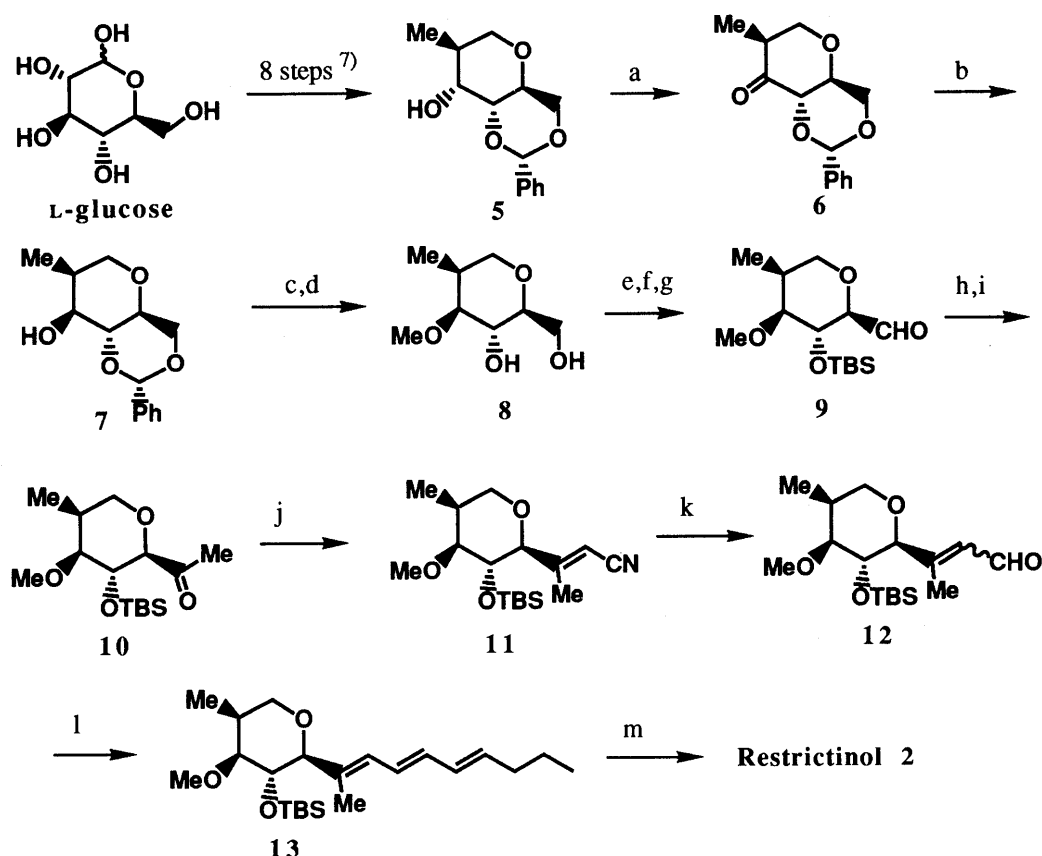
Table 1. *In vitro* Antifungal Activity of Ro 09-1571

Strains	MIC: $\mu\text{g/ml}$			
	Ketoconazole	Fluconazole	Ro 09-1571	Restricticin
<i>C.albicans</i> CY1005	>200	>200	50	>200
<i>C.albicans</i> CY3003	25	>200	25	200
<i>C.albicans</i> CY1002	>200	>200	25	>200
<i>C.neoformans</i> CY1057	0.025	12.5	3.13	1.56
<i>C.neoformans</i> CY1061	0.05	50	12.5	3.13
<i>C.neoformans</i> CY1059	0.1	25	6.25	3.13
<i>A.fumigatus</i> CF1003	3.13	>200	3.13	100
<i>A.fumigatus</i> CF1023	3.13	>200	3.13	100
<i>A.fumigatus</i> CF1004	3.13	>200	3.13	100

Agar dilution method, medium: $\text{YNB}+\text{K}_2\text{HPO}_4+\text{LMPA}$ (pH7.0), inoculum size: 1×10^5 cfu/ml, incubation : 3 days at 27°C .

The *in vitro* antifungal activity of Ro 09-1571 is summarized in Table 1 in comparison with those of Restricticin 1, Fluconazol, and Ketoconazole. Ro 09-1571 showed much more potent *in vitro* antifungal activity against *Candida albicans* and *Aspergillus fumigatus*, and nearly comparable activity against *Cryptococcus neoformans* when compared with natural product Restricticin 1. The antifungal activities of Ro 09-1571 against *Candida* and *Aspergillus* sp. are comparable with those of Ketoconazole. Moreover, it is noteworthy that the trans-1-nonenyl chain of Ro 09-1571 is no longer air-sensitive.

In summary, we have accomplished the synthesis of Restrictinol 2 and its analog, Ro 09-1571, with potent antifungal activity.

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- 8) Physicochemical data of the synthesized Restrictinol 2 were identical to those of the natural product.
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Spectral data

- 7 $^1\text{H-NMR}(\text{CDCl}_3)$ δ : 1.18(d, $J=7.3\text{Hz}$, 3H), 2.20(m, 1H), 3.33(dt, $J=4.4, 9.5\text{Hz}$, 1H), 3.6-3.8(m, 4H), 3.95(dd, $J=5.8, 9.5\text{Hz}$, 1H), 4.28(dd, $J=4.4, 10.2\text{Hz}$, 1H), 5.57(s, 1H), 7.37(m, 3H), 7.91(m, 2H); MS(EI) m/z :250(M^+).
 - 11 (E-isomer) $^1\text{H-NMR}(\text{C}_6\text{D}_6)$ δ : 0.00(s, 3H), 0.10(s, 3H), 0.81(d, $J=7.3\text{Hz}$, 1H), 0.93(s, 3H), 1.50(m, 1H), 1.89(d, $J=1.0\text{Hz}$, 3H), 2.67(dd, $J=9.0, 4.9\text{Hz}$, 1H), 2.89(s, 3H), 2.97(dd, $J=11.0, 2.0\text{Hz}$, 1H), 3.10(d, $J=9.0\text{Hz}$, 1H), 3.36(dd, $J=2.1, 11.0\text{Hz}$, 1H), 3.38(t, $J=9.0\text{Hz}$, 1H), 5.00(s, 1H); MS(EI) m/z :268($\text{M}^+ - \text{tBu}$).
 - 12 (E-isomer) $^1\text{H-NMR}(\text{C}_6\text{D}_6)$ δ : 0.00(s, 3H), 0.41(s, 3H), 0.89(d, $J=6.9\text{Hz}$, 3H), 0.94(s, 9H), 1.60(m, 1H), 1.88(d, $J=1.3\text{Hz}$, 3H), 2.75(dd, $J=8.6, 5.3\text{Hz}$, 1H), 2.93(s, 3H), 3.05(dd, $J=11.6, 2.0\text{Hz}$, 1H), 3.30(d, $J=8.6\text{Hz}$, 1H), 3.43(dd, $J=11.6, 1.5\text{Hz}$, 1H), 3.54(t, $J=8.6\text{Hz}$, 1H), 6.13(d, $J=7.6\text{Hz}$, 1H), 9.95(d, $J=7.6\text{Hz}$, 1H); MS(EI) m/z :328(M^+).
 - 13 $^1\text{H-NMR}(\text{C}_6\text{D}_6)$ δ : 0.16(s, 3H), 0.27(s, 3H), 0.89(t, $J=7.4\text{Hz}$, 3H), 1.06(s, 9H), 1.07(d, $J=6.3\text{Hz}$, 3H), 1.37(sext, $J=6.7\text{Hz}$, 2H), 1.95(s, 3H), 2.00(q, $J=7\text{Hz}$, 2H), 2.1-2.3(m, 1H), 2.97(dd, $J=8.9, 4.8\text{Hz}$, 1H), 3.06(s, 3H), 3.29(dd, $J=11.6, 2.0\text{Hz}$, 1H), 3.59(d, $J=8.9\text{Hz}$, 1H), 3.61(dd, $J=11.6, 1.7\text{Hz}$, 1H), 3.77(t, $J=8.9\text{Hz}$, 1H), 5.63(dt, $J=14.9, 7.1\text{Hz}$, 1H), 6.17(dd, $J=14.9, 10.4\text{Hz}$, 1H), 6.30(dd, $J=14.6, 10.4\text{Hz}$, 1H), 6.33(dd, $J=11.2, 1.1\text{Hz}$, 1H), 6.49(dd, $J=14.6, 11.2\text{Hz}$, 1H); MS(EI) m/z :394(M^+).
 - 14 $^1\text{H-NMR}(\text{CDCl}_3)$ δ : 0.02(s, 3H), 0.06(s, 3H), 0.84(s, 9H), 0.88(t, $J=6.6\text{Hz}$, 1H), 0.99(d, $J=7.1\text{Hz}$, 3H), 1.2-1.4(m, 11H), 2.0-2.3(m, 2H), 3.13(dd, $J=5.8, 8.8\text{Hz}$, 1H), 3.28(s, 3H), 3.43(t, $J=8.8\text{Hz}$, 1H), 3.56(dd, $J=2.2, 11.8\text{Hz}$, 1H), 3.75(dd, $J=2.2, 11.8\text{Hz}$, 1H), 3.80(t, $J=8.8\text{Hz}$, 1H), 5.35(t, $J=9.0\text{Hz}$, 1H), 5.64(dt, $J=9.0, 11.5\text{Hz}$, 1H); MS(EI) m/z 327($\text{M}^+ - \text{tBu}$).
- Ro 09-1571**
- $^1\text{H-NMR}(\text{CDCl}_3)$ δ : 0.86(t, $J=6.3\text{Hz}$, 3H), 1.04(d, $J=7.4\text{Hz}$, 3H), 1.24(m, 10H), 2.0(m, 2H), 2.2(m, 1H), 3.28(3H, s), 3.35(dd, $J=5.2, 9.4\text{Hz}$, 1H), 3.56(br.d, $J=11.2\text{Hz}$, 1H), 3.62(br.t, $J=9.4\text{Hz}$, 1H), 3.7-3.9(m, 3H), 4.90(t, $J=9.4\text{Hz}$, 1H), 5.38(1H, dd, $J=15.3, 8.2\text{Hz}$, 1H), 5.76(dt, $J=15.3, 6.0\text{Hz}$, 1H); MS(EI) m/z :327($\text{M}^+ - \text{TFA}$).

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