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

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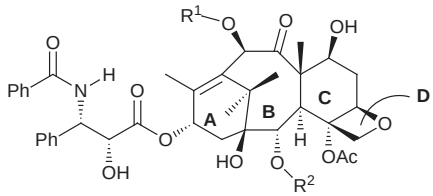
An unusual TBAF-mediated intramolecular cyclisation of diallylsilane derivatives 3 and 12 provided bicyclo[6.2.2]-dodecanes 5 and 13 in good yields.

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 taxol[2] and numerous synthetic methods have

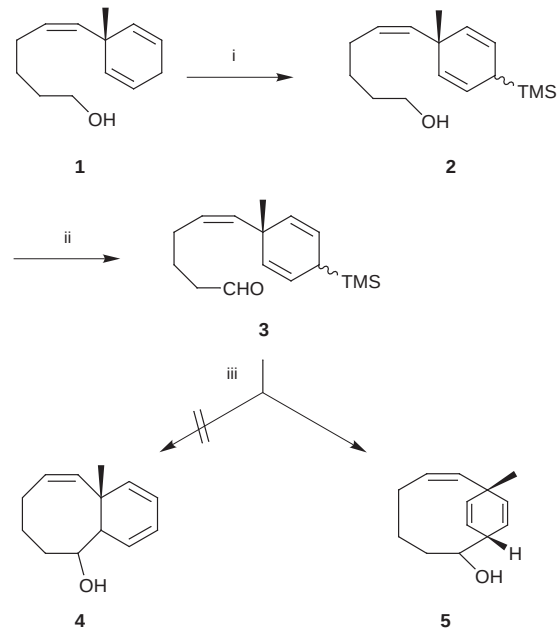


Taxol R^1 = Ac, R^2 = Bz
Taxotere R^1 = H, R^2 = Boc

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 ten-membered 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 H_2SO_4 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 NMO[6] in CH_2Cl_2 afforded the desired aldehyde **3**.

First of all, **3** was subjected to the Hosomi–Sakurai reaction[4] 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 $TiCl_4$ or $BF_3{\cdot}OEt_2$ did not provide the cyclised compound **4**, but brought about rapid decomposition of **3** (Table 1; entries 1 and 2); with $LiBF_4$ 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, TMSCl, 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.

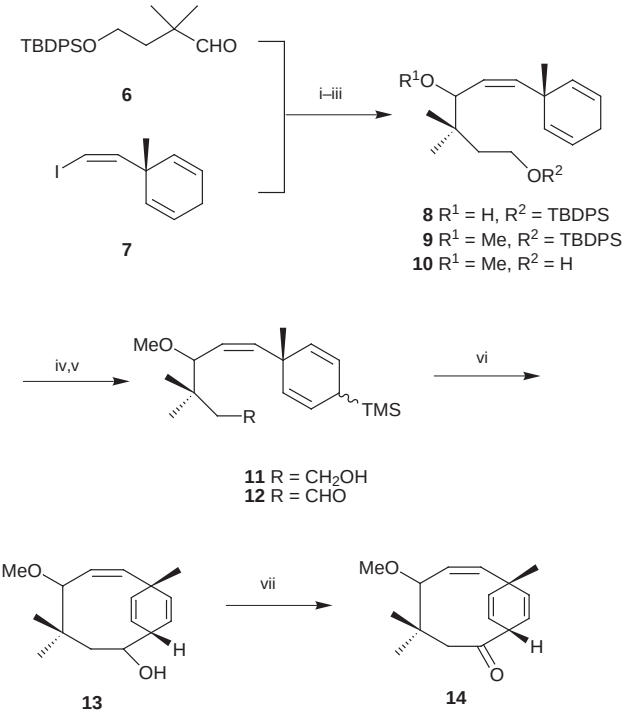
The cyclisation of the substituted material **12** was next investigated under the same conditions as above. The assembly of **12** is depicted in Scheme 2. The coupling reaction of the aldehyde **6**[9] and the vinyl iodide **7**[10] with 2.2 equiv. of Bu^{t}Li afforded the alcohol **8** in 84% yield. 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_2Cl_2	−78	1.0	0
2	$BF_3{\cdot}OEt_2$ (1.5)	CH_2Cl_2	−78 → 0	4.0	0
3	$LiBF_4$ (1.1)	THF	0 → rt	7.0	0
4	HF·Py (1.1)	THF	0 → 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	TBAF[b,c] (3.0)	MeCN	rt	1.0	38

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



Scheme 2 *Reagents and conditions*: i, Bu^t Li, THF, −78 °C (84%); ii, MeI, NaH, DMF, 0 °C → rt (96%); iii, TBAF, THF, rt (94%); iv, BuLi, TMSCl, TMEDA, THF, 0 °C, then 10% $KHSO_4$ (94%); v, 20 mol% TPAP, NMO, 4 Å molecular sieves, CH_2Cl_2, rt (77%), vi, TBAF, THF, rt (66%); vii, 20 mol% TPAP, NMO, 4 Å molecular sieves, CH_2Cl_2, 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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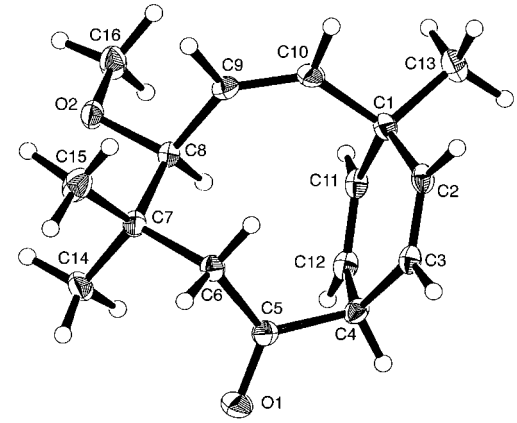

Fig. 1 Molecular structure of **14**.

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7 $EtAlCl_2$, $AlCl_3$, $SnCl_4$ and TBDMSOTf were also investigated in these reactions, however, neither **4** nor **5** was obtained.

8 *Selected data* for **5**: δ_H(300 MHz, $CDCl_3$) 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); δ_C (75 MHz, $CDCl_3$) 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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11 *Selected data* for **13**: δ_H(300 MHz, $CDCl_3$): 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, $P\bar{1}$, a = 7.641(1), b = 15.890(3), c = 6.3477(9) Å, α = 96.66(1), β = 109.31(1), γ = 99.48(1)°, V = 705.3(2) Å^3, Z = 2, μ = 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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