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## ACETYL MIGRATION OF TRICHILINS WITH ZINC BOROHYDRIDE

by

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### Abstracts

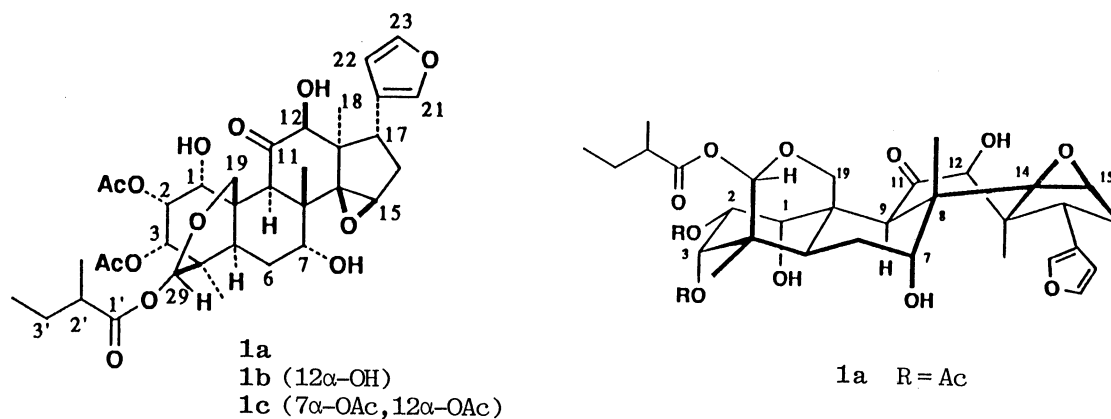
Treatment of trichilin A (**1a**), insect antifeedant limonoid, with zinc borohydride in 2-propanol led to acyl migration in ring A and gave its 1,2-diacetyl and 1,3-diacetyl isomers. Similar treatment of trichilin B (**1b**, 12-epimer of **1a**) and its 7,12-diacetate also induced 1,3- and 1,2-acetyl migrations.

**Key words** : Acyl migration, Zinc borohydride, Trichilins, Limonoid, Antifeedant

### Introduction

Trichilin A and B (**1a** and **1b**) are insect antifeeding limonoids from East African medicinal plant *Trichilia roka*.<sup>1,2)</sup> In structural and structure/activity relation studies, their 11-hydroxy derivatives were particularly interesting, for the potent active were the compounds with a 12-OH function, independent of the substitution pattern in ring A. A 11-hydroxy-12-oxo isomer (trichilin C) was inactive.<sup>3)</sup> As trichilins are sensitive to

Fig. 1



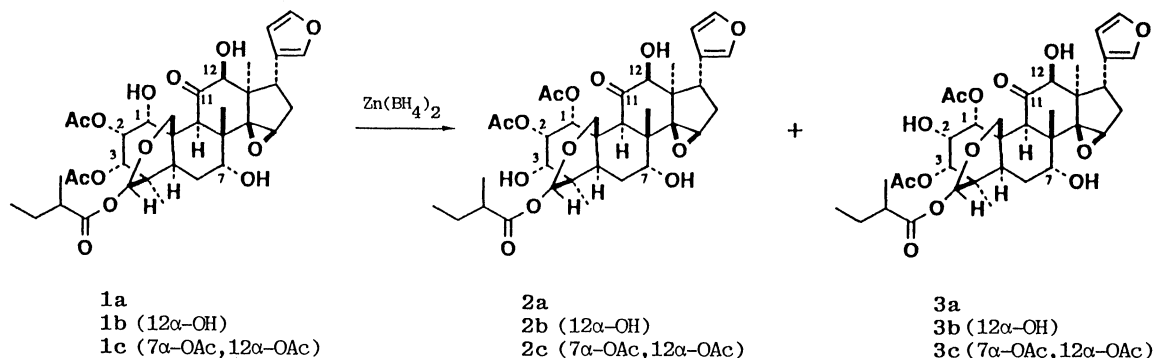
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traces of acid or base, treatment of **1a** with neutral zinc borohydride in attempt to reduce the 11-one led unexpectedly to acyl migration in ring A and gave a mixture of **1a** and its 1,2-diacetyl **2a** and 1,3-diacetyl isomers **3a** derived by 1,3- or 1,2-shift of acetyl group. Similar treatment of trichilin B (**1b**) and its 7,12-diacetate (**1c**) also induced a similar acetyl migration.

### Results and Discussion

When a solution of **1a** (10 mg, 0.015 mmol) and 1.3 M ether solution (0.1 ml, 0.13 mmol) of zinc borohydride<sup>4</sup> in dry 2-propanol (0.5 ml) was stirred at room temperature for 40 h, the product gave two compounds, **2a** (6%) and **3a** (11%) along with **1a** (79%) (Scheme 1 and Table 1). This reaction did not reduce the 11-keto group and the products, **2a** and **3a**, showed  $n-\pi^*$  absorption of  $>C=O$  at 303 ( $\Delta\epsilon - 4.3$ ) and 300 nm ( $\Delta\epsilon - 3.7$ ) in their CD spectra, respectively. Both **2a** and **3a** had the same molecular formula,  $C_{35}H_{46}O_{13}$ , as **1a** and their  $^1H$  NMR spectra were also very similar to that of **1a** except for the acylation pattern in ring A (Table 2). The acylation pattern in **1a**, namely, that **1a** has a free 1-OH, was shown by the fact that the 9-H signal in **1a** was at  $\delta$  4.72, whereas in **2a** (1,2-diacetate) and **3a** (1,3-diacetate) they were shifted upfield to  $\delta$  4.13 and 4.17, respectively. The low shift of  $\delta$  4.72 in **1a** has been attributed to the effect of the 1-OH in a 1,3-diaxial relation (Fig. 1). The isomers, **2a** and **3a**, were identical with trichilin F and E isolated from *T. roka*.<sup>5</sup>



Scheme 1

Table 1. Acetyl Migration of Trichilins with Zinc Borohydride

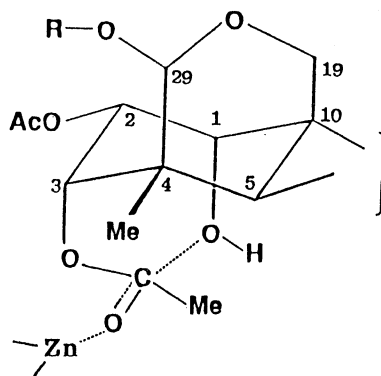
Compound	Solvent	Reaction time, h	Products, Yields %			Recovered, %	
<b>1a</b>	2-Propanol	40	<b>2a</b>	6	<b>3a</b>	11	79
<b>1b</b>	2-Propanol	50	<b>2b</b>	4	<b>3b</b>	2	88
<b>1c</b>	2-Propanol	30	<b>2c</b>	30	<b>3c</b>	23	45
<b>1c</b>	EtOH	17	<b>2c</b>	13	<b>3c</b>	7	75

As in the case of **1a**, the treatment of trichilin B (**1b**) having same acylation pattern with **1a** in ring A induced acyl migration to give its 1,2-diacetate **2b** (4%) and 1,3-diacetate **3d** (2%), the latter of which was identified as the cytotoxic aphanastatin.<sup>6</sup> As its structure has been determined by X-ray analysis, this novel conversion established the structure of trichilin B. When 7,12-diacetyltrichilin B (**1c**) was treated with zinc borohydride, the reaction proceeded smoothly, yielding 1,2-diacetate **2c** (30%) and 1,3-diacetate **3c** (23%). The reaction of **1c** in ethanol also gave a similar result to that in propanol (Table 1).

These results suggest that the 2- or 3-acetyl group in **1** would migrate to 1-position via five- or six-membered cyclic intermediate such as **4** (Fig. 2) to give the isomers, **3** or **2**, and that this acetyl migration would have been affected by another OH function or by the conformational change of the ring C in **1**.

In spite of the change of the acylation pattern in ring A, the reaction products of **2a-c** and **3a-c** showed similar antifeeding activities (leaf disk method),<sup>7</sup> respectively, with their starting materials, **1a-c**, against a North American pest insect, *Spodoptera eridania*.

Fig. 2



## Experimental

<sup>1</sup>H NMR spectra were measured in CDCl<sub>3</sub> at 250 MHz. UV and CD spectra were measured in MeOH. Final purification of compounds was done by HPLC with adsorption column using a MeOH/CH<sub>2</sub>Cl<sub>2</sub> solvent system.

**Trichilin A (1a) and B (1b).** Trichilin A (**1a**) and B (**1b**) were isolated from African Meliaceae plant *T. roka*.<sup>1</sup> **1a**: C<sub>35</sub>H<sub>46</sub>O<sub>13</sub>; UV 213 nm (ε 4050); CD 213 (Δε + 2.5) and 304 nm (Δε - 3.7). **1b**: C<sub>35</sub>H<sub>46</sub>O<sub>13</sub>; UV 209 nm (ε 4600); CD 217 (Δε + 1.2) and 306 nm (Δε - 1.9).

**7,12-Diacetyltrichilin B (1c).** Trichilin B (**1b**, 15 mg) was acetylated with Ac<sub>2</sub>O in pyridine at 55°C for 30 h to give the 12-acetate (2 mg) and 7,12-diacetate (**1c**, 8 mg). **1c**: C<sub>39</sub>H<sub>50</sub>O<sub>15</sub>; CI-MS m/z 759 (M+1)<sup>+</sup>; UV 210 nm (ε 4200); CD 215 (Δε + 1.9) and 305 nm (Δε - 2.3). 12-Acetyltrichilin B: C<sub>37</sub>H<sub>48</sub>O<sub>14</sub>; CI-MS m/z 717 (M+1); UV 210

Table 2.  $^1\text{H}$  NMR Spectra of Trichilins and Their Acyl Migration Products

H	<b>1a</b>	<b>1b</b>	<b>1c</b>	<b>2a</b>	<b>2b</b>	<b>2c</b>	<b>3a</b>	<b>3b</b>	<b>3c</b>
	$\delta$ Mult	$\delta$ Mult	$\delta$ Mult	$\delta$ Mult	$\delta$ Mult	$\delta$ Mult	$\delta$ Mult	$\delta$ Mult	$\delta$ Mult
1	3.98 brt (4.5)	4.58 brt (4.5)	4.42 m	5.40 dd (5.0, 1.0)	5.93 d (3.5)	5.75 d (5.2)	5.32 d (4.2)	5.86 d (4.8)	5.69 brd (5.0)
2	5.90 t (4.5)	5.91 t (4.5)	5.88 t (4.5)	5.91 t (5.0)	5.91 t (3.5)	5.92 t (5.2)	4.80 m	4.80 m	4.81 t (5.0)
3	5.54 brd (4.5)	5.53 brd (4.5)	5.46 d (4.5)	4.05 m	4.05 m	4.00 m	5.46 d (4.2)	5.45 d (4.8)	5.43 brd (5.0)
7	3.72 m	3.66 m	4.75 m	3.69 m	3.63 m	4.80 m	3.71 m	3.66 m	4.76 m
9	4.72 s	4.56 s	4.63 s	4.13 s	4.04 s	4.02 s	4.17 s	4.09 s	4.11 s
12	3.72 d (2.5)	4.10 s	5.39 s	3.50 d (1.7)	4.05 brd (1.0)	5.45 s	3.55 d (1.0)	4.04 brd (2.0)	5.45 s
15	3.53 s	3.78 s	3.58 s	3.48 s	3.71 s	3.58 s	3.47 s	3.72 s	3.59 s
17	3.39 dd (11, 6.0)	3.02 dd (11, 6.0)	2.95 m	3.42 dd (11, 6)	2.88 dd (11, 6)	2.95 dd (11, 6)	3.45 dd (11, 6)	3.27 dd (11, 6)	2.97 dd (11, 6)
18(Me)	1.32 s	1.15 s	1.30 s	1.16 s	1.12 s	1.19 s	1.18 s	1.11 s	1.20 s
19A									4.31 d (13)
19B	4.50 brs*	4.35 brs*	4.31 brs	4.53 brs	4.36 brs	4.34 m	4.55 brs	4.38 brs	4.45 d (13)
21	7.19	7.22	7.10	7.17	7.20	7.10	7.16	7.19	7.10
22	6.35	6.53	6.09	6.32	6.48	6.07	6.32	6.51	6.06
23	7.37	7.33	7.32	7.35	7.29	7.31	7.35	7.30	7.32
28(Me)	0.88 s	0.83 s	0.76 s	0.99 s	1.00 s	0.96 s	0.82 s	0.82 s	0.78 s
29	5.76 s	5.75 s	5.71 s	5.77 s	5.77 s	5.76 s	5.75 s	5.74 s	5.71 s
30(Me)	1.02 s	1.14 s	1.20 s	1.01 s	1.00 s	1.19 s	1.00 s	1.03 s	1.20 s
2'-Me	1.19 d (7.0)	1.19 d (7.0)	1.16 d (6.8)	1.15 d (7.1)	1.14 d (7.0)	1.13 d (7.0)	1.15 d (6.9)	1.15 d (7.5)	1.15 d (7.8)
3'-Me	0.92 t (7.5)	0.92 t (7.0)	0.88 t (7.3)	0.89 t (7.3)	0.89 t (7.0)	0.88 t (7.3)	0.89 t (7.2)	0.89 t (7.6)	0.88 t (7.1)
Ac	2.03	2.03	1.96	2.02	2.01	1.97	2.04	1.99	1.99
	2.14	2.12	1.99	2.06	2.02	2.01	2.10	2.09	2.04
			2.07			2.06			2.06
			2.16			2.18			2.18

Measured in  $\text{CDCl}_3$ . Coupling constants (Hz) are in parentheses.

\*observed as two signals at 400 MHz; **1a**:  $\delta$  4.47 (d,  $J=13$ ) and 4.53 (d,  $J=13$ ). **1b**:  $\delta$  4.32 (d,  $J=13$ ) and 4.36 (d,  $J=13$ ).

nm ( $\epsilon$  4100); CD 215 ( $\Delta\epsilon+1.5$ ) and 305 nm ( $\Delta\epsilon-2.2$ );  $^1\text{H}$  NMR  $\delta$  0.81 (3H, s), 0.89 (3H, t,  $J=7.2$ ), 1.15 (3H, s), 1.17 (3H, d,  $J=6.8$ ), 1.33 (3H, s), 1.95, 2.00, 2.10 (each 3H, s, OAc), 3.67 (1H, m), 3.74 (1H, s), 4.32 (1H, s), 4.41 (1H, t,  $J=4.5$ ), 4.61 (1H, s), 5.40 (1H, s, 12-H), 5.50 (1H, d,  $J=4.6$ ), 5.74 (1H, s), 5.88 (1H, t,  $J=4.6$ ), 6.10, 7.10, 7.31 (each 1H, furan).

**General procedure for treatment of 1 with zinc borohydride.** A solution of the compound **1** (10 mg, 0.015 mmol) in dry 2-propanol (0.5 ml) was stirred with 1.3 M ether solution (0.1 ml, 0.13 mmol) of zinc borohydride for 40 h at room temperature and then acetone (1 ml) was added. After an additional stirring of 2 h, the reaction products were purified by column chromatography and HPLC.

**Reaction products.** **2a:** CI-MS  $m/z$  675 ( $M+1$ )<sup>+</sup>; UV 210 nm ( $\epsilon$  5100); CD 211 ( $\Delta\epsilon+2.2$ ) and 303 nm ( $\Delta\epsilon-4.3$ ). **3a:** CI-MS  $m/z$  675 ( $M+1$ )<sup>+</sup>; UV 215 nm ( $\epsilon$  4100); CD 211 ( $\Delta\epsilon+2.7$ ) and 300 nm ( $\Delta\epsilon-3.7$ ). **2b:** CI-MS  $m/z$  675 ( $M+1$ )<sup>+</sup>; UV 209 nm ( $\epsilon$  4300); CD 214 ( $\Delta\epsilon+1.6$ ) and 306 nm ( $\Delta\epsilon-2.0$ ). **3b:** CI-MS  $m/z$  675 ( $M+1$ )<sup>+</sup>; UV 209 nm ( $\epsilon$  4000); CD 214 ( $\Delta\epsilon+1.4$ ) and 304 nm ( $\Delta\epsilon-2.9$ ). **2c:** CI-MS  $m/z$  759 ( $M+1$ )<sup>+</sup>. **3c:** CI-MS  $m/z$  759 ( $M+1$ )<sup>+</sup>.

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