

## Synthesis of Some Minor Quinoline Alkaloids Found in *Galipea longiflora*

Stéphane Caron, Sonia Desfossés, Renée Dionne, Nathalie Théberge, and Robert H. Burnell

*J. Nat. Prod.*, **1993**, 56 (1), 138-139 • DOI:  
10.1021/np50091a021 • Publication Date (Web): 01 July 2004

Downloaded from <http://pubs.acs.org> on April 4, 2009

### More About This Article

---

The permalink <http://dx.doi.org/10.1021/np50091a021> provides access to:

- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article



**ACS Publications**  
High quality. High impact.

Journal of Natural Products is published by the American Chemical Society, 1155 Sixteenth Street N.W., Washington, DC 20036

SYNTHESIS OF SOME MINOR QUINOLINE ALKALOIDS  
FOUND IN *GALIPEA LONGIFLORA*STÉPHANE CARON, SONIA DESFOSSÉS, RENÉE DIONNE,  
NATHALIE THÉBERGE, and ROBERT H. BURNELL\*

Département de Chimie, Université Laval, Québec, Québec G1K 7P4, Canada

ABSTRACT.—Three simple quinoline alkaloids **5a**, **5b**, and **4c** have been synthesized to corroborate the structures proposed following their recent isolation.

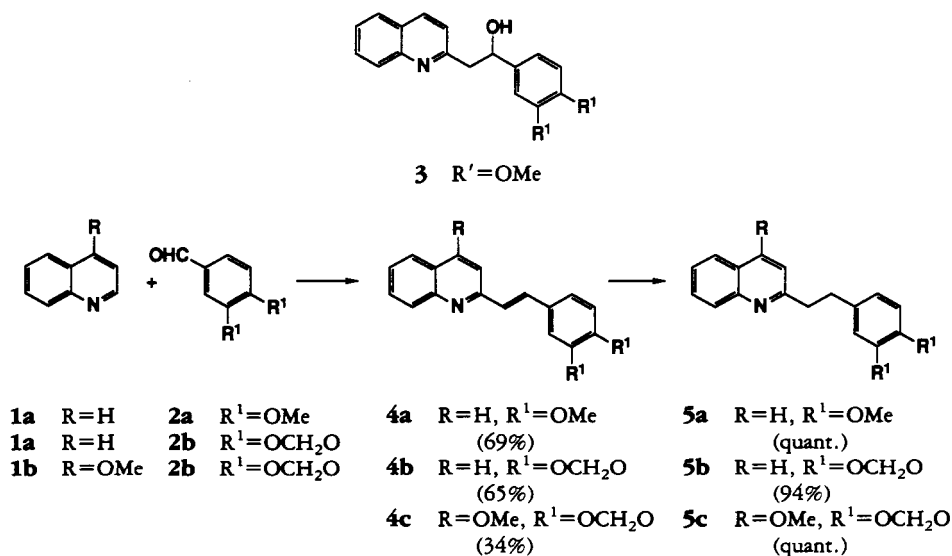
Recently the structures of several related quinoline alkaloids were proposed for a series of basic compounds extracted from *Galipea longiflora* (1). We were surprised that the synthesis of some of these compounds had not already been described in the literature. In another context, we had reason to prepare several such  $\alpha$ -substituted quinolines, and here we describe some of them which are identical with the natural products described by Fournet *et al.* (1).

Our synthesis is quite straightforward and exploits the well-known reactivity of methyl groups  $\alpha$  to the nitrogen atoms in aromatic heterocycles. In our first experiments, quinaldine **1a** for example was converted to the anion using *n*-butyllithium, and the corresponding aldehyde **2a** was introduced to afford al-

cohols such as **3**. Although the benzylic hydroxyl in the latter should be readily hydrogenolyzed, we found it advantageous to dehydrate to the conjugated trans olefin **4a** by mild reflux in glacial HOAc and then to reduce the double bond by catalytic hydrogenation to afford **5a**.

The results with this particular preparation were somewhat variable, but when the quinaldine **1a** and the aldehyde **2a** were refluxed in  $Ac_2O$  under conditions inspired by those of Kaslow and Stayner (2) the condensation was accompanied by dehydration leading directly to **4a** in excellent yield (Scheme 1).

This proved to be quite general, even if the aldehyde also contained phenolic hydroxyl residues. The products in these latter examples were of course the corresponding phenolic acetates. Like many



SCHEME 1

other examples these are not included in Scheme 1. Compounds **5a**, **4c**, **5b**, and **5c** are naturally occurring, and while the first three are new, **5c** has been known for a long time by the name cusparine (3). The physical properties of the synthetic samples agree well with those in the literature, and direct comparison of the ir and nmr spectra, kindly performed by the original authors (1), proved total structural identity.

## EXPERIMENTAL

### GENERAL EXPERIMENTAL PROCEDURES.—

The nmr spectra are for  $\text{CDCl}_3$  solutions measured on a Varian XL 200, and mass spectra were obtained on a Hewlett-Packard 8450A. Exact mass determinations were by the Centre régional de spectrométrie de masse, Université de Montréal, Montréal, Canada.

*2(3',4'-Dimethoxystyryl)quinoline [4a].*—Quinaldine [**1a**] (1.0 g, 7 mmol), veratraldehyde [**2a**] (1.118 g, 6.7 mmol) and  $\text{Ac}_2\text{O}$  (0.5 ml) were heated at  $140^\circ$  for 4.5 h. After cooling, the mixture was diluted with  $\text{Et}_2\text{O}$  (30 ml), poured into aqueous NaOH (20%, 25 ml), and extracted with more  $\text{Et}_2\text{O}$ . The combined organic phase was washed, dried, and evaporated and then chromatographed over Si gel. Elution with petroleum ether- $\text{Et}_2\text{O}$  (7:3) afforded the pure **4a**: mp  $104\text{--}105^\circ$  (1.347 g, 69%); ir (KBr) 3030, 1625, 1590, 1510, 960, 820, 810,  $755\text{ cm}^{-1}$ ;  $^1\text{H}$  nmr  $\delta$  (200 MHz,  $\text{CDCl}_3$ ) 3.89 and 3.91 (2s, OMe), 6.82 (d,  $J = 8.6\text{ Hz}$ , H-5'), 7.11 (dd,  $J = 8.2$  and  $2.0\text{ Hz}$ , H-6'), 7.20 (d,  $J = 2.0\text{ Hz}$ , H-2'), 7.25 (d,  $J_{\text{trans}} = 16.4\text{ Hz}$ , H-8'), 7.43 (t,  $J = 8.6\text{ Hz}$ , H-6), 7.56 (d,  $J_{\text{trans}} = 16.4\text{ Hz}$ , H-7'), 7.58 (m, 3H, H-7, H-5, H-3), 8.03 (d, 2H,  $J = 8.6\text{ Hz}$ , H-8 and H-4);  $^{13}\text{C}$  nmr  $\delta$  156.0 (C-2), 118.7 (C-3), 136.0 (C-4), 127.3 (C-4a), 127.3 (C-5), 125.8 (C-6), 128.8 (C-7), 129.5 (C-8), 148.0 (C-8a), 129.4 (C-1'), 108.7 (C-2'), 1149.6 (C-3'), 149.0 (C-4'), 110.9 (C-5'), 126.9 (C-7'), 134.0 (C-8'), 55.8 (MeO); ms  $m/z$  [ $\text{M}]^+$  291 (74), 276 (17), 260 (7), 233 (11), 178 (23), 150 (5), 128 (56). Exact mass calcd for  $\text{C}_{19}\text{H}_{17}\text{NO}_2$ , 291.1259; found 291.1244.

*2(3',4'-Dimethoxyphenylethyl)quinoline [5a].*—The olefin **4a** (500 mg) was hydrogenated over Pd/C (197 mg) in 95% EtOH containing  $\text{K}_2\text{CO}_3$  (178 mg) in a Parr apparatus at 5 psi for 1 h. The catalyst was filtered (Celite) and the solvent evaporated leaving the pure amorphous **5a** (quant.):  $^1\text{H}$  nmr  $\delta$  3.03 and 3.33 (2m, 4H, H-7' and H-8'), 3.78 and 3.80 (2s, OMe), 6.74 (m,

3H, H-3', H-5', H-6'), 7.20 (d,  $J = 8.2\text{ Hz}$ , H-3), 7.46 (t,  $J = 8.2\text{ Hz}$ , H-6), 7.70 (m, 2H, H-5 and H-7), 8.03 (d,  $J = 8.6\text{ Hz}$ , H-4), 8.13 (d,  $J = 8.2\text{ Hz}$ , H-8);  $^{13}\text{C}$  nmr  $\delta$  161.4, 121.4, 136.5, 126.6, 127.3, 125.8, 128.1, 129.5, 147.0, 133.7, 111.7, 148.5, 147.0, 111.0, 120.1, 35.4, 40.7, 55.6 (MeO), 55.7 (MeO); ms  $m/z$  [ $\text{M}]^+$  293 (84), 292 (68), 278 (41), 156 (66), 1561 (100), 129 (47). Exact mass calcd for  $\text{C}_{19}\text{H}_{19}\text{NO}_2$ , 293.1416; found 293.1406.

*2(3',4'-methyleneedioxyphenylethyl)-quinoline [5b].*—Mp  $64\text{--}65^\circ$  [lit. (1)  $65^\circ$ ];  $^1\text{H}$  nmr  $\delta$  3.00–3.27 (m, 4H, H-7' and H-8'), 5.84 (s, 2H,  $\text{OCH}_2\text{O}$ ), 6.62–6.74 (m, 3H, H-2', H-5', H-6'), 7.14 (d,  $J = 8.2\text{ Hz}$ , H-3), 7.43 (dt,  $J = 8.6$  and  $1.17\text{ Hz}$ , H-6), 7.61–7.72 (m, 2H, H-5 and H-7), 8.00 (d,  $J = 8.6\text{ Hz}$ , H-4) and 8.08 (d,  $J = 8.6\text{ Hz}$ , H-8);  $^{13}\text{C}$  nmr  $\delta$  161.5, 121.4, 136.0, 126.6, 127.4, 125.6, 128.7, 129.2, 147.8, 135.2, 108.9, 147.4, 147.4, 108.0, 121.1, 35.6, 41.2, 100.6 ( $\text{OCH}_2\text{O}$ ); ms  $m/z$  [ $\text{M}]^+$  277 (31), 276 (30), 156 (35), 135 (100), 129 (36), and 128 (24). Exact mass calcd for  $\text{C}_{18}\text{H}_{15}\text{NO}_2$ , 277.1103; found 277.1098.

*2(3',4'-methyleneedioxytyrlyl)-4-methoxyquinoline [4c].*—Mp  $178\text{--}180^\circ$  [lit. (1) amorphous];  $^1\text{H}$  nmr  $\delta$  4.06 (s, 3H, MeO), 5.98 (s, 2H,  $\text{OCH}_2\text{O}$ ), 6.81 (d,  $J = 8.1\text{ Hz}$ , H-5'), 6.90 (s, H-3), 7.06 (d,  $J = 8.1\text{ Hz}$ , H-6'), 7.16 (bs, H-2'), 7.18 (d,  $J = 16.5\text{ Hz}$ , H-8'), 7.42 (t, 7.7 Hz, H-6), 7.56 (d,  $J = 16.5\text{ Hz}$ , H-7'), 7.66 (t,  $J = 7.7\text{ Hz}$ , H-7), 7.99 (d,  $J = 8.1\text{ Hz}$ , H-8), 8.11 (d,  $J = 8.1\text{ Hz}$ , H-5);  $^{13}\text{C}$  nmr  $\delta$  156.9, 97.7, 162.3, 120.5, 121.5, 125.0, 128.4, 129.9, 148.9, 130.9, 105.9, 148.1, 148.0, 108.4, 122.6, 127.5, 133.6, 101.2, 55.6 (MeO); ms  $m/z$  [ $\text{M}]^+$  305 (93), 304 (100), 290 (55), 274 (51), 232 (27), 204 (38). Exact mass calcd for  $\text{C}_{19}\text{H}_{15}\text{NO}_3$ , 305.1052; found 305.1032.

## ACKNOWLEDGMENTS

We thank Dr. Pascal Richomme, Université d'Angers for his help comparing the samples and the Natural Sciences and Engineering Council of Canada (N.S.E.R.C.) and the Québec Ministère de l'éducation (F.C.A.R.) for financial help.

## LITERATURE CITED

1. A. Fournier, B. Vagneur, P. Richomme, and J. Bruneton, *Can. J. Chem.*, **67**, 2116 (1989).
2. C.E. Kaslow and R.D. Stayner, *J. Am. Chem. Soc.*, **67**, 1716 (1945).
3. E. Späth and O. Brunner, *Ber.*, **57**, 1243 (1924).

Received 3 June 1992