X-Ray Crystal Structure of Rocaglamide, a Novel Antileukemic 1*H*-Cyclopenta[*b*]benzofuran from *Aglaia elliptifolia*

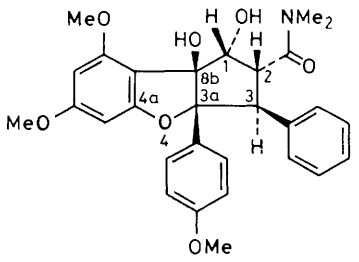
Ming Lu King,*[a] Chin-Chih Chiang,*[b] Han-Chin Ling,[b] Eiichi Fujita,*[c] Masahito Ochiai,[c] and Andrew T. McPhail*[d]

[a] *Department of Medical Research, Veterans General Hospital and Department of Pharmacology, National Yang-Ming Medical College, Taipei, Taiwan, Republic of China*
[b] *Department of Medical Research, Tri-service General Hospital and School of Pharmacy, National Defense Medical Center, Taipei, Taiwan*
[c] *Institute of Chemical Research, Kyoto University, Kyoto, Japan*
[d] *Paul M. Gross Chemical Laboratory, Duke University, Durham, North Carolina 27706, U.S.A.*

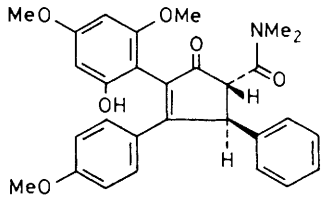
The structures and relative stereochemistries of rocaglamide, a novel antileukemic 1*H*-cyclopenta[*b*]benzofuran isolated from *Aglaia elliptifolia*, and dehydrorocaglamide, derived from rocaglamide, have been established from spectral and single-crystal *X*-ray analysis.

The alcoholic extract of dried roots and stems of *Aglaia elliptifolia* Merr. (Meliaceae) has been reported to exhibit significant antileukemic activity against P388 lymphocytic leukemia in CDF_1 mice[1] and inhibitory activity *in vitro* against cells derived from human epidermoid carcinoma of the nasopharynx (KB cell).†

Examination of the chloroform-soluble fraction of this extract has now led to the isolation of a novel 1*H*-2,3,3a,8b-tetrahydrocyclopenta[*b*]benzofuran, rocaglamide (**1**), with significant antileukemic activity against P388 leukemia in CDF_1 mice. Rocaglamide (**1**), $C_{29}H_{31}NO_7$,‡ *m/e* 505.2087 (M^+); m.p. 118—119 °C (MeOH); $[\alpha]_D^{25}$ −96° (*c*. 1.00, $CHCl_3$), λ_{max} (EtOH) 214 (log ε 4.38), 232 (sh, log ε 3.96), 273 nm (log ε 2.91). When (**1**) was treated with conc. HCl in diethyl ether solution it yielded dehydrorocaglamide (**2**), $C_{29}H_{29}NO_6$, *m/e* 487.1980 (M^+, found; 487.1972, calc.); m.p. 233—234 °C (MeOH); $[\alpha]_D^{25}$ +435° (*c* 0.2, $CHCl_3$). The similarity of the ^1H n.m.r. spectra of (**2**) and (**1**) attested to the fact that the former had retained several of the functional groups originally present in the latter. The appearance of new absorptions at 1700 cm^{-1} in its i.r. spectrum and λ_{max} (EtOH) 312 nm (log ε 3.71) in its u.v. spectrum confirmed the existence of an α,β-unsaturated cyclopentenone system and a stilbene chromophore, respectively, in (**2**).



(1)



(2)

A single-crystal *X*-ray analysis of (**1**), as the methanol solvate, unequivocally defined its complete structure and stereochemistry. *Crystal data:* $C_{29}H_{31}NO_7.CH_3OH$, M = 537.62, monoclinic, space group $P2_1$, a = 14.260(6), b = 7.822(3), c = 12.323(5) Å, β = 98.01(2)°, U = 1361.1 Å^3,

† KB-cell culture assay and P388 *in vivo* activity were conducted under the auspices of the National Cancer Institute by literature procedures (R. I. Geran, H. H. Greenberg, M. M. MacDonald, A. M. Schumacher, and B. J. Abbott, *Cancer Chemother. Rep., Part* 3, 1972, **3**, 1). The extract showed ED_{50} = 4.4 × 10° mcg/ml in the KB assay. In the P388 system, rocaglamide (**1**) exhibited optimal values of *T/C* of *ca.* 156% at a non-toxic dose of 1.0 mg/kg.

‡ Satisfactory elemental analyses were obtained; i.r., ^1H and ^{13}C n.m.r. spectra were consistent with the structures shown.

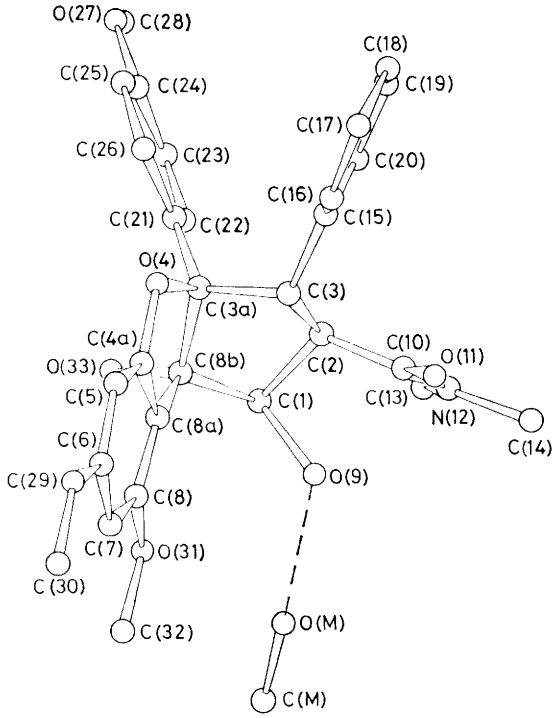


Figure 1. Structure and solid-state conformation of rocaglamide (**1**); the broken line denotes an O . . . H–O hydrogen bond to the methanol of solvation.

$Z = 2$, $D_c = 1.312$ g cm^{-3}. The structure was solved by direct methods.[2] Least-squares refinement of atomic positional§ and thermal parameters (anisotropic C, N, O; fixed H contributions) converged at R 0.061 using 1498 reflections measured on an Enraf–Nonius CAD-3 automated diffractometer[3] (Ni-filtered Cu-K_α radiation, $\lambda = 1.5418$ Å; θ–2θ scans, θ_{max} 67°). A view of the structure is shown in Figure 1.

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2 P. Main, L. Lessinger, M. M. Woolfson, G. Germain, and J.-P. Declerq, 'MULTAN 76, A System of Computer Programmes for the Automatic Solution of Crystal Structures,' Universities of York and Louvain, 1976.
3 For details, see R. W. Miller and A. T. McPhail, *J. Chem. Soc., Perkin Trans.* 2, 1979, 1527.

§ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.