Hz), 114.2, 121.8, 128.5, 128.6, 128.7, 134.0, 139.9, 152.2 (t, ²*J*_{CF} = 33.4 Hz), 158.7, 161.3; ¹⁹F-NMR (CDCl₃, 282 MHz): δ = -85.0 (s, 2F); HRMS (ES) calc. for (M+H)⁺ C₂₈H₃₆F₂NO₃Si: 500.2433; found: 500.2440.

General procedure for the preparation of propargylic amino esters 2a-m.

Imino esters **1** (1 mmol) and propargyl bromide (222 mg, 1.5 mmol) were dissolved in DMF (3 mL). The solution was cooled to 0 °C, then activated zinc powder (98 mg, 1.5 mmol) was added, followed by 2 drops of TMSCl. The reaction mixture was then slowly warmed to room temperature. After 2-10 h (the reaction was monitored by TLC) the medium was cooled to 0 °C and hydrolyzed with a saturated aqueous solution of NH₄Cl (20 mL), then extracted with Et₂O (3 × 10 mL). The combined organic layers were washed with brine (30 mL), dried with MgSO₄, filtered, and the solvents were evaporated. The residue was purified by flash chromatography over silica gel (hexanes/AcOEt, 9:1) to afford compounds **2** as colorless liquids (Table 1).¹¹

Table 1 Synthesis of propargyl α-amino esters **2a-m**.

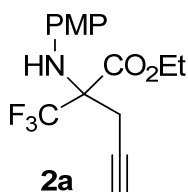
					
Entry	1	R ¹	R ²	R ³	2 (yield %) ^a
1	1a	CF ₃	PMP	Et	2a (89%)
2	1b	CF ₃	PMP	(CH ₂) ₂ TMS	2b (93%)
3	1c	ClCF ₂	PMP	Et	2c (59%) ^b
4	1d	CF ₃ CF ₂	PMP	Et	2d (98%) ^b

(11) With non-fluorinated substrates **2i-m** variable amounts (10-20%) of the corresponding allenes were formed.

5	1e	AllylCF ₂	PMP	Bn	2e (92%) ^b
6	1f	CF ₃	4-MeC ₆ H ₄	Et	2f (95%)
7	1g	CF ₃	Ph	Et	2g (97%)
8	1h	CF ₃	3,5-(MeO) ₂ C ₆ H ₃	Et	2h (84%)
9	1i	Ph	PMP	Et	2i (60%) ^b
10	1j	Me	PMP	Me	2j (50%) ^b
11	1k	4-ClC ₆ H ₄	PMP	Et	2k (52%) ^b
12	1l	PMP	PMP	Et	2l (55%) ^b
13	1m	2-naphthyl	PMP	Et	2m (84%)

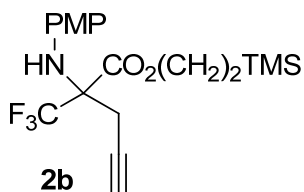
^a Isolated yields after column chromatography. ^b The reaction mixture was stirred for 10 h at room temperature.

PMP = 4-methoxyphenyl. TMS = trimethylsilyl.



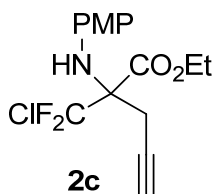
Ethyl 2-[(4-methoxyphenyl)amino]-2-(trifluoromethyl)-4-pentynoate (**2a**).

Following the general procedure described above, 281 mg of **2a** (89% yield) were obtained as a light yellow oil starting from 275 mg of **1a**. ¹H-NMR (CDCl₃, 300 MHz) δ = 1.33 (t, *J* = 7.1 Hz, 3H), 2.04 (t, *J* = 2.6 Hz, 1H), 2.93 (dd, *J*₁ = 17.0 Hz, *J*₂ = 2.6 Hz, 1H), 3.04 (dd, *J*₁ = 17.0 Hz, *J*₂ = 2.6 Hz, 1H), 3.76 (s, 3H), 4.30-4.41 (m, 2H), 4.51 (br s, 1H), 6.78 (d, *J* = 9.0 Hz, 2H), 6.99 (d, *J* = 8.9 Hz, 2H); ¹³C-NMR (CDCl₃, 75.5 MHz) δ = 13.8, 21.2, 55.3, 63.3, 68.0 (q, ²*J*_{CF} = 26.2 Hz), 72.3, 77.1, 114.1, 124.0 (q, ¹*J*_{CF} = 289.3 Hz), 124.7, 124.7, 135.1, 155.9, 167.1; ¹⁹F-NMR (CDCl₃, 282 MHz) δ = -73.7; HRMS (ES) calc. for (M+H)⁺ C₁₅H₁₇F₃NO₃: 316.1161; found: 316.1165.



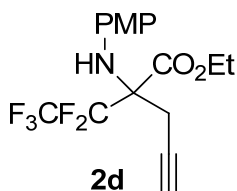
2-(Trimethylsilyl)ethyl 2-[(4-methoxyphenyl)amino]-2-(trifluoromethyl)-4-pentynoate (2b).

Following method described above 361 mg of **2b** (93% yield) were obtained as a light yellow oil starting from 347 mg of **1b**. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ = 0.07 (s, 9H), 1.06-1.11 (m, 2H), 2.04 (t, J = 2.6 Hz, 1H), 2.94 (dd, J_1 = 17.0 Hz, J_2 = 2.6 Hz, 1H), 3.04 (dd, J_1 = 17.0 Hz, J_2 = 2.6 Hz, 1H), 3.75 (s, 3H), 4.35-4.41 (m, 2H), 4.53 (br s, 1H), 6.78 (d, J = 9.0 Hz, 2H), 6.99 (d, J = 8.9 Hz, 2H); $^{13}\text{C-NMR}$ (CDCl_3 , 75.5 MHz) δ = -1.7, 17.2, 21.1, 55.3, 66.0, 68.0 (q, $^2J_{\text{CF}}$ = 26.1 Hz), 72.3, 77.1, 114.1, 124.0 (q, $^1J_{\text{CF}}$ = 289.3 Hz), 124.5, 135.2, 155.8, 167.2; $^{19}\text{F-NMR}$ (CDCl_3 , 282 MHz) δ = -73.5; HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{18}\text{H}_{25}\text{F}_3\text{NO}_3\text{Si}$: 388.1556; found: 388.1535.



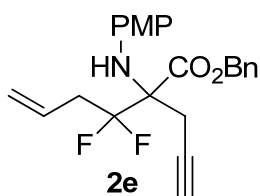
Ethyl 2-(chlorodifluoromethyl)-2-[(4-methoxyphenyl)amino]-4-pentynoate (2c).

Following method described above 196 mg of **2c** (59% yield) were obtained as a light yellow oil starting from 291 mg of **1c**. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ = 1.36 (t, J = 7.1 Hz, 3H), 2.01 (t, J = 2.6 Hz, 1H), 2.95 (dd, J_1 = 16.8 Hz, J_2 = 2.6 Hz, 1H), 3.14 (dd, J_1 = 16.9 Hz, J_2 = 2.6 Hz, 1H), 3.77 (s, 3H), 4.34-4.42 (m, 2H), 4.69 (br s, 1H), 6.78 (d, J = 8.9 Hz, 2H), 7.05 (d, J = 8.9 Hz, 2H); $^{13}\text{C-NMR}$ (CDCl_3 , 75.5 MHz) δ = 13.8, 21.0, 55.3, 63.4, 72.2, 72.4 (d, $^2J_{\text{CF}}$ = 22.1 Hz), 77.5, 114.1, 125.2, 125.2, 129.2 (dd, $^1J_{\text{CF1}}$ = 308.7 Hz, $^1J_{\text{CF2}}$ = 305.1 Hz), 135.0, 156.0, 167.4; $^{19}\text{F-NMR}$ (CDCl_3 , 282 MHz) δ = -57.3 (d, J_{FF} = 162.5 Hz, 1F), -60.6 (d, J_{FF} = 162.5 Hz, 1F); HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{15}\text{H}_{17}\text{ClF}_2\text{NO}_3$: 332.0865; found: 332.0860.



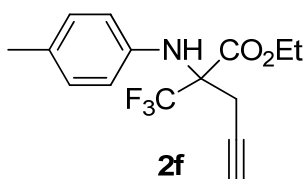
Ethyl 2-[(4-methoxyphenyl)amino]-2-(perfluoroethyl)-4-pentynoate (2d).

Following method described above 359 mg of **2d** (98% yield) were obtained as a light yellow oil starting from 325 mg of **1d**. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ = 1.36 (t, J = 7.2 Hz, 3H), 1.92 (t, J = 2.7 Hz, 1H), 2.97 (dd, J_1 = 16.8 Hz, J_2 = 2.7 Hz, 1H), 3.05 (ddd, J_1 = 16.8 Hz, J_2 = 2.7 Hz, J_3 = 0.9 Hz, 1H), 3.77 (s, 3H), 4.32-4.43 (m, 2H), 4.76 (br s, 1H), 6.78 (d, J = 9.0 Hz, 2H), 7.01 (d, J = 9.0 Hz, 2H); $^{13}\text{C-NMR}$ (CDCl_3 , 75.5 MHz) δ = 13.8, 19.9, 55.4, 63.8, 67.1 (t, $^2J_{\text{CF}}$ = 22.2 Hz), 72.2, 83.3, 114.0, 125.2, 135.0, 155.7, 167.8; $^{19}\text{F-NMR}$ (CDCl_3 , 282 MHz) δ = -79.3 (s, 3F), -77.2 (s, 2F); HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{16}\text{H}_{17}\text{F}_5\text{NO}_3$: 366.1129; found: 366.1141.



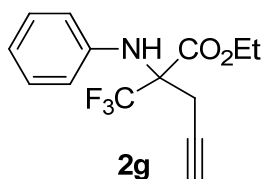
Benzyl 3,3-difluoro-2-[(4-methoxyphenyl)amino]-2-(2-propyn-1-yl)-5-hexenoate (2e).

Following method described above 368 mg of **2e** (92% yield) were obtained as a light yellow oil starting from 359 mg of **1e**. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ = 1.86 (t, J = 2.4 Hz, 1H), 2.47-2.68 (m, 1H), 2.83-2.99 (m, 1H), 2.99 (dd, J_1 = 17.1 Hz, J_2 = 2.7 Hz, 1H), 3.09 (dd, J_1 = 17.1 Hz, J_2 = 2.7 Hz, 1H), 3.76 (s, 3H), 5.08-5.21 (m, 2H), 5.25 (d, J = 12.3 Hz, 1H), 5.29 (d, J = 12.3 Hz, 1H), 5.79 (ddt, J_1 = 17.1 Hz, J_2 = 9.9 Hz, J_3 = 7.2 Hz, 1H), 6.74 (d, J = 9.0 Hz, 2H), 6.91 (d, J = 9.0 Hz, 2H), 7.36-7.41 (m, 5H); $^{13}\text{C-NMR}$ (CDCl_3 , 75.5 MHz) δ = 19.8 (t, $^3J_{\text{CF}}$ = 3.5 Hz), 37.6 (t, $^2J_{\text{CF}}$ = 23.9 Hz), 55.4, 68.5, 69.5 (t, $^2J_{\text{CF}}$ = 24.9 Hz), 71.6, 78.6, 114.1, 120.6, 122.3 (t, $^1J_{\text{CF}}$ = 228.7 Hz), 123.4, 123.5, 128.2 (t, $^3J_{\text{CF}}$ = 4.8 Hz), 128.5, 128.6, 134.7, 136.3, 155.1, 169.9; $^{19}\text{F-NMR}$ (CDCl_3 , 282 MHz) δ = -104.1 (ddd, J_{FF} = 248.2 Hz, J_{FH} = 25.4 Hz, J_{FH} = 11.9 Hz, 1F), -105.3 (ddd, J_{FF} = 248.2 Hz, J_{FH} = 25.4 Hz, J_{FH} = 11.9 Hz, 1F); HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{23}\text{H}_{24}\text{F}_2\text{NO}_3$: 400.1724; found: 400.1724.



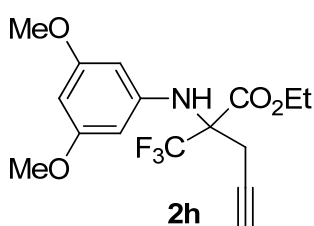
Ethyl 2-(p-tolylamino)-2-(trifluoromethyl)-4-pentynoate (2f).

Following method described above 249 mg of **2f** (96% yield) were obtained as a light yellow oil starting from 259 mg of **1f**. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ = 1.33 (t, J = 7.14 Hz, 3H), 2.02 (t, J = 2.63 Hz, 1H), 2.27 (s, 3H), 3.08 (d, J = 2.64 Hz, 2H), 4.37 (m, 2H), 4.66 (br s), 6.86 (d, J = 8.40 Hz, 2H), 7.03 (d, J = 8.04 Hz, 2H); $^{13}\text{C-NMR}$ (CDCl_3 , 75.5 MHz) δ = 13.8, 20.6, 21.3, 63.5, 67.6 (q, $^2J_{\text{CF}}$ = 26.7 Hz), 72.4, 76.7, 121.2, 121.2, 124.1 (q, $^1J_{\text{CF}}$ = 289.2 Hz), 129.6, 131.7, 139.9, 167.2; $^{19}\text{F-NMR}$ (CDCl_3 , 282 MHz) δ = -73.4; HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{15}\text{H}_{17}\text{F}_3\text{NO}_2$: 300.1211; found: 300.1211.



Ethyl 2-(phenylamino)-2-(trifluoromethyl)-4-pentynoate (**2g**).

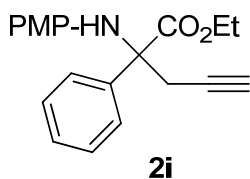
Following method described above 277 mg of **2g** (97% yield) were obtained as a light yellow oil starting from 245 mg of **1g**. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ = 1.34 (t, J = 7.1 Hz, 3H), 2.02 (t, J = 2.6 Hz, 1H), 3.15 (d, J = 2.7 Hz, 1H), 3.17 (d, J = 2.6 Hz, 1H), 4.35-4.42 (m, 2H), 4.84 (br s, 1H), 6.91-7.00 (m, 3H), 7.21-7.27 (m, 2H); $^{13}\text{C-NMR}$ (CDCl_3 , 75.5 MHz) δ = 13.8, 21.4, 63.6, 67.2 (q, $^2J_{\text{CF}}$ = 27.1 Hz), 72.5, 76.3, 120.0, 120.0, 121.7, 124.0 (q, $^1J_{\text{CF}}$ = 289.0 Hz), 129.0, 142.6, 167.1; $^{19}\text{F-NMR}$ (CDCl_3 , 282 MHz) δ = -73.3; HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{14}\text{H}_{15}\text{F}_3\text{NO}_2$: 286.1055; found: 286.1042.



Ethyl 2-[(3,5-dimethoxyphenyl)amino]-2-(trifluoromethyl)-4-pentynoate (**2h**).

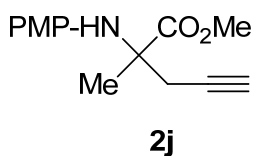
Following method described above 256 mg of **2h** (84% yield) were obtained as a light yellow oil starting from 305 mg of **1h**. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ = 1.32 (t, J = 7.1 Hz, 3H), 2.03 (t, J = 2.6 Hz, 1H), 3.11 (dd, J_1 = 17.1 Hz, J_2 = 2.64 Hz, 1H), 3.24 (dd, J_1 = 17.1 Hz, J_2 = 2.6 Hz, 1H), 3.74 (s, 6H), 4.33-4.40 (m, 2H), 4.81 (br s, 1H), 6.07-6.09 (m, 3H); $^{13}\text{C-NMR}$ (CDCl_3 , 75.5 MHz) δ = 13.8, 21.4, 55.2, 63.6, 67.1 (q, $^2J_{\text{CF}}$ = 27.4 Hz), 72.6, 76.3, 93.5, 98.1, 98.2, 124.0 (q, $^1J_{\text{CF}}$ = 289.0 Hz), 144.6, 161.2, 167.0; $^{19}\text{F-NMR}$

NMR (CDCl₃, 282 MHz) δ = -73.2; HRMS (ES) calc. for (M+H)⁺ C₁₆H₁₉F₃NO₄: 346.1266; found: 346.1262.



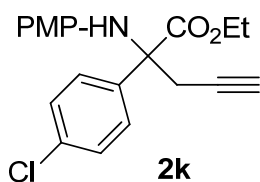
Ethyl 2-[(4-methoxyphenyl)amino]-2-phenyl-4-pentynoate (2i).

Following method described above 194 mg of **2i** (60% yield) were obtained as a light yellow oil starting from 283 mg of **1i**. ¹H-NMR (CDCl₃, 300 MHz) δ = 1.18 (t, *J* = 7.1 Hz, 3H), 2.01 (t, *J* = 2.6 Hz, 1H), 3.21 (dd, *J*₁ = 16.3 Hz, *J*₂ = 2.6 Hz, 1H), 3.40 (dd, *J*₁ = 16.4 Hz, *J*₂ = 2.6 Hz, 1H), 3.69 (s, 3H), 4.07-4.37 (m, 2H), 4.99 (br s, 1H), 6.40 (d, *J* = 9.1 Hz, 2H), 6.63 (d, *J* = 9.0 Hz, 2H), 7.32-7.40 (m, 3H), 7.55-7.63 (m, 2H); ¹³C-NMR (CDCl₃, 75.5 MHz) δ = 13.9, 24.8, 55.5, 62.1, 66.6, 71.6, 79.3, 114.3, 118.5, 126.8, 127.9, 128.7, 137.8, 139.7, 153.0, 172.3; HRMS (ES) calc. for (M+H)⁺ C₂₀H₂₂NO₃: 324.1600; found: 324.1607.



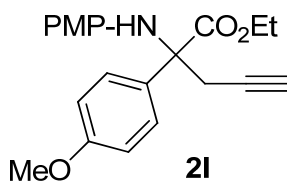
Ethyl 2-[(4-methoxyphenyl)amino]-2-methyl-4-pentynoate (2j).

Following method described above 124 mg of **2j** (50% yield) were obtained as a light yellow oil starting from 221 mg of **1j**. ¹H-NMR (CDCl₃, 300 MHz) δ = 1.56 (s, 3H), 2.09 (t, *J* = 3.0 Hz, 1H), 2.66 (dd, *J*₁ = 15.0 Hz, *J*₂ = 3.0 Hz, 1H), 2.79 (dd, *J*₁ = 18.0 Hz, *J*₂ = 3.0 Hz, 1H), 3.75 (s, 3H), 3.75 (s, 3H), 6.71 (d, *J* = 9.0 Hz, 2H), 6.76 (d, *J* = 9.0 Hz, 2H); ¹³C-NMR (CDCl₃, 75.5 MHz) δ = 23.8, 27.9, 52.5, 55.5, 61.2, 71.7, 79.6, 114.4, 121.3, 137.8, 154.6, 175.0; HRMS (ES) calc. for (M+H)⁺ C₁₄H₁₈NO₃: 248.1287; found: 248.1284.



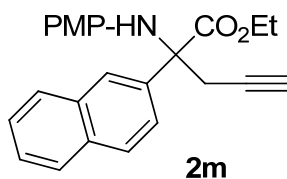
Ethyl 2-[(4-methoxyphenyl)amino]-2-(4-chlorophenyl)-4-pentynoate (2k).

Following method described above 186 mg of **2k** (52% yield) were obtained as a light yellow oil starting from 317 mg of **1k**. ¹H-NMR (CDCl₃, 300 MHz) δ = 1.18 (t, *J* = 9.0 Hz, 3H), 2.02 (t, *J* = 3.0 Hz, 1H), 3.16 (dd, *J*₁ = 18.0 Hz, *J*₂ = 3.0 Hz, 1H), 3.33 (dd, *J*₁ = 18.0 Hz, *J*₂ = 3.0 Hz, 1H), 3.69 (s, 3H), 4.06-4.17 (m, 2H), 4.95 (br s, 1H), 6.39 (d, *J* = 9.0 Hz, 2H), 6.64 (d, *J* = 9.0 Hz, 2H), 7.34 (d, *J* = 9.0 Hz, 2H), 7.52 (d, *J* = 9.0 Hz, 2H); ¹³C-NMR (CDCl₃, 75.5 MHz) δ = 13.9, 25.2, 55.5, 62.3, 66.3, 71.9, 78.8, 114.4, 118.5, 128.4, 128.8, 134.0, 137.5, 138.4, 153.2, 171.9; HRMS (ES) calc. for (M+H)⁺ C₂₀H₂₁ClNO₃: 358.1210; found: 358.1202.



Ethyl 2-[(4-methoxyphenyl)amino]-2-(4-methoxyphenyl)-4-pentynoate (**2l**).

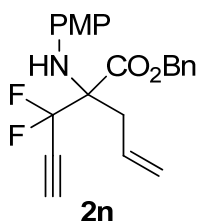
Following method described above 195 mg of **2l** (55% yield) were obtained as a light yellow oil starting from 313 mg of **1l**. ¹H-NMR (CDCl₃, 300 MHz) δ = 1.19 (t, *J* = 9.0 Hz, 3H), 2.00 (t, *J* = 3.0 Hz, 1H), 3.17 (dd, *J*₁ = 15.0 Hz, *J*₂ = 3.0 Hz, 1H), 3.35 (dd, *J*₁ = 18.0 Hz, *J*₂ = 3.0 Hz, 1H), 3.69 (s, 3H), 3.81 (s, 3H), 4.16-4.32 (m, 2H), 4.94 (br s, 1H), 6.41 (d, *J* = 9.0 Hz, 2H), 6.63 (d, *J* = 9.0 Hz, 2H), 6.85 (d, *J* = 9.0 Hz, 2H), 6.93 (d, *J* = 9.0 Hz, 2H); ¹³C-NMR (CDCl₃, 75.5 MHz) δ = 14.0, 24.9, 55.2, 55.5, 62.1, 65.8, 66.2, 71.5, 79.4, 114.0, 114.3, 118.5, 128.1, 131.7, 138.0, 153.0, 159.2, 172.6; HRMS (ES) calc. for (M+H)⁺ C₂₁H₂₄NO₄: 354.1705; found: 354.1698.



Ethyl 2-[(4-methoxyphenyl)amino]-2-(2-naphthyl)-4-pentynoate (**2m**).

Following method described above 313 mg of **2m** (84% yield) were obtained as a light yellow oil starting from 333 mg of **1m**. ¹H-NMR (CDCl₃, 300 MHz) δ = 1.17 (t, *J* = 6.0 Hz, 3H), 2.05 (t, *J* = 3.0 Hz, 1H), 3.32 (dd, *J*₁ = 15.0 Hz, *J*₂ = 3.0 Hz, 1H), 3.54 (dd, *J*₁ = 15.0 Hz, *J*₂ = 3.0 Hz, 1H), 3.66 (s, 3H), 4.04-4.16 (m, 2H), 5.03 (br s, 1H), 6.44 (d, *J* = 9.0 Hz, 2H), 6.60 (d, *J* = 9.0 Hz, 2H), 7.49-7.53 (m, 2H), 7.72 (dd, *J*_o = 9.0 Hz, *J*_m = 3.0 Hz, 1H), 7.82-7.88 (m, 3H), 8.02 (d, *J* =

3.0 Hz, 1H); ^{13}C -NMR (CDCl_3 , 75.5 MHz) δ = 13.9, 24.8, 55.4, 62.2, 66.8, 71.8, 79.2, 114.3, 118.7, 124.8, 125.9, 126.2, 126.4, 127.5, 128.4, 128.5, 132.8, 133.2, 137.5, 137.8, 153.1, 172.3; HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{24}\text{H}_{24}\text{NO}_3$: 374.1756; found: 374.1751.



Benzyl 2-(1,1-difluoroprop-2-ynyl)-2-(4-methoxyphenylamino)-4-pentenoate (2n).

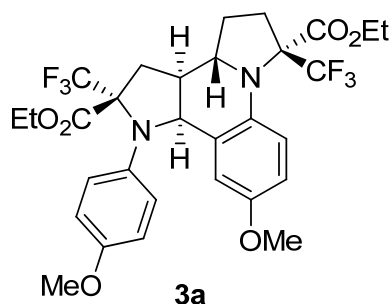
A freshly prepared solution of allylzinc bromide (1.5 mL, 1.5 mmol) was added dropwise to a solution of α -imino ester **1n** (500 mg, 1 mmol) in THF (10 mL) under inert atmosphere at -40°C . After 10 minutes, the reaction mixture was quenched with a saturated aqueous solution of NH_4Cl (20 mL) and the aqueous layer was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were washed with brine (3 x 7 mL) and dried over anhydrous Na_2SO_4 , and the solvent removed under reduced pressure to afford the desired α -amino ester in almost quantitative yield, that was used in the next step without further purification.

To a solution of TBAF (1.2 mL, 1.0 M solution in THF) and acetic acid (0.18 mL, 2.8 mmol) in dry THF (10 mL) at room temperature was added dropwise a solution of the previously obtained amino ester in dry THF (10 mL). The reaction mixture was stirred at this temperature until TLC showed total consumption of the starting material (2 h), then quenched with water and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with brine (30 mL) and dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure and the crude mixture was purified by means of *flash* column chromatography [*n*-hexane-AcOEt (10:1)]. The deprotected amino ester **2n** was obtained in 60% yield (232 mg) as a light yellow oil. ^1H -NMR (CDCl_3 , 300 MHz): δ = 2.76 (t, J = 5.4 Hz, 1H), 2.92 (dd, J_1 = 14.7 Hz; J_2 = 8.7 Hz, 1H), 3.06 (ddt, J_1 = 14.7 Hz; J_2 = 6.0 Hz; J_3 = 1.2 Hz, 1H), 3.75 (s, 3H), 4.61 (br s, 1H), 4.94-5.01 (m, 2H), 5.26 (dd, J_1 = 16.8 Hz; J_2 = 12.0 Hz, 2H), 5.56-5.42 (m, 1H), 6.74 (d, J = 9.0 Hz, 2H), 6.88 (d, J = 9.0 Hz, 2H), 7.37 (s, 5H); ^{13}C -NMR (CDCl_3 , 75.5 MHz): δ = 33.3, 55.4, 68.4, 70.2, 74.8 (t, $^2J_{\text{CF}}$ = 39.0 Hz), 77.5 (t, $^3J_{\text{CF}}$ = 6.4 Hz), 109.2, 113.5 (t,

$^1J_{\text{CF}} = 246.9$ Hz), 119.9, 122.2, 128.4, 128.5, 130.8, 134.6, 136.8, 154.6, 169.4; ^{19}F -NMR (CDCl_3 , 282 MHz): $\delta = -98.6$ (dd, $J_{\text{FF}} = 274.5$ Hz; $J_{\text{FH}} = 5.4$ Hz, 1F), -101.6 (dd, $J_{\text{FF}} = 274.5$ Hz; $J_{\text{FH}} = 5.4$ Hz, 1F); HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{22}\text{H}_{22}\text{F}_2\text{NO}_3$: 386.1568; found: 386.1569.

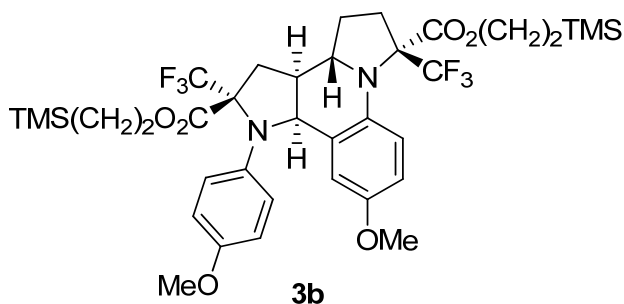
General procedure for the gold catalysis.

Active catalyst was formed by stirring at 0 °C a suspension of AuClPPh_3 (5 mol %) and AgOTf (5 mol %) in dry toluene (0.6 mL, 0.2 M) for 5 minutes. The corresponding α -propargylamino ester **2** (0.24 mmol) was added next. The reaction mixture was stirred at this temperature until TLC showed total consumption of starting material. Then, solvents were removed under reduced pressure and crude mixture was purified by flash chromatography in [hexanes: ethyl acetate] (10:1).



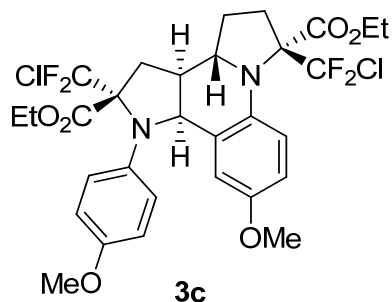
(2R*,3aS*,3bS*,6R*,11bS*)-Diethyl 10-Methoxy-1-(4-methoxyphenyl)-2,6-bis(trifluoromethyl)-2,3,3a,3b,4,5,6,11b-octahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6-dicarboxylate (**3a**).

Following method described above 57 mg of **3a** (76% yield) were obtained as a white solid starting from 76 mg of **2a**. m.p. = 121-123 °C. ^1H -NMR (CDCl_3 , 300 MHz): $\delta = 0.91$ (t, $J = 7.1$ Hz, 3H), 1.23 (t, $J = 7.2$ Hz, 3H), 1.91-1.98 (m, 1H), 2.16-2.24 (m, 1H), 2.40-2.56 (m, 4H), 2.78 (dd, $J_1 = 14.6$ Hz, $J_2 = 7.4$ Hz, 1H), 3.33 (s, 3H), 3.75 (s, 3H), 3.94 (q, $J = 7.2$ Hz, 2H), 4.01-4.09 (m, 1H), 4.13-4.24 (m, 2H), 4.72 (d, $J = 5.1$ Hz, 1H), 6.09 (d, $J_{\text{m}} = 3.0$ Hz, 1H), 6.55 (dd, $J_{\text{o}} = 9.0$ Hz, $J_{\text{m}} = 3.0$ Hz, 1H), 6.75 (d, $J_{\text{o}} = 9.0$ Hz, 2H), 6.78 (d, $J_{\text{o}} = 9.0$ Hz, 1H), 7.18 (d, $J_{\text{o}} = 8.7$ Hz, 2H). ^{13}C -NMR (CDCl_3 , 75.5 MHz): $\delta = 13.6$, 13.8, 27.4, 33.4, 35.7, 36.6, 55.3, 55.3, 59.3, 61.9, 62.0, 62.5, 72.4 (q, $^2J_{\text{CF}} = 25.6$ Hz), 74.8 (q, $^2J_{\text{CF}} = 27.5$ Hz), 113.4, 115.3, 116.4, 117.1 (q, $^5J_{\text{CF}} = 6.0$ Hz), 123.1, 125.5 (q, $^1J_{\text{CF}} = 287.5$ Hz), 126.3 (q, $^1J_{\text{CF}} = 291.7$ Hz), 132.4, 134.7, 135.5, 151.9, 158.1, 168.3, 169.1; ^{19}F -NMR (CDCl_3 , 282 MHz): $\delta = -69.1$ (s, 3F), -71.7 (s, 3F); HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{30}\text{H}_{33}\text{F}_6\text{N}_2\text{O}_6$: 631.2243; found: 631.2232.



(2R*,3aS*,3bS*,6R*,11bS*)-Bis[2-(trimethylsilyl)ethyl] 10-Methoxy-1-(4-methoxyphenyl)-2,6-bis(trifluoromethyl)-2,3,3a,3b,4,5,6,11b-octahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6-dicarboxylate (3b).

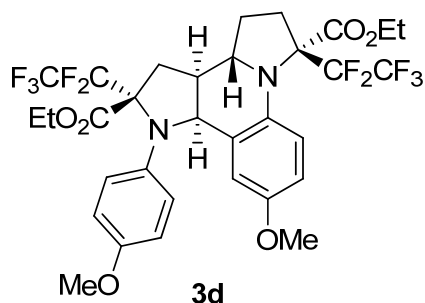
Following method described above 48 mg of **3b** (52% yield) were obtained as a yellow oil starting from 93 mg of **2b**. ¹H-NMR (CDCl₃, 300 MHz): δ = 0.02 (s, 9H), 0.06 (s, 9H), 0.51-0.72 (m, 2H), 0.91-1.00 (m, 2H), 1.90-1.99 (m, 1H), 2.16-2.25 (m, 1H), 2.43-2.54 (m, 4H), 2.78 (dd, *J*₁ = 14.1 Hz, *J*₂ = 7.2 Hz, 1H), 3.35 (s, 3H), 3.75 (s, 3H), 3.92-4.02 (m, 2H), 4.03-4.15 (m, 1H), 4.15-4.28 (m, 2H), 4.72 (d, *J* = 4.5 Hz, 1H), 6.10 (d, *J*_m = 3.0 Hz, 1H), 6.54 (dd, *J*_o = 9.0 Hz, *J*_m = 3.0 Hz, 1H), 6.77 (d, *J*_o = 9.0 Hz, 1H), 6.75 (d, *J* = 9.0 Hz, 2H), 7.19 (d, *J* = 9.0 Hz, 2H); ¹³C-NMR (CDCl₃, 75.5 MHz): δ = -1.7, -1.8, 17.2, 16.9, 27.5, 33.3, 35.8, 36.8, 55.3, 55.3, 59.3, 62.6, 64.5, 64.6, 72.5 (q, ²*J*_{CF} = 25.5 Hz), 74.8 (q, ²*J*_{CF} = 27.4 Hz), 113.4, 115.2, 116.4, 117.1 (q, ⁵*J*_{CF} = 5.5 Hz), 123.2, 132.4, 134.8, 135.5, 151.9, 158.0, 168.6, 169.4; ¹⁹F-NMR (CDCl₃, 282 MHz): δ = -69.0 (s, 3F), -71.5 (s, 3F); HRMS (ES) calc. for (M+H)⁺ C₃₆H₄₉F₆N₂O₆Si₂: 775.3033; found: 775.3043.



(2R*,3aS*,3bS*,6R*,11bS*)-Diethyl 2,6-Bis(chlorodifluoromethyl)-10-methoxy-1-(4-methoxyphenyl)-2,3,3a,3b,4,5,6,11b-octahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6-dicarboxylate (3c).

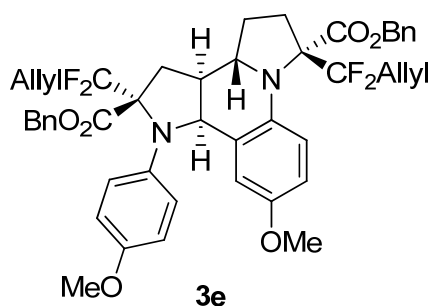
Following method described above 48 mg of **3c** (60% yield) were obtained as a yellow oil starting from 79 mg of **2c**. ¹H-NMR (CDCl₃, 300 MHz): δ = 0.96 (t, *J* = 7.2 Hz, 3H),

1.20 (t, $J = 7.2$ Hz, 3H), 1.89-1.99 (m, 1H), 2.16-2.34 (m, 1H), 2.47-2.76 (m, 4H), 2.82 (dd, $J_1 = 14.4$ Hz, $J_2 = 6.9$ Hz, 1H), 3.34 (s, 3H), 3.67 (s, 3H), 3.98 (q, $J = 7.2$ Hz, 2H), 4.03-4.11 (m, 1H), 4.16 (qd, $J_1 = 7.2$ Hz, $J_2 = 1.5$ Hz, 2H), 4.77 (d, $J = 4.8$ Hz, 1H), 6.09 (d, $J_m = 3.0$ Hz, 1H), 6.53 (dd, $J_o = 9.0$ Hz, $J_m = 3.0$ Hz, 1H), 6.73 (d, $J_o = 9.0$ Hz, 1H), 6.73 (d, $J = 9.0$ Hz, 2H), 7.13 (d, $J = 9.0$ Hz, 2H); ^{13}C -NMR (CDCl_3 , 75.5 MHz): $\delta = 13.6, 13.8, 27.7, 35.0, 36.9, 37.3, 55.2, 55.3, 59.7, 61.9, 62.0, 63.6, 77.1$ (t, $^2J_{\text{CF}} = 22.2$ Hz), 78.5 (t, $^2J_{\text{CF}} = 22.1$ Hz), 113.1, 115.2, 116.4 (t, $^5J_{\text{CF}} = 9.1$ Hz), 116.7, 122.2, 130.7 (t, $^1J_{\text{CF}} = 302.9$ Hz), 131.4 (t, $^1J_{\text{CF}} = 304.2$ Hz), 132.9, 134.6, 135.5, 151.5, 158.9, 168.4, 168.8; ^{19}F -NMR (CDCl_3 , 282 MHz): $\delta = -54.8$ (s, 2F), -54.8 (s, 2F); HRMS (ES) calc. for $(\text{M}+\text{H})^+ \text{C}_{30}\text{H}_{33}\text{Cl}_2\text{F}_4\text{N}_2\text{O}_6$: 663.1652; found: 663.1667.



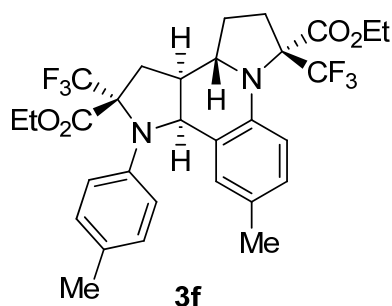
(2R*,3aS*,3bS*,6R*,11bS*)-Diethyl 10-Methoxy-1-(4-methoxyphenyl)-2,6-bis(perfluoroethyl)-2,3,3a,3b,4,5,6,11b-octahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6-dicarboxylate (3d).

Following method described above 45 mg of **3d** (51% yield) were obtained as a yellow oil starting from 88 mg of **2d**. ^1H -NMR (CDCl_3 , 300 MHz): $\delta = 1.06$ (t, $J = 7.2$ Hz, 3H), 1.18 (t, $J = 7.2$ Hz, 3H), 1.83-1.95 (m, 1H), 2.10-2.18 (m, 1H), 2.35-2.53 (m, 2H), 2.60-2.75 (m, 2H), 2.86 (d, $J = 13.8$ Hz, 1H), 3.40 (s, 3H), 3.74 (s, 3H), 3.83-3.91 (m, 1H), 4.02-4.23 (m, 4H), 4.70 (d, $J = 4.2$ Hz, 1H), 6.05 (d, $J_m = 2.7$ Hz, 1H), 6.53 (dd, $J_o = 9.0$ Hz, $J_m = 2.7$ Hz, 1H), 6.58 (d, $J_o = 9.0$ Hz, 1H), 6.73 (d, $J = 9.0$ Hz, 2H), 7.12 (d, $J = 9.0$ Hz, 2H); ^{13}C -NMR (CDCl_3 , 75.5 MHz): $\delta = 13.6, 13.7, 28.1, 34.0, 34.1, 37.9, 55.2, 55.4, 58.7, 62.1, 62.2, 64.4, 71.2-71.7$ (m), 73.3-73.9 (m), 112.9, 114.6-114.9 (m), 115.2, 117.0, 120.9, 133.3, 135.2, 135.3, 151.0, 158.0, 168.0, 168.8; ^{19}F -NMR (CDCl_3 , 282 MHz): $\delta = -78.7$ (s, 3F), -79.0 (s, 3F), -108.1 (d, $J_{\text{FF}} = 279.0$ Hz, 1F), -110.9 (d, $J_{\text{FF}} = 279.3$ Hz), -113.5 (d, $J_{\text{FF}} = 266.3$ Hz, 1F), -118.2 (d, $J_{\text{FF}} = 266.3$ Hz, 1F); HRMS (ES) calc. for $(\text{M}+\text{H})^+ \text{C}_{32}\text{H}_{33}\text{F}_{10}\text{N}_2\text{O}_6$: 731.2179; found: 731.2190.



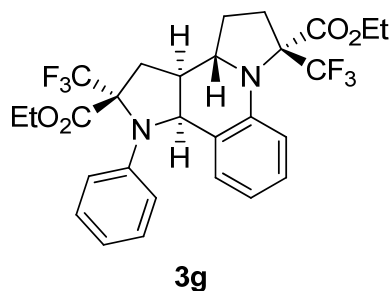
(2R*,3aS*,3bS*,6R*,11bS*)-Dibenzyl 2,6-Bis(1,1-difluorobut-3-enyl)-10-methoxy-1-(4-methoxyphenyl)-2,3,3a,3b,4,5,6,11b-octahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6-dicarboxylate (3e).

Following method described above 59 mg of **3e** (62% yield) were obtained as a yellow oil starting from 96 mg of **2e**. ¹H-NMR (CDCl₃, 300 MHz): δ = 1.76-1.92 (m, 2H), 2.01-2.29 (m, 5H), 2.49-2.84 (m, 5H), 3.30 (s, 3H), 3.52-3.57 (m, 1H), 3.67 (m, 3H), 4.53 (d, *J* = 4.2 Hz, 1H), 4.83 (d, *J* = 12.3 Hz, 2H), 4.96 (d, *J* = 12.3 Hz, 2H), 5.11-5.20 (m, 4H), 5.56-5.73 (m, 1H), 5.75-5.90 (m, 1H), 6.06 (d, *J_m* = 3.0 Hz, 1H), 6.37 (dd, *J_o* = 9.0 Hz, *J_m* = 3.0 Hz, 1H), 6.50 (d, *J_o* = 9.0 Hz, 1H), 6.64 (d, *J* = 9.0 Hz, 2H), 6.94 (d, *J* = 9.0 Hz, 2H), 7.13-7.26 (m, 10H); ¹³C-NMR (CDCl₃, 75.5 MHz): δ = 36.0, 37.1, 38.9, 39.5 (t, ²*J_{CF}* = 24.0 Hz), 40.2 (t, ²*J_{CF}* = 23.7 Hz), 56.3, 56.4, 60.7, 64.6, 68.4, 68.5 (t, ²*J_{CF}* = 31.5 Hz), 68.9, 76.2 (t, ²*J_{CF}* = 24.1 Hz), 76.4 (t, ²*J_{CF}* = 25.6 Hz), 114.4, 115.5, 119.4, 121.2, 121.3, 125.9 (t, ¹*J_{CF}* = 252.6 Hz), 126.6 (t, ¹*J_{CF}* = 253.1 Hz), 129.4, 129.6, 129.8, 130.0, 130.1, 130.6, 134.1, 137.0, 137.1, 137.5, 138.0, 151.9, 159.1, 171.6, 172.9; ¹⁹F-NMR (CDCl₃, 282 MHz): δ = -97.1 (ddd, *J_{FF}* = 252.5 Hz, *J_{FF}* = 30.8 Hz, *J_{FH}* = 7.1 Hz, 1F), -98.8 (dd, *J_{FF}* = 254.7 Hz, *J_{FF}* = 28.5 Hz, 1F), -99.8 (ddd, *J_{FF}* = 252.2 Hz, *J_{FF}* = 27.9 Hz, *J_{FH}* = 7.1 Hz, 1F), -104.6 (dd, *J_{FF}* = 253.9 Hz, *J_{FF}* = 29.0 Hz, 1F); HRMS (ES) calc. for (M+H)⁺ C₄₆H₄₇F₄N₂O₆: 799.3370; found: 799.3388.



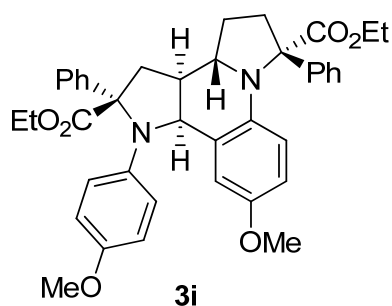
(2R*,3aS*,3bS*,6R*,11bS*)-Diethyl 10-Methyl-1-*p*-tolyl-2,6-bis(trifluoromethyl)-2,3,3a,3b,4,5,6,11b-octahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6-dicarboxylate (3f).

Following method described above 24 mg of **3f** (34% yield) were obtained as a yellow oil starting from 72 mg of **2f**. ¹H-NMR (CDCl₃, 300 MHz): δ = 0.97 (t, *J* = 7.2 Hz, 3H), 1.24 (t, *J* = 7.2 Hz, 3H), 1.91 (s, 3H), 1.91-1.99 (m, 1H), 2.16-2.23 (m, 1H), 2.28 (s, 3H), 2.42-2.54 (m, 4H), 2.79 (dd, *J*₁ = 14.4 Hz, *J*₂ = 7.2 Hz, 1H), 3.96-4.28 (m, 5H), 4.78 (d, *J* = 4.5 Hz, 1H), 6.46 (d, *J*_m = 2.1 Hz, 1H), 6.66 (d, *J*_o = 8.4 Hz, 1H), 6.75 (dd, *J*_o = 8.4 Hz, *J*_m = 2.1 Hz, 1H), 7.02 (d, *J*_o = 8.4 Hz, 2H), 7.12 (d, *J*_o = 8.4 Hz, 2H); ¹³C-NMR (CDCl₃, 75.5 MHz): δ = 13.5, 13.8, 20.0, 20.9, 27.8, 33.5, 36.0, 37.5, 59.1, 61.9, 62.0, 62.1, 72.5 (q, ²*J*_{CF} = 25.7 Hz), 74.1 (q, ²*J*_{CF} = 27.6 Hz), 114.9 (q, ⁵*J*_{CF} = 5.4 Hz), 121.5, 125.7 (q, ¹*J*_{CF} = 288.3 Hz), 126.3 (q, ¹*J*_{CF} = 292.1 Hz), 128.5, 128.7, 130.4, 133.2, 135.9, 139.2, 139.4, 168.5, 169.2; ¹⁹F-NMR (CDCl₃, 282 MHz): δ = -69.0 (s, 3F), -71.1 (s, 3F); HRMS (ES) calc. for (M+H)⁺ C₃₀H₃₃F₆N₂O₄: 599.2345; found: 599.2337



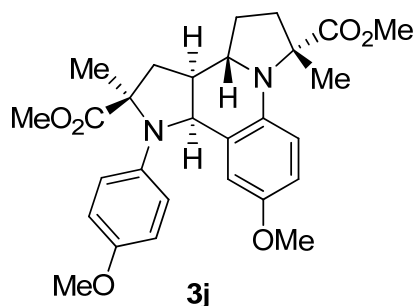
(2R*,3aS*,3bS*,6R*,11bS*)-Diethyl 1-Phenyl-2,6-bis(trifluoromethyl)-2,3,3a,3b,4,5,6,11b-octahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6-dicarboxylate (3g).

Following method described above 10 mg of **3g** (14% yield) were obtained as a yellow oil starting from 68 mg of **2g**. ¹H-NMR (CDCl₃, 300 MHz): δ = 0.96 (t, *J* = 7.2 Hz, 3H), 1.22 (t, *J* = 7.2 Hz, 3H), 1.89-2.00 (m, 1H), 2.19-2.26 (m, 1H), 2.42-2.58 (m, 4H), 2.80 (dd, *J*₁ = 14.4 Hz, *J*₂ = 7.5 Hz, 1H), 3.97-4.07 (m, 2H), 4.12-4.26 (m, 4H), 4.86 (d, *J* = 4.8 Hz, 1H), 6.37-6.43 (m, 1H), 6.66-6.69 (m, 1H), 6.73-6.84 (m, 1H), 6.91-6.96 (m, 1H), 7.09-7.17 (m, 1H), 7.19-7.23 (m, 4H); ¹³C-NMR (CDCl₃, 75.5 MHz): δ = 13.6, 13.8, 28.0, 33.6, 36.2, 37.8, 59.0, 62.1, 62.2, 63.7, 72.7 (q, ²*J*_{CF} = 25.6 Hz), 74.1 (q, ²*J*_{CF} = 27.2 Hz), 115.0 (q, ⁵*J*_{CF} = 3.3 Hz, 118.2, 125.7 (q, ¹*J*_{CF} = 286.5 Hz), 126.2, 126.2 (q, ¹*J*_{CF} = 290.0 Hz), 128.1, 128.2, 129.2, 130.2, 132.5, 141.6, 142.2, 168.4, 169.2; ¹⁹F-NMR (CDCl₃, 282 MHz): δ = -48.8 (s, 3F), -50.9 (s, 3F); HRMS (ES) calc. for (M+H)⁺ C₂₈H₂₉F₆N₂O₄: 571.2032; found: 571.2025.



(2S*,3aS*,3bS*,6S*,11bS*)-Diethyl 10-Methoxy-1-(4-methoxyphenyl)-2,6-diphenyl-2,3,3a,3b,4,5,6,11b-octahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6-dicarboxylate (3i).

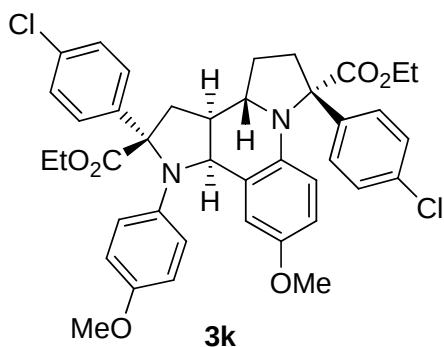
Following method described above 47 mg of **3i** (60% yield) were obtained as a yellow oil starting from 78 mg of **2i**. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 0.93 (t, J = 7.0 Hz, 3H), 1.11 (t, J = 7.0 Hz, 3H), 1.75-1.84 (m, 1H), 1.95-2.06 (m, 2H), 2.53-2.64 (m, 3H), 2.71 (dd, J_1 = 12.5 Hz, J_2 = 6.5 Hz, 1H), 3.31 (s, 3H), 3.61 (s, 3H), 3.92-4.02 (m, 2H), 4.04-4.18 (m, 3H), 4.72 (d, J = 6.5 Hz, 1H), 6.25 (d, J_o = 9.0 Hz, 1H), 6.35 (dd, J_o = 9.0 Hz, J_m = 3.0 Hz, 1H), 6.39 (d, J_m = 3.0 Hz, 1H), 7.15-7.36 (m, 10H); $^{13}\text{C-NMR}$ (CDCl_3 , 75.5 MHz): δ = 14.0, 14.1, 30.2, 42.2, 42.5, 44.3, 55.4, 55.4, 60.4, 61.2, 61.3, 73.7, 75.5, 113.3, 113.4, 115.6, 117.0, 123.7, 126.1, 127.0, 127.2, 127.4, 127.8, 127.9, 128.4, 136.7, 138.8, 140.4, 142.3, 151.4, 153.9, 173.2, 174.9; HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{40}\text{H}_{43}\text{N}_2\text{O}_6$: 647.3121; found: 647.3146.



(2R*,3aS*,3bS*,6R*,11bS*)-Dimethyl 10-Methoxy-1-(4-methoxyphenyl)-2,6-dimethyl-2,3,3a,3b,4,5,6,11b-octahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6-dicarboxylate (3j).

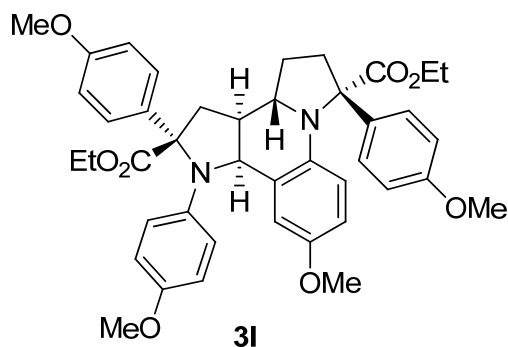
Following method described above 44 mg of **3j** (70% yield) were obtained as a yellow oil starting from 63 mg of **2j**. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ = 1.36 (s, 3H), 1.55 (s, 3H), 1.78-1.86 (m, 1H), 1.88-1.99 (m, 2H), 2.22-2.41 (m, 4H), 2.76 (dt, J_1 = J_2 = 9.0 Hz, 1H), 3.40 (s, 3H), 3.65 (s, 3H), 3.66 (s, 3H), 3.76 (s, 3H), 4.57 (d, J = 6.0 Hz, 1H),

6.30 (d, $J_o = 9.0$ Hz, 1H), 6.34 (d, $J_m = 3.0$ Hz, 1H), 6.56 (dd, $J_o = 9.0$ Hz, $J_m = 3.0$ Hz, 1H), 6.80 (d, $J = 9.0$ Hz, 2H), 7.01 (d, $J = 9.0$ Hz, 2H); ^{13}C -NMR (CDCl_3 , 75.5 MHz) $\delta = 19.9, 23.2, 29.2, 39.4, 41.9, 41.9, 52.1, 52.4, 55.4, 58.4, 61.5, 66.3, 67.6, 113.1, 113.7, 113.8, 116.3, 124.8, 127.7, 137.1, 138.3, 150.5, 155.9, 176.5, 176.8$; HRMS (ES) calc. for $(\text{M}+\text{H})^+ \text{C}_{28}\text{H}_{35}\text{N}_2\text{O}_6$: 495.2495; found: 495.2497.



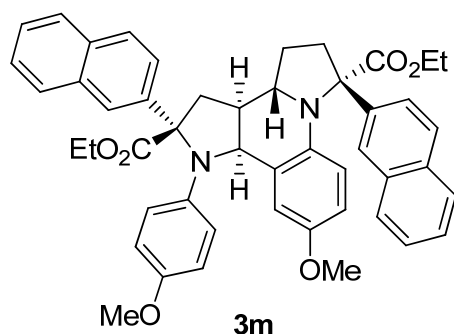
(2R*,3aS*,3bS*,6R*,11bS*)-Diethyl 2,6-Bis(4-chlorophenyl)-10-methoxy-1-(4-methoxyphenyl)-2,3,3a,3b,4,5,6,11b-octahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6-dicarboxylate (3k).

Following method described above 63 mg of **3k** (74% yield) were obtained as a yellow oil starting from 86 mg of **2k**. ^1H -NMR (CDCl_3 , 300 MHz) $\delta = 0.94$ (t, $J = 9.0$ Hz, 3H), 1.12 (t, $J = 9.0$ Hz, 3H), 1.76-1.87 (m, 1H), 1.92-2.06 (m, 2H), 2.49-2.67 (m, 4H), 2.75-2.86 (m, 1H), 3.36 (s, 3H), 3.65 (s, 3H), 3.93-4.01 (m, 2H), 4.06-4.20 (m, 2H), 4.72 (d, $J = 6.0$ Hz, 1H), 6.24 (d, $J_o = 9.0$ Hz, 1H), 6.39 (dd, $J_o = 9.0$ Hz, $J_m = 3.0$ Hz, 1H), 6.44-6.47 (m, 1H), 6.58 (d, $J = 9.0$ Hz, 2H), 6.59 (d, $J = 9.0$ Hz, 2H), 7.16 (d, $J = 9.0$ Hz, 2H), 7.21 (d, $J = 9.0$ Hz, 2H), 7.25 (d, $J = 9.0$ Hz, 2H), 7.30 (d, $J = 9.0$ Hz, 2H); ^{13}C -NMR (CDCl_3 , 75.5 MHz) $\delta = 13.9, 14.0, 30.2, 42.1, 42.8, 44.6, 55.4, 55.4, 60.1, 60.9, 61.5, 61.5, 73.2, 75.2, 113.1, 113.6, 115.7, 117.0, 122.9, 126.4, 127.8, 128.0, 129.0, 129.8, 132.8, 133.1, 136.3, 138.5, 140.8, 151.8, 153.9, 172.8, 174.5$; HRMS (ES) calc. for $(\text{M}+\text{H})^+ \text{C}_{40}\text{H}_{41}\text{Cl}_2\text{N}_2\text{O}_6$: 715.2342; found: 715.2330.



(2R*,3aS*,3bS*,6R*,11bS*)-Diethyl 10-Methoxy-1,2,6-tris(4-methoxyphenyl)-2,3,3a,3b,4,5,6,11b-octahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6-dicarboxylate (3l)

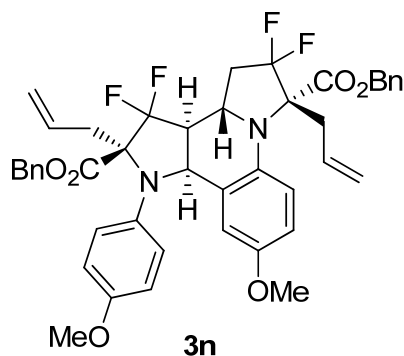
Following method described above 61 mg of **3l** (72% yield) were obtained as a yellow oil starting from 85 mg of **2l**. ¹H-NMR (CDCl₃, 300 MHz) δ = ¹H-NMR (CDCl₃, 300 MHz) δ 1.01 (t, *J* = 6.0 Hz, 3H), 1.18 (t, *J* = 6.0 Hz, 3H), 1.78-1.93 (m, 1H), 1.99-2.13 (m, 2H), 2.51-2.66 (m, 3H), 2.69-2.90 (m, 2H), 3.40 (s, 3H), 3.70 (s, 3H), 3.80 (s, 3H), 3.82 (s, 3H), 4.11-4.25 (m, 4H), 4.75 (d, *J* = 6.0 Hz, 1H), 6.44 (s, 1H), 6.54 (d, *J* = 9.0 Hz, 2H), 6.62 (d, *J* = 9.0 Hz, 2H), 6.79-6.90 (m, 6H), 7.18 (d, *J* = 9.0 Hz, 2H), 7.32 (d, *J* = 9.0 Hz, 2H); ¹³C-NMR (CDCl₃, 75.5 MHz) δ = 14.0, 14.1, 30.0, 42.2, 42.5, 44.3, 55.2, 55.2, 55.4, 55.4, 60.2, 61.2, 73.1, 75.0, 113.0, 113.1, 113.2, 113.3, 115.6, 116.7, 123.8, 126.0, 128.6, 129.5, 132.4, 134.1, 136.8, 138.9, 151.3, 153.9, 158.5, 158.6, 173.4, 175.1; HRMS (ES) calc. for (M+H)⁺ C₄₂H₄₇N₂O₈: 707.3332; found: 707.3323.



(2R*,3aS*,3bS*,6R*,11bS*)-Diethyl 10-Methoxy-1-(4-methoxyphenyl)-2,6-di(naphthalen-2-yl)-2,3,3a,3b,4,5,6,11b-octahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6-dicarboxylate (3m).

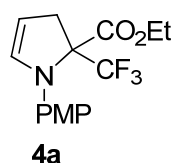
Following method described above 67 mg of **3m** (75% yield) were obtained as a yellow oil starting from 90 mg of **2m**. ¹H-NMR (CDCl₃, 300 MHz) δ = 1.05 (t, *J* = 6.0 Hz, 3H), 1.22 (t, *J* = 6.0 Hz, 3H), 1.81-1.97 (m, 1H), 2.14-2.32 (m, 2H), 2.71-2.82 (m, 2H), 2.88-3.03 (m, 2H), 3.41 (s, 3H), 3.69 (s, 3H), 3.82-3.88 (m, 1H), 4.94 (d, *J* = 3.0 Hz, 1H), 6.44-6.71 (m, 6H), 7.29-7.59 (m, 8H), 7.65-7.86 (m, 9H); ¹³C-NMR (CDCl₃, 75.5 MHz)

δ = 14.0, 14.1, 30.1, 41.8, 42.7, 44.6, 55.4, 55.4, 60.4, 61.2, 61.3, 61.4, 73.8, 76.1, 113.2, 113.5, 115.6, 117.6, 123.4, 125.9, 126.0, 126.0, 127.1, 127.4, 127.5, 127.5, 128.3, 128.4, 136.8, 138.9, 151.7, 153.9, 173.1, 174.9; HRMS (ES) calc. for (M+H)⁺ C₄₈H₄₇N₂O₆: 747.3434; found: 747.3411.



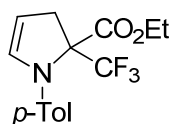
(2S*,3aS*,3bS*,6S*,11bS*)-dibenzyl 2,6-diallyl-3,3,5,5-tetrafluoro-10-methoxy-1-(4-methoxyphenyl)-2,3,3a,3b,4,5,6,11b-octahydro-1H-dipyrrolo[1,2-a:3',2'-c]quinoline-2,6-dicarboxylate (3n).

Following method described above 86 mg of **3n** (90% yield) were obtained as a yellow oil as a 7:1 mixture of diastereoisomers starting from 96 mg of **2n**. ¹H-NMR (CDCl₃, 300 MHz): δ = 2.37-2.51 (m, 1H), 2.55-2.74 (m, 2H), 2.95-3.16 (m, 4H), 3.37 (s, 3H), 3.76 (s, 3H), 4.00-4.09 (m, 1H), 4.70 (d, J = 7.5 Hz, 1H), 4.91-5.02 (m, 4H), 5.06-5.12 (m, 4H), 5.29-5.46 (m, 1H), 5.68-5.79 (m, 1H), 6.40 (d, J_m = 2.4 Hz, 1H), 6.52 (d, J_o = 8.4 Hz, 1H), 6.56 (dd, J_o = 8.4 Hz, J_m = 2.7 Hz, 1H), 6.71 (d, J = 9.3 Hz, 2H), 6.77 (d, J = 9.3 Hz, 2H), 7.23-7.35 (m, 10H); ¹³C-NMR (CDCl₃, 75.5 MHz): (major diastereoisomer) δ = 34.9, 35.0, 36.9, 37.0, 55.2, 55.5, 55.6, 57.0, 67.5, 67.6 (t, $^2J_{CF}$ = 39.7 Hz), 67.6, 74.1 (t, $^2J_{CF}$ = 24.5 Hz), 74.3 (t, $^2J_{CF}$ = 24.0 Hz), 114.1, 115.1, 116.1, 116.1 (t, $^1J_{CF}$ = 282.6 Hz), 116.2 (t, $^1J_{CF}$ = 279.1 Hz), 119.7, 120.2, 124.9, 125.7, 127.9, 128.5, 128.5, 128.5, 131.8, 131.9, 135.1, 135.1, 135.4, 136.8, 152.4, 155.4, 169.2, 169.4; ¹⁹F-NMR (CDCl₃, 282 MHz): δ = -95.5 (dt, J_{FF} = 234.7 Hz, J_{FH} = 17.5 Hz, 1F), -101.1 (dt, J_{FF} = 239.5 Hz, J_{FH} = 13.8 Hz, 1F), -102.1 (dt, J_{FF} = 234.7 Hz, J_{FH} = 12.7 Hz, 1F), -106.1 (dt, J_{FF} = 239.2 Hz, J_{FH} = 11.0 Hz, 1F); HRMS (ES) calc. for (M+H)⁺ C₄₄H₄₃F₄N₂O₆: 771.3057; found: 771.3035.



Ethyl 1-(4-methoxyphenyl)-2-(trifluoromethyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (4a).

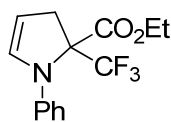
Following method described above 10 mg of **4a** (13% yield) were obtained as a colorless oil starting from 76 mg of **2a**. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 1.15 (t, J = 7.2 Hz, 3H), 3.75 (s, 3H), 4.21 (qd, J_1 = 7.2 Hz, J_2 = 0.9 Hz, 2H), 4.26-4.33 (m, 1H), 4.44 (dt, J_1 = 14.4 Hz, J_2 = 2.1 Hz, 1H), 5.80-5.84 (m, 1H), 6.40 (dt, J_1 = 6.0 Hz, J_2 = 2.1 Hz, 1H), 6.66 (d, J = 9.0 Hz, 1H), 6.82 (d, J = 9.0 Hz, 1H); $^{13}\text{C-NMR}$ (CDCl_3 , 75.5 MHz): δ = 13.9, 55.6, 58.4, 114.4, 114.7 (q, $^5J_{\text{CF}}$ = 2.0 Hz), 124.4 (q, $^1J_{\text{CF}}$ = 288.5 Hz), 124.9, 133.5, 138.2, 152.5, 167.6; $^{19}\text{F-NMR}$ (CDCl_3 , 282 MHz): δ = -70.3 (s, 3F); HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{15}\text{H}_{17}\text{F}_3\text{NO}_3$: 316.1161; found: 316.1155.



4f

Ethyl 1-p-tolyl-2-(trifluoromethyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (4f).

Following method described above 25 mg of **4f** (34% yield) were obtained as a colorless oil starting from 72 mg of **2f**. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 1.62 (t, J = 7.2 Hz, 3H), 2.25 (s, 3H), 4.23 (q, J = 7.2 Hz, 2H), 4.31 (d, J = 14.1 Hz, 1H), 4.45 (dt, J_1 = 14.4 Hz, J_2 = 1.8 Hz, 1H), 8.81-5.85 (m, 1H), 6.41 (dt, J_1 = 6.3 Hz, J_2 = 1.8 Hz, 1H), 6.60 (d, J = 8.7 Hz, 2H), 7.04 (d, J = 8.4 Hz, 2H); $^{13}\text{C-NMR}$ (CDCl_3 , 75.5 MHz): δ = 13.9, 20.2, 58.0, 62.3, 77.8 (q, $^2J_{\text{CF}}$ = 28.9 Hz), 113.3, 124.4 (q, $^1J_{\text{CF}}$ = 286.4 Hz), 124.9, 127.5, 129.4, 133.3, 141.7, 167.5; $^{19}\text{F-NMR}$ (CDCl_3 , 282 MHz): δ = -69.7 (s, 3F); HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{15}\text{H}_{17}\text{F}_3\text{NO}_2$: 300.1211; found: 300.1221.

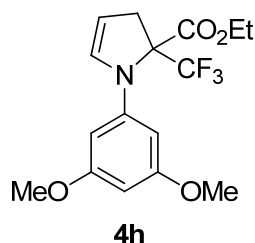


4g

Ethyl 1-phenyl-2-(trifluoromethyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (4g).

Following method described above 44 mg of **4g** (64% yield) were obtained as a colorless oil starting from 68 mg of **2g**. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ 1.46 (t, J = 7.2 Hz, 3H), 4.23 (qd, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 2H), 4.34 (d, J = 14.7 Hz, 1H), 4.47 (dt, J_1 = 14.4 Hz, J_2 = 2.1 Hz, 1H), 5.82-5.86 (m, 1H), 6.42 (ddd, J_1 = 6.0 Hz, J_2 = J_3 = 1.8 Hz,

1H), 6.69 (d, $J = 8.4$ Hz, 2H), 6.81 (tt, $J_1 = 7.2$ Hz, $J_2 = 1.2$ Hz, 1H), 7.20-7.25 (m, 1H). ^{13}C -NMR (CDCl_3 , 75.5 MHz): δ 13.8, 57.9, 62.4, 113.2, 118.3, 124.3 (q, $^1J_{\text{CF}} = 288.5$ Hz), 124.9 (q, $^5J_{\text{CF}} = 8.4$ Hz), 128.9, 133.3, 144.0, 167.3. ^{19}F -NMR (CDCl_3 , 282 MHz): δ -50.1 (s, 3F). HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{14}\text{H}_{15}\text{F}_3\text{NO}_2$: 286.1055; found: 286.1047.



Ethyl 1-(3,5-dimethoxyphenyl)-2-(trifluoromethyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (4h).

Following method described above 28 mg of **4h** (34% yield) were obtained as a colorless oil starting from 83 mg of **2h**. ^1H -NMR (CDCl_3 , 300 MHz): δ = 1.10 (t, $J = 7.2$ Hz, 3H), 3.68 (s, 6H), 4.16 (dd, $J_1 = 7.2$ Hz, $J_2 = 0.9$ Hz, 2H), 4.27 (d, $J = 15.1$ Hz, 1H), 4.35 (dt, $J_1 = 14.4$ Hz, $J_2 = 2.1$ Hz, 1H), 5.74-5.77 (m, 1H), 5.84 (d, $J_{\text{m}} = 2.1$ Hz, 2H), 5.93 (t, $J_{\text{m}} = 2.1$ Hz, 1H), 6.33 (dt, $J_1 = 6.3$ Hz, $J_2 = 2.1$ Hz, 1H); ^{13}C -NMR (CDCl_3 , 75.5 MHz): δ = 18.9, 55.1, 58.1, 62.4, 77.4 (q, $^2J_{\text{CF}} = 29.4$ Hz), 90.8, 92.7, 124.3 (q, $^1J_{\text{CF}} = 288.0$ Hz), 124.9, 133.1, 145.9, 161.3, 167.3; ^{19}F -NMR (CDCl_3 , 282 MHz): δ = -69.4 (s, 3F); HRMS (ES) calc. for $(\text{M}+\text{H})^+$ $\text{C}_{16}\text{H}_{19}\text{F}_3\text{NO}_4$: 346.1266; found: 346.1276.

X-Ray ORTEP Of compound 3a¹²

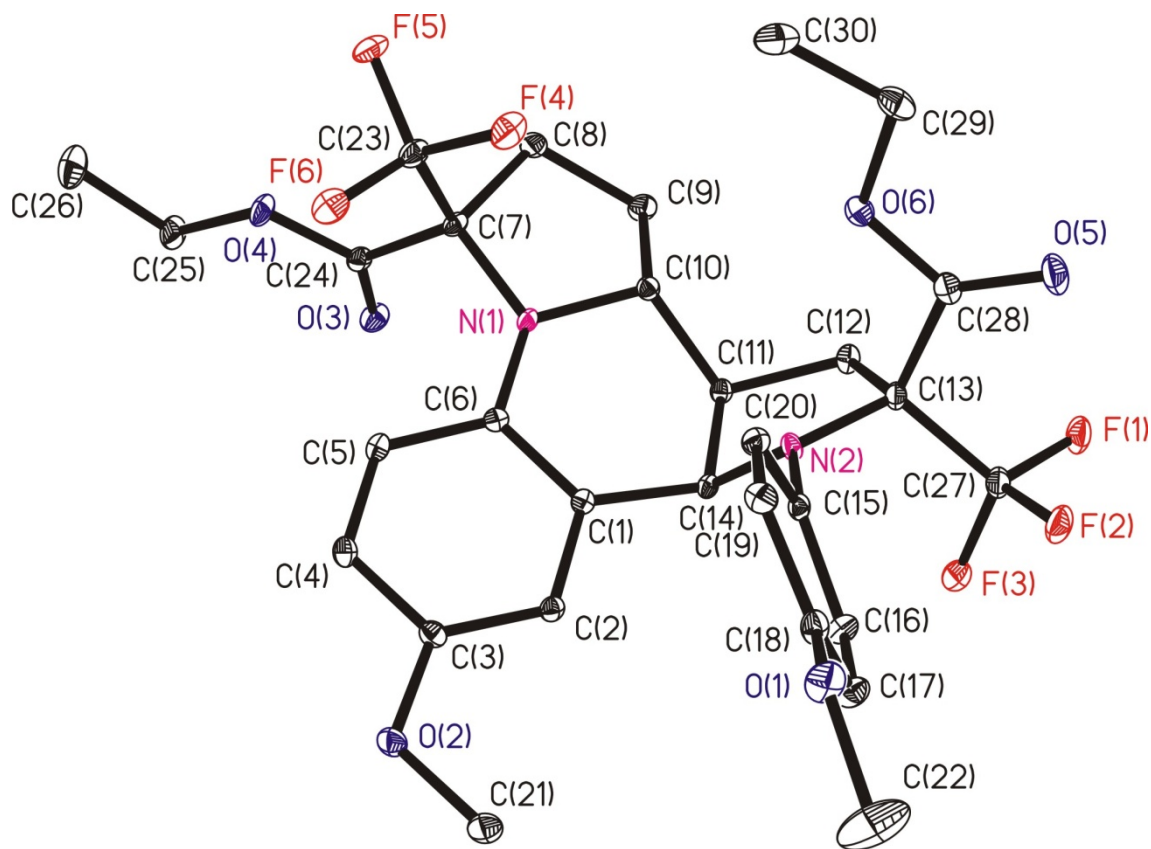


Figure 1. ORTEP of compound 3a

(12) CCDC 894411 contains the supplementary crystallographic data of compound **3a**. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44(1223)336-033, e-mail: deposit@ccdc.cam.ac.uk].

