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Uncatalysed intermolecular aza-Michael reactions

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ARTICLE INFO

Article history:

Received 25 August 2012

Accepted after revision 12 November 2012

Available online 5 January 2013

Keywords:

aza-Michael

Hydroamination

Alkenes

Amines

Catalyst-free reactions

N-heterocycles

ABSTRACT

The catalyst-free reactions of activated alkenes with primary and secondary amines were investigated leading to various mono- and di-hydroamination products, the latter being rare and original. These reactions were shown to depend first on the strength of the nucleophile. Temperature and steric hindrance of the reagents were the other key factors controlling the selectivity of these aza-Michael reactions. In spite of their poor nucleophilicities, some *N*-heterocyclic amines could react with different activated alkenes affording valuable intermediates. Such results tended to demonstrate the hydrogen-bonding interactions between activated alkenes and poly-nitrogen aromatic cycles may control these concerted or fully conjugate aza-Michael additions.

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1. Introduction

Highly selective and atom-economic reactions can be reached using catalysis but challenges remain for some reactions like the synthesis of amines through hydroamination reactions [1]. The aza-Michael reaction involving the reaction of activated alkenes and amines can be considered as a hydroamination reaction. It was largely applied in organic synthesis with the use of various metal or organic catalysts [2]. Surprisingly, the uncatalysed “background” aza-Michael reaction has only been scarcely reported [3,4] and, to the best of our knowledge, no comprehensive study has been carried out so far. Such data could be of interest for highly selective aza-Michael reactions through a rational choice of reagents and experimental conditions. Herein, we would like to report

on advantages and limits of uncatalysed aza-Michael reactions. The reactivity scope will be exposed leading to original mono- and di-hydroamination products.

2. Results and discussion

As a start, several weak amine nucleophiles were allowed to react with 10 equivalents of methylvinylketone **1** (Table 1). The use of an excess of alkene to react with an amine is known to increase drastically the conversions; indeed, such a reactivity enhancement was already observed for several catalysed hydroamination reactions of unactivated alkenes [1c,d,g].

In order to check the reactivity issues at a sufficient level of activation, reactions were performed at 100 °C in polar or apolar solvents, respectively tetrachloroethane (TCE) or toluene. Reaction of **1** proceeded with imine **2e** to lead to product **3e** most likely because of higher amine nucleophilicity (entry 5). The use of toluene instead of TCE proved to increase drastically the yield of **3e**, acid traces in TCE decomposing imine **2e**. By comparing reactivity and

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Table 1
Amine reactivity towards methylvinylketone 1.

Entry	Equivalents of alkene 1	Amine	Conversion (%) ^a
1	10		0
2	10		0
3	10		0
4	10		0
5	10		77 ^b
6	10		100 (79 + 21) ^c
7	2		76 (60 + 16) ^c
8	1		71 (64 + 7) ^c

^a Conversions measured by ¹H NMR.

^b Performed in toluene at 100 °C for 40 h.

^c Yields of compounds **3f**₁ (branched) + **3f**₂ (linear).

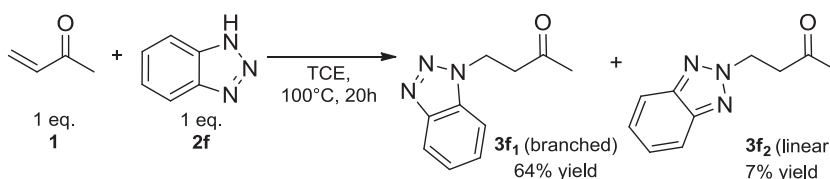
pKa values in DMSO of the involved amine reagents, imine **2e** (pKa 31.0) was found to be the strongest nucleophile of that series as compared to benzamide **2a** (pKa 23.3), oxazolidone **2b** (pKa 20.8) or the amines **2c-d,f**. By allowing a 71% yield of products **3f**₁ and **3f**₂, benzotriazole **2f** (pKa 11.9) first appeared to be an exception regarding the poor nucleophilicity of **2f** (Table 1, entry 8 and Scheme 1). It was worth noting the reaction was quantitative as respect to the amine by using 10 equivalents of alkene **1** (entry 6). Moreover, the observed rearrangement of branched product **3f**₁ into linear product **3f**₂ was already reported in other syntheses [5].

However, Wang et al. recently described catalyst-free aza-Michael reactions of azoles with β,γ-unsaturated-α-keto esters [3e]. The hydrogen bonding between the carbonyl oxygen of the activated alkene and the NH moiety of the *N*-heterocyclic nucleophile was proposed to form the key reaction intermediate. Then, the fully conjugate

nucleophile addition afforded an enol intermediate and later the final addition product after a retro-enolization. Hence, as a general trend, the catalyst-free reactions of amines with activated alkenes appeared to depend on the strength of the nucleophile. Nevertheless, in spite their poor pKas, *N*-heterocyclic amines could react with different activated alkenes affording valuable intermediates. Such results tended to demonstrate the hydrogen-bonding interactions between activated alkenes and such polynitrogen aromatic cycles may control these concerted or fully conjugate aza-Michael additions.

Next, we studied the reactivity of acrylate derivatives **4a,b** with primary and secondary amines **2f-s** at 100 °C and 30 °C in toluene. The last was preferred to TCE as far as basic amines proved to be more sensitive to acidic residues of chlorinated solvents (Table 2).

With the exception of amine **2f** which afforded poor yields of compounds **5fa**, **5fa**₂ and **5fb**₁ (entries 1–2), the reactions proceeded quite well for secondary amines **2i-k** at 100 °C affording mono-hydroamination products **5ia**, **5ib**, **5ja** and **5ka** in good yields (entries 3–6). For these last products, yields were quite low at 30 °C except for reaction with *N*-methylbenzylamine **2k** (entry 6). Regarding *N*-methylaniline **2l** and diisopropylamine **2m** (entries 7,8), no conversion was obtained. On the whole, these results confirmed that the less the nitrogen atom was hindered, the more the hydroamination reaction was enabled. The reactivity of primary amines **2n-t** with acrylates **4a,b** was then investigated in detail. At 100 °C, mono-hydroamination **5(n-t)a** and di-hydroamination **6(n-t)a** products were obtained with average to good yields (entries 9–16). It was worth noting methyl crotonate **4b** afforded only mono-hydroamination product **5pb** (entry 12) and aniline **2q** did not react (entry 13). Strikingly, cyclohexylamine **2o**, tertbutylamine **2s** led selectively to mono-hydroamination products **5oa** and **5sa** (entries 10, 15) whereas butylamine **2r** and methylamine **2t** afforded only di-hydroamination products **6ra** and **6ta** (entries 14, 16). Hence, we could state a sterically bulky primary amine reagent would privilege a mono-hydroamination product whereas a less hindered amine would mainly lead to a di-hydroamination product. However, γ-substituted activated alkenes would offer exclusively mono-hydroamination products. Moreover, lowering the temperature to 30 °C induced the selective formation of mono-hydroamination compounds **5na**, **5oa**, **5pa** and **5ra** but in low yields (entries 9–11, 14). The use of a large excess of alkene **4a** proved to be crucial in order to reach average to good yields of mono-hydroamination product **5pa** and di-hydroamination product **6pa** (entries 11, 17–19). To the best of our knowledge, such results are rare examples of controlled di-hydroamination reactions [6].



Scheme 1.

Table 2
Primary and secondary amine reactivity towards acrylate derivatives **4a,b**.

$RR'NH + R_1-CH=CH-C(=O)OR_2 \xrightarrow[\text{20h}]{\text{Toluene}}$

2f - s **4a** $R_1=H$ $R_2=nBu$ **5(f-t)(a-b)** (if $R'=alkyl, amine$)
4b $R_1=Me$ $R_2=Me$ **6(n-t)(a-b)** (if $R'=H$)

Entry	Amine	Alkene (eq.)	Yield (%) 5(f-t)(a-b) at 100 °C ^a	Yield (%) 6(n-t)(a-b) at 100 °C ^a	Yield (%) 5(f-t)(a-b) at 30 °C ^{a,b}
1 ^c	2f	4a (10 eq.)	15 (6+9) ^f (5fa ₁ + 5fa ₂)	0	< 5 (5fa) ^g
2		4b (10 eq.)	< 5 (5fb ₁) ^g	0	0
3 ^{c,d}	2i	4a (10 eq.)	70 (5ia)	0	< 5 (5ia) ^g
4		4b (10 eq.)	77 (5ib)	0	-
5 ^e	2j (nBu) ₂ NH	4a (10 eq.)	90 (5ja)	0	15 (5ja)
6	2k MeBnNH	4a (10 eq.)	96 (5ka)	0	55 (5ka)
7	2l MePhNH	4a (10 eq.)	0	0	0
8	2m (iPr) ₂ NH	4a (10 eq.)	0	0	0
9	2n iPrNH ₂	4a (10 eq.)	37 (5na) ^h	38 (6na)	8 (5na)
10	2o CyNH ₂	4a (10 eq.)	100 (5oa)	0	23 (5oa)
11	2p BnNH ₂	4a (10 eq.)	58 (5pa)	42 (6pa)	38 (5pa)
12	2p BnNH ₂	4b (10 eq.)	95 (5pb)	0	-
13	2q PhNH ₂	4a (10 eq.)	0	0	-
14	2r nBuNH ₂	4a (10 eq.)	0	90 (6ra)	44 (5ra)
15	2s tBuNH ₂	4a (10 eq.)	32 (5sa)	0	0
16	2t MeNH ₂	4a (10 eq.)	0	42 (6ta) ⁱ	0
17	2p BnNH ₂	4a (5 eq.)	84 (5pa)	12 (6pa)	25 (5pa) ^g
18	2p BnNH ₂	4a (2 eq.)	83 (5pa)	11 (6pa)	-
19	2p BnNH ₂	4a (1 eq.)	99 (5pa)	0	-

^a Isolated yield; all reactions performed with 0.5 mmol of amine.

^b 20 h reactions.

^c TCE as solvent.

^d 23 h reaction.

^e 26 h reaction.

^f Compounds **5fa**₁ (branched) and **5fa**₂ (linear).

^g Measured by ¹H NMR.

^h 40 h reactions.

ⁱ Same result at 30 °C.

Table 3
Solvent and additive effects on the reaction of butylacrylate **4a** and benzylamine **2p**.

$BnNH_2 + CH_2=CH-C(=O)OnBu \xrightarrow[\text{30 °C, 20h}]{\text{Solvent}}$

2p 1 eq. **4a** 10 eq. **5pa** $n=1, R=H$
6pa $n=2, R=-$

Entry	Solvent	Additive	Yield (%) ^a 5pa	Yield (%) ^a 6pa
1	Toluene	-	38	0
2	Toluene	Undistilled alkene	59	0
3	Toluene	H ₂ O (2 eq.)	65	0
4	Toluene	hydroquinone (10 mol%)	90	10
5	Toluene	Silica (10 mol%)	87	Traces
6	Dioxane	-	37	0
7	THF	-	31	0
8	Et ₂ O	-	43	0
9	DCM	-	62	0
10	None	-	85	9

^a Alkene and solvent were distilled. Amine was not distilled.

Table 4
Benzotriazole reactivity towards activated alkenes.

Entry	Alkene 7a-f	Time (h)	Yield (%) at 100 °C ^a	Conversion (%) at 30 °C ^b
1	7a	20	86 ^c (69 + 17) (8a1 , 8a2)	100 ^c (84 + 26) (8a1 , 8a2)
2	7b	20	82 (8b1)	94 (8b1)
3	7c	20	97 ^c (84 + 13) (8c1 , 8c2)	86 (8c1)
4	7d	20	69 ^c (46 + 23) (8d1 , 8d2)	< 5 (8d1)
5	7e	65	51 (8e1)	11 ^d (8e1)
6	7f	65	100 ^c (83 + 17) (8f1 , 8f2)	–

^a Isolated yield.

^b Performed in CH₂Cl₂ for 30 h, conversions by ¹H NMR.

^c Products **5fa1**, **8a1**, **c1**, **d1**, **f1** from addition and **5fa2**, **8a2**, **c2**, **d2**, **f2** from rearrangement.

^d 20 h reaction.

Finally, the reaction of compounds **4a** and **2p** using 10 mol% of mono-hydroamination compound **5pa** as catalyst afforded **5pa** in a 17% yield which was lower than the 38% yield of the reaction run without catalyst at 30 °C (Table 2, entry 11). Hence, product **5pa** could not perform any autocatalysis for the reaction of reagents **4a** and **2p** [7]. Moreover, reactions of amine **2p** with alkene **4a** proved to be sensitive to the nature of the solvent used, neat reaction running also very well (Table 3, entries 1, 6–10). It is worth noting the yields of **5pa** were drastically increased by the addition of water to the reaction medium (entries 2, 3). The use of protic additives like hydroquinone and silica did also enhance the yields of **5pa** and small amounts of **6pa** could be isolated (entries 4, 5) [8]. Such rate enhancement in aza-Michael reactions, though known but rarely quoted, can be described as an external proton transfer activation by protic media [6d,8a].

In order to clarify the scope of these catalyst-free aza-Michael reactions, we next studied reactions of different activated alkenes with an amine. Considering the raising interest on conjugate addition reactions of nitrogen-centered heterocyclic nucleophiles to electron-deficient olefins [3e,9], we chose benzotriazole **2f** which is also a useful synthetic auxiliary (Table 4) [10]. At 100 °C in TCE, reactions of **2f** with alkenes **7a-f** afforded addition

products **8a1-f1** in good yields (Table 4, entries 1–6). Moreover, alkenes **7a**, **7c**, **7d**, **7f** afforded rearranged products **8a2**, **8c2**, **8d2**, **8f2** in low yields (entries 1, 3, 4, 6) [5]. At 30 °C in dichloromethane, the uncatalysed reactions using alkenes **7a-c** were almost quantitative and there was no evidence for any polymerisation of the alkene reagents at such a reaction temperature according NMR spectra of the corresponding crude mixtures (Table 4, entries 1–3). However, at 30 °C, reactions of benzotriazole **2f** with alkenes **7d-f** offered lower conversions or none (Table 4, entries 4–6). Finally, no reactivity was observed for ethylcrotonate, acrylonitrile, 2-butenitrile, 3-penten-2-one, ethylcinnamate and phenyltrans-styryl sulphone, independently of the reaction conditions used.

3. Conclusion

The studied aza-Michael reactions were shown to be performed without the use of any catalyst depending on a combination of different factors. The strength of the nucleophile appeared to be the key parameter to control the reactivity, temperature and steric hindrance of the reagents being the other factors mastering the selectivity of these mono- and di-hydroamination reactions. The last were shown to proceed only when heat and large excesses

of activated alkenes were used. This allowed the synthesis of rare products resulting from a double-addition of an amine on two equivalents of an activated alkene. Moreover, the catalyst-free conjugate addition reaction of various electron-deficient olefins and poor nucleophiles like *N*-heterocyclic amines was demonstrated and afforded valuable intermediates for organic synthesis. Such results tended to demonstrate the hydrogen-bonding interactions between activated alkenes and poly-nitrogen aromatic cycles may control these concerted or fully conjugate aza-Michael additions. Finally, when a catalysed aza-Michael reaction is performed, it may be asked whether a strict catalysed reaction is involved or if any competitive background reaction is taking place.

4. Experimental

4.1. General remarks

All solvents were dried using standard methods. Alkenes were distilled under vacuum over CaH₂ and stored over molecular sieves (4 Å). Amine substrates were placed under vacuum during one hour before use, or distilled over CaH₂ if they were liquid. All reactions were carried out under a dry nitrogen atmosphere. Analytical thin layer chromatography (TLC) was performed on Merck pre-coated 0.20 mm silica gel Alugram Sil 60 G/UV₂₅₄ plates. Flash chromatography was carried out with Macherey silica gel 60 M. ¹H (300 MHz or 400 MHz), ¹³C (75 MHz) and ³¹P (121 MHz) NMR spectra were acquired on Bruker Avance spectrometers. Chemical shifts are reported downfield of Me₄Si and coupling constants are expressed in Hz. 1,3,5-trimethoxybenzene and 1,2,4,5-tetrachlorobenzene were used as internal standards when needed. Gas chromatography analyses were done on GC Varian 3900 and 430 using Alltech EconoCap EC-5TM column (30 m, 0.25 mm, 0.25 μm) with program (5 °C/min, 100–230 °C, 36 min) and with tetradecane as internal standard. GC-MS analyses were performed on a Shimadzu QP2010+ using Supelco column SLBTM-5ms (30 m, 0.25 mm, 0.25 μm). Infrared spectra were recorded on a ThermoScientific-Nicolet 6700 spectrometer; the samples being prepared with KBr powder. HRMS-ESI analyses were performed at CUMA-University Lille Nord de France. Elemental analyses were performed on a Elementar Vario Micro Cube apparatus at UCCS, University Lille Nord de France. See [supporting information](#) for other details.

4.2. General procedures

4.2.1. General procedure for amine reactivity screening with methylvinylketone

Amine substrate (0.5 mmol) (if solid) was added in a Schlenk flask and dried under vacuum for 30 minutes. Next, dry 1,1',2,2'-tetrachloroethane or toluene (1 mL), methylvinylketone (5.0 mmol, 0.4 mL), and amine substrate (0.5 mmol) (if liquid) were added. After stirring at 100 °C for the corresponding time, the mixture was concentrated under vacuum, and the resulting product was isolated by flash chromatography.

4.2.2. General procedure for amine substrate screening

Amine substrate (0.5 mmol) (if solid) was added in a Schlenk flask and dried during 30 minutes under vacuum. Then, dry toluene (1 mL), butylacrylate (5.0 mmol, 0.7 mL), and freshly distilled amine substrate (0.5 mmol) (if liquid) were added under a nitrogen atmosphere. After stirring at 100 °C for the corresponding time, the mixture was concentrated under vacuum, and the resulting product was isolated by flash chromatography.

4.2.3. General procedure for activated alkene screening

Benzotriazole (0.5 mmol, 59.6 mg) and activated alkene (5.0 mmol) (if solid) were added in a Schlenk flask and dried during 30 min under vacuum. Then, dry 1,1',2,2'-tetrachloroethane (1 mL), and activated alkene (5.0 mmol) (if liquid) were added under a nitrogen atmosphere. After stirring at 100 °C at the corresponding time, the mixture was concentrated under vacuum, and the corresponding product was isolated by flash chromatography.

4.3. Physical and spectra data for 5ja, 5ka, 6na, 6pa, 6ra, 6ta, 8e₁, 8f₁, 8f₂

4.3.1. Butyl-3-(dibutylamino)propanoate 5ja

Isolated after flash chromatography with petroleum ether/NEt₃ (9:1), as a colourless oil (from 0.5 mmol, 0.45 mmol-116 mg, 90% yield). ¹H NMR (CDCl₃, 300 MHz): δ = 0.85–0.95 (*q*^{*}, 9H), 1.20–1.45 (*m*, 10H), 1.58 (*quin*, *J*(H,H) = 7.2 Hz, 2H), 2.30–2.45 (*m*, 6H), 2.75 (*t*, *J*(H,H) = 7.5 Hz, 2H), 4.05 (*t*, *J*(H,H) = 6.7 Hz, 2H). ¹³C NMR (CDCl₃, 75 MHz): δ = 13.7 (CH₃), 14.1 (2 CH₃), 19.1 (CH₂), 20.6 (2 CH₂), 29.3 (2 CH₂), 30.7 (CH₂), 32.4 (CH₂), 49.4 (CH₂), 53.6 (2 CH₂), 64.2 (CH₂), 173.1 (C). IR (KBr): ν̃ = 2959, 2933, 2873, 1717, 1202 cm⁻¹. HMRS (ESI) *m/z* calcd for C₁₅H₃₂NO₂: 258.2428 [MH⁺], found: 258.2423.

4.3.2. Butyl-3-(benzyl(methyl)amino)propanoate 5ka

Isolated after flash chromatography with petroleum ether/ethylacetate/NEt₃ (9:1:1) (R_f = 0.75) as a colourless oil (from 0.5 mmol, 0.48 mmol-120 mg, 96% yield). ¹H NMR (CDCl₃, 300 MHz): δ = 0.95 (*t*, *J*(H,H) = 7.4 Hz, 3H), 1.39 (*sex*, *J*(H,H) = 7.4 Hz, 2H), 1.63 (*quin*, *J*(H,H) = 7.1 Hz, 2H), 2.22 (*s*, 3H), 2.54 (*t*, *J*(H,H) = 7.2 Hz, 2H), 2.77 (*t*, *J*(H,H) = 7.2 Hz, 2H), 3.53 (*s*, 2H), 4.10 (*t*, *J*(H,H) = 6.7 Hz, 2H), 7.20–7.40 (*m*, 5H). ¹³C NMR (CDCl₃, 75 MHz): δ = 13.8 (CH₃), 19.2 (CH₂), 30.7 (CH₂), 33.0 (CH₂), 41.8 (CH₃), 52.9 (CH₂), 62.1 (CH₂), 64.3 (CH₂), 127.0 (CH), 128.2 (2 CH), 129.0 (2 CH), 138.9 (C), 172.7 (C). IR (KBr): ν̃ = 2954, 2841, 2791, 1734, 1124 cm⁻¹. HMRS (ESI) *m/z* calcd for C₁₅H₂₄NO₂: 250.1802 [MH⁺], found: 250.1798.

4.3.3. Dibutyl-3,3'-(isopropylazanediyldip)propanoate 6na

Isolated after flash chromatography with petroleum ether/NEt₃ (9:1) as a colourless oil (from 0.50 mmol, 0.19 mmol-60 mg, 38% yield). ¹H NMR (CDCl₃, 300 MHz): δ = 0.85–1.00 (*m*, 12H), 1.34 (*sex*, *J*(H,H) = 7.5 Hz, 4H), 1.57 (*quin*, *J*(H,H) = 6.9 Hz, 4H), 2.38 (*t*, *J*(H,H) = 7.2 Hz, 4H), 2.68 (*t*, *J*(H,H) = 7.2 Hz, 4H), 2.85 (*sep*, *J*(H,H) = 6.6 Hz, 1H), 4.03 (*t*, *J*(H,H) = 6.6 Hz, 4H). ¹³C NMR (CDCl₃, 75 MHz): δ = 13.8 (2 CH₃), 18.4 (2 CH₃), 19.2 (2 CH₂), 30.8 (2 CH₂), 34.8 (2 CH₂), 45.8 (2 CH₂), 50.7 (CH), 64.2 (2 CH₂), 173.0 (2 C). IR

(KBr): ν^{\sim} = 2979, 1733, 1137 cm^{-1} . HMRS (ESI) m/z calcd for $\text{C}_{17}\text{H}_{34}\text{NO}_4$: 316.24824 $[\text{MH}^+]$, found: 316.24873.

4.3.4. Dibutyl-3,3'-(benzylazanediyldipropoanoate 6pa

Isolated after flash chromatography with petroleum ether/ethylacetate/ NEt_3 (8:2:1), R_f = 0.7, as a colourless oil (from 0.50 mmol, 0.21 mmol-76 mg, 42% yield). ^1H NMR (CDCl_3 , 300 MHz): δ = 0.85 (t, $J(\text{H,H})$ = 7.3 Hz, 6H), 1.28 (sex, $J(\text{H,H})$ = 7.3 Hz, 4H), 1.49 (quin, $J(\text{H,H})$ = 6.9 Hz, 4H), 2.38 (t, $J(\text{H,H})$ = 7.2 Hz, 4H), 2.73 (t, $J(\text{H,H})$ = 7.2 Hz, 4H), 3.52 (s, 2H), 3.98 (t, $J(\text{H,H})$ = 6.7 Hz, 4H), 7.15–7.25 (m, 5H). ^{13}C NMR (CDCl_3 , 75 MHz): δ = 13.7 (2 CH_3), 19.1 (2 CH_2), 30.6 (2 CH_2), 32.7 (2 CH_2), 49.2 (2 CH_2), 58.2 (CH_2), 64.3 (2 CH_2), 127.0 (CH), 128.2 (2 CH), 128.7 (2 CH), 139.1 (C), 172.7 (2 C). IR (KBr): ν^{\sim} = 2959, 2873, 1734, 1176 cm^{-1} . HMRS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{34}\text{NO}_4$: 364.2482 $[\text{MH}^+]$, found: 364.2475.

4.3.5. Dibutyl-3,3'-(butylazanediyldipropoanoate 6ra

Isolated after flash chromatography with petroleum ether: NEt_3 (9:1) as a colourless oil (from 0.5 mmol, 0.45 mmol-148 mg, 90% yield). ^1H NMR (CDCl_3 , 300 MHz): δ = 0.80–0.95 (m, 9H), 1.15–1.40 (m, 8H), 1.55 (quin, $J(\text{H,H})$ = 7.5 Hz, 4H), 2.35 (q, $J(\text{H,H})$ = 7.5 Hz, 6H), 2.71 (t, $J(\text{H,H})$ = 7.3 Hz, 4H), 4.01 (t, $J(\text{H,H})$ = 6.7 Hz, 4H). ^{13}C NMR (CDCl_3 , 75 MHz): δ = 13.7 (2 CH_3), 14.0 (CH_3), 19.1 (2 CH_2), 20.4 (CH_2), 29.3 (CH_2), 30.6 (2 CH_2), 32.6 (2 CH_2), 49.2 (2 CH_2), 53.4 (CH_2), 64.2 (2 CH_2), 172.8 (2 C). IR (KBr): ν^{\sim} = 2960, 2934, 2873, 1734, 1189 cm^{-1} . HMRS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{36}\text{NO}_4$: 330.2639 $[\text{MH}^+]$, found: 330.2632.

4.3.6. Dibutyl-3,3'-(methylazanediyldipropoanoate 6ta

Isolated after flash chromatography with petroleum ether/ NEt_3 (9:1) as a colourless oil (from 0.5 mmol, 0.2 mmol-60 mg, 42% yield). ^1H NMR (CDCl_3 , 300 MHz): δ = 0.88 (t, $J(\text{H,H})$ = 7.2 Hz, 6H), 1.34 (hex, $J(\text{H,H})$ = 7.2 Hz, 4H), 1.55 (quin, $J(\text{H,H})$ = 6.9 Hz, 4H), 2.20 (s, 3H), 2.42 (t, $J(\text{H,H})$ = 7.2 Hz, 4H), 2.66 (t, $J(\text{H,H})$ = 7.2 Hz, 4H), 4.03 (t, $J(\text{H,H})$ = 6.6 Hz, 4H). ^{13}C NMR (CDCl_3 , 75 MHz): δ = 12.8 (2 CH_3), 18.2 (2 CH_2), 29.7 (2 CH_2), 31.7 (2 CH_2), 40.8 (CH_3), 51.6 (CH_2), 63.3 (2 CH_2), 171.7 (CO). IR (KBr): ν^{\sim} = 2960, 2930, 2850, 1738, 1180 cm^{-1} .

4.3.7. 1-(2-(phenylsulfonyl)ethyl)-1H-benzo[d][1,2,3]triazole 8e₁

Isolated after flash chromatography with petroleum ether/ethylacetate (1:1), R_f = 0.3, as a white solid (from 0.50 mmol, 0.25 mmol-72 mg, 51% yield). M.p. = 97–99 °C. ^1H NMR (CDCl_3 , 300 MHz): δ = 3.89 (t, $J(\text{H,H})$ = 6.9 Hz, 2H), 5.01 (t, $J(\text{H,H})$ = 6.9 Hz, 2H), 7.30–7.45 (m, 3H), 7.45–7.60 (m, 3H), 7.71 (d, $J(\text{H,H})$ = 7.8 Hz, 2H), 7.94 (d, $J(\text{H,H})$ = 8.3 Hz, 1H). ^{13}C NMR (CDCl_3 , 75 MHz): δ = 41.5 (CH_2), 54.9 (CH_2), 109.13 (CH), 120.1 (CH), 124.3 (CH), 127.6 (2 CH), 127.9 (CH), 129.3 (2 CH), 132.9 (C), 134.1 (CH), 138.2 (C), 145.7 (C). IR (KBr): ν^{\sim} = 2989, 1308, 1140 cm^{-1} . HMRS (ESI) m/z calcd for $\text{C}_{14}\text{H}_{14}\text{N}_3\text{O}_2\text{S}$: 288.08012 $[\text{MH}^+]$, found: 288.08004.

4.3.8. 3-(3-(1H-benzo[d][1,2,3]triazol-1-yl)butanoyl)oxazolidin-2-one 8f₁

Isolated after flash chromatography with petroleum ether/ethylacetate (8:2), R_f = 0.3, as a white solid (from

0.50 mmol, 0.42 mmol-114 mg, 83% yield). M.p. = 123–125 °C. ^1H NMR (CDCl_3 , 300 MHz): δ = 1.70 (d, $J(\text{H,H})$ = 6.9 Hz, 3H), 3.47 (dd, $J(\text{H,H})$ = 4.6 Hz and $J(\text{H,H})$ = 18.2 Hz, 1H), 3.70–3.95 (m, 2H), 4.08 (dd, $J(\text{H,H})$ = 9.0 Hz and $J(\text{H,H})$ = 18.2 Hz, 1H), 4.30 (sex, $J(\text{H,H})$ = 8.4 Hz, 2H), 5.35–5.50 (m, 1H), 7.31 (t, $J(\text{H,H})$ = 7.5 Hz, 1H), 7.45 (t, $J(\text{H,H})$ = 7.5 Hz, 1H), 7.62 (d, $J(\text{H,H})$ = 8.4 Hz, 1H), 7.98 (d, $J(\text{H,H})$ = 8.4 Hz, 1H). ^{13}C NMR (CDCl_3 , 75 MHz): δ = 21.2 (CH_3), 41.4 (CH_2), 42.3 (CH_2), 50.6 (CH), 62.3 (CH_2), 109.9 (CH), 119.8 (CH), 124.0 (CH), 127.2 (CH), 132.7 (C), 145.9 (C), 153.5 (C), 169.8 (C). IR (KBr): ν^{\sim} = 2985, 2928, 1777, 1698, 1221, 1120 cm^{-1} . HMRS (ESI) m/z calcd for $\text{C}_{13}\text{H}_{15}\text{N}_4\text{O}_3$: 275.11387 $[\text{MH}^+]$, found: 275.1139.

4.3.9. 3-(3-(2H-benzo[d][1,2,3]triazol-2-yl)butanoyl)oxazolidin-2-one 8f₂

Isolated after flash chromatography with petroleum ether/ethylacetate (8:2), R_f = 0.5, as a white solid (from 0.500 mmol, 0.085 mmol-23 mg, 17% yield). M.p. = 82–84 °C. ^1H NMR (CDCl_3 , 300 MHz): δ = 1.75 (d, J = 6.8 Hz, 3H), 3.52 (dd, J = 4.7 Hz and $J(\text{H,H})$ = 18 Hz, 1H), 3.85–4.00 (m, 2H), 4.04 (dd, $J(\text{H,H})$ = 8.8 Hz and $J(\text{H,H})$ = 18 Hz, 1H), 4.30–4.45 (m, 2H), 5.50–5.65 (m, 1H), 7.34 (dd, $J(\text{H,H})$ = 3.0 Hz and $J(\text{H,H})$ = 6.5 Hz, 2H), 7.83 (dd, $J(\text{H,H})$ = 3.0 Hz and $J(\text{H,H})$ = 6.5 Hz, 2H). ^{13}C NMR (CDCl_3 , 75 MHz): δ = 21.6 (CH_3), 41.5 (CH_2), 42.3 (CH_2), 58.6 (CH), 62.3 (CH_2), 118.1 (2 CH), 126.2 (2 CH), 144.0 (2 C), 153.5 (C), 169.7 (C). IR (KBr): ν^{\sim} = 2958, 2927, 1780, 1703, 1275, 1116 cm^{-1} . HMRS (ESI) m/z calcd for $\text{C}_{13}\text{H}_{15}\text{N}_4\text{O}_3$: 275.11387 $[\text{MH}^+]$, found: 275.1135.

Acknowledgements

This work is first financed by the French National Research Agency with project ANR-09-BLAN-0032-02 (with a PhD fellowship to F.M.). Support from CNRS is warmly acknowledged. Partial funding from Région Nord-Pas de Calais with “Projet Prim: État-Région” and with “Fonds européen de développement régional (FEDER)” are also appreciated. Mrs C. Méliet (UCCS) is thanked for elemental analyses. Ms C. Delabre (UCCS) is thanked for GC-MS analyses.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.crci.2012.11.001>.

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