DOI: 10.1002/adsc.200505488

Palladium/Lewis Acid-Catalyzed Reactions of Bicyclic Hydrazines with Organostannanes: A General Methodology for the Stereoselective Synthesis of 3,4-Disubstituted Cyclopentenes

V. S. Sajisha, K. V. Radhakrishnan*

Organic Chemistry Section, Chemical Sciences Division, Regional Research Laboratory (C.S.I.R), Thiruvananthapuram – 695019, Kerala, India
Fax: (+91)-471-249-1712, e-mail: radhupreethi@rediffmail.com

Received: December 22, 2005; Revised: January 23, 2006; Accepted: February 20, 2006

Dedicated with respect to Professor Yoshinori Yamamoto, Tohoku University, Sendai, Japan on the occasion of his 63rd birthday.

Abstract: Pd/Lewis acid-catalyzed reactions of bicyclic hydrazines with organostannanes afforded the 3,4-disubstituted cyclopentenes in excellent yields. The reaction is milder and is the first general methodology developed for the stereoselective synthesis of *trans*, vicinal disubstituted cyclopentenes. The results show that organostannanes with easily functionalizable moieties can be efficiently utilized in the ring opening of bicyclic hydrazines leading to the stereoselective formation of 3,4-disubstituted cyclopentenes. The products, having a wide range of substituents, are important intermediates in the synthesis of biologically active molecules like cyclopentenyl nucleosides, glycosidase inhibitors etc.

Keywords: bicyclic hydrazines; disubstituted cyclopentenes; homogeneous catalysis; organostannanes; palladium

Introduction

Substituted cyclopentanes have been extensively utilized as synthons in the preparation of a number of biologically active molecules. For example, cyclopentenyl nucleosides such as carbovir have been shown to act as potential anti-HIV agents[1] and some of them are known to have potent *in vitro* antitrypanosomal activity.[2] 1,2-Disubstituted cyclopentanes are well known for their activity as small, potent potentiators of AMPA receptors[3] and COX-2 inhibitors.[4] Aminocyclopentane-based α-L-fucosidase inhibitors serve as novel therapeutic agents for treating inflammation and cancer.[5] Nikkomycins and polyoxins, a family of cyclopentene-derived molecules are used as nucleoside-type antibodies.[6] Mannostatins and trehazolins, a class of glycosidase inhibitors, are derived from substituted cyclopentanes.[7] Some hydrazinocyclopentitols itself are shown to be active as mannosidase inhibitors.[8] Polyhydroxycyclopentitol-containing natural products like pactamycin,[9] bacteriohopanetetrol,[10] funiculosin,[11] epoxyqueuosine,[12] keruffarides,[13] crasserides[14] and caryose[15] also belong to the substituted cyclopentane derivatives. Some of the biologically active substituted cyclopentanes are shown in Figure 1.

Various strategies have been adopted for the synthesis of substituted cyclopentane derivatives[16] starting from carbohydrates, inositols etc. In most of the reports, the synthetic strategy involves disubstituted cyclopentene as a key intermediate. Synthesis of disubstituted cyclopentenic intermediates is a challenging problem in synthetic organic chemistry since it allows access to a wide range of biologically active cyclopentanoids. However, there are no general methods available for the synthesis of 3,4-disubstituted cyclopentenes. Most of the reported syntheses involve several steps and usually result in low or moderate yields.

Functionalization of the unsaturated cyclopentane skeleton is a promising strategy towards substituted cyclopentanes. In this context, bicyclic hydrazines have been evaluated as versatile building blocks for the synthesis of disubstituted cyclopentenes. Earlier attempts for the desymmetrization of these substrates resulted in the formation of 3,5-disubstituted cyclopentenes.[17] In a few cases, 3,4-disubtituted cyclopentenes were observed as minor products from *meso*-bicyclic hydrazines[18] and *N*-acyl-nitroso hetero-Diels–Alder cycloadducts.[19] It is to be noted that 3,5-disubstituted cyclopentenes were formed as the major product in all these transformations. Hence it is of considerable interest to

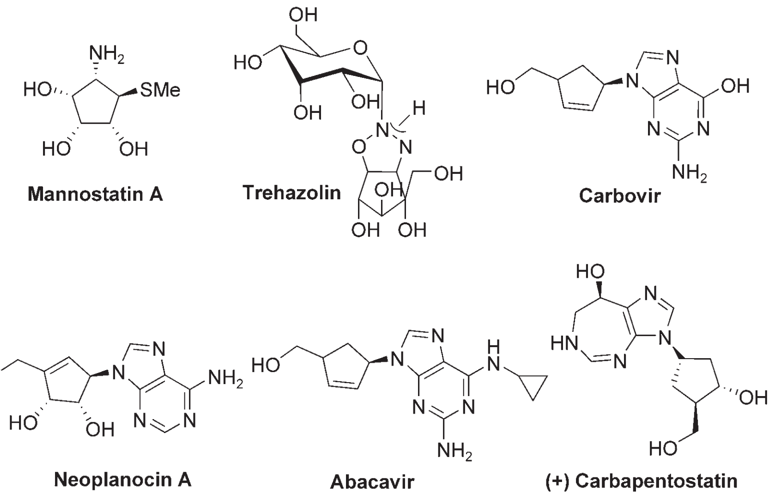
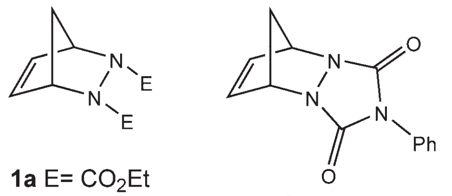


Figure 1. Biologically active substituted cyclopentanes.



1a E= CO_2Et

1b E= CO_2-*i*-Pr

1c E= CO_2-*t*-Bu

2

Figure 2. Bicyclic hydrazines studied.

develop a general and efficient methodology for the synthesis of 3,4-disubstituted cyclopentenes. Herein, we report an expedient synthesis of 3,4-disubstituted cyclopentenes by the palladium-catalyzed reaction of bicyclic hydrazines with organostannanes. The bicyclic hydrazines[20] selected for our studies are shown in Figure 2.

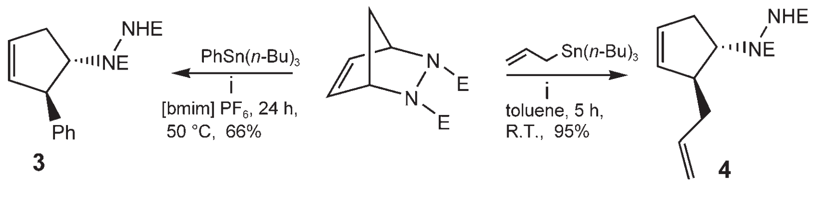
Results and Discussion

We have recently reported the Pd/Lewis acid-catalyzed reaction of allyltributylstannane with bicyclic hydrazines which afforded the 3-allyl-4-hydrazinocyclopentenes **4** in excellent yields. The role of ionic liquid, [bmim]PF_6, as a solvent as well as a promoter was also established by carrying out the reactions in the ionic liquid. Phenyltributylstannane was also found to react in the same manner yielding the phenyl-substituted hydrazinocyclopentene **3**.[21] The reaction is illustrated in Scheme 1.

In the present paper, we report the synthesis of more interesting and structurally diverse 3,4-disubstituted cyclopentenes. With the aim of exploiting the reactivity of organostannanes with bicyclic hydrazines, we investigated the palladium/Lewis acid-catalyzed reactions of 2-(tributylstannyl)furan and 2-(tributylstannyl)thiophene with bicyclic hydrazines. To the best of our knowledge, this is the first report on the single step, stereoselective synthesis of furyl- and thienyl-substituted hydrazinocyclopentenes.

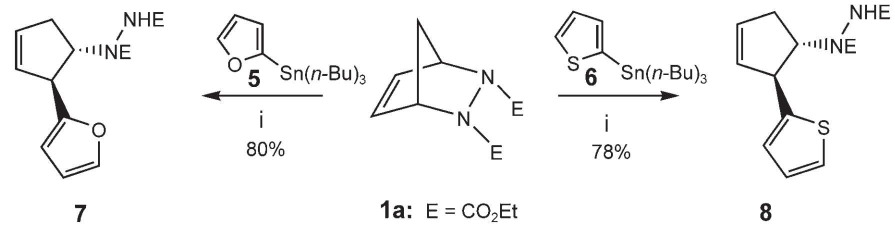
Our initial studies involved the reaction of bicyclic hydrazine **1a** with 2-(tributylstannyl)furan in the presence of $[Pd(allyl)Cl]_2$, dppe and $Sc(OTf)_3$. The reaction proceeded smoothly affording 3-(2-furyl)-4-hydrazinocyclopentene **7** in 80% yield. Similar reactivity was observed with **1a** and 2-(tributylstannyl)thiophene leading to the formation of thiophene-substituted hydrazinocyclopentene **8** in 78% yield. The reaction is shown in Scheme 2.

The structures of **7** and **8** were assigned based on spectral analysis and by comparison to the literature.[8,18] The



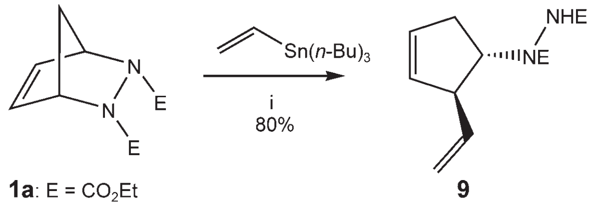
i = $[Pd(allyl)Cl]_2$ (5 mol %), dppe (10 mol %), $Sc(OTf)_3$ (2 mol %)

Scheme 1.



i = [Pd(allyl)Cl]$_2$ (5 mol %), dppe (10 mol %), Sc(OTf)$_3$ (2 mol %), toluene, 60 °C, 12 h

Scheme 2.



i = [Pd(allyl)Cl]$_2$ (5 mol %), dppe (10 mol %), Sc(OTf)$_3$ (2 mol %), toluene, 60 °C, 18 h

Scheme 3.

4-phenyl-1,2,4-triazoline-3,5-dione-derived tricyclic hydrazine **2** was also examined for its reactivity towards 2-(tributylstannyl)furan and 2-(tributylstannyl)thiophene and similar products were obtained. In solvents like toluene and THF, the rate of the reaction was found to be very low for the tricyclic hydrazine. On the other hand, the reactions were found to be high yielding in ionic liquid. The results of our investigations are summarized in Table 1.

Inspired by the reactivity of stannylfuran and stannylthiophene and the excellent yield of the reaction, we have carried out the ring-opening reaction of bicyclic hydrazine with vinyltributyltin. Interestingly, 3-vinyl-4-hydrazinocyclopentene **9** was formed in 80% yield (Scheme 3).

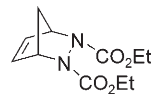
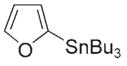
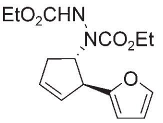
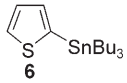
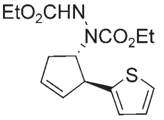
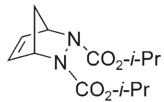
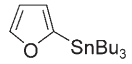
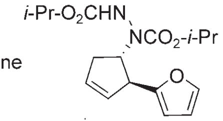
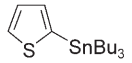
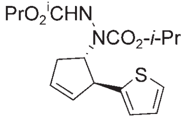
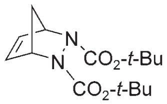
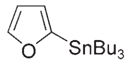
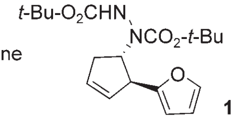
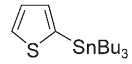
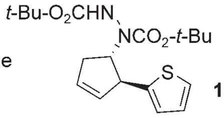
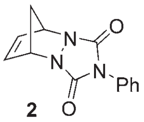
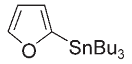
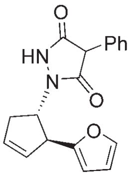
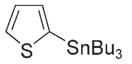
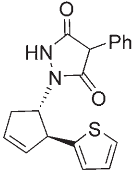
The mechanism of the reaction appears similar to the one proposed by Kaufmann and co-workers[18] in the palladium-catalyzed C–N bond cleavage of azabicyclic olefins in the hydroarylation reaction under Pd(OAc)$_2$/AsPh$_3$/HCOOH/Et$_3$N conditions in DMF/DMSO and is outlined in Scheme 4. Alternately the present reaction may involve the initial formation of a tin amide, which can be hydrolyzed in the work-up process.

Since the completion of this work, an article by Pineschi et al.[22] has appeared which describes the catalytic asymmetric ring opening of 1,3-cyclopentadiene-heterodienophile cycloadducts with dialkylzinc and trialkylaluminium reagents in the presence of copper-phosphoramidate catalyst. According to their report, the copper-phosphoramidate-catalyzed reaction of 3-azaoxabicyclo[2.2.1]-hept-5-enes with dialkylzinc afforded *trans*-1,2-hydroxamic acid. Except in the case of dimethylzinc, the reaction afforded ring opened products in 20 to 50% yield. In the case of trialkylaluminium, only tricyclic and tetracyclic Diels–Alder adducts afforded the ring opened product. Moreover, they could introduce only small alkyl groups like methyl, ethyl etc. to the cyclopentene moiety. It is noteworthy that our method, utilizing the [Pd(allyl)Cl]$_2$-dppe-Sc(OTf)$_3$ catalyst system afforded the *trans*-disubstituted derivatives in good yields. Our results show that organostannanes with easily functionalizable moieties can be efficiently utilized in the ring opening of bicyclic hydrazines leading to the stereoselective formation of 3,4-disusbtituted cyclopentenes.

Conclusions

In conclusion, we have developed a general and efficient methodology for the stereoselective synthesis of *trans*, vicinal disubstituted hydrazinocyclopentenes in excellent yields. This is the first report on the one-step stereoselective ring opening of bicyclic hydrazines with a variety of organostannanes. The described palladium/Lewis acid-mediated ring opening with the formation of a new carbon-carbon bond is a viable and general methodology for the synthesis of aza-functionalized substituted cyclopentanes under mild conditions. The synthesized molecules are amenable to a number of synthetic transformations and they can be used for the synthesis of cyclopentenyl nucleosides and glycosidase inhibitors. The results show that 3,4-disubstituted cyclopentenes with substituents ranging from allyl, phenyl, heteroaryl to vinyl can be synthesized easily under very mild conditions from easily available 1,3-cyclopentadiene-heterodienophile cycloadducts. The method described in this paper affords 3,4-disubstituted cyclopentenes in excellent yields under very mild conditions, irrespective of the bicyclic hydrazine. The double bond in the cyclopentene ring, furan and thiophene ring and the hydrazine moiety can be considered as latent functional groups. Transformations like dihydroxylation, Diels–Alder reaction, conversion of the hydrazine moiety to amine etc. will result in the formation of versatile synthons for the preparation of novel carbonucleosides, glycosidase inhibitors and other biologically active compounds. Further work in this line is in progress and will be reported in due course.

Table 1. Palladium/Lewis acid-catalyzed reaction of bicyclic hydrazines with 2-(tributylstannyl)furan and 2-(tributylstannyl)thiophene.[a]

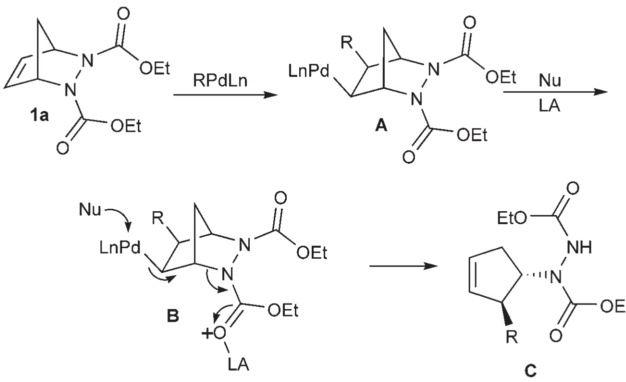
Entry	Substrate	Stannane	Solvent	Product	Yield [%]
1	 **1a**	 **5**	Toluene	 **7**	80
		 **6**	Toluene	 **8**	78
2	 **1b**	 **5**	Toluene	 **10**	85
		 **6**	Toluene	 **11**	75
3	 **1c**	 **5**	Toluene	 **12**	88
		 **6**	Toluene	 **13**	78
4	 **2**	 **5**	[bmim]PF$_6$	 **14**	78
		 **6**	[bmim]PF$_6$	 **15**	76

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

Experimental Section

General Methods

All reactions were conducted in oven-dried glassware. Solvents used for the experiments were distilled and dried as specified. Bicyclic hydrazines were prepared as per the literature procedures.[20] All other reagents were purchased from local suppliers. All reactions were monitored by TLC (silica gel 60 F254, 0.25 mm, Merck), visualization was effected with UV and/or by staining with Enholm yellow solution. Chromatography refers to open column chromatography on silica gel (100–200 mesh). NMR spectra were recorded at 300 (^{1}H) and 75 (^{13}C) MHz respectively on a Bruker Advance DPX-300 MHz. Chemical shifts are reported in δ (ppm) relative to TMS (^{1}H) or CDCl$_3$ (^{13}C) as internal standards. IR spectra were recorded on a Bomem MB series FT-IR spectrometer; absorptions are reported in cm^{-1}. Mass spectra were recorded under EI-HR-MS or FAB-LR-MS using a JEOL JMS 600H mass spectrometer.



Scheme 4.

Typical Experimental Procedure

Bicyclic hydrazine (2 equivs.), organostannane (1 equiv.), [Pd (allyl)Cl]$_2$ (5 mol %), dppe (10 mol %) were charged in a Wheaton vial, degassed with argon and the mixture was dissolved in dry toluene (4 mL). Sc(OTf)$_3$ (2 mol %) was added and the reaction mixture was stirred at 60 °C for 12 hours. The reaction mixture was diluted with dichloromethane (2 × 25 mL) and washed with aqueous KF solution (2 × 25 mL), followed by water (2 × 25 mL) and saturated brine (25 mL) solution. The organic layer was then dried over anhydrous sodium sulfate and the solvent was evaporated under vacuum. The residue on silica gel (100–200 mesh) column chromatography using 20% ethyl acetate in hexane afforded the product in good yield.

Compound 7

Following the general experimental procedure, the bicyclic hydrazine **1a** (100 mg, 0.42 mmol), 2-tributylstannylfuran (0.06 mL, 0.21 mmol), [Pd(allyl)Cl]$_2$ (4 mg, 5 mol %), dppe (8 mg, 10 mol %), Sc(OTf)$_3$ (2 mg, 2 mol %) in 4 mL dry toluene at 60 °C for 12 h gave the product as a colorless viscous liquid; yield: 51 mg (80%). IR (neat): ν_{max} = 3295, 3055, 2986, 2934, 2866, 1750, 1681, 1412, 1057, 1017, 942, 862, 754 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.31 (s, 1H), 6.52 (s, 1H), 6.27 (m, 1H), 6.09 (s, 1H), 5.82 (m, 1H), 5.70 (m, 1H), 4.94 (m, 1H), 4.19 (q, 4H), 4.11 (m, 1H), 2.65 (m, 2H), 1.26 (t, 6H); ^{13}C NMR (75 MHz, CDCl$_3$): δ = 156.8, 155.7, 141.2, 129.9, 128.7, 110.1, 105.1, 63.9, 62.3, 61.9, 57.4, 47.0, 34.8, 14.3; HR-MS (EI): *m/z* = 308.1377, calculated for $C_{15}H_{20}N_2O_5$ (M$^+$): 308.1372.

Compound 8

Following the general experimental procedure, the bicyclic hydrazine **1a** (100 mg, 0.42 mmol), 2-tributylstannylthiophene (0.06 mL, 0.21 mmol), [Pd(allyl)Cl]$_2$ (4 mg, 5 mol %), dppe (8 mg, 10 mol %), Sc(OTf)$_3$ (2 mg, 2 mol %) in 4 mL dry toluene at 60 °C for 12 h gave the product as a colorless viscous liquid; yield: 52 mg (78%). IR (neat): ν_{max} = 3295, 3060, 2980, 2935, 2866, 1750, 1680, 1515, 1475, 1412, 1126, 1057, 948, 759, 691 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.13 (d, J = 4.2 Hz, 1H), 6.91 (d, J = 3 Hz, 2H), 6.57 (s, 1H), 5.76 (m, 1H), 5.62 (m, 1H), 4.80 (m, 1H), 4.20 (q, 4H), 4.10 (m, 1H), 2.65 (m, 2H), 1.27 (t, 6H); ^{13}C NMR (75 MHz, CDCl$_3$): δ = 156.9, 155.8, 136.4, 133.0, 132.8, 129.9, 124.0, 123.5, 67.4, 63.0, 62.4, 49.0, 34.9, 14.4, 14.3; HR-MS (EI): *m/z* = 324.1160, calculated for $C_{15}H_{20}N_2O_4S$ (M$^+$): 324.1144.

Compound 9

Following the general experimental procedure, the bicyclic hydrazine 1a (100 mg, 0.42 mmol), vinyltributyltin (0.06 mL, 0.21 mmol), [Pd(allyl)Cl]$_2$ (4 mg, 5 mol %), dppe (8 mg, 10 mol %), Sc(OTf)$_3$ (2 mg, 2 mol %) in 4 mL dry toluene at 60 °C for 18 h gave the product as a colorless viscous liquid; yield: 44.5 mg (80%). IR (neat): ν_{max} = 3295, 3055, 2975, 2929, 1716, 1521, 1418, 1177, 1132, 1097, 1069, 914, 765, 719 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 6.31 (s, 1H), 5.71–5.82 (m, 1H), 5.51–5.63 (m, 2H), 4.94–5.05 (m, 2H), 4.56–4.58 (m, 1H), 4.12–4.13 (m, 4H), 3.34–3.44 (m, 1H), 2.41–2.51 (m, 2H), 1.22 (t, J = 5.4 Hz, 6H); ^{13}C NMR (75 MHz, CDCl$_3$): δ = 156.4, 155.9, 116.3, 115.1, 111.56, 64.2, 62.4, 51.1, 44.6, 35.0, 14.5, 13.6; HR-MS (EI): *m/z* = 268.1391, calculated for $C_{13}H_{20}N_2O_4$ (M$^+$): 268.1423.

Compound 10

Following the general experimental procedure, the bicyclic hydrazine **1b** (100 mg, 0.37 mmol), 2-tributylstannylfuran (0.06 mL, 0.19 mmol), [Pd(allyl)Cl]$_2$ (3 mg, 5 mol %), dppe (7 mg, 10 mol %), Sc(OTf)$_3$ (2 mg, 2 mol %) in 4 mL dry toluene at 60 °C for 12 h gave the product as a colorless viscous liquid; yield: 53 mg (85%). IR (neat): ν_{max} = 3295, 3061, 2980, 2941, 2883, 1750, 1681, 1510, 1469, 1304, 1240, 1178, 1109, 1040, 960, 926, 765, cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.31 (s, 1H), 6.42 (s, 1H), 6.27 (m, 1H), 6.09 (s, 1H), 5.80 (m, 1H), 5.71 (m, 1H), 4.98 (m, 1H), 4.90 (m, 2H), 4.07 (s, 1H), 2.63 (m, 2H), 1.25 (d, 12H); ^{13}C NMR (75 MHz, CDCl$_3$): δ = 156.6, 155.9, 141.3, 136.4, 130.0, 116.3, 111.1, 110.1, 70.1, 69.7, 63.8, 47.1, 34.9, 22.1, 22.0, 21.9; HR-MS (EI): *m/z* = 337.1768, calculated for $C_{17}H_{24}N_2O_5$ (M + 1): 337.1717.

Compound 11

Following the general experimental procedure, the bicyclic hydrazine **1b** (100 mg, 0.37 mmol), 2-tributylstannylthiophene (0.06 mL, 0.19 mmol), [Pd(allyl)Cl]$_2$ (3 mg, 5 mol %), dppe (7 mg, 10 mol %), Sc(OTf)$_3$ (2 mg, 2 mol %) in 4 mL dry toluene at 60 °C for 12 h gave the product as a colorless viscous liquid; yield: 49 mg (75%). IR (neat): ν_{max} = 3301, 3060, 2980, 2935, 2877, 1744, 1687, 1515, 1378, 1240, 1177, 1103, 1034, 954, 914, 828, 759, 697 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.13 (m, 1H), 6.91 (d, J = 3.9 Hz, 2H), 6.41 (s, 1H), 5.83 (m, 1H), 5.76 (m, 1H), 4.96 (m, 2H), 4.84 (m, 1H), 4.28 (s, 1H), 2.61 (m, 2H), 1.26 (d, 12H); ^{13}C NMR (75 MHz, CDCl$_3$): δ = 156.5, 155.8, 132.3, 129.9, 126.7, 124.0, 123.5, 70.1, 69.8, 49.0, 34.9, 22.1, 22.0; HR-MS (E1): m/z = 352.1462, calculated for $C_{17}H_{24}N_2O_4S$ (M$^+$): 352.1457.

Compound 12

Following the general experimental procedure, the bicyclic hydrazine **1c** (50 mg, 0.17 mmol), 2-tributylstannylfuran (0.03 mL, 0.08 mmol), $[Pd(allyl)Cl]_2$ (2 mg, 5 mol %), dppe (3 mg, 10 mol %), $Sc(OTf)_3$ (1 mg, 2 mol %) in 3 mL dry toluene at 60 °C for 12 h gave the product as a colorless viscous liquid; yield: 27 mg (88%). IR (neat): ν_{max} = 3318, 3060, 2980, 2935, 1744, 1688, 1550, 1481, 1452, 1389, 1366, 1246, 1155, 1046, 1012, 948, 851, 754 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (s, 1H), 6.43 (s, 1H), 6.27 (s, 1H), 6.09 (s, 1H), 5.61–5.81 (m, 2H), 4.89 (s, 1H), 4.02 (s, 1H), 2.58 (m, 2H), 1.47 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.2, 155.6, 141.2, 130.2, 116.16, 110.2, 108.9, 105.1, 81.2, 63.7, 47.2, 37.6, 35.0, 28.2, 26.8, 26.6, 22.6; HR-MS (E1): m/z = 365.1912, calculated for $C_{19}H_{28}N_2O_5$ (M + 1): 365.1998.

Compound 13

Following the general experimental procedure, the bicyclic hydrazine **1c** (50 mg, 0.17 mmol), 2-tributylstannylthiophene (0.03 mL, 0.08 mmol), $[Pd(allyl)Cl]_2$ (2 mg, 5 mol %), dppe (3 mg, 10 mol %), $Sc(OTf)_3$ (1 mg, 2 mol %) in 4 mL dry toluene at 60 °C for 12 h gave the product as a colorless viscous liquid; yield: 25 mg (78%). IR (neat): ν_{max} = 3309, 3058, 2980, 2938, 1748, 1685, 1475, 1368, 1245, 1155, 1015, 948, 850, 754 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.13 (d, *J* = 5.4 Hz, 1H), 6.92 (d, *J* = 3.6 Hz, 2H), 6.49 (s, 1H), 5.76–5.83 (m, 2H), 4.76 (s, 1H), 4.24 (s, 1H), 2.51–2.64 (m, 2H), 1.47 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.6, 155.9, 132.5, 127.7, 125.6, 123.1, 122.6, 81.3, 64.0, 49.0, 37.8, 34.9, 28.3, 26.8, 26.5, 22.7; HRMS (EI): *m/z* = 381.1774, calculated for $C_{19}H_{28}N_2O_4S$ (M + 1): 381.1770.

Compound 14

The bicyclic hydrazine **2** (100 mg, 0.41 mmol), 2-tributylstannylfuran (0.07 mL, 0.21 mmol), $[Pd(allyl)Cl]_2$ (4 mg, 5 mol %), dppe (8 mg, 10 mol %) and $Sc(OTf)_3$ (2 mg, 2 mol %) were taken up in 3 mL ionic liquid $[bmim]PF_6$ and stirred at 60 °C for 12 h. The reaction mixture was extracted several times with diethyl ether and the solvent was evaporated off. The crude sample on silica gel column chromatography using 25% EtOAc/hexane afforded the product as a colorless viscous liquid; yield: 50 mg (78%). IR (neat): ν_{max} = 3352, 3060, 2958, 2923, 2854, 1681, 1595, 1578, 1504, 1412, 1320, 1149, 1012, 943, 868, 725, 668 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.51 (s, 1H), 7.50 (m, 2H), 7.39 (m, 3H), 7.31 (d, *J* = 0.9 Hz, 1H), 6.25 (m, 1H), 6.14 (d, 1H), 5.85 (m, 1H), 5.81 (m, 1H), 5.04 (m, 1H), 4.28 (s, 1H), 2.77 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.2, 151.8, 141.5, 130.2, 129.68, 128.6, 126.8, 125.0, 116.2, 113.3, 110.2, 104.9, 58.5, 48.5, 35.1; LR-MS (FAB): *m/z* = 310.12, calculated for $C_{17}H_{15}N_3O_3$ (M + 1): 310.1113.

Compound 15

The bicyclic hydrazine **2** (100 mg, 0.41 mmol), 2-tributylstannylthiophene (0.07 mL, 0.21 mmol), $[Pd(allyl)Cl]_2$ (4 mg, 5 mol %), dppe (8 mg, 10 mol %) and $Sc(OTf)_3$ (2 mg, 2 mol %) were taken up in 3 mL ionic liquid $[bmim]PF_6$ and stirred at 60 °C for 12 h. The reaction mixture was extracted several times with diethyl ether and the solvent was evaporated off. The crude sample on silica gel column chromatography using 25% EtOAc/hexane afforded the product as a white solid; yield: 51 mg (76%). IR (KBr): ν_{max} = 3350, 3061, 2958, 2924, 2854, 1682, 1595, 1579, 1320, 1148, 1012, 943, 868, 725, 668 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ = 8.52 (s, 1H), 7.41 (m, 5H), 7.16 (d, *J* = 5.1 Hz, 1H), 6.92 (m, 2H), 5.91 (m, 1H), 5.85 (m, 1H), 4.83 (m, 1H), 4.44 (m, 1H), 2.74 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.1, 151.7, 144.7, 131.1, 130.7, 128.7, 127.8, 127.4, 126.7, 125.9, 124.5, 123.1, 123.0, 63.7, 47.3, 33.9; LR-MS (FAB): *m/z* = 326.03, calculated for $C_{17}H_{15}N_3O_2S$ (M + 1): 326.0885.

Acknowledgements

VSS thanks Council of Scientific and Industrial Research (CSIR), Government of India for Junior Research Fellowship. The authors thank Council of Scientific and Industrial Research (CSIR), Government of India for financial assistance (Task Force Project-CMM-005 on Specialty Chemicals). Thanks are due to one of the referees for suggesting the alternate mechanism involving the formation of tin amide.

References and Notes

[1] a) R. Vince, M. Hua, S. Daluge, F. Lee, W. M. Shannon, G. C. Lavelle, J. Qualls, O. S. Weislow, R. Kiser, P. G. Canonico, R. H. Schultz, V. L. Narayanan, J. G. Mayo, R. H. Shoemaker, M. R. Boyd, *Biochem. Biophys. Res. Commun*. **1988**, *156*, 1046–1053; b) R. Vince, M. Hua, *J. Med. Chem*. **1990**, *33*, 17–21.

[2] J. Guo, Y. Q. Wu, D. Rattendi, C. J. Bacchi, P. M. Woster, *J. Med. Chem*. **1995**, *38*, 1770–1777.

[3] T. A. Shepherd, J. A. Aikins, D. Bleakman, B. E. Cantrell, J. P. Rearick, R. L. Simon, E. C. R. Smith, G. A. Stephenson, D. M. Zimmerman, A. Mandelzys, K. R. Jarvie, K. Ho, M. Deverill, R. K. Kamboj, *J. Med. Chem*. **2002**, *45*, 2101–2111.

[4] A. Balsamo, I. Coletta, A. Guglielmotti, C. Landolfi, F. Mancini, A. Martinelli, C. Milanese, F. Minutolo, S. Nencetti, E. Orlandini, M. Pinza, S. Rapposelli, A. Rosello, *Eur. J. Med. Chem*. **2003**, *38*, 157–168.

[5] a) P. G. Schultz, R. A. Lerner, *Science* (Washington, D. C.) **1995**, *269*, 1835; b) R. A. Lerner, S. J. Benkovic, P. G. Schultz, *Science* (Washington, D. C.) **1991**, *252*, 659; c) N. R. Thomas, *Natl. Prod. Rep*. **1996**, 479; d) *Carbohydrate antigens*, (Eds.: P. J. Garegg, A. A. Lindberg), ACS Symposium Series 519, Washington, D. C., **1993**; e) E. E. Simanek, G. J. McGarvey, J. A. Jablonowski, C.-H. Wong, *Chem. Rev*. **1998**, *98*, 833.

[6] a) H. Hagenmaier, A. Keckeisen, H. Zähner, W. A. König, *Liebigs Ann. Chem*. **1979**, 1494; b) H. Hagenmaier, A. Keckeisen, W. Dehler, H. P. Fiedler, H. Zähner, W. A. König, *Liebigs Ann. Chem*. **1981**, 1018; c) W. A. König, W. Hass, W. Dehler, H. P. Fiedler, H. Zähner, *Liebigs Ann. Chem*. **1980**, 622; d) K. Kobinata, M. Uramoto,

M. Nishii, H. Kusakabe, G. Nakamura, K. Isono, *Agric. Biol. Chem.* **1980**, *44*, 1709; e) M. Uramoto, K. Kobinata, K. Isono, T. Higashijima, T. Miyazawa, E. E. Jenkins, J. A. McCloskey, *Tetrahedron*, **1982**, *38*, 1599.

[7] a) K. W. Moremen, R. B. Trimble, A. Herscoviks, *Glycobiology* **1994**, *4*, 133; b) P. F. Daniel, B. Winchester, C. D. Warren, *Glycobiology* **1994**, *4*, 551; c) A. Berecibar, C. Grandjean, A. Siriwardena, *Chem. Rev.* **1999**, *99*, 779–844.

[8] C. Bournaud, D. Robic, M. Bonin, L. Micouin, *J. Org. Chem*. **2005**, *70*, 3316–3317.

[9] a) A. D. Argoudelis, H. K. Jahnke, J. A. Fox, *Antimicrob. Agents. Chemother*. **1961**, *3*, 191.

[10] M. Rohmer, B. Sutter, H. Sahm, *J. Chem. Soc. Chem. Commun*. **1989**, 1471.

[11] K. Ando, S. Suzuki, T. Saeki, G. Tamura, K. Arima, *J. Antibiot*. **1969**, *22*, 189.

[12] H. Kersten, *Biofactors* **1988**, *1*, 27.

[13] M. Ishibashi, C.-M. Zeng, J. Kabayashi, *J. Nat. Prod*. **1993**, *56*, 1856.

[14] V. Constantino, E. Fattorusso, A. Mangoni, *J. Org. Chem*. **1993**, *58*, 186.

[15] M. Adinolfi, M. M. Corsaro, C. De Castro, A. Evidente, R. Lanzetta, A. Molinaro, M. Parrilli, *Carbohydr. Res.* **1996**, *284*, 111.

[16] a) V. H. Lillelund, H. H. Jensen, X. Liang, M. Bols, *Chem. Rev.* **2002**, *102*, 515; b) B. M. Trost, D. L. Van Vranken, *J. Am. Chem. Soc*. **1993**, *115*, 444; c) G. Hu, A. Vasella, *Helv. Chim. Acta* **2004**, *87*, 2405; d) G. Hu, M. Zimmermann, C. V. Ramana, A. Vasella, *Chem. Commun.* **2003**, 952; e) S. Ogawa, T. Morikawa, *Eur. J. Org. Chem*. **2000**, 1759.

[17] A. Perez Luna, M. Cesario, M. Bonin, L. Micouin, *Org. Lett*. **2003**, *25*, 4771–4774.

[18] M.-L. Yao, G. Adiwidjaja, D. E. Kaufmann, *Angew. Chem. Int. Ed*. **2002**, *41*, 3375–3378.

[19] a) M. D. Surman, M. J. Miller, *J. Org. Chem*. **2001**, *66*, 2466–2469; b) M. D. Surman, M. J. Mulvihill, M. J. Miller, *J. Org. Chem*. **2002**, *67*, 4115–4121.

[20] a) O. Diels, J. H. Blom, W. Knoll, *Justus Liebigs Ann. Chem*. **1925**, *443*, 242–262; b) J. E. Herweh, M. F. Richard, *Tetrahedron Lett*. **1973**, 2101–2104.

[21] K. V. Radhakrishnan, V. S. Sajisha, S. Anas, K. S. Krishnan, *Synlett* **2005**, 2273–2276.

[22] M. Pineschi, F. D. Moro, P. Crotti, F. Macchia, *Org.Lett*. **2005**, *17*, 3605–3607.