Tetrahedron 67 (2011) 9885–9889

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

NHC-catalyzed annulation of enals and chalcones: further explorations on the novel synthesis of 1,3,4-trisubstituted cyclopentenes

Vijay Nair *, Rony Rajan Paul, D.V.M. Padmaja, N. Aiswarya, C.R. Sinu, Anu Jose

Organic Chemistry Section, National Institute for Interdisciplinary Science and Technology (CSIR), Trivandrum 695019, India

ARTICLE INFO

Article history:
Received 8 August 2011
Received in revised form 23 September 2011
Accepted 23 September 2011
Available online 1 October 2011

This paper is dedicated with best wishes and warm regards to Professor Gilbert Stork on the occasion of his 90th birthday

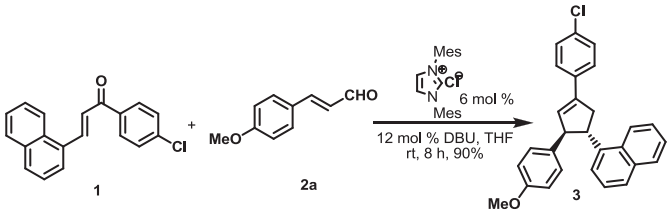
Keywords:
Homoenolate
N-Heterocyclic carbene
Chalcone
Heterocycle
Cyclopentene

ABSTRACT

The facile synthesis of 1,3,4-trisubstituted cyclopentenes via homoenolate annulation of enals with heterocycle substituted chalcones is described.

1. Introduction

Catalysis of organic reactions by small organic molecules, commonly called organocatalysis,[1] has been an area of immense research activity in recent years. Contemporaneously, the use of nucleophilic heterocyclic carbenes (NHCs) as catalysts[2] in organic reactions was pursued by a number of groups. From a historical perspective, the origins of NHC-catalysis can be traced to the preliminary experiments of Ugai[3] as well as Mizuhara[4] followed by the pathbreaking work of Breslow[5] that demonstrated the catalysis of benzoin condensation by the ylide/carbene generated from a thiazolium salt. Surprisingly NHCs received very little attention for more than four decades except for their role in Stetter reaction and benzoin condensation. However a dramatic change occurred during the last decade; presently work on the NHC-catalysis is proceeding at a torrid pace in many laboratories. Recent investigations have revealed a number of synthetic protocols triggered by NHCs, a unique one being the generation of homoenolates from enals, discovered by Glorius[6] and Bode.[7] Subsequent to their original work on the synthesis of γ-lactones, a multitude of NHC-catalyzed homoenolate reactions have emerged.[8] Inter alia, the synthesis of γ-spirolactones,[9] pyrazolidinones,[10] pyridazininones,[11] lactams,[12] and cyclopentanols[13] are noteworthy. Homoenolates have also been shown to add efficiently to nitrostyrenes[14] and sulfonimines leading to precursors for novel γ-aminobutyric acid (GABA) derivatives.[15] A reaction that intrigued us most was the NHC mediated annulation of enals with chalcones leading to cyclopentenes,[16] observed in our laboratory (Scheme 1).



Scheme 1. Reaction of enals with chalcones.

The early studies on this reaction were confined to the annulation of aryl enals with aryl enones. Subsequently we found that the homoenolate annulations afforded cyclopentenes and/or spirocyclopentanones depending on the structural features of the dienones employed.[17] In our continuing efforts to define the scope of the cyclopentene annulation employed we have now examined

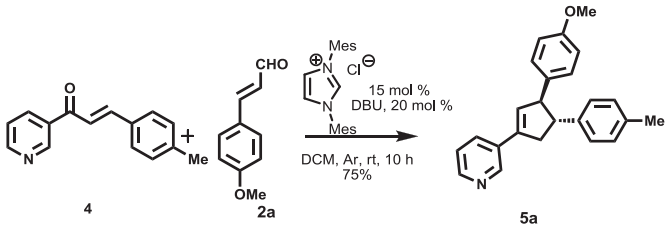
* Corresponding author. Tel.: +91 471 2490406; fax: +91 471 491712; e-mail address: vijaynair_2001@yahoo.com (V. Nair).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.09.113

the reaction of enals with a variety of heteroaryl substituted chalcones. In addition to aryl enals we have examined the reaction with a typical aliphatic enal viz., crotonaldehyde. The results of these investigations which broaden the scope of the cyclopentene synthesis are presented in this paper.

2. Results and discussion

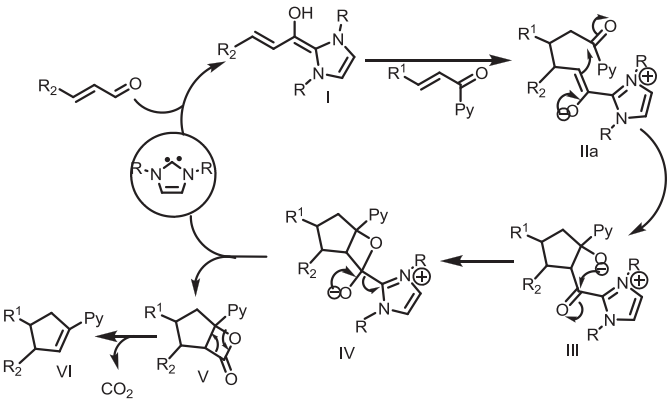
The present studies were initiated by exposing a mixture of 4-methoxycinnamaldehyde and (*E*)-1-(pyridin-3-yl)-3-*p*-tolylprop-2-en-1-one in presence of IMes under an inert atmosphere of argon for about 10 h. The reaction mixture on column chromatography yielded the product, 4-(3-(4-methoxyphenyl)-4-tolylcyclopent-1-enyl)pyridine **5a** as an yellow liquid in 75% yield (Scheme 2).



Scheme 2. Reaction with pyridine substituted chalcone.

The structure of compound **5a** was elucidated by usual spectroscopic analysis. The ^{1}H NMR spectrum showed a singlet at δ 3.65 corresponding to the methoxy group and the alkenyl proton of the pentene core was observed at δ 6.19. This was supported by the ^{13}C NMR spectrum, which showed peaks at δ 123.4 and 141.6 indicating the alkenyl carbons and a peak at δ 158.4 indicating the aromatic carbon bearing $-OCH_3$ group. It also displayed a peak at δ 55.1 corresponding to methoxy carbon. Compound **5a** gave satisfactory LRMS data also. The stereochemistry for the two substituents was assigned on the basis of X-ray crystal data obtained for the analogous compound **3**.[15]

A mechanistic rationale for the cyclopentene formation postulated earlier is invoked here (Scheme 3). As might be expected, the homoenolate I formed by the reaction of IMes with enal undergoes conjugate addition to the chalcone and consequent to a proton transfer generates the enolate IIa, which participates in intramolecular aldol reaction to deliver the cyclopentane carbinolate III. The latter undergoes lactone formation concomitant with the ejection of IMes. The β-lactone V thus formed is unstable and liable to undergo retro [2+2] process to yield the cyclopentene VI with the loss of carbon dioxide.



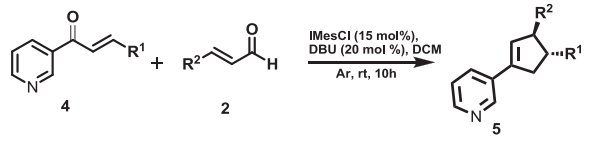
Scheme 3. Mechanistic rationale.

Our original report on the stereoselective synthesis of cyclopentene derivatives was followed by a number of instances of similar reactions such as the asymmetric, intramolecular, and enone–imine variants of the cylopentannulation from other groups.[18] Bode proposed an aldehyde-enone crossed benzoin condensation and a subsequent oxy-cope rearrangement to rationalize the enhanced enantioselectivity and preferential formation of *cis*-substituted cyclopentenes.[18a] Scheidt isolated a bicyclic β-lactone from the intramolecular variant of the cyclopentannulation thus accruing indirect support to our β-lactone intermediate.[18b]

Importantly, in addition to the experimental proof obtained for the lactone formation by IR spectroscopy,[16] theoretical calculations involving DFT studies by two different research groups support the formation of cyclopentenes via the proposed pathway.[19] In concurrence with our proposal, Domingo's theoretical studies point out that the step involving conjugate addition of homoenolate to enone is responsible for the trans relationship at the final cyclopentene. Furthermore, Domingo has concluded that "the high energy associated with the NHC-catalyzed crossed benzoin reaction allows for the rejection of the mechanism through an oxy-Cope rearrangement" proposed by Bode.

In subsequent experiments it was found that a variety of pyridine substituted chlacones readily undergo annulations to afford cyclopentenes. The results of our studies are consolidated in Table 1. It is interesting to note that in addition to aromatic enals, the aliphatic enal crotonaldehyde also participates in this reaction.

Table 1
Reaction with 3-pyridyl chalcones

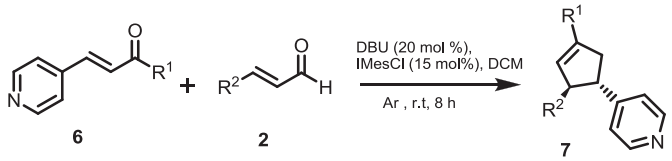


Entry	R^1	R^2	Product	Yield (%)
1	4-Methylphenyl	4-Methoxyphenyl	**5a**	75
2	4-Methylphenyl	2-Methoxyphenyl	**5b**	84
3	4-Methylphenyl	Phenyl	**5c**	75
4	4-Methylphenyl	Methyl	**5d**	80
5	4-Methoxyphenyl	4-Methoxyphenyl	**5e**	81
6	4-Methoxyphenyl	2-Methoxyphenyl	**5f**	73
7	4-Methoxyphenyl	Phenyl	**5g**	77
8	4-Fluorophenyl	4-Methoxyphenyl	**5h**	66
9	4-Fluorophenyl	2-Methoxyphenyl	**5i**	80
10	4-Fluorophenyl	Phenyl	**5j**	70
11	4-Fluorophenyl	Methyl[a]	**5k**	80
12	Naphthyl	4-Methoxyphenyl	**5l**	89

[a] THF, 70 °C, 12 h.

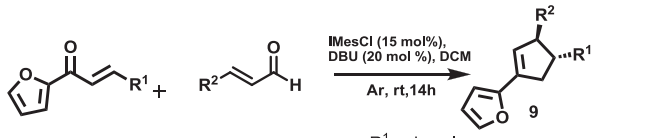
In view of the success of the reaction with 3-pyridyl chalcones, it was of interest to extend it to other chlacones such as 4-pyridyl chalcones. The expected cyclopentene was obtained in every case examined, albeit in lower yields (Table 2).

Table 2
Reaction with 4-pyridyl chalcones



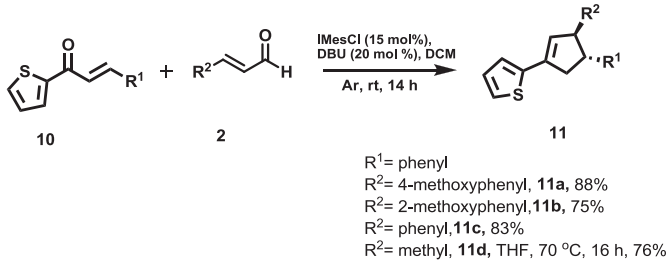
Entry	R^1	R^2	Product	Yield (%)
1	Phenyl	4-Methoxyphenyl	**7a**	65
2	Phenyl	Phenyl	**7b**	63
3	4-Methoxyphenyl	4-Methoxyphenyl	**7c**	58
4	4-Methoxyphenyl	2-Methoxyphenyl	**7d**	67
5	4-Methylphenyl	4-Methoxyphenyl	**7e**	60

The facile formation of pyridine substituted cyclopentenes prompted us to extend the reaction with other heterocycle substituted chalcones. The results of our experiments with furan substituted chalcones are depicted in Scheme 4.



Scheme 4. Reaction with furan substituted chalcones.

Further, the reaction was extended to a few thiophene substituted chalcones. The protocol was found to be effective for the synthesis of thiophene substituted cyclopentenes (Scheme 5).



Scheme 5. Reaction with thiophene substituted chalcones.

In conclusion a series of pyridine, furan, and thiophene substituted cyclopentenes are synthesized via homoenolate protocol. The simple and mild reaction conditions and the high yields of products are likely to make the reaction attractive for its application in the synthesis of a variety of cyclopentene derivatives. The present work expands the scope of the unique cyclopentannulation.

3. Experimental section

3.1. General experimental procedure

The α,β-unsaturated aldehyde (1.5 equiv), IMesCl (0.15 equiv), and heterocycle substituted chalcone (1 equiv) were taken in DCM (6 ml/1 mmol of chalcone). After addition of DBU (0.2 equiv), the reaction mixture was allowed to stir at room temperature for the time mentioned in the table. The reaction mixture on column chromatography on silica (100–200 mesh) using 15:85 ethylacetate/hexane mixture yielded the corresponding cyclopentene as an yellow viscous liquid.

3.1.1. Compound ***5a***. ^{1}H NMR (500 MHz, $CDCl_3$): 8.69 (s, 1H), 8.4 (s, 1H), 7.65 (d, 1H, J=8 Hz), 7.16–7.13 (m, 1H), 7.01–6.96 (m, 4H), 6.70–6.65 (m, 2H), 6.91 (d, 2H, J=8.5 Hz), 6.20 (s, 1H), 3.95 (dd, 1H, J_1=5 Hz, J_2=5 Hz), 3.65 (s, 3H), 3.30–3.25 (m, 1H), 3.2–3.15 (m, 1H), 2.89–2.84 (m, 1H), 2.22 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 158.4, 148.2, 147.1, 147.6, 138.9, 136.4, 135.8, 132.9, 131.8, 130.7, 129.2, 128.3 127.2, 123.4, 113.9, 60.0, 55.1, 54.4, 53.4, 41.6, 21.1; LRMS-FAB $(M+H)^+$ calculated: 342.45; found: 342.85.

3.1.2. Compound ***5b***. ^{1}H NMR (500 MHz, $CDCl_3$): 8.67 (d, 1H, J=2 Hz), 8.37 (dd, 1H, J_1=5 Hz, J_2=1 Hz), 7.65–7.63 (m, 1H), 7.14–7.12 (m, 1H), 7.10–7.05 (m, 4H), 6.96 (d, 2H, J=2 Hz), 6.80–6.77 (m, 1H), 6.70 (d, 1H, J=8 Hz), 6.20 (s, 1H), 4.45 (dd, 1H, J_1=6 Hz, J_2=2.5 Hz), 3.51 (s, 3H), 3.3–3.34 (m, 2H), 3.20–3.16 (m, 1H), 2.21 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 157.2, 148.3, 147.3, 143.0, 139.0, 135.3, 132.6, 132.5, 131.8, 130.5, 128.9, 128.2, 127.8, 127.6, 127.5, 126.9, 123.3, 120.7, 110.6, 55.2, 53.4, 52.1, 41.4, 21.1; LRMS-FAB $(M+H)^+$ calculated: 342.45; found: 342.71.

3.1.3. Compound ***5c***. ^{1}H NMR (500 MHz, $CDCl_3$): 8.67 (d, 1H, J=1.5 Hz), 8.39 (dd, 1H, J_1=4.5 Hz, J_2=1.5 Hz), 7.66–7.64 (m, 1H), 7.16–7.13 (m, 3H), 7.11–7.07 (m, 1H), 7.01–6.97 (m, 6H), 6.22 (d, 1H, J=1.5 Hz), 4.01–3.99 (m, 1H), 3.33–3.14 (m, 2H), 3.19–2.90 (m, 1H), 2.22 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 148.4, 147.3, 144.3, 141.7, 139.3, 135.8, 133.3, 132.7, 131.6, 130.3, 129.3, 128.5, 127.9, 127.5, 127.4, 126.7, 123.3, 60.9, 54.3, 45.7, 41.7, 21.1; LRMS-FAB $(M+H)^+$ calculated: 312.42; found: 312.78.

3.1.4. Compound ***5d***. ^{1}H NMR (300 MHz, $CDCl_3$): 8.77 (d, 1H, J=13.8 Hz), 8.49 (d, 1H, J=4.5 Hz), 7.71 (d, 1H, J=7.5 Hz), 7.27–7.15 (m, 5H), 6.25 (s, 1H), 3.21–3.16 (m 1H), 3.07–3.04 (m, 2H), 3.04–2.89 (m, 1H), 2.38 (s, 3H), 1.21 (d, 3H, J=6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): 147.9, 147.1, 137.2, 135.5, 133.4, 131.8, 129.1, 128.7, 127.2, 123.1, 52.9, 49.3, 44.3, 21.0, 19.6; LRMS-FAB $(M+H)^+$ calculated: 250.35; found: 250.58.

3.1.5. Compound ***5e***. ^{1}H NMR (500 MHz, $CDCl_3$): ^{1}H NMR (500 MHz, $CDCl_3$): 8.66 (d, 1H, J=2 Hz), 8.38 (d, 1H, J=8.5 Hz), 7.64 (d, 1H, J=7.5 Hz), 7.15–7.13 (m, 1H), 7.01 (d, 2H, J=8.5 Hz), 6.92–6.90 (m, 2H), 6.71–6.68 (m, 4H), 6.19 (s, 1H), 3.93–3.91 (m, 1H), 3.66 (s, 3H), 3.64 (s, 3H), 3.28–3.23 (m, 1H), 3.16–3.14 (m, 1H), 2.87–2.82 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 158.4, 158.2, 148.2, 147.1, 138.9, 136.6, 136.3, 132.8, 131.7, 130.7, 129.6, 129.3, 128.3, 123.3, 113.9, 113.1, 60.1, 55.1, 54.2, 41.6; LRMS-FAB $(M+H)^+$ calculated: 358.44; found: 358.78.

3.1.6. Compound ***5f***. ^{1}H NMR (500 MHz, $CDCl_3$): 8.77 (d, 1H, J=2 Hz), 8.48 (dd, 1H, J_1=5 Hz, J_2=1.5 Hz), 7.77–7.75 (m, 1H), 7.26–7.24 (m, 1H), 7.19–7.15 (m, 4H), 6.91–6.87 (m, 1H), 6.82–6.78 (m, 3H), 6.30 (s, 1H), 4.52 (d, 1H, J=4 Hz), 3.76 (s, 3H), 3.65–3.63 (m, 3H), 3.46–3.43 (m, 1H), 3.30–3.25 (m, 1H), 2.92–2.87 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 157.9, 157.1, 148.2, 147.2, 139.0, 138.0, 132.7, 132.5, 131.8, 130.6, 129.8, 129.1, 127.9, 127.6, 127.5, 123.3, 120.7, 113.6, 112.5, 110.6, 55.2, 55.1, 41.3; LRMS-FAB $(M+H)^+$ calculated: 358.33; found: 358.83.

3.1.7. Compound ***5g***. ^{1}H NMR (300 MHz, $CDCl_3$): 8.79 (s, 1H), 8.52 (d, 1H, J=4.2 Hz), 7.79 (d, 1H, J=7.8 Hz), 7.29–7.21 (m, 4H), 7.16–7.10 (m, 4H), 6.83 (d, 2H, J=8.4 Hz), 6.36 (s, 1H), 4.11–4.08 (m, 1H), 3.79 (s, 3H), 3.56–3.36 (m, 2H), 3.01–2.96 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 158.2, 158.1, 148.2, 147.0, 144.2, 139.2, 136.5, 132.7, 131.7, 130.2, 128.4, 127.3, 126.5, 123.2, 113.9, 60.9, 53.9, 41.6, 29.6; LRMS-FAB $(M+H)^+$ calculated: 328.42; found: 328.90.

3.1.8. Compound ***5h***. ^{1}H NMR (500 MHz, $CDCl_3$): 8.69 (d, 1H, J=1.5 Hz), 8.43 (d, 1H, J=4 Hz), 7.70–7.69 (m, 1H), 7.20 (dd, 1H, J_1=8 Hz, J_2=5 Hz), 7.10–7.08 (m, 2H), 6.94–6.84 (m, 2H), 6.73–6.72 (m, 4H), 6.23 (d, 1H, J=1 Hz), 3.95–3.93 (m, 1H), 3.72 (s, 3H), 3.33–3.12 (m, 2H), 2.93–2.82 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 162.5, 160.6, 158.5, 147.4, 147.2, 140.3, 138.9, 135.9, 132.7, 131.5, 130.5, 129.5, 128.7, 123.3, 115.2, 113.9, 60.2, 55.1, 54.1, 41.5, 29.1; LRMS-FAB $(M+H)^+$ calculated: 346.41; found: 346.91.

3.1.9. Compound ***5i***. ^{1}H NMR (500 MHz, $CDCl_3$): 8.68 (d, 1H, J=2 Hz), 8.40 (dd, 1H, J_1=4.5 Hz, J_2=1 Hz), 7.69–7.66 (m, 1H), 7.18–7.19 (m, 1H), 7.13–7.09 (m, 2H), 7.08–7.06 (m, 2H), 6.86–6.79 (m, 3H), 6.71 (d, 1H, J=8 Hz), 6.21 (d, 1H, J=2.5 Hz), 4.43–4.41 (m,

1H), 3.51 (s, 3H), 3.37–3.30 (m, 1H), 3.23–3.17 (m, 1H), 2.83–2.81 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 162.4, 160.4, 157.0, 148.2, 147.1, 141.6, 139.1, 132.8, 131.7, 129.6, 123.4, 120.7, 119.9, 115.0, 113.8, 110.5, 60.3, 55.1, 53.5, 52.1, 41.3, 39.6; LRMS-FAB $(M+H)^+$ calculated: 346.41; found: 346.77.

3.1.10. Compound ***5j***. ^{1}H NMR (300 MHz, $CDCl_3$): 8.82 (s, 1H), 8.52 (d, 1H, J=7 Hz), 7.79 (d, 1H, J=7.8 Hz), 7.31–6.95 (m, 8H), 6.80–6.71 (m, 2H), 6.34 (s, 1H), 4.08 (d, 1H, J=5.1 Hz), 3.50–3.30 (m, 2H), 3.14–3.03 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 162.5, 148.6, 147.3, 143.9, 140.2, 139.3, 132.7, 131.4, 130.1, 128.7, 127.9, 127.3, 126.7, 123.3, 115.4, 61.0, 53.9, 41.6; LRMS-FAB $(M+H)^+$ calculated: 316.38; found: 316.75.

3.1.11. Compound ***5k***. ^{1}H NMR (300 MHz, $CDCl_3$): 8.69 (s, 1H), 8.45 (dd, 1H, J_1=3.9 Hz, J_2=1.5 Hz), 7.68 (d, 1H, J=7.8 Hz), 7.26–7.22 (m, 3H), 7.01–6.96 (m, 2H), 6.18 (s 1H), 3.22–3.14 (m, 1H), 3.07–2.96 (m, 1H), 2.87–2.85 (m, 1H), 2.29–2.15 (m, 1H), 1.17 (d, 3H, J=6.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): 162.5, 160.5, 148.1, 147.1, 140.6, 137.2, 132.5, 131.7, 129.1, 128.6, 123.2, 115.2, 52.5, 49.5, 41.9, 19.7; LRMS-FAB $(M+H)^+$ calculated: 254.31; found: 254.63.

3.1.12. Compound ***5l***. ^{1}H NMR (500 MHz, $CDCl_3$): 8.82 (d, 1H, J=1.5 Hz), 8.52 (dd, 1H, J_1=4.5 Hz, J_2=1.5 Hz), 7.90 (d, 1H, J=8 Hz), 7.86 (d, 1H, J=7.5 Hz), 7.82–7.79 (m, 1H), 7.73 (d, 1H, J=8 Hz), 7.47–7.39 (m, 4H), 7.30–7.28 (m, 1H), 7.08 (d, 2H, J=8.5 Hz), 6.80–6.78 (m, 2H), 6.44 (d, 1H, J=2 Hz), 4.14–4.10 (m, 2H), 3.77 (s, 3H), 3.55–3.49 (m, 1H), 3.16–3.12 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 148.4, 147.4, 141.1, 139.1, 136.8, 136.3, 134.2, 132.8, 131.6, 130.7, 129.1, 128.3, 127.1, 125.8, 125.5, 125.4, 123.9, 123.7, 123.3, 114.0, 112.9, 112.2, 59.0, 55.2, 41.4; LRMS-FAB $(M+H)^+$ calculated: 378.48; found: 378.67.

3.1.13. Compound ***7a***. ^{1}H NMR (500 MHz, $CDCl_3$): 8.41 (d, 2H, J=6 Hz), 7.43 (d, 2H, J=7.5 Hz), 7.28 (t, 2H, J=7.5 Hz), 7.21 (m, 1H), 7.06 (d, 2H, J=6 Hz), 6.96 (d, 2H, J=8.5 Hz), 6.73 (d, 2H, J=8.5 Hz), 6.13 (s, 1H), 3.96 (t, 1H, J=2.5 Hz), 3.70 (s, 3H), 3.32–3.23 (m, 2H), 2.93–2. 88 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 158.5, 154.1, 149.9, 141.7, 136.0, 135.5, 128.5, 128.3, 128.1, 127.7, 125.8, 122.6, 114.2, 59.7, 55.1, 53.9, 40.9; LRMS-FAB $(M+H)^+$ calculated: 328.16; found: 328.71.

3.1.14. Compound ***7b***. ^{1}H NMR (500 MHz, $CDCl_3$): 8.38 (d, 2H, J=6 Hz), 7.40 (d, 2H, J=7.5 Hz), 7.25 (t, 2H, J=7.5 Hz), 7.17 (t, 3H, J=7.5 Hz), 7.12 (m, 1H), 7.01–7.03 (m, 4H), 6.13 (s, 1H), 3.98–3.96 (m, 1H), 3.32–3.21 (m, 2H), 2.90–2.85 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 154.1, 149.9, 148.9, 144.0, 142.1, 135.5, 128.7, 128.6, 128.5, 128.1, 127.8, 127.7, 127.3, 127.6, 127.3, 126.9, 126.7, 125.8, 123.8, 122.6, 60.4, 53.7, 41.1; LRMS-FAB $(M+H)^+$ calculated: 298.15; found: 298.47.

3.1.15. Compound ***7c***. ^{1}H NMR (500 MHz, $CDCl_3$): 8.50 (d, 2H, J=5 Hz), 7.43 (d, 2H, J=8.5 Hz), 7.18 (d, 2H, J=36 Hz), 7.02 (d, 2H, J=8.5 Hz), 6.88 (d, 2H, J=9 Hz), 6.80 (d, 2H, J=8 Hz), 6.07 (s, 1H), 4.02–3.99 (m, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 3.37–3.29 (m, 2H), 2.95–2.89 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 159.3, 158.5, 155.5, 148.7, 141.4, 136.1, 129.8, 129.2, 128.2, 127.0, 125.8, 122.9, 114.3, 59.8, 55.1, 54.0, 41.0, 30.2; LRMS-FAB $(M+H)^+$ calculated: 358.17; found: 358.37.

3.1.16. Compound ***7d***. ^{1}H NMR (500 MHz, $CDCl_3$): 8.61 (d, 2H, J=5 Hz), 7.95 (d, 2H, J=9 Hz), 7.45–7.42 (m, 2H), 7.38 (d, 2H, J=9 Hz), 7.20 (d, 2H, J=10 Hz), 6.89 (m, 2H), 6.00 (s, 1H), 4.40–3.39 (m, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 3.29–3.26 (m, 1H), 3.23–3.18 (m, 1H), 2.80–2.76 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 158.2, 156.4, 155.7, 140.7, 130.6, 129.9, 128.9, 128.0, 126. 6, 123.9, 119.5, 112.8, 109.0, 54.1, 54.0, 51.7, 51.1, 39.7; LRMS-FAB $(M+H)^+$ calculated: 358.17; found: 358.42.

3.1.17. Compound ***7e***. ^{1}H NMR (500 MHz, $CDCl_3$): 8.39 (d, 2H, J=6 Hz), 7.30 (d, 2H, J=8 Hz), 7.04–7.07 (m, 4H), 6.93 (d, 2H, J=8.5 Hz), 6.71 (d, 2H, J=8.5 Hz), 6.05 (s, 1H), 3.93–3.91 (m, 1H), 3.68 (s, 3H), 3.29–3.19 (m, 2H), 2.88–2.82 (m, 1H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 158.5, 154.5, 149.6, 141.6, 137.5, 136.2, 132.7, 129.2, 128.3, 127.0, 125.7, 122.7, 114.0, 59.6, 55.1, 54.0, 40.9, 21.3; LRMS-FAB $(M+H)^+$ calculated: 342.18; found: 342.52.

3.1.18. Compound ***9a***. ^{1}H NMR (500 MHz, $CDCl_3$): 7.36 (s, 1H), 7.26–7.23 (m, 2H), 7.18–7.17 (m, 3H), 7.01–6.99 (m, 3H), 6.76 (d, 2H, J=8.5 Hz), 6.38–6.36 (m, 1H), 6.11 (s, 1H), 4.04–4.03 (m, 1H), 3.73 (s, 3H), 3.35–3.30 (m, 1H), 3.21–3.16 (m, 1H), 2.89–2.86 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 157.4, 152.0, 146.4, 145.1, 141.9, 133.1, 132.9, 128.5, 128.3, 127.8, 127.5, 127.3, 127.1, 126.9, 125.9, 120.7, 110.8, 110.5, 55.3, 48.5, 40.7, 39.4; LRMS-FAB $(M+H)^+$ calculated: 316.39; found: 316.78.

3.1.19. Compound ***9b***. ^{1}H NMR (500 MHz, $CDCl_3$): 7.38 (s, 1H), 7.25–7.24 (m, 1H), 7.21–7.13 (m, 1H), 7.16–7.13 (m, 2H), 6.98–6.90 (m, 2H), 6.89–6.86 (m, 1H), 6.78–6.76 (s, 1H), 6.38–6.37 (m, 1H), 6.24–6.23 (m, 1H), 6.11 (s, 1H), 4.52–4.51 (m, 1H), 3.56 (s, 3H), 3.55–3.45 (m, 1H), 3.39–3.35 (m, 1H), 3.21–3.16 (m, 1H), 2.84–2.80 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 157.3, 145.1, 140.5, 136.7, 136.2, 128.5, 128.3, 127.8, 127.4, 127.3, 126.3, 124.4, 124.1, 113.9, 58.4, 55.1, 54.9, 42.8, 39.4; LRMS-FAB $(M+H)^+$ calculated: 315.78; found: 315.78.

3.1.20. Compound ***9c***. ^{1}H NMR (300 MHz, $CDCl_3$): 7.45 (s, 1H), 7.35–7.25 (m, 8H), 7.16–7.14 (m, 2H), 6.45 (s, 1H), 6.35 (d, 1H, J=3 Hz), 6.21 (s, 1H), 4.13–4.05 (m, 1H), 3.51–3.41 (m 1H), 3.36–3.33 (m, 1H), 3.01–2.93 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 145.1, 144.6, 140.4, 136.5, 128.5, 127.5, 127.4, 126.5, 124.5, 124.2, 61.0, 54.7, 42.9, 29.7; LRMS-FAB $(M-H)^+$ calculated: 285.14; found: 285.79.

3.1.21. Compound ***9d***. ^{1}H NMR (300 MHz, $CDCl_3$): 7.39 (s, 1H), 7.33–7.23 (m, 5H), 6.42–6.39 (m, 1H), 6.21 (d, 1H, J=3 Hz), 6.04 (s, 1H), 2.87–2.81 (m, 1H), 3.16–3.03 (m, 3H), 1.21 (d, 3H, J=6.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): 152.1, 145.2, 141.9, 141.4, 128.5, 127.5, 111.2, 110.5, 60.2, 49.3, 44.1, 41.3, 40.6, 19.9; LRMS-FAB $(M+H)^+$ calculated: 224.30; found: 224.67.

3.1.22. Compound ***11a***. ^{1}H NMR (500 MHz, $CDCl_3$): 7.27–7.24 (m, 2H), 7.20–7.16 (m, 4H), 7.02–6.96 (m, 4H), 6.77 (d, 2H, J=8.5 Hz), 6.04 (s, 1H), 4.04–4.03 (m, 1H), 3.75 (s, 3H), 3.39–3.35 (m, 1H), 3.32–3.27 (m, 1H), 2.99–2.95 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 158.3, 145.1, 140.5, 136.7, 136.2, 128.4, 128.2, 127.8, 127.4, 127.3, 126.3, 124.4, 124.1, 113.9, 60.9, 55.1, 54.9, 42.8; LRMS-FAB $(M-H)^+$ calculated: 331.46; found: 331.90.

3.1.23. Compound ***11b***. ^{1}H NMR (500 MHz, $CDCl_3$): 7.26–7.24 (m, 4H), 7.23–7.21 (m, 2H), 7.20–7.17 (m, 1H), 7.04–6.98 (m, 2H), 6.97–6.93 (m, 1H), 6.90–6.87 (m, 1H), 6.82–6.77 (m, 1H), 6.05 (s, 1H), 4.52–4.50 (m, 1H), 3.58 (s, 3H), 3.44–3.12 (m, 1H), 3.29–3.26 (m, 1H), 2.95–2.89 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 157.4, 146.4, 145.1, 140.8, 136.8, 136.5, 133.1, 128.3, 127.8, 127.5, 126.3, 124.3, 120.7, 110.8, 58.5, 55.3, 52.9, 41.3; LRMS-FAB $(M-H)^+$ calculated: 332.46; found: 332.67.

3.1.24. Compound ***11c***. ^{1}H NMR (500 MHz, $CDCl_3$): 7.29–7.22 (m, 8H), 7.16–7.14 (m, 2H), 7.04–7.03 (m, 3H), 6.12 (s, 1H), 4.13–4.05 (m, 1H), 3.15–3.41 (m, 1H), 3.36–3.33 (m, 1H), 3.08–3.03 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 145.1, 144.6, 140.4, 136.5, 128.6, 128.5, 127.5,

127.4, 127.3, 126.5, 126.4, 124.5, 124.2, 60.9, 54.7, 42.9; LRMS-FAB $(M-H)^+$ calculated: 301.11; found: 301.74.

3.1.25. Compound ***11d***. ^{1}H NMR (300 MHz, $CDCl_3$): 7.33–7.27 (m, 2H), 7.26–7.23 (m, 2H), 7.20–7.17 (m, 1H), 7.01–6.94 (m, 3H), 5.97 (s, 1H), 3.25–3.19 (m, 1H), 3.10–2.95 (m, 2H), 2.87–2.82 (m, 1H), 1.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 145.3, 140.8, 134.5, 130.1, 128.5, 127.5, 127.2, 126.3, 124.5, 60.3, 53.5, 49.5, 44.1, 19.9; LRMS-FAB $(M-H)^+$ calculated: 239.11; found: 239.69.

Acknowledgements

V.N. acknowledges the Department of Science and Technology for the Raja Ramanna Fellowship. The authors also thank the Council of Scientific and Industrial Research, New Delhi for financial assistance. Thanks are due to Mrs. Soumini Mathew and Mrs. Viji S. for spectral data.

References and notes

1. For a recent review on organocatalysis see: Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. *Chem. Rev.* **2007**, *107*, 5471.
2. For reviews on NHC chemistry see: (a) Nair, V.; Bindu, S.; Vellalath, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 5130; (b) Zeitler, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 7506; (c) Marion, N.; Diez Gonzalez, S.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2988; (d) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606; (e) Phillips, E. M.; Chan, A.; Scheidt, K. A. *Aldrichimica Acta* **2009**, *42*, 55; (f) Moore, J. L.; Rovis, T. In *Asymmetric Organocatalysis*; List, B., Ed.; Topics in Current Chemistry; Springer: Berlin, 2009; Vol. 291, p 77; (g) Chiang, P.-C.; Bode, J. W. N-Heterocyclic carbenes as organic catalysts In *N-Heterocyclic Carbenes: From Laboratory Curiosities to Efficient Synthetic Tools*; Díez-González, S., Ed.; RSC Catalysis Series No. 6; Royal Society of Chemistry: Cambridge, 2010; p 399.
3. Ugai, T.; Tanaka, R.; Dokawa, T. *J. Pharm. Soc. Jpn.* **1943**, *63*, 296.
4. (a) Mizuhara, S.; Tamura, R.; Arata, H. *Proc. Jpn. Acad.* **1951**, *27*, 302; (b) Mizuhara, S.; Handler, P. *J. Am. Chem. Soc.* **1954**, *76*, 571.
5. Breslow, R. *J. Am. Chem. Soc.* **1958**, *80*, 3719.
6. Burstein, C.; Glorius, F. *Angew. Chem., Int. Ed.* **2004**, *43*, 6205.
7. Sohn, S. S.; Rosen, E. L.; Bode, J. W. *J. Am. Chem. Soc.* **2004**, *126*, 14370.
8. For reviews on homoenolate chemistry see: (a) Nair, V.; Vellalath, S.; Babu, B. P. *Chem. Soc. Rev.* **2008**, *37*, 2691; (b) Nair, V.; Menon, R. S.; Biju, A. T.; Sinu, C. R.; Paul, R. R.; Jose, A.; Vellalath, S. *Chem. Soc. Rev.* **2011**, doi:10.1039/c1cs15139h.
9. (a) Nair, V.; Vellalath, S.; Poonoth, M.; Mohan, R.; Suresh, E. *Org. Lett.* **2006**, *8*, 507; (b) Nair, V.; Vellalath, S.; Poonoth, M.; Suresh, E.; Viji, S. *Synthesis* **2007**, 3195.
10. Chan, A.; Scheidt, K. A. *J. Am. Chem. Soc.* **2008**, *130*, 2741.
11. Chan, A.; Scheidt, K. A. *J. Am. Chem. Soc.* **2007**, *129*, 5334.
12. (a) He, M.; Bode, J. W. *Org. Lett.* **2005**, *7*, 3131; (b) He, M.; Bode, J. W. *J. Am. Chem. Soc.* **2008**, *130*, 418.
13. Nair, V.; Babu, B. P.; Vellalath, S.; Varghese, V.; Raveendran, A. E.; Suresh, E. *Org. Lett.* **2009**, *11*, 2507.
14. Nair, V.; Sinu, C. R.; Babu, B. P.; Varghese, V.; Jose, A.; Suresh, E. *Org. Lett.* **2009**, *11*, 5570.
15. Nair, V.; Vargehse, V.; Babu, B. P.; Sinu, C. R.; Suresh, E. *Org. Biomol. Chem.* **2010**, *8*, 761.
16. Nair, V.; Vellalath, S.; Poonoth, M.; Suresh, E. *J. Am. Chem. Soc.* **2006**, *128*, 8736.
17. (a) Nair, V.; Vellalath, S.; Babu, B. P.; Varghese, V.; Paul, R. R.; Suresh, E. *Org. Biomol. Chem.* **2010**, *8*, 4861; (b) Nair, V.; Babu, B. P.; Vellalath, S.; Suresh, E. *Chem. Commun.* **2008**, 747.
18. (a) Chiang, P.-C.; Kaeobamrung, J.; Bode, J. W. *J. Am. Chem. Soc.* **2007**, *129*, 3520; (b) Wadamoto, M.; Phillips, E. M.; Reynolds, T. E.; Scheidt, K. A. *J. Am. Chem. Soc.* **2007**, *129*, 10098; (c) He, M.; Bode, J. W. *J. Am. Chem. Soc.* **2007**, *128*, 418.
19. (a) Verma, P.; Patni, P. A.; Sunoj, R. B. *J. Org. Chem.* **2011**, *76*, 5606; (b) Domingo, L. R.; Zaragozá, R. J.; Arnó, M. *Org. Biomol. Chem.* **2010**, *8*, 4884.