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Borax as an Efficient Metal-Free Catalyst for Hetero-Michael Reactions in an Aqueous Medium

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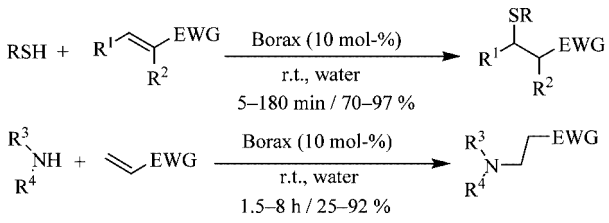
Borax, a naturally occurring material, very efficiently catalyzed the conjugate addition of thiols, dithiols and amines to α,β-unsaturated ketones, nitriles, amides, aldehydes and esters in an aqueous medium to afford the corresponding Michael adducts in good yields at room temperature. Recycling of the catalyst and scaling up of the reactions are important attributes of this catalysis. The reactions of thiols and dithiols were relatively more facile than those of the corresponding amines.

Introduction

The construction of C–S and C–N bonds is the key step in the synthesis of organo-sulfur and -nitrogen compounds, respectively. While organo-sulfur compounds have multiple applications[1] in the production of biologically active molecules, including calcium antagonistic dilthiazem,[2] β-amino ketones exhibit a wide range of biological activities,[3] possess pharmacological properties and also serve as essential intermediates in the synthesis of β-amino acids[4] and β-lactams.[5] Consequently, the development of novel protocols for the conjugate addition of thiols and amines to electron-deficient olefins leading to the formation of C–S and C–N bonds, respectively, have attracted a great deal of attention in synthetic organic chemistry. Notably, the success of conjugate addition reactions lie in the use of either acidic or basic conditions which, if not selected judiciously, can be detrimental to the desired synthesis allowing unwanted side-reactions to contaminate the product. Moreover, the possibility of poisoning metal-based catalysts with thiols, alkyl- or arylamines[6] cannot be completely ruled out. In order to alleviate some of these problems, the Michael reaction has metamorphosed over the years to allow a number of reagents and catalysts and alternative procedures to be used, for instance, a variety of inorganic salts,[7] quaternary ammonium salts,[8] ionic liquids (IL),[9] a combination of IL and water,[10] palladium,[6] supported $CeCl_3 \cdot 7H_2O/NaI$,[11] clay,[12] silica gel,[13a] $SiO_2/HClO_4$,[13b] solid acid,[13c] KF/alumina,[14] polyethylene glycol (PEG),[15] $Cu(acac)_2$/IL,[16] boric acid in water,[17] cyclodextrin in water[18] and even a micellar solution of sodium dodecyl sulfate (SDS).[19] Each method has some advantages over the others; however, the search still continues for improved versions of the Michael reaction. Notably, most of the methods recently developed have involved metal-based acidic catalysts, presumably because the Michael reactions in basic media are rather sluggish without providing satisfactory yields even with long reaction times.[20] However, there is an intrinsic interest in the Michael addition of thiols to enones in basic aqueous media under mild conditions[21] and such reactions are highly relevant to "dynamic combinatorial chemistry" which offers a conceptually new approach to the investigation of host–guest interactions.[22] Considering all these and being intrigued by the fact that the pH of an aqueous solution of borax is 9.5, we thought it worthwhile to carry out both thia- and aza-Michael reactions using borax as the catalyst and water as the reaction medium. Environmental benignity and appreciable solubility in water are important attributes of the chosen catalyst. In addition, the reactions in water not only contribute to "green chemistry" but also to pseudonatural catalysis chemistry. Reported in this paper are the borax-catalyzed Michael reactions of thiols and amines with α,β-unsaturated ketones, nitriles and esters in water at room temperature (Scheme 1).



R = alkyl / aryl; R^1 = alkyl / aryl / $-(CH_2)-$;
EWG = CO_2Me, CN, $CONH_2$, COMe, COPh

Scheme 1.

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Results and Discussion

In order to ascertain the efficacy of the catalyst in water, the conjugate addition reactions of thiophenol to methyl acrylate were separately conducted in water and four different organic solvents. The results are summarized in Table 1. It is evident that the reaction takes place in each case with the best performance being in water containing 10 mol-% of the catalyst. Accordingly, all the reactions discussed hereafter were conducted with this combination of solvent and catalyst.

Table 1. Michael addition of thiophenol with methyl acrylate under different reaction conditions.

Run	Borax [mol-%]	Solvent	Time [min]	Yield [%]
1	0	H_2O	5	5
2	20	H_2O	5	95
3	10	H_2O	5	95
4	1	H_2O	5	40
5	10	MeOH	5	30
6	10	CH_3CN	5	64
7	10	$(CH_3)_2CO$	5	70
8	10	AcOEt	5	70

A variety of electron-deficient olefins such as methyl acrylate, acrylonitrile, acrylamide, cyclohexanone and methyl methacrylate underwent facile 1,4-addition with a wide range of thiols catalyzed by borax (10 mol-%) in water at room temperature to afford the corresponding β-adducts in high to very high yields (Table 2). Unsaturated ketones, nitriles, amides, aldehydes and esters reacted readily with both aliphatic and aromatic thiols to provide the corresponding Michael adducts (Table 2, Runs 1–20).

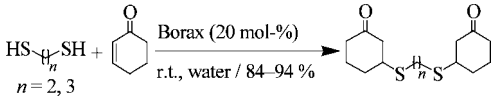
The reactions were clean. The borax/water system also worked very well with α- and β-substituted Michael acceptors at ambient temperatures. It was found that with a methyl group either at the α- or β-position, the reaction gave good yields (Table 2, Runs 12–15) in 5–10 min, while with a phenyl group at the β-position longer reaction times were required (1.5–3 h, Table 2, Runs 23–25). Acceptors like carvone and pulegone reacted readily with aliphatic thiols (Table 2, Runs 21 and 22). Notably, this protocol worked well for the conjugate addition of cysteine to acrylamide (Table 2, Run 11) giving 88% isolated yield of the adduct. Incidentally, our experimental conditions, especially the involvement of a weakly alkaline aqueous reaction medium, mild reaction conditions capable of working efficaciously at room temperature and with no particular precautions necessary to prevent di- or polymerization, compare very well with those required for the synthesis of dynamic chemical libraries (DCLs)[21] by base-mediated Michael addition of thiols to enones. This reaction is important in the context of the alkylation of cysteine in proteins with acrylamide under mild aqueous alkaline conditions and is considered to be useful for cysteine identification during protein sequencing.[23]

Table 2. Borax-catalyzed Michael addition of thiols to olefins in water at room temperature.

Run	Thiol	Olefin	Product	Time [min (h)]	Yield [%][a]
1			**1a**	5	95, 97[b]
2			**2a**	5	92
3			**3a**	5	92
4	C_2H_5SH		**4a**	5	89
5	$C_{12}H_{25}SH$		**5a**	(3)	75
6			**6a**	5	94
7	C_2H_5SH		**7a**	5	87
8	$C_{12}H_{25}SH$		**8a**	(2.5)	72
9			**9a**	5	93, 96[b]
10	C_4H_9SH		**10a**	5	87
11			**11a**	30	88
12			**12a**	5	88
13	C_4H_9SH		**13a**	5	82
14			**14a**	10	85
15			**15a**	10	86
16			**16a**	5	92
17			**17a**	5	90
18			**18a**	5	88
19	C_2H_5SH		**19a**	5	90
20	$C_{12}H_{25}SH$		**20a**	(2.5)	70
21	C_2H_5SH		**21a**	(3)	85
22	C_2H_5SH		**22a**	(3)	82
23	C_2H_5SH		**23a**	(1.5)	89
24			**24a**	(3)	75
25			**25a**	(2)	80

[a] Isolated Yield. [b] Yield on a 7 g scale.

The borax-catalyzed Michael addition reaction in water is also readily applicable to dithiols, as shown in Scheme 2.



Scheme 2.

The reactions proceeded with alacrity giving bis(adducts) in very good yields (Table 3). Such reactions are expected to be useful in the designed synthesis of organo-sulfur polymers, supramolecular architectures and macromolecules.

Incidentally, $H_2N–CO–CH_2–CH_2–S–CH_2–CH_2–CH_2–S–CH_2–CH_2–CO–NH_2$ obtained from the reaction of 1,3-propanedithiol and 2 equiv. of acrylamide (Table 3, Run 2) is an interesting compound,[24] the preparation of which does not seem to be available in the open literature. The use of the compound as a photographic development accelerator and as a constituent of colour photographic developer has, however, been reported in two Japanese patents.[24] It has also been used in lithographic plate processing solutions.

Table 3. Borax-catalyzed Michael addition of dithiols to olefins in water at room temperature.

Run	$HS\text{-}(CH_2)_n\text{-}SH$	Olefins	Product	Time [min]	Yield[a] [%]
1	$n = 2$	$CONH_2$	**26a**	15	92
2	$n = 3$	$CONH_2$	**27a**	15	94
3	$n = 2$	=O	**28a**	15	84
4	$n = 3$	=O	**29a**	20	87
5	$n = 2$	CO_2Me	**30a**	15	86
6	$n = 2$	CO_2Me	**31a**	20	85

[a] Isolated yields.

The borax/water protocol is applicable to aza-Michael reactions as well. A variety of α,β-unsaturated compounds underwent 1,4-addition with a wide range of aliphatic amines in the presence of 10 mol-% of borax at ambient temperature to afford the corresponding β-amino compounds in high yields. Some representative examples are listed in Table 4. A comparison of the results of the thiol and amine addition reactions under similar experimental conditions shows that the former are more facile than the latter. Indeed, this observation is in agreement with the results of an earlier kinetic study.[20a] Based on kinetic data, it was predicted that –SH groups are many times more reactive than amines in aqueous alkaline solution. A comparison of the results obtained in this work with those of the corresponding boric acid catalyzed aza-Michael reactions[17] (Table 4) suggests that under similar experimental conditions borax is either as good as or slightly better than boric acid in catalyzing the chosen reactions.

Table 4. Borax-catalyzed Michael addition of amines to olefins in water at room temperature.

Run	Amine	Olefin	Product	Borax: time [h] / yield [%][a]	Boric acid:[17] time [h] / yield [%][a]
1	NH	CO_2Me	**1b**	3 / 86	1.5 / 90
2	O NH	CO_2Me	**2b**	3 / 92	1.5 / 85
3	NH_2	CO_2Me	**3b**	2 / 89	2.5 / 90
4	nBu H N nBu	CO_2Me	**4b**	2 / 92	4 / 88
5	NH	CN	**5b**	2 / 90	1.5 / 95
6	NH_2	CN	**6b**	1.5 / 86	2.5 / 92
7	nBu H N nBu	CN	**7b**	2 / 92	2 / 90
8	MeO NH_2	CO_2Me	**8b**	8 / 25	12 / 15
9	H_2N O OPh	CO_2Me	**9b**	8 / 0	– / –

[a] Isolated yields.

Finally, upon completion of the reaction, recyclability of the catalyst was examined through a series of reactions with thiophenol and methyl acrylate using an aqueous phase containing borax. The reaction continued to give good results from the second through to the fifth cycle with the yields being 95, 94, 92 and 90%, respectively. However, the yield was reduced to 80% in the sixth cycle. This is explained by attrition and leaching of the catalyst. It is also important to note that the borax/water protocol can be applied to a relatively larger scale (7 g) of operation, giving very good yields (Table 2, Runs 1 and 9).

Conclusions

Borax has emerged as an efficacious, environmentally acceptable and highly cost-effective novel catalyst for thia- and aza-Michael reactions thereby making an important addition to the existing toolbox of the Michael reaction. The fact that the reactions work very well in water is an important attribute of this protocol. The controlled basicity of the catalyst causes thiol additions to α,β-unsaturated ketones, nitriles, amides, aldehyde, and esters to be relatively more facile than the corresponding amine addition reactions. Moreover, borax, being a naturally occurring material, soluble and capable of functioning efficiently in water, satisfies some tenets of "green chemistry." The reactions are thus more conducive to the environment and provide scope for further studies. The thia-Michael reaction between cysteine and acrylamide (Table 2, Run 11) may be relevant to the understanding of the alkylation of cysteine in proteins with acrylamide under mildly alkaline conditions.

Experimental Section

Experimental Procedure: Borax (0.2 mmol, 0.076 g) was dissolved in water (2 mL) followed by the addition of a thiol or an amine (2 mmol) or a dithiol (1 mmol) and an α,β-unsaturated compound (2.2 mmol) and the mixture was stirred at room temperature. The reaction was monitored by TLC. After completion of the reaction, the mixture was extracted with ethyl acetate (3 × 5 mL). The combined extracts (dried with Na_2SO_4) were concentrated in vacuo and the resulting product was purified on silica gel with ethyl acetate and *n*-hexene (1:9 for thia and 3:7 for aza adduct) as eluent to afford the pure adduct. The aqueous layer containing borax can be reused in the next run. A 25% solution of methanol in water was used as the reaction medium for Runs 23–25 of Table 2. Precipitation occurred in the reactions of amide with thiols (Table 2, Runs 9–11, 21 and 22, and Table 3, Runs 3 and 4). The precipitates were filtered and washed with water and then recrystallized from MeOH or hot water. ^1H and ^{13}C NMR spectra were recorded with a Bruker 200 MHz and a Varian 400 MHz spectrometer. IR spectra were recorded either in KBr or neat with a Nicolet Impact 410 spectrophotometer. GC-MS data were recorded with a Perkin-Elmer Precisely Clarus 500 instrument using a capillary column (30 × 0.25 × 0.25 mμ). Elemental analyses were carried out with a Perkin-Elmer 2400 automatic C,H,N,S analyzer.

Spectral Data of Some Selected Compounds

3a: Yield: 0.443 g, 92%, light yellow solid (m.p. 56–57 °C). IR (KBr): $\tilde{\nu}$ = 1340 and 1511 (NO_2), 1733 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.71 (t, J = 7.6 Hz, 2 H), 3.30 (t, J = 7.2 Hz, 2 H), 3.71 (s, 3 H), 7.34 (d, J = 8.8 Hz, 2 H), 8.12 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.39, 33.73, 52.37, 124.20 (2 C), 126.76 (2 C), 145.21, 146.27, 171.89 ppm. $C_{10}H_{11}NO_4S$ (241.27): calcd. C 49.78, H 4.60, N 5.81, S 13.29; found C 49.62, H 4.65, N 5.85, S 13.25.

4a: Yield: 0.264 g, 89%, pale yellow liquid. IR (neat): $\tilde{\nu}$ = 1744 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, J = 7.2 Hz, 3 H), 2.54 (q, J = 7.2 Hz, 2 H), 2.59 (t, J = 7.6 Hz, 2 H), 2.77 (t, J = 7.6 Hz, 2 H), 3.67 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.87, 26.11, 26.67, 34.83, 51.84, 172.24 ppm. $C_6H_{12}O_2S$ (148.23): calcd. C 48.62 H 8.16, S 21.63; found C 48.47, H 8.20, S 21.55.

5a: Yield: 0.433 g, 75%, colorless oil. IR (neat): $\tilde{\nu}$ = 1747 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, J = 6.4 Hz, 3 H), 1.25–1.59 (m, 20 H), 2.51 (t, J = 7.6 Hz, 2 H), 2.60 (t, J = 7.2 Hz, 2 H), 2.77 (t, J = 7.2 Hz, 2 H), 3.69 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.80, 23.36, 27.66, 29.53, 29.88, 29.99 (2 C), 30.18 (2 C), 30.25 (2 C), 32.56, 32.86, 35.40, 52.37, 172.38 ppm. $C_{16}H_{32}O_2S$ (288.50): calcd. C 66.61, H 11.18, S 11.11; found C 66.52, H 11.25, S 11.07.

8a: Yield: 0.368 g, 72%, colorless oil. IR (neat): $\tilde{\nu}$ = 2340 (CN) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, J = 6.8 Hz, 3 H), 1.25–1.60 (m, 20 H), 2.58 (t, J = 8 Hz, 2 H), 2.62 (t, J = 7.2 Hz, 2 H), 2.77 (t, J = 7.2 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.24, 19.05, 22.79, 27.76, 28.87, 29.28, 29.43, 29.57 (2 C), 29.72 (3C), 32.00, 32.44, 118.25 ppm. $C_{15}H_{29}NS$ (255.47): calcd. C 70.52, H 11.44, N 5.48, S 12.55; found C 70.32, H 11.49, N 5.49, S 12.48.

10a: Yield: 0.280 g, 87%, white solid (m.p. 78 °C). IR (KBr): $\tilde{\nu}$ = 1657 (C=O), 3197 and 3374 (NH_2) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, J = 7.6 Hz, 3 H), 1.41 (sext., J = 7.6 Hz, 2 H), 1.57 (quint., J = 7.6 Hz, 2 H), 2.48–2.56 (m, 4 H), 2.79 (t, J = 7.2 Hz, 2 H), 6.02 (br. s, NH), 6.02 (br. s, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.95, 22.21, 27.71, 31.85, 32.24, 36.23, 174.14 ppm. $C_7H_{15}NOS$ (161.27): calcd. C 54.14, H 9.38, N 8.69, S 19.88; found C 52.09, H 9.39, N 8.72, S 19.79.

18a: Yield: 0.442 g, 88%, yellow solid (m.p. 70 °C). IR (KBr): $\tilde{\nu}$ = 1340 and 1508 (NO_2), 1717 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.81–1.89 (m, 2 H), 2.15–2.26 (m, 2 H), 2.39–2.49 (m, 3 H), 2.76–2.80 (dd, J_1 = 4.4 Hz, J_2 = 14 Hz, 1 H), 3.68–3.75 (m, 1 H), 7.40 (d, J = 8.4 Hz, 2 H), 8.12 (d, J = 8.4 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.25, 31.22, 41.09, 44.73, 47.50, 124.22 (2 C), 129.21 (2 C), 144.28, 146.04, 207.27 ppm. $C_{12}H_{13}NO_3S$ (251.31): calcd. C 57.35, H 5.21, N 5.57, 12.76; found C 57.17, H 5.27, N 5.60, S 12.73.

20a: Yield: 0.417 g, 70%, colorless oil. IR (neat): $\tilde{\nu}$ = 1717 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, J = 6.4 Hz, 3 H), 1.25–1.59 (m, 20 H), 1.67–1.73 (m, 2 H), 2.10–2.15 (m, 2 H), 2.32–2.39 (m, 3 H), 2.53 (t, J = 7.6 Hz, 2 H), 2.67–2.72 (m, 1 H), 3.10–3.11 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.80, 23.35, 24.96, 29.61, 29.86, 29.99, 30.15, 30.27 (2 C), 30.39 (2 C), 31.24, 32.36, 32.55, 41.59, 43.41, 48.89, 209.22 ppm. $C_{18}H_{34}OS$ (298.54): calcd. C 72.42, H 11.48, S 10.74; found C 72.20, H 11.54, S 10.71.

26a: Yield: 0.217 g, 92%, white solid (m.p. 179–181 °C). IR(KBr): $\tilde{\nu}$ = 1646 (C=O), 3200 and 3395 (NH_2) cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 2.32 (t, J = 7.2 Hz, 4 H), 2.68–2.71 (m, 6 H), 6.83 (br. s, NH), 7.33 (br. s, NH) ppm. ^{13}C NMR (100 MHz, [D_6]-DMSO): δ = 26.87 (2 C), 31.27 (2 C), 35.65 (2 C), 172.22 (2 C) ppm. $C_8H_{16}N_2O_2S_2$ (236.36): calcd. C 40.65, H 6.82, N 11.85, S 27.13; found C 40.54, H 6.88, N 11.90, S 27.10.

27a: Yield: 0.235 g, 94%, white solid (m.p. 147–149 °C). IR (KBr): $\tilde{\nu}$ = 1648 (C=O), 3200 and 3397 (NH_2) cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 1.74 (quint, J = 7.2 Hz, 2 H), 2.30 (t, J = 7.2 Hz, 4 H), 2.55 (t, J = 7.2 Hz, 4 H), 2.64 (t, J = 7.6 Hz, 4 H), 6.81 (br. s, NH), 7.31 (br. s, NH) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 26.88 (2 C), 29.03, 29.89 (2 C), 35.54 (2 C), 172.21 (2 C) ppm. $C_9H_{18}N_2O_2S_2$ (250.38): calcd. C 43.17, H 7.25, N 11.19, S 25.61; found C 43.05, H 7.29, N 11.17, S 25.53.

30a: Yield: 0.229 g, 86%, colourless oil. IR (neat): $\tilde{\nu}$ = 1732 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.62 (t, J = 7.2 Hz, 4 H), 2.74 (s, 4 H), 2.82 (t, J = 7.2 Hz 4 H), 3.69 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.33 (2 C), 32.39 (2 C), 34.96 (2 C), 52.12 (2 C), 171.22 (2 C) ppm. $C_{10}H_{18}O_4S_2$ (266.38): calcd. C 45.09, H 6.81, S 24.07; found C 44.94, H 6.85, S 24.11.

31a: Yield: 0.238 g, 85%, colourless oil. IR (neat): $\tilde{\nu}$ = 1735 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.85 (quint, J = 7.2 Hz, 2 H), 2.60 (t, J = 7.6 Hz, 4 H), 2.62 (t, J = 7.6 Hz, 4 H), 2.76 (t, J = 7.2 Hz, 4 H), 3.68 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.26 (2 C), 29.32, 31.14 (2 C), 34.93 (2 C), 52.04 (2 C), 172.28 (2 C) ppm. $C_{11}H_{20}O_4S_2$ (280.41): calcd. C 47.12, H 7.19, S 22.87; found C 47.02, H 7.25, S 22.79.

3b: Yield: 0.344 g, 89%, colourless liquid. IR (neat): $\tilde{\nu}$ = 3467 (N–H) 1742(C=O) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.87 (s, 1NH), 2.52 (t, J = 6.8 Hz, 2 H), 2.88 (t, J = 6 Hz, 2 H), 3.66 (s, 2 H), 3.79 (s, 3 H), 7.20–7.30 (m, 5 H) ppm. $C_{11}H_{15}NO_2$ (193.25): C 68.37, H 7.28, N 7.25; found C 68.32, H 7.33, N 7.29.

4b: Yield: 0.396 g, 92%, colourless liquid. IR (neat): $\tilde{\nu}$ = 1743 (C=O) cm^{-1}. ^1H NMR: ($CDCl_3$, 400 MHz): δ = 0.90 (t, J = 6.8 Hz, 6 H), 1.26–1.44 (m, 8 H), 2.39 (t, J = 7.2 Hz, 2 H), 2.60 (t, J = 7.2 Hz, 2 H), 2.77 (t, J = 7.6 Hz, 2 H), 3.66 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.50, 21.04, 29.70, 32.68, 47.18, 49.70, 50.17, 51.82, 54.00, 173.42 ppm. MS (EI): m/z (%) = 215 (33) $[M]^+$, 172 (100). $C_{12}H_{25}NO_2$ (215.34): calcd. C 66.93, H 11.70, N 6.50; found C 66.78, H 11.69, N 6.52.

5b: Yield: 0.248 g, 90%, colourless liquid. IR (KBr): $\tilde{\nu}$ = 2259 (CN) cm^{-1}. ^1H NMR: ($CDCl_3$, 200 MHz): δ = 1.44–1.49 (m, 2 H), 1.57–1.65 (m, 4 H), 2.40–2.50 (m, 6 H), 2.62–2.69 (m, 2 H) ppm. MS (EI): m/z (%) = 138 (23) $[M]^+$, 98 (100). $C_8H_{14}N_2$ (138.21): C 69.52, H 10.21, N 20.27; found C 69.49, H 10.25, N 20.29.

6b: Yield: 0.275 g, 86%, colorless liquid. IR (neat): $\tilde{\nu}$ = 3334 (N–H), 2254 (CN) cm^{-1}. ^1H NMR: ($CDCl_3$, 200 MHz): δ = 1.50 (s, 1 H), 2.47 (t, J = 4.4 Hz, 2 H), 2.90 (t, J = 4.6 Hz, 2 H), 3.81 (s, 2 H), 7.24–7.28 (m, 5 H) ppm. MS (EI): m/z (%) = 160 (10) $[M]^+$, 91 (100). $C_{10}H_{12}N_2$ (160.22): C 74.97, H 7.55, N 17.48; found C 74.77 H 7.61, N 17.52.

Supporting Information (see footnote on the first page of this article): Experimental details, analytical data and the ^1H and ^{13}C NMR spectra of selected compounds.

Acknowledgments

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