PERGAMON

Phytochemistry 54 (2000) 897–899

PHYTOCHEMISTRY

www.elsevier.com/locate/phytochem

Spectral comparisons of coniferyl and cinnamyl alcohol epoxide derivatives with a purported *cis*-epoxyconiferyl alcohol isolate

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Received 18 October 1999; received in revised form 11 February 2000

Abstract

The reported isolation of *cis*-epoxyconiferyl alcohol must be incorrect, based upon comparison of the reported Nuclear Magnetic Resonance (NMR) spectral data for the isolate with those for synthesized coniferyl and cinnamyl alcohol epoxide derivatives. Attempts to prepare *cis*- and *trans*-coniferyl alcohols were unsuccessful, although their acetate derivatives could be synthesized. The NMR spectral data for a synthetic sample of pinoresinol were in excellent agreement with those for the purported isolate.

Keywords: *Fraxinus oxycarpa*; Oleaceae; Pinoresinol; Epoxyconiferyl alcohol

1. Introduction

As part of another project we required samples of epoxyconiferyl or epoxycinnamyl alcohols for Nuclear Magnetic Resonance (NMR) spectral data comparisons with an isolate. We found no literature reports of epoxyconiferyl alcohols as synthetics and only a single isolation reference to *cis*-epoxyconiferyl alcohol (**1**) as an isolate from *Fraxinus oxycarpa* (Kostova et al., 1995). Examination of the reported NMR spectral data for this isolate, however, did not seem consistent with literature data for other epoxycinnamyl alcohols. We therefore attempted to synthesize some epoxy derivatives which, along with literature data, might confirm or negate the isolation report.

2. Results and discussion

Epoxidations of *cis*- and *trans*-coniferyl alcohols were attempted with *m*-chloroperoxybenzoic acid, transition metal catalyzed reactions (Sharpless and Michaelson, 1973), in situ generation of dimethyldioxirane (DDO) (Frohn et al., 1998), and dilute DDO solutions (Murray and Singh, 1996). We were unable to prepare these epoxides with any of the above methods, and a multitude of products, mostly unidentified, resulted from our attempts. These methods, however, were successful for the preparation of *trans*-epoxycinnamyl alcohol and the diacetates of *cis*- and *trans*-epoxyconiferyl alcohols. Attempts to epoxidize *cis*- or *trans*-coniferyl alcohols and then generate the acetate in situ failed, but subjecting the prior acetylated coniferyls to epoxidation produced the desired acetate-derived epoxyconiferyl alcohols. Deacetylation of the epoxyconiferyl alcohol acetates was unsuccessful. We feel the *p*-phenol on **1** creates a labile benzylic position which makes epoxidation extremely difficult, if not impossible.

The NMR spectral data (Table 1) for the epoxides we prepared, when compared with the *Fraxinus oxycarpa* isolate NMR spectral data (Kostova et al., 1995), clearly indicate that the isolate cannot be *cis*-epoxyconiferyl alcohol. Data from the literature for a few isomeric epoxides which might be considered for

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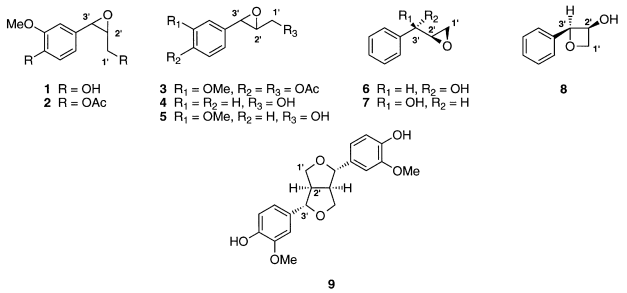
0031-9422/00/$ - see front matter
PII: S0031-9422(00)00101-1



1 R = OH
2 R = OAc

3 R_1 = OMe, R_2 = R_3 = OAc
4 R_1 = R_2 = H, R_3 = OH
5 R_1 = OMe, R_2 = H, R_3 = OH

6 R_1 = H, R_2 = OH
7 R_1 = OH, R_2 = H

8

9

the isolate (Table 1) were in some cases somewhat closer to the reported data for **1**, but still not within good agreement. At the suggestion of a reviewer, we compared pertinent NMR spectral data for the purported epoxide **1** with the data for a synthetic sample of (±)-pinoresinol (**9**) (Table 1). These data are essentially identical, as were the IR and UV data for **1** and **9** (Tandon and Rastogi, 1976). An optical rotation of $+51.65^{\circ}$ ($CHCl_3$) was reported for **1** and $+84.0^{\circ}$ (acetone) for **9** (Tandon and Rastogi, 1976). The 70 eV mass spectrum for **1** was reported as (*m*/*z*, rel. int.) 196(8), 165(8), 151(100), 137(38). The direct probe EI mass spectrum of synthetic sample **9** showed a strong M^+ at 358(70) and peaks at 163(38), 151(100), and 137(72), but not 196; if the isolate **1** was really **9**, the *m*/*z* 358 peak should have been easily observable. It is clear from the NMR spectral data that **1** cannot be the purported isolate, but its positive identification as **9** is somewhat clouded by the nonidentity of mass spectra, at least as reported for **1**. No answer to a request for a standard sample of **1** was received, so this question cannot be fully resolved at this time.

3. Experimental

3.1. Preparation of diacetate cis- and trans-epoxyconiferyl alcohols

trans-Coniferyl alcohol was purchased from Aldrich Chemical and *cis*-coniferyl alcohol was prepared according to a previously published procedure (Ralph and Zhang, 1998). The diacetates of coniferyl alcohol were prepared using standard pyridine/acetic anhydride conditions. Acetylation of *cis*- and *trans*-coniferyl alcohols produced a clear oil that was used directly in the epoxidations. Epoxidation with the neutral species DDO (approximately 0.06 M in acetone), was performed by adding an equivalent of DDO to an acetone solution of the coniferyl diacetates or cinnamyl alcohol. An equivalent of DDO was added every 15 min for 1.5 h. In each case, removal of the solvent in

Table 1
Comparison of ^1H and ^{13}C NMR spectral data between **1**, our synthetics, and literature data ($CDCl_3$)[a]

Compound	1′		2′		3′	
	^{13}C	^1H	^{13}C	^1H	^{13}C	^1H
1	71.7	3.88 (*dd*) *J* = 9.0, 3.7 4.25 (*dd*) *J* = 9.0, 7.0	54.2	3.10 (*m*)	85.9	4.74 (*d*) *J* = 4.2
2[b]	62.2	3.85 (*m*) 4.09 (*dd*) *J* = 12.4, 4.0	55.9	3.45 (*m*)	56.1	4.15 (*d*) *J* = 4.0
3[b]	63.9	4.10 (*dd*) *J* = 12.2, 5.7 4.45 (*dd*) *J* = 12.3, 3.3	56.2	3.20 (*m*)	59.3	3.81 (*m*)
4[b c]	62.5	3.81 (*dd*) *J* = 13, 5 4.18 (*dd*) *J* = 13, 3	55.6	3.25–3.3 (*m*)	61.2	3.95 (*d*) *J* = 3
5[d]	62.3	3.80 (*ddd*) *J* = 12.8, 7.9, 3.8 4.07 (*ddd*) *J* = 12.8, 5.2, 2.3	55.6	3.21 (*ddd*) *J* = 3.8, 2.3, 2.1	61.3	3.92 (*d*) *J* = 2.1
6[e]	43.6	4.85 (*d*) *J* = 2.9	55.0	3.16–3.19 (*m*)	70.8	2.72 (*dd*) *J* = 5.4, 3.9 2.92 (*dd*) *J* = 5.4, 2.9
7[e]	45.3	4.40 (*t*) *J* = 4.9	56.0	3.16–3.19 (*m*)	74.5	2.76 (*dd*) *J* = 4.9, 2.9 2.77–2.81 (*m*)
8[f]	79.3	4.40 (*m*) 4.8 (*m*)	67.5	4.8 (*m*)	88.6	5.77 (*d*) *J* = 5.6
9[b]	71.7	3.88 (*dd*) *J* = 9.2, 3.2 4.25 (*dd*) *J* = 9.0, 6.8	54.2	3.10 (*m*)	85.9	4.74 (*d*) *J* = 4.4

[a] We denote side chains with C-1′, etc. instead of IUPAC nomeclature to remain consistent with the Kostova et al. publication.
[b] Synthetics prepared in our labs.
[c] Gao et al. (1987).
[d] Evans et al. (1991).
[e] Kawakami et al. (1993).
[f] Ruotsalainen and Karki (1983).

vacuo gave pure epoxides as clear oils in excellent yield (>95%). The diacetate coniferyl epoxides rapidly degraded when not stored in solution ($CHCl_3$ for our experiments).

3.2. cis-Epoxyconiferyl alcohol diacetate

^{1}H NMR spectral data (300 MHz, $CDCl_3$): δ 2.08 (*s*, 3H, CH_3) 2.32 (*s*, 3H, CH_3), 3.47 (*m*, 1H, CH), 3.85 (*s*, 3H, OCH_3), 3.87 (*m*, 1H, CH), 4.09 (*dd*, 2H, J = 12.0, 4.0 Hz, CH_2), 4.17, (*d*, 1H, J = 4.0 Hz, CH), 6.92 (*d*, 1H, J = 2.0 Hz, CH), 6.95 (*dd*, 1H, J = 12.0, 2.0 Hz, CH), 7.03 (*d*, 1H, J = 8.0 Hz, CH); ^{13}C NMR spectral data (75 MHz, $CDCl_3$): δ 20.55 (CH_3), 20.65 (CH_3), 55.85 (OCH_3), 55.91 (CH), 56.12 (CH), 62.22 (CH_2), 110.09 (CH), 118.37 (CH), 122.72 (CH), 132.94 (C), 139.33 (C), 151.01 (CH), 168.83 (C═O), 170.65, (C═O); HR-FABMS (MH^+): calculated: 281.1020; found: 281.1017.

3.3. trans-Epoxyconiferyl alcohol diacetate

^{1}H NMR spectral data (300 MHz, $CDCl_3$): δ 2.16 (*s*, 3H, CH_3), 2.32 (*s*, 3H, CH_3), 3.20 (*m*, 1H, CH), 3.81 (*m*, 1H, CH), 3.82 (*s*, 3H, OCH_3), 4.10 (*dd*, 1H, CH, J = 12.2, 5.7 Hz), 4.45 (*dd*, 1H, CH, J = 12.3, 3.3 Hz), 6.84 (*d*, 1H, CH, J = 1.8 Hz), 6.89 (*dd*, 1H, CH, J = 8.1, 1.8 Hz), 7.01, (*d*, 1H, CH, J = 8.1 Hz); ^{13}C NMR spectral data (75 MHz, $CDCl_3$): δ 20.57 (CH_3), 20.70 (CH_3), 55.83 (OCH_3), 56.19 (CH), 59.31 (CH), 63.95 (CH_2), 108.94 (CH), 118.16 (CH), 122.80 (CH), 135.19 (C), 139.71 (C), 151.33 (C), 168.96 (C═O), 170.61 (C═O); HR-FABMS (MH^+): calculated: 281.1020; found: 281.1020.

3.4. (±) Pinoresinol

This was prepared according to a procedure by Quideau and Ralph (1994).

^{1}H NMR spectral data (400 MHz, $CDCl_3$): δ 3.10 (*m*, 2H, CH), 3.88 (*dd*, 2H, CH, J = 9.2, 3.2 Hz), 3.91 (*s*, 6H, OCH_3), 4.25 (*dd*, 2H, CH, J = 9.0, 6.8), 4.74 (*d*, 2H, CH, J = 4.4 Hz), 5.59 (*bs*, 2H, OH), 6.82 (*dd*, 2H, CH, J = 8.0, 2.0), 6.88 (*d*, 2H, CH, J = 8.0), 6.90 (*d*, 2H, J = 1.6), ^{13}C NMR spectral data (100 MHz, $CDCl_3$): δ 54.17 (CH), 55.95 (OCH_3), 71.67 (CH_2), 85.87 (CH), 108.58 (CH), 114.26 (CH), 118.96 (CH), 132.94 (C), 145.24 (C), 146.69 (C); EIMS (direct probe, m/z rel. int.): 358(70), 327(11), 235(15), 205(30), 163(38), 151(100), 137(72).

Acknowledgements

This research was supported by grant CHE-9619213 from the National Science Foundation. Mass spectra were obtained on an instrument supported by National Institutes of Health grant GM49631.

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