

Supporting Information Available

Click Linker: Efficient and High Yielding Synthesis of a New Family of SPOS Resins by 1,3-Dipolar Cycloaddition

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Experimental details:

Preparation of the FAMT and FIMT resins 3a-f:

Merrifield resin (5.0 g, 1.1-1.7mmol/g) was reacted in a parallel synthesizer (Advanced ChemTech PLS) with NaN₃ (5eq) in DMSO (50mL) at 60 °C for 48 h. After being cooled to rt, the suspension was filtrated and the resin was washed alternatingly with MeOH (5x30mL) and CH₂Cl₂ (5x30mL) to give azidomethyl polystyrene **4** (FT-IR: 2096cm⁻¹). Addition of **1a-e** or **6** (5eq), CuI (0.02eq), THF (35mL) and DIPEA (15mL) was followed by agitation at 35 °C. Reaction was stopped when the IR-signal of the azido group had completely disappeared. The resin was collected by filtration and washed alternatingly with pyridine (5x30mL), MeOH (5x30mL) and CH₂Cl₂ (5x30mL). Drying of the residue in vacuum gave **3a-f** showing an IR signal for the aldehyde C=O at 1650-1690 cm⁻¹.

Parallel synthesis of the arylcarbamides 10a-t:

Five teflon reactors (AdvancedChemtech PLS) were charged each with the resin **3f** (200mg), one of the amines **A1-A5** (5eq), Na(OAc)₃BH (5eq) and CH₂Cl₂ (5mL). Agitation for 16 h at rt was followed by filtration and alternating washing of the resin with MeOH (5x5mL), MeOH/H₂O 1:1 (5x5mL), MeOH (5x5mL) and CH₂Cl₂ (5x5mL). Each resin was quartered, transferred into four teflon vessels and treated with DMF (2mL). Addition of a mixture of one of the carboxylic acids **B1-B4** (5eq) and TFFH (5eq), being preincubated in DMF/DIPEA (4:1) for 1h at rt, was followed by agitation for 24 h. IR analyses indicated the appearance of an amide signal at 1620-1630cm⁻¹. Filtration and washing of the resins with MeOH (5x5mL) and CH₂Cl₂ (5x5mL) and subsequent agitation with TFA (2% in CH₂Cl₂, 3mL) was followed by filtration. Evaporation gave the crude carboxamides **10a-f**. HPLC analysis (CH₃CN/0.1N CH₃COOH; UV detection at 240nm) was conducted after extraction with Et₂O/aq. NaHCO₃.

Dopamine receptor affinity of the test compounds **10a-t** displayed as the percental displacement of [³H]-spiperone from the human D2_{long}, D2_{short}, D3 and D4.4 receptor subtypes.

Cpd.	Concentration (test compound)[mol/l]	Displacement of [³ H]-spiperone			
		hD2 _{long}	hD2 _{short}	hD3	hD4.4
11a	10 ⁻⁷	<5	<5	<5	<5
	10 ⁻⁵	36	31	48	58
11b	10 ⁻⁷	<5	<5	7	11
	10 ⁻⁵	20	19	16	23
11c	10 ⁻⁷	<5	<5	<5	15
	10 ⁻⁵	9	15	21	24
11d	10 ⁻⁷	<5	<5	<5	<5
	10 ⁻⁵	<5	<5	10	24
11e	10 ⁻⁷	<5	<5	<5	<5
	10 ⁻⁵	18	6	7	34
11f	10 ⁻⁷	<5	5	8	60
	10 ⁻⁵	28	26	32	96
11g	10 ⁻⁷	<5	<5	<5	21
	10 ⁻⁵	19	16	13	97
11h	10 ⁻⁷	<5	<5	<5	<5
	10 ⁻⁵	<5	<5	<5	8
11i	10 ⁻⁷	<5	<5	<5	77
	10 ⁻⁵	23	16	27	94
11j	10 ⁻⁷	19	<5	9	65
	10 ⁻⁵	26	29	40	>99
11k	10 ⁻⁷	<5	<5	10	9
	10 ⁻⁵	27	24	73	78
11l	10 ⁻⁷	<5	<5	<5	<5
	10 ⁻⁵	<5	11	11	34
11m	10 ⁻⁷	<5	5	10	<5
	10 ⁻⁵	33	45	73	57
11n	10 ⁻⁷	<5	<5	<5	36
	10 ⁻⁵	70	58	45	>99
11o	10 ⁻⁷	<5	<5	<5	10

	10^{-5}	13	12	18	24
11p	10^{-7}	<5	<5	8	19
	10^{-5}	42	47	40	95
11q	10^{-7}	<5	<5	<5	<5
	10^{-5}	31	24	17	55
11r	10^{-7}	<5	<5	<5	<5
	10^{-5}	7	8	11	19
11s	10^{-7}	18	6	<5	70
	10^{-5}	66	67	40	>99
11t	10^{-7}	<5	5	10	<5
	10^{-5}	17	18	25	57

The authors thank Dr. J.-C. Schwartz and Dr. P. Sokoloff (INSERM, Paris), Dr. H. H. M. Van Tol (Clarke Institute of Psychiatry, Toronto) as well as Dr. J. Shine (The Garvan Institute of Medical Research, Sydney) for providing dopamine D3, D4 and D2 receptor expressing cell lines, respectively.