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Rearrangements of 2,6-Diaryl-3,7-dioxabicyclo[3.3.0]octane Lignans[1] Reactions of Paulownin and Wodeshiol with Triethylsilane and BF_3-Etherate

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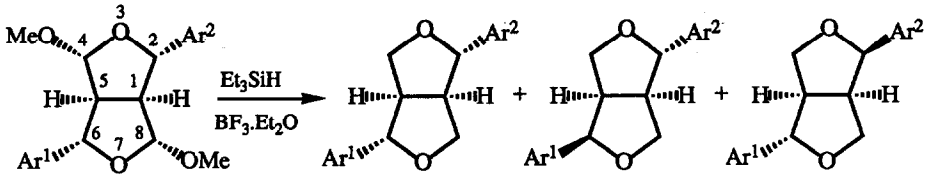
Abstract:

Paulownin on treatment with triethylsilane and BF_3-etherate reacts in a similar manner to gmelinol, giving an aryltetralin as the product. In contrast, wodeshiol under the same conditions rearranges to two isomeric tetrahydropyran derivatives, the structures of which have been deduced on the basis of their ^1H and ^{13}C n.m.r. spectra, including NOE and spin decoupling experiments.

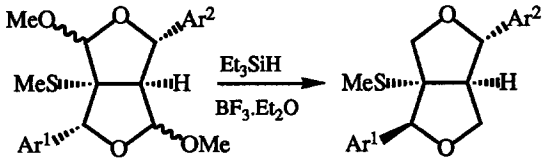
We have previously shown that triethylsilane and BF_3-etherate can be used to reduce acetals such as (1) and (2) to the corresponding cyclic ethers[2] (Scheme 1). We have also shown that this reagent converts either arboreol (3) or gummadiol (4) into a mixture of paulownin (5) and isopaulownin (6).[3] Treatment of gmelinol (7), however, with $Et_3SiH/BF_3.Et_2O$ gives as the major product the aryltetralin (8).[1] Furthermore, we have now shown that treatment of paulownin (5) with this reagent gives an analogous rearrangement product (9) (Scheme 2). This product, m.p. 116°, was obtained in 85% yield, after allowing for recovered paulownin, and gave very similar ^1H and ^{13}C n.m.r. spectra to (8) (see Tables 1 and 2).

Treatment of wodeshiol (12) with 2.2 equivalents of $BF_3.Et_2O$ followed by a large excess of triethylsilane gave two products (13) and (14) along with unreacted wodeshiol. Both products were obtained in 44% yield each, after allowing for recovered wodeshiol, and both gave a molecular ion at *m/z* 388 in their mass spectra. On acetylation both products gave diacetates having M^+ 472. The ^1H and ^{13}C n.m.r. spectra of these compounds are presented in Tables 3 and 4.

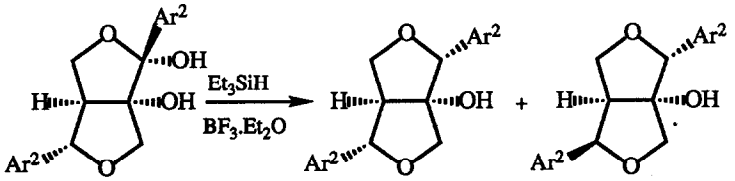
The ^{13}C n.m.r. spectra of (13) - (16) showed that the aromatic rings were intact and largely unaffected by the reaction. The ^{13}C n.m.r. spectra also showed that (13) amd (14)



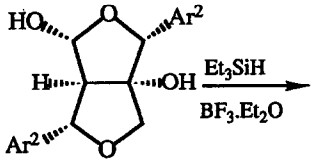
(1)



(2)



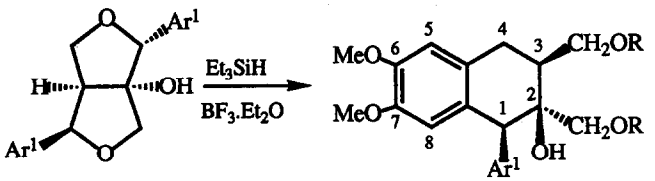
(3) (5) (6)



(4) (5) + (6)

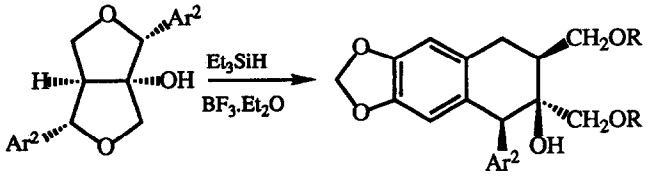
Scheme 1

Ar^1 = 3,4-dimethoxyphenyl
Ar^2 = 3,4-methylenedioxyphenyl



(7)

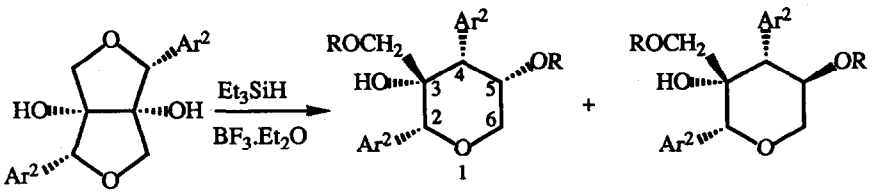
(8) R = H
(10) R = Ac



(5)

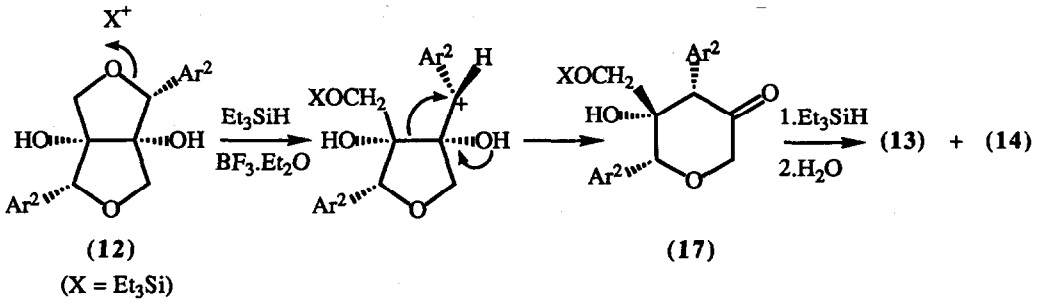
(9) R = H
(11) R = Ac

Scheme 2

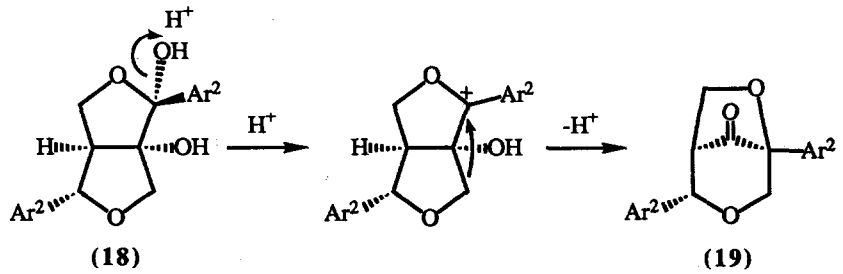


(12) (13) R = H (14) R = H
(15) R = Ac (16) R = Ac

Scheme 3



(12) (17)
(X = Et_3Si)



(18) (19)

Scheme 4

contained two different aliphatic CH_2 groups in addition to the two methylenedioxy groups. There were also three aliphatic methine groups and one aliphatic quaternary carbon in both compounds.

The ^1H n.m.r. spectra indicated that both products contained one isolated CH_2 group giving rise to a simple AB system, and one isolated CH giving rise to a singlet. The singlet was not shifted by acetylation in either compound but the AB system was shifted downfield by approx. 0.35 p.p.m. in both compounds, suggesting the presence of a CH_2OH group.

The remaining parts of the ^1H n.m.r. spectra of both products were significantly different. In (13) the second CH_2 group showed only very small coupling to other protons and indeed the other two methine protons also showed very small coupling constants. The structure of the aliphatic part of this compound was eventually rationalised by carrying out NOE experiments on the 400 MHz spectrum of the diacetate (15) (see Figure 1), and an analysis of its COSY spectrum (see Table 3) and spin decoupling. As a result, structure (13) was assigned to this product from the triethylsilane/BF_3-etherate reaction. NOE measurements on (13) itself (Figure 2) also supported this assignment.

The structure of the second product was more readily arrived at since the second CH_2 group, giving signals at 4.33 and 3.48 p.p.m. in the spectrum of the acetate, was clearly part of an ABX system. Furthermore, the X proton of the ABX system at 5.60 p.p.m. was also very clearly coupled to a second methine proton at 3.15 p.p.m. It was deduced therefore that the structure of this product was very similar to that of other product and indeed that the two compounds were epimers differing only in their configuration at C-5. The structure of the second product is therefore (14) and its diacetate is (16).

It is envisaged that products (13) and (14) result from a rearrangement of wodeshiol (12) to the tetrahydropyrone (17) followed by reduction (Scheme 4). It is particularly interesting that the pinacol-type rearrangement of (12) takes a very different course from the acid-catalysed pinacol rearrangement of arboreol (18).[4] This may indicate that the conversion of (12) to (17) is a stepwise process *via* a carbonium ion and that the migratory aptitude of C5 (tertiary) is greater than that of C8 (primary). Rearrangement of (18) to gmelanone (19) may be a concerted process and hence stereocontrolled. Alternatively, the rearrangement of (18) may also involve a stepwise mechanism. However, the ion formed by loss of water after protonation of (18) would provide very poor overlap between the vacant p orbital of the carbocation and the intrabridgehead C-C bond orbital and this would inhibit migration of this bond which would, in any case, lead to a four membered ring.

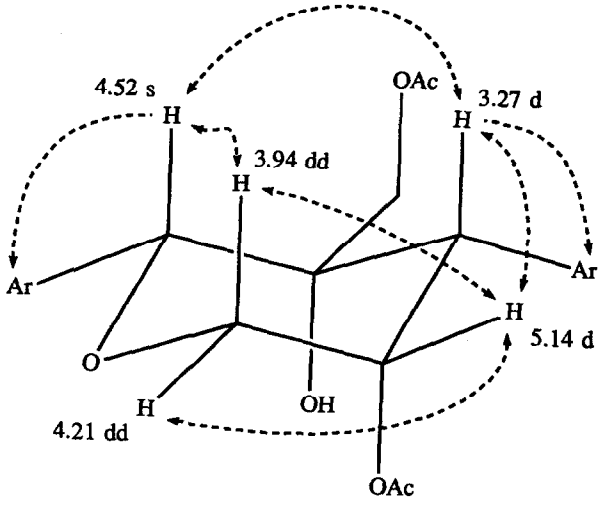


Figure 1 (compound **15**) ----→ = NOE observed

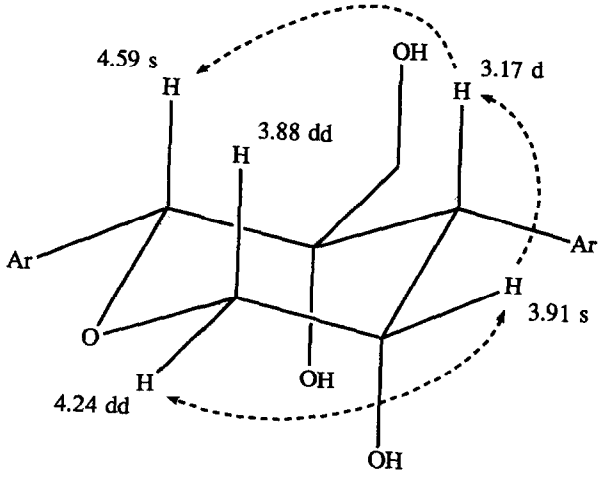


Figure 2 (compound **13**) ----→ = NOE observed

Table 1

^{1}H N.m.r. spectra of (8) and (9) and their diacetates (10) and (11)

	(8)[a]	(9)[b]	(10)[a]	(11)[a]
H-1	4.22s	4.21s	4.22s	4.18s
H-3	2.29s	2.20m	2.47m	2.43m
H-4	(2.61dd (5,16) (3.03br.t(14.5)	2.60dd(5.0, 16.1) 3.15t (15.1)	2.77dd(5,16) 3.04br.t (14.3)	2.72dd(4.9, 16.1) 3.03br.t (14.4)
2-CH_2	(3.40d (11.5) (3.60d(11.5)	3.31dd(6.7, 10.8) 3.55dd(5.0, 10.8)	3.81d (11.3) 3.96d (11.3)	3.73d(11.3) 4.01d (11.3)
3-CH_2	(3.80dd (2, 10.5) (3.95dd (7.6, 10.6)	)3.91m)	4.15dd(6, 11.3) 4.39dd (5.6, 11.3)	4.13dd (5.7, 11.3) 4.37dd(5.5, 11.3)
OH	(2.87br. (2.44br. (2.01s	4.48t (4.2) 4.06t (5.0) 2.94s	- - 1.79s	- -
H-5	6.19s	6.08s	6.19s	6.18s
H-8	6.62s	6.60s	6.63s	6.60s
H-2′	6.73d(2)	6.72d(1.0)	6.63d(2)	
H-5′ H-6′	6.84d(8) 6.77dd(2,8)	)6.78m)	6.83d(8) 6.68dd(2,8)	6.79d(8.5)
OMe	(3.89s (3.85s (3.79s (3.56s	-	3.88s 3.86s 3.77s 3.55s	-
OCH_2O	-	(5.85s (5.95s	-	5.86s 5.97s
OAc	-	-	(2.05s (2.10s	2.06s 2.11s

[a] in $CDCl_3$. [b] in d_6-acetone.

Table 2.

^{13}C N.m.r. spectra of (8) and (9)

	(8)[a]	(9)[b]
C-1	50.32	52.14
C-2	73.06	74.31
C-3	39.90	41.11
C-4	28.52	c
CH_2	62.93	64.65
CH_2	61.50	63.38
C-5	115.44	112.68
C-8	114.21	110.54
C-2′	111.44	108.31
C-5′	110.62	107.78
C-6′	147.64	147.94
C-7	147.28	147.09
C-3′	146.84	146.36 (x 2)
C-4′	146.38	
C-1′	133.91	136.47
C-8a	131.27	133.24
C-4a	128.88	130.56
C-6	124.00	125.89
OMe	(55.63 (55.37	-
OCH_2O	-	101.37 101.62

[a] in d_6-DMSO. [b] in d_6-acetone. [c] hidden by solvent peak.

Table 3

^{1}H N.m.r. spectra of (13) and (14) and their diacetates (15) and (16)[a]

	(13)	(14)	(15)	(16)
H-2	4.59s	4.54s	4.52s	4.56s
H-4	3.17d (2.3)[c]	2.93d (10.5)[c]	3.27d (3.11)[c]	3.15d (11.5)[c]
H-5	3.91s[bd]	4.40m[be]	5.14d (3.11)[bde]	5.60dt (4.9, 10.7)[bde]
CH_2	(3.26d (10.7) (2.99d (10.7)	3.15d (10.8) 3.00d (10.8)	3.63d (11.16) 3.34d (11.14)	3.51d(11.2) 3.28d (11.2)
H-6 eq	4.24dd (1.92, 12.30)	4.30m	4.21dd (1.25, 13.08)[ce]	4.33dd (5.3, 10.7)[ce]
H-6 ax	3.88dd (1.23, 12.30)	3.48t (10.2)[c]	3.94dd (1.47, 13.04)[cd]	3.48t (10.5)[cd]
OH	3.3br.		3.36s	
OAc			2.16s 2.06s	1.83s 2.10s
OCH_2O	5.94s 5.95s	5.95s 5.96s	(5.92d (1.42) (5.93d (1.49) (5.94s	5.94s 5.95s
arom.	6.76-7.29m	6.8-7.0m	(6.75s (6.94s (6.70d (8.01) (6.81dd (1.53, 8.05) (7.07d (1.41)	6.7-6.9m

[a] all spectra in $CDCl_3$
[b] coupled to H-4 by COSY and spin decoupling
[c] " " H-5 " " " " "
[d] " " H-6 eq. " " " " "
[e] " " H-6 ax. " " " " "

Table 4.

^{13}C N.m.r. spectra of (13) - (16)[a]

	(13)	(14)	(15)	(16)
C-2	83.87	83.40	84.81	83.00
C-3	75.61	74.46	74.01	73.87
C-4	49.01	55.44	48.99	52.28
C-5	71.75	67.01	73.34	68.31
CH_2	63.44	63.87	64.43	64.87
C-6	73.96	72.31	71.55	69.63
OAc	-	-	(20.94 (21.49 (169.58 (	20.67 20.76 169.53 169.97
OCH_2O	(100.98 (101.08	101.11	101.19 101.24	101.01 101.22
1/1//	(131.15 (132.33	130.10 130.98	130.29 130.38	129.24 129.90
2/2//	(107.99 (108.22	108.13	107.95 108.36	108.07
3/3//4/4//	(146.81 (147.56 (147.75	147.24 147.59 147.86	147.21 147.74 147.79	147.08 147.83 147.95
5/5//	(108.69 (110.65	108.39	108.68 110.21	108.25
6/6//	(121.27 (123.20	120.95	121.65 123.33	121.03

[a] all spectra in $CDCl_3$

EXPERIMENTAL

^1H and ^{13}C n.m.r. spectra were recorded on a Bruker 250 MHz instrument, with high field ^1H n.m.r. spectra being recorded on a Bruker 400 MHz instrument. Mass spectra were recorded on a VG12-253 quadrupole instrument and on a double focussing VG ZAB-E instrument. Silica gel G was used for column chromatography and for tlc. Melting points are uncorrected.

Reaction of paulownin with BF_3-etherate and triethylsilane.

To a solution of paulownin (**5**) (0.5g, 1.35 mmole) in dichloromethane (10 cm^3) cooled to 0° was added BF_3-etherate (0.43g, 3.03 mmole) and the mixture stirred at 0° for 1 hr. Triethylsilane (3 cm^3, 2.18g, 18.8 mmole) was added and the mixture allowed to warm to room temperature and left stirring overnight. Aq. $NaHCO_3$ (10 cm^3) was added and the mixture stirred for 2 hr. before being extracted with chloroform (3 x 30 cm^3). The organic layer was washed with aq. $NaHCO_3$ (3 x 20 cm^3), brine (3 x 20 cm^3) and dried ($MgSO_4$). After removal of the solvent, a colourless gum (0.55g) was obtained. This was separated by column chromatography using hexane-ethyl acetate (1:1) to give unreacted paulownin (0.29g), and the product (**9**) (0.18g) which was crystallised from chloroform to give a colourless amorphous powder, m.p. 116° (yield 36%, 85% after allowing for recovered paulownin). For ^1H and ^{13}C n.m.r. spectra see Tables 1 and 2, *m /z* 372 (36%, M^+), 293 (13%), 268 (31%), 267 (24%), 255 (20%), 239 (10%), 238 (36%), 177 (16%), 135 (17%), 133 (50%), 131 (15%), 103 (11%). Acc. masses found : 372.12112 ($C_{20}H_{20}O_7$), 293.08118 ($C_{18}H_{13}O_4$), 268.07375 ($C_{16}H_{12}O_4$), 267.06624 ($C_{16}H_{11}O_4$), 267.04468 ($C_{19}H_7O_2$), 255.06436 ($C_{15}H_{11}O_4$), 239.06851 ($C_{15}H_{11}O_3$), 238.06358 ($C_{15}H_{10}O_3$), 135.04430 ($C_8H_7O_2$).

Preparation of compound (11).

Compound (**9**) (40 mg) in dry pyridine (1 cm^3) was treated with acetic anhydride (1 cm^3) at 0°C and allowed to stand at room temperature for 0.5 hr. The reaction mixture was poured onto crushed ice and extracted with chloroform (3 x 10 cm^3). The organic layer was washed with 1% aq. HCl (3 x 10 cm^3), brine (3 x 10 cm^3) and dried ($MgSO_4$). After removal of the organic solvent a gum was obtained (40 mg) which was purified by column chromatography, using dichloromethane, to yield the acetate (**11**). For ^1H and ^{13}C n.m.r. spectra see Tables 1 and 2. *m/z* 456 (4%, M^+), 378 (4%), 336 (3%), 319 (6%), 279 (10%), 267 (10%), 238 (15%), 223 (8%), 205 (12%), 149 (100%). *m/z* (CI) 474 (100%, M + NH_4^+), 279 (55%).

Reaction of wodeshiol (12) with BF_3-etherate and triethylsilane.

To a solution of wodeshiol (0.21g, 0.544 mmole) in dichloromethane (6 cm^3) cooled to 0°C was added BF_3-etherate (0.17g, 1.20 mmole) and the mixture stirred at 0° for half an hour. Triethylsilane (2 cm^3, 1.46g, 12.5 mmole) was added and the mixture stirred for 2 hr. at 0° and then left overnight at room temperature. The reaction mixture was poured onto ice-water (50 cm^3) and extracted with chloroform (3 x 20 cm^3). The organic layer was washed with aq. $NaHCO_3$ (3 x 20 cm^3), brine (3 x 20 cm^3) and dried ($MgSO_4$). After removal of the solvent a pale brown residue (0.22g) was obtained which showed two spots in addition to wodeshiol on tlc (benzene-ethyl acetate 9:1). The crude product was purified by column chromatography using dichloromethane-ethyl acetate (9:1) to give wodeshiol (0.12g), and the two products (**13**) and (**14**) (40 mg each, 44% yield each after allowing for recovered wodeshiol). The products were further purified by prep. tlc using dichloromethane-ethyl acetate (9:1). For ^1H and ^{13}C n.m.r. spectra see Tables 3 and 4. Spectral data for (**13**) : *m/z* 388 (2%, M^+), 194 (40%), 161 (20%), 149 (45%)m 135 (100%). *m/z* (CI) 406 (25%, M + NH_4^+), 371 (100%), 353 (20%), 212 (20%), 195 (10%), 161 (20%), 135 (35%). Found : M^+ 388.1158 ($C_{20}H_{20}O_8$). Spectral data for (**14**) : *m/z* 388 (25%, M^+), 194 (75%), 161 (40%), 149 (60%), 135 (100%). *m/z* (CI) 406 (100%, M + NH_4^+), 371 (100%), 353 (50%), 212 (40%), 195 (30%), 161 (25%), 135 (45%). Found : M^+ 388.1158 ($C_{20}H_{20}O_8$).

Preparation of compound (15).

The acetate (**15**) was prepared using the method described for the preparation of (**11**). For ^1H and ^{13}C n.m.r. spectra see Tables 3 and 4. *m/z* 472 (100, M^+), 237 (100%). *m/z* (CI) 490 (20%, M + NH_4^+), 237 (100%). Found : M^+ 472.1369 ($C_{24}H_{24}O_{10}$).

Preparation of compound (16).

The acetate (**16**) was prepared using the method described for the preparation of (**11**). For ^1H and ^{13}C n.m.r. spectra see Tables 3 and 4. *m/z* 472 (40%, M^+), 237 (100%). *m/z* (CI) 490 (10%, M + NH_4^+), 395 (25%), 237 (100%). Found : M^+ 472.1369 ($C_{24}H_{24}O_{10}$).

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