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ACETYL MIGRATION OF TRICHILINS WITH ZINC BOROHYDRIDE

by

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Abstracts

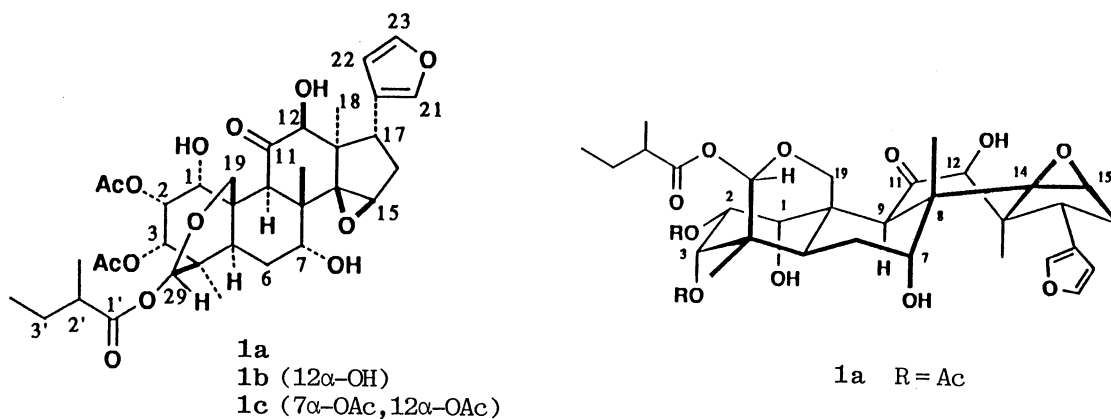
Treatment of trichilin A (**1a**), insect antifeedant limonoid, with zinc borohydride in 2-propanol led to acyl migration in ring A and gave its 1,2-diacetyl and 1,3-diacetyl isomers. Similar treatment of trichilin B (**1b**, 12-epimer of **1a**) and its 7,12-diacetate also induced 1,3- and 1,2-acetyl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

Fig. 1



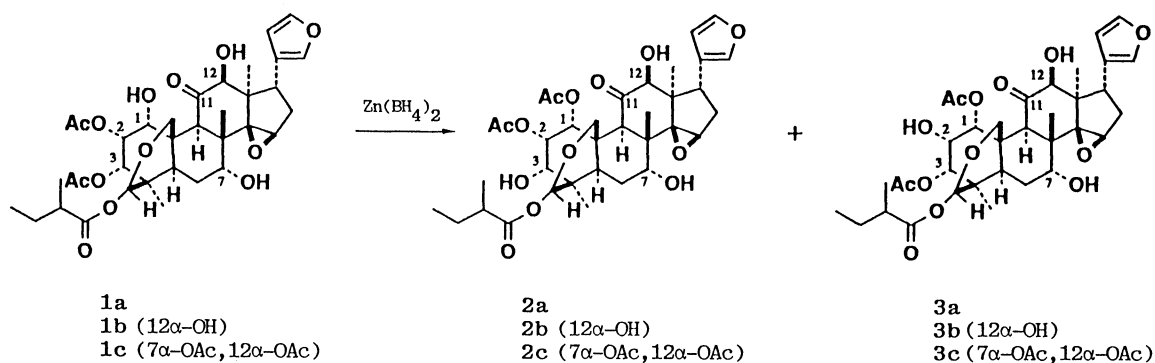
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traces of acid or base, treatment of **1a** with neutral zinc borohydride in attempt to reduce the 11-one led unexpectedly to acyl migration in ring A and gave a mixture of **1a** and its 1,2-diacetyl **2a** and 1,3-diacetyl isomers **3a** derived 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 borohydride⁴⁾ 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 δ 4.72, whereas in **2a** (1,2-diacetate) and **3a** (1,3-diacetate) they were shifted upfield to δ 4.13 and 4.17, respectively. The low shift of δ 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*.⁵⁾



Scheme 1

Table 1. Acetyl Migration of Trichilins with Zinc Borohydride

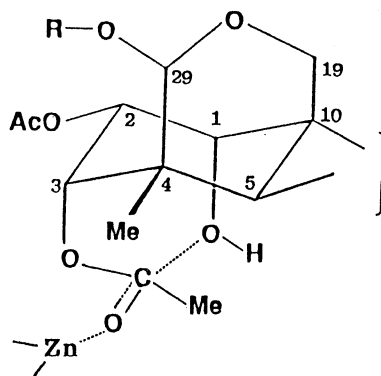
| Compound | Solvent | Reaction time, h | Products, Yields % | | | | Recovered, % |
|-----------|------------|------------------|--------------------|----|-----------|----|--------------|
| 1a | 2-Propanol | 40 | 2a | 6 | 3a | 11 | 79 |
| 1b | 2-Propanol | 50 | 2b | 4 | 3b | 2 | 88 |
| 1c | 2-Propanol | 30 | 2c | 30 | 3c | 23 | 45 |
| 1c | EtOH | 17 | 2c | 13 | 3c | 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.⁶ 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),⁷ respectively, with their starting materials, **1a-c**, against a North American pest insect, *Spodoptera eridania*.

Fig. 2



Experimental

¹H NMR spectra were measured in CDCl₃ 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/CH₂Cl₂ solvent system.

Trichilin A (1a) and B (1b). Trichilin A (**1a**) and B (**1b**) were isolated from African Meliaceae plant *T. roka*.¹⁾ **1a**: C₃₅H₄₆O₁₃; UV 213 nm (ε 4050); CD 213 (Δε + 2.5) and 304 nm (Δε - 3.7). **1b**: C₃₅H₄₆O₁₃; 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 Ac₂O in pyridine at 55°C for 30 h to give the 12-acetate (2 mg) and 7,12-diacetate (**1c**, 8 mg). **1c**: C₃₉H₅₀O₁₅; CI-MS m/z 759 (M+1)⁺; UV 210 nm (ε 4200); CD 215 (Δε + 1.9) and 305 nm (Δε - 2.3). 12-Acetyltrichilin B: C₃₇H₄₈O₁₄; CI-MS m/z 717 (M+1); UV 210

Table 2. ^1H NMR Spectra of Trichilins and Their Acyl Migration Products

| H | 1a | 1b | 1c | 2a | 2b | 2c | 3a | 3b | 3c |
|--------|----------------------|----------------------|-----------------|-----------------------|--------------------|--------------------|--------------------|--------------------|--------------------|
| | δ Mult | δ Mult | δ Mult | δ Mult | δ Mult | δ Mult | δ Mult | δ Mult | δ 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 CDCl_3 . Coupling constants (Hz) are in parentheses.*observed as two signals at 400 MHz; **1a**: δ 4.47 (d, $J=13$) and 4.53 (d, $J=13$). **1b**: δ 4.32 (d, $J=13$) and 4.36 (d, $J=13$).

nm (ϵ 4100); CD 215 ($\Delta\epsilon+1.5$) and 305 nm ($\Delta\epsilon-2.2$); ^1H NMR δ 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 ($M+1$)⁺; UV 210 nm (ϵ 5100); CD 211 ($\Delta\epsilon+2.2$) and 303 nm ($\Delta\epsilon-4.3$). **3a:** CI-MS m/z 675 ($M+1$)⁺; UV 215 nm (ϵ 4100); CD 211 ($\Delta\epsilon+2.7$) and 300 nm ($\Delta\epsilon-3.7$). **2b:** CI-MS m/z 675 ($M+1$)⁺; UV 209 nm (ϵ 4300); CD 214 ($\Delta\epsilon+1.6$) and 306 nm ($\Delta\epsilon-2.0$). **3b:** CI-MS m/z 675 ($M+1$)⁺; UV 209 nm (ϵ 4000); CD 214 ($\Delta\epsilon+1.4$) and 304 nm ($\Delta\epsilon-2.9$). **2c:** CI-MS m/z 759 ($M+1$)⁺. **3c:** CI-MS m/z 759 ($M+1$)⁺.

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