

Cite this: *Org. Biomol. Chem.*, 2011, **9**, 8483

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PAPER

Multi-component, regio-selective aldol addition of β -ketoesters to aldehydes: scope and applications†

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Received 22nd July 2011, Accepted 27th September 2011

DOI: 10.1039/c1ob06229h

Simple and effective multi-component one-pot aldol addition/protection reactions of β -ketoesters to a series of aldehydes in the presence Me_3SiCl and $i\text{-Pr}_2\text{EtN}$ have been described. The analysis of the scope of the reaction revealed a dramatic dependence of the reactivity on the substrates used. Thus the effect of a catalytic amount of DMF and different reaction conditions was widely investigated. Further transformations of the aldol adducts were particularly useful to give valuable diols and compounds with quaternary stereocenters, while X-ray structural analysis gave also important stereochemical information about this challenging reaction.

1. Introduction

The aldol addition of readily enolizable 1,3-dicarbonyl compounds is still an important challenge in organic chemistry. Even though the obtained adducts are valuable intermediates in the total synthesis of natural products,^{1,2} a general approach is not available yet. In the past very few effective methods have been developed with a limited scope^{3,4} and the literature witnessed a plethora of unsuccessful attempts under both metal and organocatalysed conditions.^{3,5,6} The main difficulties can be attributed to the scarce stability of the adducts and to the inadequacy of the current methodologies that favour condensation (Knoevenagel reaction) or retro-aldol process instead of the aldol reaction. For these reasons different strategies and multi-step non-flexible syntheses have been developed in some cases.^{7–10}

Only very recently a multicomponent one-pot aldol addition/protection reaction (MCR) of malonates to aldehydes for the obtaining of a large class of new aldol adducts in the presence of Me_3SiCl and $i\text{-Pr}_2\text{EtN}$ was developed by our group.¹¹ In these studies it was clearly demonstrated that the success of this challenging aldol addition is mainly related to the *in situ* trapping of the unstable aldol adducts by chlorosilanes reagents^{11a,b} or by their intramolecular trapping.^{11c} In this way a series of aromatic, hetero-aromatic and even simple aliphatic aldehydes

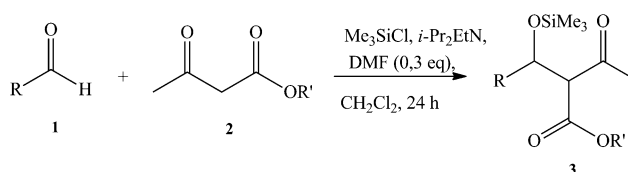
were reacted with malonates to give protected aldol adducts^{11a,b} and a number of novel 3-substituted isoindolinones were obtained reacting 2-cyanobenzaldehyde in the presence of several 1,3-dicarbonyl compounds.^{11c} However, under the MCR conditions, β -ketoesters were almost completely unreactive.^{11b}

Since the branched aldol adducts derived from β -ketoesters have been obtained only in few cases with a very limited aldehyde scope,^{3,11b} as part of our program toward a general procedure for the aldol addition of active methylene compounds, in this article we disclose of our efforts about the development of multi-component one-pot aldol addition/protection reactions to β -ketoesters. Then the usefulness of the obtained adducts is explored in the synthesis of substituted diols and alkylated products; important mechanistic insights have been obtained performing ¹H NMR experiments.

2. Results and discussion

2.1 Multi-component one-pot aldol addition/protection reaction of β -ketoesters

Under the conditions used for the one-pot aldol addition/protection reaction of malonates at $-20\text{ }^\circ\text{C}$, β -ketoesters revealed themselves to be almost completely unreactive. Only *p*-nitro benzaldehyde in the presence of *t*-butyl acetoacetate **2a** and (–)-methyl acetoacetate **2b** gave the silylated adducts in about a 30% yield at $-20\text{ }^\circ\text{C}$ (Scheme 1, Table 1 entries 1–3). In order

Scheme 1 Multicomponent aldol addition of β -ketoesters.

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† Electronic supplementary information (ESI) available: General reaction procedures and spectroscopic data. CCDC reference numbers 837214–837215. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob06229h

Table 1 Multicomponent aldol addition/protection reaction *t*-butyl acetoacetate **2a** with aldehydes in the presence of Me₃SiCl and *i*-Pr₂EtN at –20 °C

Entry	Aldehyde (R)	DMF (eq.)	3	Yield (%) ^a	d.r. ^b
1	Ph	0	3a	No reaction	
2	4-NO ₂ C ₆ H ₄	0	3b	31	1/1
3 ^c	4-NO ₂ C ₆ H ₄	0	3c	35	1/2/1 ^d
4	4-NO ₂ C ₆ H ₄	0.3	3b	75	2.5/1
5	Ph	0.3	—	No reaction	
6	4-CNC ₆ H ₄	0.3	3d	79	2.5/1
7	4-CNC ₆ H ₄	—	3d	55	2.5/1
8	2-CNC ₆ H ₄	0.3	3e	80	2/1
9	2-CNC ₆ H ₄	—	3e	58	
10	4-ClC ₆ H ₄	0.3	3f	20	2/1
11	4-OMeC ₆ H ₄	0.3	—	No reaction	
12	3-Ph propionaldehyde	0.3	—	No reaction	

^a Yields refer to chromatographically pure compounds. ^b Determined by ¹H NMR analysis of crude. ^c Reaction performed in the presence of (–)-menthyl acetoacetate **2b**. ^d Mixture of 3 diastereomers.

Table 2 Multicomponent aldol addition/protection reaction of *tert*-butyl acetoacetate with aldehydes in the presence of Me₃SiCl and *i*-Pr₂EtN

Entry	Aldehyde (R)	T °C	DMF (eq.)	Time (h)	3	Yield (%) ^a	d.r. ^b
1	Ph	–20 °C	0.3	48	3a	No reaction	
2	Ph	0 °C	—	48	3a	No reaction	
3	Ph	rt	—	72	3a	42%	1/1
4	Ph	rt	0.3	72	3a	51%	2/1
5	4-MeOC ₆ H ₄	rt	—	72	—	No reaction	
6	4-MeOC ₆ H ₄	rt	0.3	72	—	No reaction	
7	4-ClC ₆ H ₄	rt	—	72	3f	60%	1.5/1
8	4-ClC ₆ H ₄	rt	0.3	72	3f	72%	1.6/1
9	3-Ph propionaldehyde	rt	—	72	3g	45%	1.5/1
10	3-Ph propionaldehyde	rt	0.3	72	3g	66%	1.7/1
11 ^c	Ph	rt	0.3	72	3h	10%	1.3/1

^a Yields refer to chromatographically pure compounds. ^b Determined by ¹H NMR analysis of crude. ^c Methyl acetoacetate **2c** was used instead of *tert*-butyl acetoacetate.

to overcome this disappointing situation several conditions and strategies were explored. A significant increase of the reactivity was observed when a catalytic amount of DMF was used (Table 1, entry 4). Thus, we were pleased to observe high yields of the silylated aldol adducts in the presence of several aromatic aldehydes bearing strong electron-withdrawing groups like nitro and cyano both in *para* and *ortho* position (Table 1, entries 4, 6 and 8), while without DMF a significant lower yield was observed (Table 1, *cf* entries 7 and 9). The presence of a chlorine substituent, strongly decreased the reactivity, while benzaldehyde and non-activated aldehydes did not react at all (Table 1, entries 5, 11 and 12). As could have been expected, this MCR guarantees high regioselectivity in all the cases for the attack of the aldehydes at the methylene group only, even if **3** were obtained with rather low diastereoselectivity.

The use of DMF was suggested by the well-known effect of activation of trimethylsilyl nucleophiles, like silyl enol ethers, by Lewis bases in a number of C–C bond forming reactions.^{12,13} ¹H NMR experiments at room temperature in CDCl₃ of mixture of TMS-Cl, *t*-butyl acetoacetate and *i*-Pr₂EtN revealed the formation of silyl enol ether intermediates in 1/1 ratio with unreacted starting materials after only 2 h, while similar experiments in the presence of di-*t*-butyl malonate left the starting materials unreacted. Probably the improvement of the reaction rate is a consequence of DMF activation of these silyl enol ether intermediates.

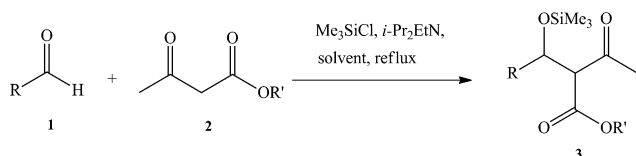
In order to improve the reactivity of less reactive aldehydes, different reaction temperature, higher concentrated reaction medium, different solvents and even in solvent-free conditions, different amines and bases in combination with Me₃SiCl were tried. The most relevant results are summarized in Table 2 and 3. Starting from the conditions of Scheme 1, it can be seen that the modification of three parameters leads to a sufficient reactivity. In the presence of 0.3 eq of DMF, at room temperature and after 72 h, we obtained a 51% yield for **3a** (Table 2, entries 1–4). In these new conditions, the effect of DMF is still evident for benzaldehyde (Table 2, *cf* entries 3 and 4) and other aldehydes. For example when *p*-chloro benzaldehyde and the aliphatic 3-phenyl propionaldehyde were used, we observed 72% and 66% yields respectively, whereas without the Lewis base the yields were lower (*cf* entries 7–8 and 9–10 of Table 2). The result of the aliphatic aldehyde is particular interesting because self-condensation products have not been observed, while also under these conditions, *p*-methoxy benzaldehyde was not reactive (Table 2, entries 5–6). Moreover another disappointing result was observed with methyl acetoacetate **2c** for which the aldol adduct **3h** was obtained in a 10% yield only (Table 2, entry 11).

Since a positive effect on the reaction rate was exerted by the increasing of the temperature, we used higher boiling solvents like 1,2-dichloroethane and THF at refluxing conditions (Scheme 2, Table 3). Focusing on less reactive substrates, a good yield was

Table 3 Multicomponent aldol addition/protection reaction of *tert*-butyl acetoacetate with aldehydes in the presence of Me₃SiCl and *i*-Pr₂EtN

Entry	Aldehyde (R)	R'	Solvent	Time (h)	3	Yield (%) ^a	d.r. ^b
1	Ph	Me	1,2-Dichloroethane	8	3h	55	1.3/1
2 ^c	Ph	Me	1,2-Dichloroethane	8	3h	50	1.5/1
3	Ph	Me	1,2-Dichloroethane	18	3h	32	1.3/1
4	Ph	<i>t</i> -Bu	1,2-Dichloroethane	8	3a	57	1.2/1
5	<i>p</i> -OMeC ₆ H ₄	<i>t</i> -Bu	1,2-Dichloroethane	8	3i	42	1.3/1
6	<i>p</i> -ClC ₆ H ₄	<i>t</i> -Bu	1,2-Dichloroethane	8	3f	84	1.4/1
7	<i>p</i> -BrC ₆ H ₄	<i>t</i> -Bu	1,2-Dichloroethane	8	3l	78	1.5/1
8	2-Furfural	<i>t</i> -Bu	1,2-Dichloroethane	8	3m	68	1.6/1
9	3-Ph propionaldehyde	<i>t</i> -Bu	1,2-Dichloroethane	8	3g	56	1.3/1
10	Ph	<i>t</i> -Bu	THF	18	3a	62	1.3/1
11	<i>p</i> -OMeC ₆ H ₄	<i>t</i> -Bu	THF	18	3i	35	1.2/1
12	Ph	Me	THF	18	3h	39	1/1

^a Yields refer to chromatographically pure compounds. ^b Determined by ¹H NMR analysis of crude. ^c Reaction performed with 0.3 eq of DMF.

**Scheme 2** Multicomponent aldol addition of β -ketoesters.

obtained with methyl acetoacetate and benzaldehyde (entry 1, Table 3).

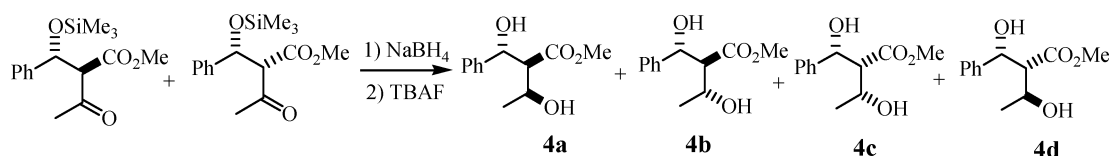
However the use of DMF did not give any significant improvement to the reactivity and for this reason all the experiments of Table 3 were performed without this additive (Table 3, entry 2). Longer reaction time led to the disappearance of the starting materials with the concomitant decrease of the yield due to the formation of decomposition products (Table 3, entry 3). Among the tested aldehydes, we observed a moderate reactivity even with the poorly reactive *p*-methoxybenzaldehyde (Table 3, entry 5). Furfural, *p*-chlorobenzaldehyde and *p*-bromobenzaldehyde showed good results (Table 3, entries 6–8), while only in the presence of 3-phenyl propionaldehyde we observed a lower yield for the formation of decomposition products (*cf* entry 9 of Table 3 with entry 11 of Table 2) The use of THF led to an increase of the yield in the presence of benzaldehyde and *t*-butyl acetoacetate (entry 10), while we did not observe any improvement when methyl acetoacetate and *p*-methoxybenzaldehyde were used (Table 3, entries 11 and 12).

2.2 Synthetic applications of aldol adducts

All the developed methods can be easily employed for gram scale synthesis of the aldol adducts, a feature that is particularly

useful for preparative purposes. In fact the adducts **3** show very interesting functionalities that could be subjected to different sets of transformations to give valuable compounds. For example, according to Scheme 3, the versatility and the stability of **3** was firstly tested treating **3h** with NaBH₄ and with TBAF for the deprotection of the resulting crude mixture. This sequence easily provided the valuable known diols **4**,^{14a,d} that otherwise require longer synthesis with the use of toxic metal reagents, but that can be readily converted into β -lactams and β -lactones.¹⁴ According to ¹H NMR analysis on the crude, all the 4 diastereomers were detected in comparison with those reported by Fleming *et al.*^{14a} and the two major isomers **4a** and **4c** were easily isolated by chromatography. From the comparison of the diastereomeric ratios of **3h** and **4**, we can confidently attribute the stereochemistry of the isomers of **3h** as those described in Scheme 3. This stereochemical outcome can be generalised to all the adducts **3** for the analogy of ¹H NMR spectra. All the aldols **3** have usually been obtained as an inseparable mixture of diastereomers. However the minor isomer of **3e** has been isolated by chromatography and easily crystallised in CH₂Cl₂. Fortunately these crystals were suitable for X-ray structural analysis, the obtained structure is reported in Fig. 1. As it can be seen, the relative configuration of the minor isomer of **3e** (*SR,RS*) is in agreement with what was previously supposed for **3h** in Scheme 3 even though with a different ester group.

Moreover, when we submitted a 1.3/1 mixture of the two diastereomers **3a** with the supposed configuration as shown in Scheme 4, to NaBH₄ reduction, we obtained quantitatively a 3/1.5/1 mixture for the three main diastereomers of **5**, as observed by carefully analysis of ¹H NMR spectrum. The major diastereomer **5a** was isolated by chromatography and treated with TBAF to give the deprotected diol **6** quantitatively. This compound was

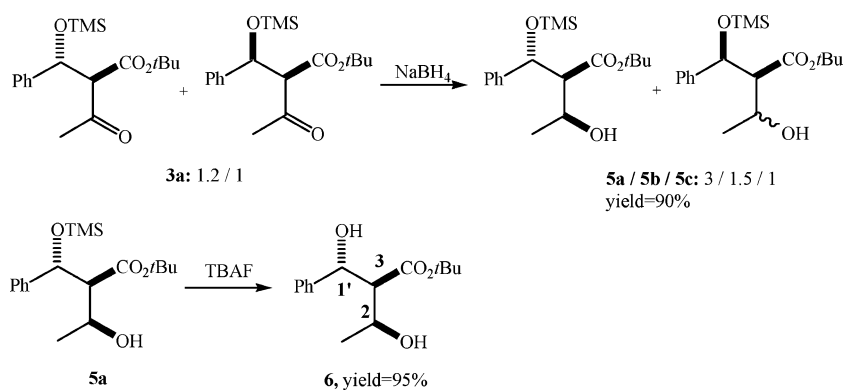
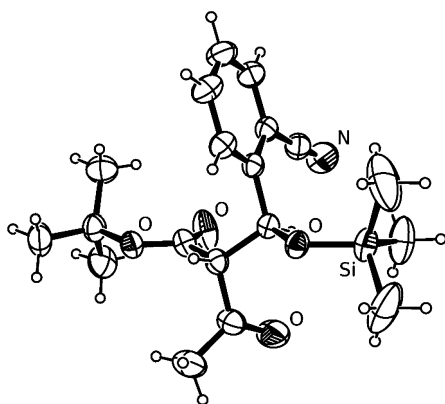
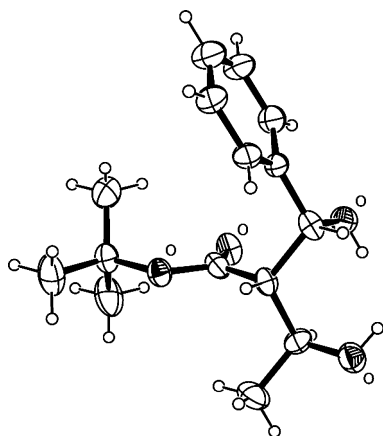


3h: ratio = 1.3 / 1

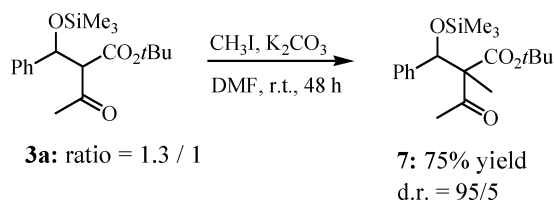
4 95% yield from **3h**

ratio **4a** / **4b** / **4c** / **4d** = 4.7 / 1.3 / 4 / 1

Scheme 3 Reduction and deprotection reactions of aldol **3h**.

Scheme 4 Reduction and deprotection reactions of aldol **3a**.Fig. 1 ORTEP structure of **3e**.Fig. 2 ORTEP structure of **6**.

crystallised again by slow evaporation of CH_2Cl_2 solution and the X-ray scattering gave the structure reported in Fig. 2. The configuration of the three stereocentres $1'RS$, $2SR$, $3SR$, confirmed what was previously supposed by simple analogy. The aldol addition of ethyl 2-methyl acetoacetate to benzaldehyde so as to give an aldol adduct with contiguous tertiary and quaternary stereocenters was unsuccessful under conditions of both Scheme 1 and 2. However, in order to further expand the range of applications of the obtained aldols **3**, we examined the reactivity of **3a** as nucleophile under alkylation conditions in the presence of CH_3I and K_2CO_3 in DMF

Scheme 5 Diastereoselective alkylation of aldol **3a**.

(Scheme 5). Very interestingly, employing the usual 1.3/1 mixture of the two diastereomers, we obtained the alkylated product **7** in the enriched 95/5 ratio in 75% yield in 48 h.

Shorter reaction time (24 h) gave **7** in rather low yield (35%). However in this case the unreacted **3a** was recovered in 35% yield with an enriched 70/30 diastereomeric ratio. Unfortunately **7** was obtained as an oil and we were not able to crystallise it for X-ray analysis for a rationalization of the stereochemical outcome. Considering the importance in the construction of quaternary centers in stereoselective manner and the fact that, to the best of our knowledge, similar diastereoselective alkylations are rare,¹⁵ further studies are in course to expand the scope of the aldols in this field.

3. Conclusions

In conclusion we have developed a series of multicomponent one-pot aldol addition/protection reactions of β -ketoesters with a wide range of aldehydes to give protected aldol adducts in the presence of Me_3SiCl and $i\text{-Pr}_2\text{EtN}$. The use of catalytic amounts of DMF led to an increase in the reactivity with aldehydes bearing electron-withdrawing groups, while less reactive aldehydes required different solvents and refluxing conditions. Subsequently, the investigation of the formation of silyl enol ethers of β -ketoesters also gave important mechanistic insights into the role that DMF can play. Finally, as examples of the possibilities of further functionalization of the obtained aldols, **3a** and **3h** were submitted to a sequence of reduction and deprotection reactions to give valuable diols, while alkylation reactions afforded quaternary stereocentre with high diastereoselectivity. Considering the variety of versions and reaction conditions that this MCR of β -ketoesters can tolerate, we think that this work can give important perspective for a general approach to the aldol addition of other readily enolizable active methylene compounds. Since the class of active

methylene compounds is very large and presents different structural motifs, in future studies particular emphasis will be given to other applications of this methodology and of the obtained aldol adducts in the synthesis of valuable compounds. Other studies are also in course for the development of enantioselective versions of these difficult aldol additions.

Experimental

General remarks

All reactions were performed in oven-dried (140 °C) or flame-dried glassware under dry N₂. Dichloromethane was reagent grade and was dried and distilled immediately from CaH₂ before use. Column chromatographic purification of products was carried out using silica gel 60 (230–400 mesh, Merck). The reagents (Aldrich and Fluka) were used without further purification. The NMR spectra were recorded on Bruker DRX 400, 300, 250 spectrometers (400 MHz, 300 MHz, 250 MHz, ¹H; 100 MHz, 75 MHz, 62.5 MHz ¹³C). Spectra were referenced to residual CHCl₃ (7.26 ppm, ¹H, 77.23 ppm, ¹³C). Coupling constants *J* are reported in Hz. Yields are given for isolated products showing one spot on a TLC plate and no impurities detectable in the NMR spectrum. Mass spectral analyses were carried out using an electrospray spectrometer, Waters 4 micro quadrupole. Elemental analyses were performed with FLASHEA 1112 series-Thermo Scientific for CHNS-O apparatus.

Procedure for one pot aldol-silylation reaction in the presence of Me₃SiCl and *i*-Pr₂EtN (Scheme 1)

In a flame-dried, 2-necked, round-bottom flask, aldehyde (0.40 mmol) was added to a solution of *i*-Pr₂EtN (2.3 eq., 0.92 mmol), β-ketoester (1.5 eq., 0.60 mmol) and Me₃SiCl (2.0 eq., 0.80 mmol) in dry dichloromethane (2.0 mL) under nitrogen at –20 °C. At the end of the reaction, the mixture was quenched with saturated aqueous NaHCO₃ (5 mL), extracted with 15 × 3 mL of CH₂Cl₂ and dried over anhydrous Na₂SO₄. After removing the solvent under reduced pressure, the crude oil was purified by flash chromatography from hexane to 95/5 hexane/AcOEt mixture to afford the pure products 3.

Procedure for one pot aldol-silylation reaction in the presence of Me₃SiCl and *i*-Pr₂EtN (Scheme 2)

In a flame-dried, 2-necked, round-bottom flask equipped with a condenser, aldehyde (0.80 mmol) was added to a solution of *i*-Pr₂EtN (2.0 eq., 1.60 mmol), β-ketoester (1.1 eq., 0.88 mmol) and Me₃SiCl (2.0 eq., 1.60 mmol) in dry 1,2-dichloroethane or THF (4.0 mL), under nitrogen. The solution was kept refluxing until the end of the reaction, monitored by TLC; then the mixture was cooled down at room temperature, quenched with saturated aqueous NaHCO₃ (5 mL), extracted with 15 × 3 mL of CH₂Cl₂ and dried over anhydrous Na₂SO₄. After removing the solvent under reduced pressure, the crude oil was purified by flash chromatography from hexane to 95/5 hexane/AcOEt mixture to afford the pure products 3.

Procedure for conversion of 3a into 5

NaBH₄ (0.27 mmol) was added to a solution of 3a (0.25 mmol) in methanol (1.0 mL), at 0 °C and reacted for 20 min. Then

the reaction was quenched with saturated aqueous NaHCO₃ (5 mL), extracted with 15 × 3 mL of CH₂Cl₂ and dried over anhydrous Na₂SO₄. After removing the solvent under reduced pressure, the crude oil was purified by flash chromatography with hexane/AcOEt mixture from 90/10 to 1/1 to afford the pure products 5.

Procedure for conversion of 5a into 6

5a was dissolved in THF (1.0 mL) and TBAF (25 μl of 1.0 M solution in THF) was added at 0 °C and reacted for 30 min. Then the mixture was treated with saturated aqueous NaCl (5 mL), extracted with 15 × 3 mL of CH₂Cl₂ and dried over anhydrous Na₂SO₄. After removing the solvent under reduced pressure, the crude oil was purified by flash chromatography with 1/1 mixtures of hexane and AcOEt to afford the pure product 6.

Procedure for alkylation of 3a

K₂CO₃ (0.27 mmol) was added to a solution of 3a (0.11 mmol) and CH₃I (0.33 mmol) in DMF (1.0 mL), at r.t. and reacted for 48 h. Then ethyl acetate (20 mL) was added and the mixture was extracted with brine (10 × 3 mL) and dried over anhydrous Na₂SO₄. After removing the solvent under reduced pressure, the crude oil was purified by flash chromatography with hexane/AcOEt mixture from 95/5 to 90/10 to afford the pure products 7.

Acknowledgements

The corresponding author wants to thank the University of Salerno for financial support.

References

- For aldol additions of malonates in total synthesis of epolactaene, see: (a) S. Marumoto, H. Kogen and S. Naruto, *J. Org. Chem.*, 1998, **63**, 2068–2069.
- For aldol additions of malonates in the total synthesis of carbohydrates, see: A. Saba, V. Adovasio and M. Nardelli, *Tetrahedron: Asymmetry*, 1992, **3**, 1573–1582.
- For catalyst-free aldol additions of 1,3-dicarbonyl compounds to activated aldehyde see: K. Rohra and R. Mahrwald, *Adv. Synth. Catal.*, 2008, **350**, 2877–2880.
- Aldol addition of formaldehyde to 1,3-dicarbonyl compounds is a well-established reaction and several examples are available. For selected examples see: (a) Y. Tsuda, A. Ishiura, S. Takamura, S. Hosoi, K. Isobe and K. Mohri, *Chem. Pharm. Bull.*, 1991, **39**, 2797–2802; (b) T. H. Chan and A. E. Schwerdtfeger, *J. Org. Chem.*, 1991, **56**, 3294–3298. For aldol addition of formaldehyde to activated ketones see: V. Lecomte and C. Bolm, *Adv. Synth. Catal.*, 2005, **347**, 1666–1672. For enantioselective aldol addition of formaldehyde in the presence of chiral palladium complexes: I. Fukuchi, Y. Hamashima and M. Sodeoka, *Adv. Synth. Catal.*, 2007, **349**, 509–512. For an aldol addition of aqueous formaldehyde with bicyclic β-keto ester, see: S. Shirakawa and S. Shimizu, *Synlett*, 2007, 3160–3164.
- The failure of a planned aldol addition of substituted cyclohexane-1,3-dione in the total synthesis of coleophomones is described by K. C. Nicolaou, T. Montagnon, G. Vassilikogiannakis and C. J. N. Mathison, *J. Am. Chem. Soc.*, 2005, **127**, 8872–8888.
- For early unsuccessful attempts of direct aldol additions see: (a) L. Birkofer, A. Ritter and H. Vernaleken, *Chem. Ber.*, 1966, **99**, 2518–2520; (b) B. D. Wilson, *J. Org. Chem.*, 1963, **28**, 314–320; (c) H. Hellmann and D. Dieterich Liebigs, *Ann. Chem.*, 1962, **656**, 89–96; (d) R. Mayer and B. Gebhardt, *Chem. Ber.*, 1960, **93**, 1212–1219; (e) W. Schroth, W. Treibs and Justus Liebigs, *Ann. Chem.*, 1961, **639**, 214–228; (f) W. Chen and B. M. Pinto, *Carbohydr. Res.*, 2007, **342**, 2163–2172.

- 7 P. Camps and J. M. Drudis, *Tetrahedron Lett.*, 1978, **19**, 2597–2598.
- 8 R. Antonioletti, F. Bonadies and A. Scettri, *J. Org. Chem.*, 1988, **53**, 5540–5542.
- 9 N. Umebayashi, Y. Hamashima, D. Hashizume and M. Sodeoka, *Angew. Chem.*, 2008, **120**, 4264–4267, (*Angew. Chem., Int. Ed.*, 2008, **47**, 4196–4199).
- 10 D. J. Buchanan, D. J. Dixon and F. A. Hernandez-Juan, *Org. Lett.*, 2004, **6**, 1357–1360.
- 11 (a) A. Massa, A. Scettri, R. Filosa and L. Capozzolo, *Tetrahedron Lett.*, 2009, **50**, 7318–7321; (b) A. Massa, A. Roscigno, P. De Caprariis, R. Filosa and A. Di Mola, *Adv. Synth. Catal.*, 2010, **352**, 3348–3354; (c) V. More, A. Di Mola, M. Perillo, P. De Caprariis, R. Filosa, A. Peduto and A. Massa, *Synthesis*, 2011, 3027.
- 12 For a recent review: J. Gawronski, N. Wascinska and J. Gajewy, *Chem. Rev.*, 2008, **108**, 5227–5252.
- 13 A. Scettri, V. De Sio, R. Villano, P. Manzo and M. R. Acocella, *Tetrahedron Lett.*, 2010, **51**, 3658–3661.
- 14 (a) M. S. Betson, I. Fleming and J. V. A. Ouzman, *Org. Biomol. Chem.*, 2003, **1**, 4017–4024; (b) P. Swaren, I. Massova, J. R. Bellettini, A. Bulychev, L. Maveyraud, L. P. Kotra, M. J. Miller, S. Mobashery and J.-P. Samama, *J. Am. Chem. Soc.*, 1999, **121**, 5353–5359; (c) S. N. Greszler and J. S. Johnson, *Org. Lett.*, 2009, **11**, 827–830; (d) J.-H. Gu, M. Terada, K. Mikami and T. Nakai, *Tetrahedron Lett.*, 1992, **33**, 1465.
- 15 H. S. Prakash Rao, K. S. Reddy and S. N. Balasubrahmanyam, *Tetrahedron Lett.*, 1994, **35**, 1759.