Novel concise ring closure leading to bridged ten-membered ring compounds

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An unusual TBAF-mediated intramolecular cyclisation of diallylsilane derivatives 3 and 12 provided bicyclo[6.2.2]-dodecanes 5 and 13 in good yields.

The taxol derivatives have attracted the attention of synthetic chemists due to their novel mode of action and the complexity of their structures.¹ So far, several groups have achieved the total synthesis of taxol² and numerous synthetic methods have



been developed for the construction of the key bicyclic (BC ring) system. However, assembly of the eight-membered ring (B ring) needs multiple steps owing to its highly oxygenated structural features and, therefore, the establishment of a novel and concise route is highly desirable. In order to achieve an efficient construction of the B ring framework, we have been studying various intramolecular cyclisations.³ In particular, cyclisation reactions employing allylsilanes^{4,5} attracted our attention. During our investigations, we found that an unusual cyclisation took place when the diallylsilanes **3** and **12** were treated with TBAF, leading to the formation of the bridged tenmembered ring compounds **5** and **13**, respectively. Herein we describe the outcome of this novel TBAF-promoted cyclisation and the structural determination of the cyclised products.

The synthesis of substrate **3** is summarized in Scheme 1. The alcohol 1^{3a} was treated with BuLi and TMSCl in the presence of TMEDA to give the *C*- and *O*-silylated product, which was reacted with 2 M H₂SO₄ to furnish the diallylsilane **2** as a mixture of diastereoisomers (diastereoselection 3 : 1). Oxidation of **2** with a catalytic amount of tetrapropylammonium perruthenate (TPAP) and NMO⁶ in CH₂Cl₂ afforded the desired aldehyde **3**.

First of all, 3 was subjected to the Hosomi-Sakurai reaction⁴ in the presence of Lewis acids,7 that is, the solution of material in solvent was treated with 1.1-3.0 equiv. of Lewis acid. Contrary to our expectations, reactions with TiCl₄ or BF₃·OEt₂ did not provide the cyclised compound 4, but brought about rapid decomposition of 3 (Table 1; entries 1 and 2); with LiBF₄ and HF·Py, compound 3 was recovered (entries 3 and 4). However, the α -carbon of the allylsilane moiety of **3** added as a nucleophile to the aldehyde in the presence of TBAF yielding the bicyclic products 5^8 in fair to good yield (entries 5–8). It is important to note that this reaction proceeds with a catalytic amount of TBAF (0.05 equiv.) at room temperature for 1 h to afford 5 in 47% yield (entry 5). Moreover, the addition of 4 Å molecular sieves gave the best result and 4 was obtained in 79% yield (entry 7). The ten-membered structure (the so-called dihydro[6]paracyclophane) of 5, obtained as a single isomer,



Scheme 1 Reagents and conditions: i, BuLi, TMSCI, TMEDA, THF, 0 °C, then 2 M H_2SO_4 (93%); ii, 20 mol% TPAP, NMO, 4 Å molecular sieves, CH_2Cl_2 , rt (71%); iii, see Table 1.

was suggested by the absence of absorptions due to the conjugated diene in the UV spectrum.

The cyclisation of the substituted material 12 was next investigated under the same conditions as above. The assembly of 12 is depicted in Scheme 2. The coupling reaction of the aldehyde 6^9 and the vinyl iodide 7^{10} with 2.2 equiv. of Bu^tLi afforded the alcohol 8 in 84% yield. Methylation of 8 followed by desilylation of 9 gave the alcohol 10. Upon treatment of 10 as above, the diallylsilanes 11 were obtained as a mixture of diastereoisomers (diastereoselection 13:1). Oxidation of 11 with TPAP as above afforded the aldehyde 12, which was converted into the bridged ten-membered ring products 13^{11} as a 14:1 mixture of two diastereoisomers with 1.1 equiv. of TBAF at room temperature in 66% yield.

The structure of the product 13 was determined by X-ray analysis (Fig. 1), after its conversion into the ketone 14^{12}

Table 1 Reactions of 3 with various Lewis acids or TBAF

Entry	Reagent (equiv.)	Solvent	T/°C	t∕h	Yield(%) ^a
1	TiCl ₄ (1.1)	CH ₂ Cl ₂	-78	1.0	0
2	BF ₃ ·OEt ₂ (1.5)	CH_2Cl_2	$-78 \rightarrow 0$	4.0	0
3	$LiBF_4$ (1.1)	THF	$0 \rightarrow rt$	7.0	0
4	HF·Py (1.1)	THF	$0 \rightarrow rt$	7.0	0
5	$TBAF^{b}(0.05)$	THF	rt	1.0	47
6	$TBAF^{b}(1.0)$	THF	rt	0.7	44
7	$TBAF^{b,c}$ (3.0)	THF	rt	0.3	79
8	$\text{TBAF}^{b,c}$ (3.0)	MeCN	rt	1.0	38
. T 1	. 1 . 11 . 10		1	4 %	

 a Isolated yield. b 1.0 M THF solution was used. c 4 Å molecular sieves were added.



Scheme 2 Reagents and conditions: i, But Li, THF, -78 °C (84%); ii, MeI, NaH, DMF, 0 °C \rightarrow rt (96%); iii, TBAF, THF, rt (94%); iv, BuLi, TMSCI, TMEDA, THF, 0 °C, then 10% KHSO₄ (94%); v, 20 mol% TPAP, NMO, 4 Å molecular sieves, CH₂Cl₂, rt (77%), vi, TBAF, THF, rt (66%); vii, 20 mol% TPAP, NMO, 4 Å molecular sieves, CH₂Cl₂, rt (95%).

obtained as a single stereoisomer. It is well documented by Birch that cyclopentadienyl anions react in the middle position.¹³

In summary, the Hosomi–Sakurai type reaction of **3** and **12** possessing the diallylsilane moiety afforded the bicyclic compounds **5** and **13** under mild conditions. We thank Dr C. Kabuto, Instrumental Analysis Center, Faculty of Science, Tohoku University, for the X-ray analysis of **14**.

Notes and references

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- 2 For a recent total synthesis: K. Morihara, R. Hara, S. Kawahara, T. Nishimori, N. Nakamura, H. Kusama and I. Kuwajima, J. Am. Chem. Soc., 1998, 120, 12980 and references therein.



Fig. 1 Molecular structure of 14.

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- 7 EtAlCl₂, AlCl₃, SnCl₄ and TBDMSOTf were also investigated in these reactions, however, neither **4** nor **5** was obtained.
- 8 Selected data for 5: $\delta_{\rm H}(300$ MHz, CDCl₃) 1.17 (s, 3H), 1.35–1.59 (m, 4H), 1.84–1.99 (m, 2H), 2.90–3.01 (m, 1H), 3.11 (dt, *J* 4.8, 3.2, 1H), 3.79 (dd, *J* 8.8, 3.2, 1H), 5.25 (ddd, *J* 11.6, 9.2, 7.6, 1H), 5.31 (d, *J* 11.6 Hz), 5.71 (ddd, *J* 9.6, 5.2, 1.6 Hz), 5.81 (dd, *J* 9.6, 1.6 Hz), 5.83–5.92 (m, 2H); $\delta_{\rm C}$ (75 MHz, CDCl₃) 137.3, 137.2, 136.0, 128.7, 126.0, 123.8, 77.6, 44.5, 40.0, 31.1, 29.6, 25.9, 25.6.
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- Selected data for 13: δ_H(300 MHz, CDCl₃): 0.79 (s, 3H), 0.93–0.99 (m, 4H), 1.21 (s, 3H), 1.40–1.60 (br s, 1H), 1.98 (dd, J 15.0, 8.8 Hz), 3.08–3.13 (m, 1H), 3.20 and 3.25 (each s, 2.8H and 0.2H), 3.99 (dd, J 8.8, 2.2 Hz), 4.67 (dd, J 9.2, 1.1 Hz), 5.09 (dd, J 12.5, 9.2 Hz), 5.52 (dd, J 12.5, 1.1 Hz), 5.70–5.90 (m, 4H); m/z 230 (M⁺ – 18).
- 12 Crystal data for 14: $C_{16}H_{22}O_2$, plates, mp 34–35 °C, triclinic, $P\overline{1}$, a = 7.641(1), b = 15.890(3), c = 6.3477(9) Å, $\alpha = 96.66(1)$, $\beta = 109.31(1)$, $\gamma = 99.48(1)^\circ$, V = 705.3(2) Å³, Z = 2, $\mu = 0.75$ cm⁻¹, $D_c = 1.169$ g cm⁻³, F000 = 272, T = 150 K, R, Rw = 0.039, 0.038 for 2302 absorption–corrected reflections with $I > 3.10 \sigma$ (I). CCDC 182/1220. see http://www.rsc.org/suppdata/cc/1999/893/ for crystallographic files in .cif format.
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