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Tetrahedron
Tetrahedron 62 (2006) 3997–4002

A facile synthesis of 3-allyl-4-hydrazinocyclopentenes by the palladium/Lewis acid mediated ring opening of bicyclic hydrazines with allyltributyltin and allyltrimethylsilane

V. S. Sajisha, Mohanlal Smitha, S. Anas and K. V. Radhakrishnan*

Chemical Sciences Division, Organic Chemistry Section, Regional Research Laboratory (CSIR), Trivandrum 695 019, India

Received 9 November 2005; revised 25 January 2006; accepted 10 February 2006

Available online 9 March 2006

Abstract—A facile method for the synthesis of 3-allyl-4-hydrazinocyclopentenes from bicyclic hydrazines by the Pd/Lewis acid catalyzed reaction of allyltributyltin and allyltrimethylsilane is described. The role of ionic liquid [bmim]PF_6 as a solvent as well as a promoter is also demonstrated by carrying out the reactions in ionic liquid without Lewis acid.

1. Introduction

Disubstituted cyclopentanes are versatile synthons for the construction of numerous biologically active molecules.[1] They are well utilized for the preparation of glycosidase inhibitors, antiviral and antitumor carbonucleosides and in prostaglandin research.[2] Among the disubstituted cyclopentenes, hydrazinocyclopentenes are of great importance because they have been extensively utilized for the preparation of carbocyclic ribavirin, which is supposed to have greater metabolic stability to the phosphorylase enzymes.[3] Substituted cyclopentenyl hydroxamic acid derived inhibitors of metal containing enzymes like 5-lipoxygenase are used for the treatment of many diseases like rheumatoid arthritis, asthma, inflammatory bowel disease, psoriasis and allergy.[4] Some of the bioactive cyclopentane derivatives are shown in Figure 1.

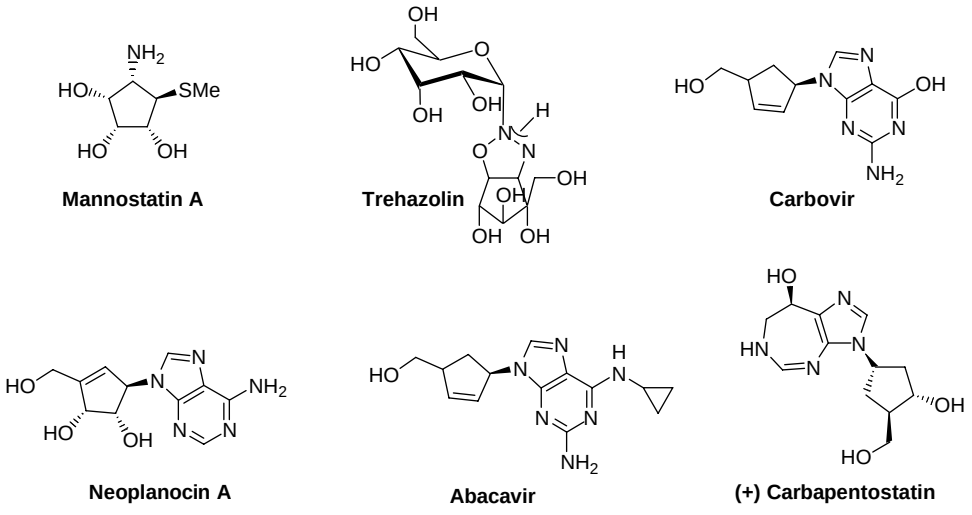

Figure 1.

Keywords: Bicyclic hydrazines; Disubstituted cyclopentanes; [bmim]PF_6; Allyltri-*n*-butyltin; Lewis acids; Palladium catalyst.
* Corresponding author. Tel.: +91 471 2515275; fax: +91 471 2491712; e-mail: radhupreethi@rediffmail.com

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doi:10.1016/j.tet.2006.02.028

Various methods are known in the literature for the preparation of disubstituted cyclopentene derivatives.[5] Trost has utilized π-allyl palladium chemistry for introducing a variety of substituents to the cyclopentenic core.[6] Miller and co-workers achieved the synthesis of disubstituted cyclopentenes by using acyl nitroso-hetero Diels–Alder cycloadducts.[7] Desymmetrization of the bicyclic hydrazines is another tool for the synthesis of disubstituted cyclopentenes and it has been well utilized by Kaufmann[8] and Micouin.[9] But all of the reported methods lead to the formation of 3,5-disubstituted cyclopentenes. In some of the above cases, 3,4-disubstituted cyclopentenes were observed as minor products.[7,8,10]

2. Results and discussion

2.1. Pd/Lewis acid mediated ring opening

Owing to our interest in the cascade carbopalladation of bicyclic alkenes, we undertook an investigation of the domino Heck–Stille coupling of bicyclic hydrazines. The Stille protocol have been employed by Kosugi and co-workers[11] for the synthesis of 2,3-disubstituted norbornanes from organic halide, organostannane and norbornene. Bicyclic hydrazines are suitable candidates for the preparation of disubstituted cyclopentenes due to their good reactivity and an internal point of fracture, the C–N bond. Moreover, they are easily accessible. The bicyclic hydrazines selected for our studies are given in Figure 2.

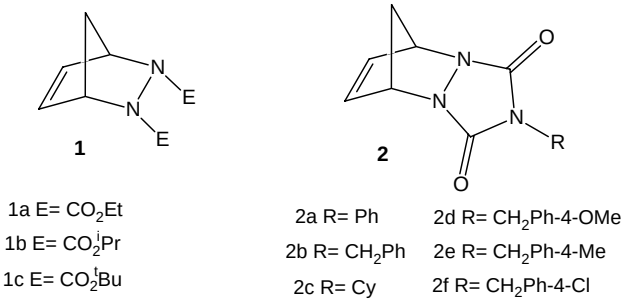
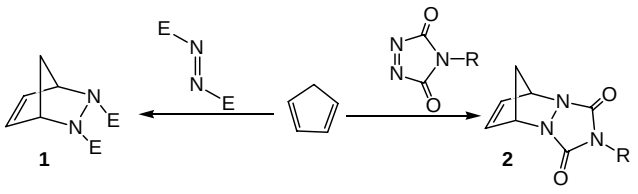


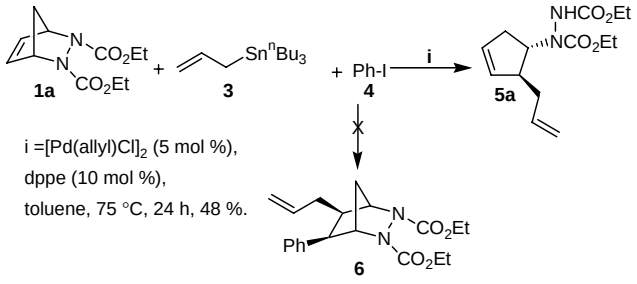
Figure 2.

Bicyclic hydrazines, the starting materials for our investigations were prepared by the Diels–Alder cycloaddition reaction between cyclopentadiene and the corresponding dialkylazodicarboxylate[12] or 1,2,4,-triazoline-3,5-dione (Scheme 1).[13]



Scheme 1.

Our experiments started with the reaction of 2,3-diazabicyclo[2.2.1]heptene with aryl iodide and allyltributyl tin in the presence of $[Pd(allyl)Cl]_2$ and dppe in dry toluene. Contrary to the expected addition product, the reaction afforded allylated hydrazinocyclopentene (Scheme 2).



Scheme 2.

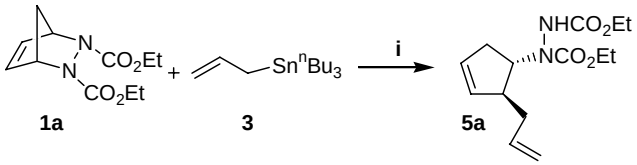
The reaction was optimized under different conditions. Details of the optimization studies are shown in Table 1.

Table 1

Catalyst	Ligand	Solvent	Time/ temperature	Yield
$Pd_2(dba)_3 \cdot CHCl_3$	dppm	Toluene	20 h, 70 °C	Complicated reaction
$Pd_2(dba)_3 \cdot CHCl_3$	dppe	Toluene	20 h, 70 °C	Complicated reaction
$PdCl_2(PPh_3)_2$	—	Toluene	24 h, 100 °C	20%
$PdCl_2(PhCN)_2$	—	Toluene	24 h, 60 °C	No reaction
$Pd(OAc)_2$	—	THF	24 h, 60 °C	Complicated reaction
$[Pd(allyl)Cl]_2$	—	Toluene	36 h, 75 °C	30%
$[Pd(allyl)Cl]_2$	dppe	Toluene	24 h, 75 °C	48%
$[Pd(allyl)Cl]_2$	PPh_3	Toluene	24 h, 75 °C	15%
$[Pd(allyl)Cl]_2$	dppm	Toluene	24 h, 75 °C	Complicated reaction

After a series of experiments, 5 mol% $[Pd(allyl)Cl]_2$ along with 10 mol% dppe as ligand was found to be the best catalyst system with toluene as the solvent.

It was interesting to note that aryl iodide was recovered almost completely and no reaction could be observed in the absence of aryl iodide. The question remained as to the role of aryl iodide in the reaction. We suspected that the trace amount of iodine present in the aryl iodide or aryl iodide itself may be acting as a nucleophile facilitating the C–N bond cleavage. Molecular iodine is known to bring about various organic transformations with high selectivity under convenient conditions.[14] The possibility of iodine acting as a promoter for various reactions, has been a topic of discussion for organic chemists in recent years. The role of iodine as a promoter, facilitating the formation of **5a** was proved by carrying out the reaction with catalytic amount of iodine instead of aryl iodide. The reaction afforded **5a** in 85% yield (Scheme 3).[15]



Scheme 3. i=$[Pd(allyl)Cl]_2$ (5 mol%), dppe (10 mol%), I_2 (2 mol%), toluene, 75 °C, 24 h, 85%.

This prompted us to investigate the effect of other Lewis acids and the reaction was found to be general with a number of Lewis acids. Scandium triflate was found to be the best, the reaction was complete in 5 h at rt and our observations are given in Table 2.

Table 2. Effect of different Lewis acids

No.	Lewis acid	Time (h)	Temperature	Yield (%)
1	I_2	24	75 °C	85
2	$Yb(OTf)_3$	5	rt	80
3	$Sc(OTf)_3$	5	rt	95
4	AgOTf	12	rt	62
5	$Cu(OTf)_2$	12	rt	68
6	$Sn(OTf)_2$	24	50 °C	60

Amount of Lewis acid=2 mol%.

The structure of the compound **5a** was assigned based on the spectral data. In the IR spectrum the stretching vibrations of NH and CO were observed at 3294 and 1713 cm^{-1}, respectively. In the ^1H NMR spectrum, the NH proton and the carboethoxy protons were seen at δ 6.52, 4.19 and 1.27 ppm, respectively, while the CH proton of the allyl group was observed at δ 5.79 ppm. The carbonyl carbons were discernible at δ 156.7 and 155.9 in the ^{13}C NMR spectrum. The structure was further confirmed by elemental analysis and high resolution mass spectral analysis. The HOMO-COSY and HETERO-COSY analyses were also in agreement with the proposed structure. The stereochemistry of the product was assigned by comparison to the literature data.[8,21]

Due to our continuing interest in this field, we decided to investigate the reactivity of some tricyclic hydrazines derived from triazoline dione. The common solvents like toluene and THF were not suitable for these substrates as the yields were substantially low. In an attempt to optimize the yield of the reaction by changing solvents, we decided to use rt ionic liquid $[bmim]PF_6$ as the solvent.

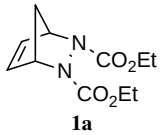
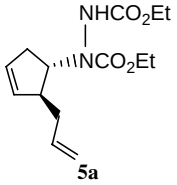
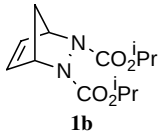
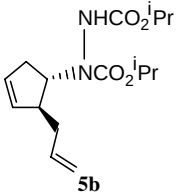
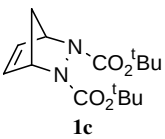
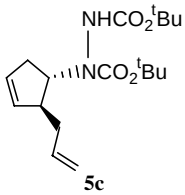
2.2. Reactions in ionic liquid $[bmim]PF_6$

It is well known that the microenvironment generated by a solvent can change the outcome of a reaction in terms of both equilibria and rate. Since ionic liquids have the potential to provide reaction media that are unique at rt, it is possible that they will have dramatic effects on reactions carried out in them.[16] Ionic liquids are composed of anions and cations; either of which may interact with solutes and therefore affect the outcome of the reaction. Some ionic liquids have also been shown to act as catalysts further augmenting their wide spread introduction into general synthetic chemistry. The ionic liquids offer an attractive alternative to conventional organic solvents for clean synthesis, as they are easy to recycle and possess no effective vapor pressure.[17]

When the reaction of bicyclic hydrazine **1** was carried out in ionic liquid instead of toluene, the reaction rate was found to enhance but with similar yield. In addition to this we observed that the reaction occurs in $[bmim]PF_6$ even in the absence of Lewis acid, but with longer reaction time. This demonstrates the ability of ionic liquid to act as a promoter. The results of our investigations are given in Table 3.

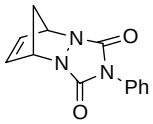
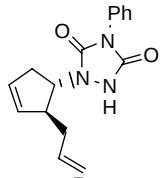
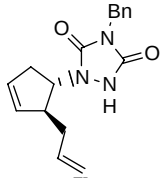
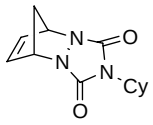
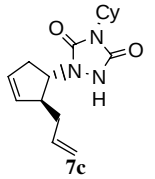
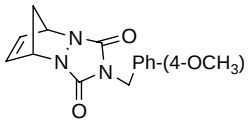
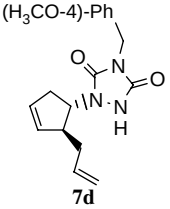
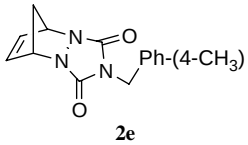
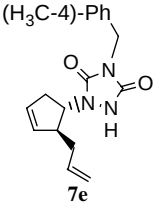
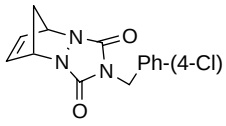
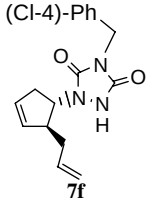
Similar reactivity was observed in the case of azatricyclic olefins. To prove the generality of this strategy we have extended the Pd(0)/Lewis acid catalyzed reaction of allyltributyltin to various tricyclic substrates. Our observations are summarized in Table 4.

Table 3. Palladium-catalyzed reaction of azabicyclic olefins with allyltributyltin

Entry	Substrate	Lewis acid	Time (h)	Solvent/ temperature (°C)	Yield (%)	Product
1	 **1a**	$Sc(OTf)_3$	5	Toluene, rt	95	 **5a**
		$Sc(OTf)_3$	1	$[bmim]PF_6$, rt	90	
		—	12	$[bmim]PF_6$, 60 °C	76	
2	 **1b**	$Sc(OTf)_3$	12	Toluene, 60 °C	75	 **5b**
		$Sc(OTf)_3$	8	$[bmim]PF_6$, 60 °C	80	
		—	24	$[bmim]PF_6$, 60 °C	78	
3	 **1c**	$Sc(OTf)_3$	12	Toluene, 60 °C	77	 **5c**
		$Sc(OTf)_3$	8	$[bmim]PF_6$, 60 °C	72	

Reaction conditions=$[Pd(allyl)Cl]_2$ (5 mol%), dppe (10 mol%), $Sc(OTf)_3$ (2 mol%).

Table 4. Palladium-catalyzed reaction of azatricyclic olefins with allyltributyltin

Entry	Substrate	Lewis acid	Time (h)	Solvent/temperature (°C)	Yield (%)	Product
1	 **2a**	$Sc(OTf)_3$ $Sc(OTf)_3$ —	36 8 24	Toluene, 60 °C [bmim]PF_6, 60 °C [bmim]PF_6, 60 °C	20 89 90	 **7a**
2	 **2b**	$Sc(OTf)_3$ —	8 24	[bmim]PF_6, 60 °C [bmim]PF_6, 60 °C	95 97	 **7b**
3	 **2c**	$Sc(OTf)_3$ —	8 24	[bmim]PF_6, 60 °C [bmim]PF_6, 60 °C	88 85	 **7c**
4	 **2d**	$Sc(OTf)_3$ —	10 24	[bmim]PF_6, 60 °C [bmim]PF_6, 60 °C	85 81	 **7d**
5	 **2e**	$Sc(OTf)_3$ —	10 24	[bmim]PF_6, 60 °C [bmim]PF_6, 60 °C	95 93	 **7e**
6	 **2f**	$Sc(OTf)_3$ —	10 24	[bmim]PF_6, 60 °C [bmim]PF_6, 60 °C	78 76	 **7f**

Reaction conditions = $[Pd(allyl)Cl]_2$ (5 mol%), dppe (10 mol%), $Sc(OTf)_3$ (2 mol%).

2.3. Reactions with allyltrimethylsilane

Organometals containing relatively electronegative metals such as organoboranes and organosilanes are also known to participate in palladium-catalyzed cross-coupling reactions.[18] These reactions are thought to proceed via transmetallation on palladium. The carbon–silicon bond of allyltrimethylsilane, although less polarized, has sufficient nucleophilicity to react with palladium complexes.[19] As expected, the reaction of bicyclic hydrazine **1a** with allyltrimethylsilane in the presence of Pd/Lewis acid catalyst afforded allyl substituted hydrazinocyclopentene as the product, but with low yield. The reaction was found to be general for bicyclic and tricyclic olefins. The results of our investigations with allyltrimethylsilane are summarized in Table 5.

Table 5. Reaction of allyltrimethysilane

Entry	Starting material	Solvent/temperature (°C)	Product	Yield (%)
1	**1a**	Toluene, 60 °C	**5a**	30
2	**2a**	[bmim]PF_6, 60 °C	**7a**	28
3	**2c**	[bmim]PF_6, 60 °C	**7c**	32

Reaction conditions = $[Pd(allyl)Cl]_2$ (5 mol%), dppe (10 mol%), $Sc(OTf)_3$ (2 mol%), 12 h.

3. Conclusions

In conclusion, we have developed a new methodology for the synthesis of 3,4-disubstituted cyclopentenes. The products are suitable for further synthetic transformations. Transformations like dihydroxylation and conversion of

the hydrazine to amine could result in the formation of versatile synthons, which can be used for the synthesis of many biologically active molecules like glycosidase inhibitors,[20] carbocyclic nucleosides, antiviral and anti-tumor agents[22] etc. The role of ionic liquid as a solvent as well as a promoter was also established by carrying out the reactions in ionic liquid without Lewis acid.

4. Experimental

4.1. General

All reactions were carried out in oven-dried glass wares under nitrogen atmosphere. Progress of the reaction was monitored by thin-layer chromatography, which was performed on Merck precoated plates (silica gel 60 F_{254}, 0.25 mm) and was visualized by fluorescence quenching under UV light or by staining with Enholm yellow solution. Column chromatography was done using 100–200 mesh silica gel and appropriate mixture of petroleum ether (60–80 °C) and ethyl acetate for elution. The solvents were removed using Buchi rotary evaporator. The IR spectra were recorded on Nicolet FT-IR spectrometer. NMR spectra were recorded on Bruker FT-NMR spectrometer using $CDCl_3$ or $CDCl_3$–CCl_4 mixture (7/3) as solvent. TMS was used as internal standard and chemical shifts are in δ-scale. High-resolution mass spectra were recorded under EI/HRMS using JEOL JMS 600H mass spectrometer. Abbreviations used in ^{1}H NMR are s-singlet, t-triplet, q-quartet and m-multiplet.

4.2. General procedure for the reaction of bicyclic hydrazines with organostannanes and organosilanes

Method A. The bicyclic hydrazine (1 equiv) and organostannane/organosilane (1 equiv) were taken in a Wheaton reactor and dissolved in dry toluene (4 mL). The ligand dppe (10 mol%) was added, followed by the catalyst $[Pd(allyl)Cl]_2$ (5 mol%). To this $Sc(OTf)_3$ (2 mol%) was added. The reaction mixture was stirred at 60 °C for 12 h. Completion of the reaction was monitored by TLC and the reaction mixture was subjected to column chromatography (silica gel 100–200 mesh, 15% EtOAc–hexane) to afford the product in good yield.

Method B. The bicyclic hydrazine (1 equiv) and the organostannane/organosilane (1 equiv) were taken in a Wheaton reactor and dissolved in ionic liquid [bmim]PF_6 (2 mL). The ligand dppe (10 mol%) was added, followed by the catalyst $[Pd(allyl)Cl]_2$ (5 mol%). To this $Sc(OTf)_3$ (2 mol%) was added. The reaction mixture was stirred at 60 °C for 12 h. Completion of the reaction was monitored by TLC. The reaction mixture was extracted several times with diethyl ether until the ether layer contains no compound. Ether was evaporated off and the crude sample was subjected to column chromatography (silica gel 100–200 mesh, 15% EtOAc–hexane) to afford the product in good yield. The ionic liquid was washed, dried and reused.

4.2.1. Data for compound 5a. Method A. Colorless viscous liquid. Yield=95%. IR (neat) ν_{max}: 3294, 3057, 2979, 2923, 1713, 1517, 1414, 1295, 1239, 1125, 1063, 909, 759, 713 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.52 (s, 1H), 5.72–5.86 (m, 1H), 5.59–5.63 (m, 2H), 4.99–5.09 (m, 2H), 4.55–4.57 (m, 1H), 4.19 (q, 4H), 2.85 (br s, 1H), 2.31–2.53 (m, 3H), 2.10–2.17 (m, 1H), 1.27 (t, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.7, 155.9, 136.4, 132.8, 128.5, 116.3, 63.1, 62.4, 61.9, 47.6, 37.6, 35.2, 14.5, 14.4. MS (LR-FAB): *m/z* calculated for $C_{14}H_{22}N_2O_4$ (M+1): 283.1658. Found: 283.1666 (M+1). Anal. Calc for $C_{14}H_{22}N_2O_4$ C, 59.56; H, 7.85; N, 9.92. Found C, 59.86; H, 7.94; N, 10.23.

4.2.2. Data for compound 5b. Method B. Colorless viscous liquid. Yield=80%. IR (neat) ν_{max}: 3296, 2981, 2934, 1732, 1689, 1468, 1411, 1297, 1109, 956 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.29 (s, 1H), 5.72–5.85 (m, 1H), 5.60–5.62 (m, 2H), 5.08 (s, 1H), 4.98–5.02 (m, 2H), 4.91–4.95 (m, 2H), 2.83 (s, 1H), 2.45–2.48 (m, 2H), 2.30–2.37 (m, 1H), 2.07–2.16 (m, 1H), 1.24–1.26 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.1, 156.6, 136.6, 133.1, 128.7, 116.4, 70.2, 69.8, 63.1, 47.8, 37.8, 37.6, 27.1, 22.3, 22.2, 17.6. HRMS (EI): *m/z* calculated for $C_{16}H_{26}N_2O_4$: 310.1893. Found: (M^+) 310.1895.

4.2.3. Data for compound 5c. Method A. Colorless viscous liquid. Yield=77%. IR (neat) ν_{max}: 3318, 2979, 2931, 1703, 1641, 1478, 1395, 1248, 1170, 950 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.16 (s, 1H), 5.77–5.79 (m, 1H), 5.61 (m, 2H), 4.97–5.07 (m, 2H), 4.45 (br s, 1H), 2.78 (s, 1H), 2.42–2.45 (m, 2H), 2.11 (m, 2H), 1.45 (s, 18H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.3, 156.8, 136.4, 133.2, 128.5, 116.8, 63.3, 62.2, 47.5, 35.9, 28.4, 26.9, 22.5, 22.1. HRMS (EI): *m/z* calculated for $C_{18}H_{30}N_2O_4$: 338. 2206. Found: (M^+) 338.2175.

4.2.4. Data for compound 7a. Method B. Colorless viscous liquid. Yield=90%. IR (neat) ν_{max}: 3433, 3175, 3067, 2954, 2923, 2851, 1769, 1697, 1604, 1506, 1429, 1249, 1130, 914, 770, 708 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.22 (br s, 1H), 7.37–7.75 (m, 5H), 5.73–5.75 (m, 1H), 5.66–5.69 (m, 2H), 5.02–5.11 (m, 2H), 4.58–4.61 (m, 1H), 2.89 –2.90 (m, 1H), 2.69–2.70 (m, 1H), 2.48–2.49 (m, 1H), 2.16–2.26 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.7, 151.6, 135.2, 132.7, 131.3, 128.8, 128.3, 127.9, 125.3, 117.1, 115.9, 59.8, 48.4, 37.6, 35.4. MS (LR-FAB): *m/z* calculated for $C_{16}H_{17}N_3O_2$ (M+1): 284.1399. Found: (M+1) 284.6529.

4.2.5. Data for compound 7b. Method B. Colorless viscous liquid. Yield=97%. IR (neat) ν_{max}: 3435, 3178, 3064, 2956, 2923, 2850, 1767, 1698, 1609, 1508, 1432, 1250, 1140, 916, 767, 718 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.06 (s, 1H), 7.29–7.50 (m, 5H), 5.74–5.79 (m, 1H), 5.65–5.72 (m, 2H), 4.99–5.09 (m, 2H), 4.65 (s, 2H), 4.48–4.55 (m, 1H), 2.82–2.84 (m, 1H), 2.63–2.72 (m, 1H), 2.34–2.42 (m, 1H), 2.09–2.29 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.7, 154.7, 135.3, 132.7, 128.5, 128.3, 128.2, 127.9, 116.9, 76.5, 64.5, 59.9, 48.4, 43.2, 42.7, 37.7, 35.3. MS (LR-FAB): *m/z* calculated for $C_{17}H_{19}N_3O_2$ (M+1): 298.1477. Found: (M+1) 298.20.

4.2.6. Data for compound 7c. Method B. Colorless viscous liquid. Yield=88%. IR (neat) ν_{max}: 3298, 2932, 1767, 1698, 1484, 1092, 956 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.59 (s, 1H), 5.79–5.82 (m, 1H), 5.70–5.73 (m, 2H), 5.04–5.07 (m, 2H), 4.48–4.56 (m, 1H), 3.85 (m, 1H), 2.86 (m, 1H), 2.71–2.74 (m, 2H), 2.65–2.68 (m, 2H), 1.66–1.76 (m, 10H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 155.4, 153.7, 135.7, 133.1, 128.7, 117.3, 60.2, 52.2, 48.8, 38.1, 35.6, 29.9, 29.7, 29.6, 26.1, 25.3. HRMS (EI): *m/z* calculated for $C_{16}H_{23}N_3O_2$: 289.1790. Found: (M^+) 289.1796.

4.2.7. Data for compound 7d. Method B. Colorless viscous liquid. Yield=85%. IR (neat) ν_{max}: 3302, 2982, 1728, 1698, 1396, 1180, 948 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.03 (s, 1H), 7.24–7.49 (m, 4H), 5.67 (m, 1H), 5.61 (m, 2H), 4.93–5.03 (m, 2H), 4.51 (s, 2H), 4.38–4.45 (m, 1H), 3.70 (s, 3H), 2.74 (m, 1H), 2.56–2.64 (m, 1H), 2.26–2.32 (m, 1H), 2.07–2.20 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.9, 153.8, 137.5, 135.1, 133.4, 132.6, 129.1, 128.6, 128.2, 118.1, 60.1, 52.3, 48.3, 42.5, 38.0, 35.1. HRMS (EI): *m/z* calculated for $C_{18}H_{21}N_3O_3$: 327.1583. Found: (M^+) 327. 1536.

4.2.8. Data for compound 7e. Method B. Colorless viscous liquid. Yield=95%. IR (neat) ν_{max}: 3297, 2980, 2932, 1767, 1685, 1458 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.01 (s, 1H), 7.21–7.01 (m, 4H), 5.67–5.73 (m, 1H), 5.60–5.65 (m, 2H), 4.93–5.02 (m, 2H), 4.53 (s, 2H), 4.40–4.46 (m, 1H), 2.75–2.76 (m, 1H), 2.56–2.64 (m, 1H), 2.32–2.34 (m, 1H), 2.25 (s, 3H), 2.02–2.16 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.1, 153.2, 137.9, 135.6, 133.0, 132.9, 129.6, 128.9, 128.6, 117.3, 60.1, 48.8, 42.9, 37.9, 35.7, 21.4. MS (FAB): *m/z* calculated for $C_{18}H_{21}N_3O_2$: 312.1634 (M+1). Found: 312. 21.

4.2.9. Data for compound 7f. Method B. Colorless viscous liquid. Yield=78%. IR (neat) ν_{max}: 3295, 3066, 2854, 1767, 1688, 1492, 1355, 1093, 916 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.82 (s, 1H), 7.25–7.34 (m, 4H), 5.74–5.80 (m, 1H), 5.68–5.72 (m, 2H), 5.01–5.10 (m, 2H), 4.60 (s, 2H), 4.47–4.53 (m, 1H), 2.80 (m, 1H), 2.64–2.73 (m, 1H), 2.33–2.39 (m, 1H), 2.12–2.27 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.8, 153.0, 135.5, 134.2, 131.3, 130.3, 130.1, 129.1, 128.7, 117.4, 60.1, 48.9, 42.8, 37.9, 35.7, 24.3, 13.9. HRMS (EI): *m/z* calculated for $C_{17}H_{18}N_3O_2Cl$ (M+2): 333.1088. Found: (M+2) 333.1092.

Acknowledgements

V.S.S. thanks Council of Scientific and Industrial Research, New Delhi for Junior Research Fellowship. Financial assistance from CSIR, New Delhi is gratefully acknowledged (Task Force Project CMM-005 on Specialty Chemicals). We thank Ms. Soumini Mathew and Ms. Viji S. for NMR and HRMS data reported in this paper.

References and notes

1. (a) Crimmins, M. T. *Tetrahedron* **1998**, *54*, 9229–9272. (b) Berecibar, A.; Grandjean, C.; Siriwardena, A. *Chem. Rev.* **1999**, *99*, 779–844. (c) Ogawa, S.; Morikawa, T. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1047–1050.
2. Corey, E. J.; Narasaka, K.; Shibasaki, M. *J. Am. Chem. Soc.* **1976**, *98*, 6417–6423.
3. (a) Kuang, R.; Ganguly, A. K.; Chan, T.-M.; Pramanik, B. N.; Blythin, D. J.; McPhail, A. T.; Saksena, A. K. *Tetrahedron Lett.* **2000**, *41*, 9575–9579. (b) Noble, S. A.; Beddal, N. E.; Beveridge, A. J.; Marr, C. L. P.; Mo, C. L.; Penn, C. R.; Storrer, R.; Woods, J. M. *Nucleosides Nucleotides* **1991**, *10*, 478–490.
4. (a) Surman, M. D.; Mulvihill, M. J.; Miller, M. J. *J. Org. Chem.* **2002**, *67*, 4115–4121. (b) Young, R. N. *Eur. J. Med. Chem.* **1999**, *34*, 671–685.
5. (a) Lillelund, V. H.; Jensen, H. H.; Liang, X.; Bols, M. *Chem. Rev.* **2002**, *102*, 515–554. (b) Trost, B. M.; VanVranken, D. L. *J. Am. Chem. Soc.* **1993**, *115*, 444–458.
6. (a) *Organometallics in Synthesis*; Schlosser, M., Ed.; Wiley: New York, 1994; Chapter 5, pp 383–461. (b) *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 1999; Chapter 24, pp 833–881. (c) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921–2943. (d) Trost, B. M. *Chem. Pharm. Bull.* **2002**, *50*, 1–14.
7. (a) Surman, M. D.; Miller, M. J. *Org. Lett.* **2001**, *3*, 519–521. (b) Mulvihill, M. J.; Surman, M. D.; Miller, M. J. *J. Org. Chem.* **1998**, *63*, 4874–4875.
8. Yao, M.-L.; Adiwidjaja, G.; Kaufmann, D. E. *Angew. Chem., Int. Ed.* **2002**, *41*, 3375–3378.
9. Luna, A. P.; Cesario, M.; Bonin, M.; Micouin, L. *Org. Lett.* **2003**, 4771–4774.
10. Surman, M. D.; Miller, M. J. *J. Org. Chem.* **2001**, *66*, 2466–2469.
11. (a) Kosugi, M.; Kumura, T.; Oda, H.; Migita, T. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3522–3529. (b) Oda, H.; Ito, K.; Kosugi, M.; Migita, T. *Chem. Lett.* **1994**, 1443–1444.
12. Diels, O.; Bolm, J. H.; Koll, W. *Justus Liebigs Ann. Chem.* **1925**, *443*, 242–262.
13. Gupta, R. C.; Raynor, C. M.; Stoodley, R. J.; Slawin, A. M. Z.; William, D. J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1773–1785.
14. (a) Yadav, J. S.; Reddy, B. V. S.; Sadasiv, K.; Satheesh, G. *Tetrahedron Lett.* **2002**, *43*, 9695–9697 see also 9703–9706. (b) Wang, S.-Y.; Ji, S. J.; Loh, T. P. *Synlett* **2003**, *15*, 2377–2379.
15. Radhakrishnan, K. V.; Sajisha, V. S.; Anas, S.; Syamkrishnan, K. *Synlett* **2005**, *15*, 2273–2276.
16. (a) *Ionic Liquids in Synthesis*; Wasserscheid, P., Welton, T., Eds.; Wiley-VCH: Germany, 2002. (b) Leveque, J. M.; Luche, J. L.; Pefrier, C.; Roux, R.; Bonrath, K. *Green Chem.* **2002**, *4*, 357–360.
17. Recent reviews on ionic liquids: (a) Dupont, J.; de Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002**, *102*, 3667–3692. (b) Zhao, H.; Malhotra, S. V. *Aldrichim. Acta* **2002**, *35*, 75. (c) Zhao, D.; Wu, M.; Kou, Y.; Min, E. *Catal. Today* **2002**, *74*, 157–189. (d) Olivier-Bourbigou, H.; Magna, L. *J. Mol. Catal. A: Chem.* **2002**, *182–183*, 419–437. (e) Sheldon, R. *Chem. Commun.* **2001**, *23*, 2399–2407. (f) Gordon, C. M. *Appl. Catal., A* **2001**, *222*, 101–117. (g) Earle, M. J.; Seddon, K. R. *Pure Appl. Chem.* **2000**, *72*, 1391–1398. (h) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3772–3789. (i) Welton, T. *Chem. Rev.* **1999**, *99*, 2071–2084.
18. (a) Hallberg, A.; Westerlund, C. *Chem. Lett.* **1993**, 1982. (b) Hatanaka, Y.; Hiyama, T. *Synlett* **1991**, *12*, 845–853. (c) Miyaura, N.; Yamada, K.; Suginome, H.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, *107*, 972–980.
19. Negishi, E., Ed.; Hand Book of Organopalladium Chemistry for Organic Synthesis; Wiley-Interscience: New York, 2002.
20. Bournaud, C.; Robic, D.; Bonin, M.; Micouin, L. *J. Org. Chem.* **2005**, *70*, 3316–3317.
21. Pineschi, M.; Moro, F. D.; Crotti, P.; Macchia, F. *Org. Lett.* **2005**, *17*, 3605–3607.
22. (a) Vince, R.; Hua, M.; Daluge, S.; Lee, F.; Shannon, W. M.; Lavelle, G. C.; Qualls, J.; Weislow, O. S.; Kiser, R.; Canonico, P. G.; Schultz, R. H.; Narayanan, V. L.; Mayo, J. G.; Shoemaker, R. H.; Boyd, M. R. *Biochem. Biophys. Res. Commun.* **1988**, *156*, 1046–1053. (b) Vince, R.; Hua, M. *J. Med. Chem.* **1990**, *33*, 17–21.