

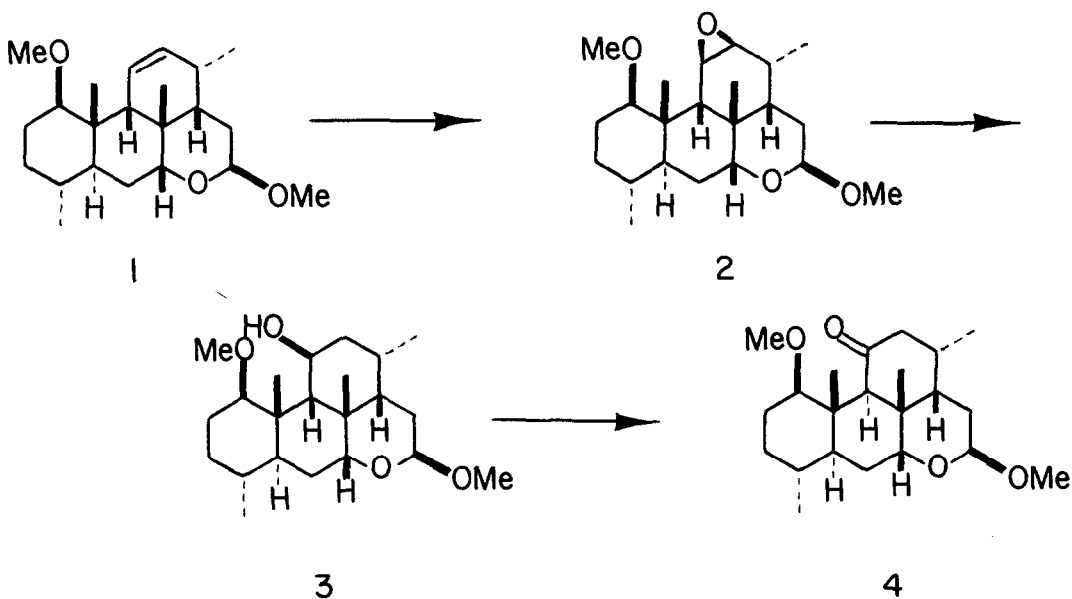
NOVEL TRANSFORMATIONS IN THE QUASSIN SERIES

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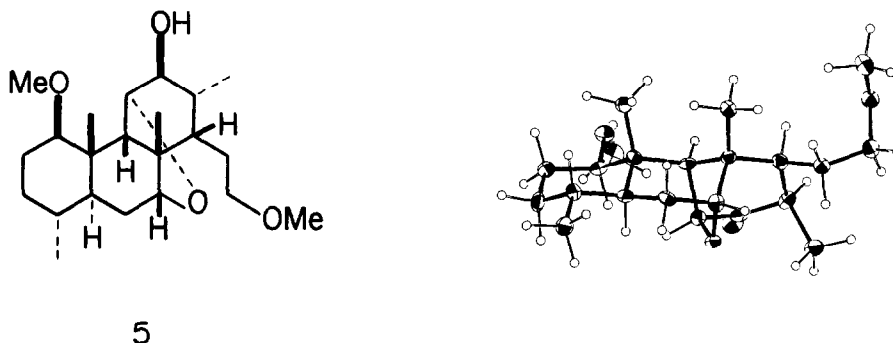
Summary: A series of remarkable rearrangement reactions involving (1 β ,9 β)-1-methoxypicras-11-en-16-one and related derivatives are described.

During our total synthesis² of quassin,³ the bitter principle of *Quassia amara*, we prepared [C₆H₅CN, KHCO₃, MeOH, 50% H₂O₂]⁴ in 83% yield, epoxide 2,⁵ mp 129-130°C, from the picrasene derivative 1⁶ in order to indirectly provide access to the quassinoid intermediate 4 via alcohol 3.

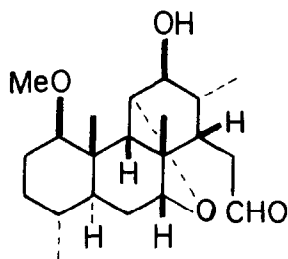


It was anticipated that once 3 was in hand, oxidation followed by epimerization at C(9) would give rise to the complete carbon framework of quassin with all chiral centers established (cf. structure 4). Much to our surprise, treatment of epoxide 2 with lithium aluminum hydride (THF, reflux) provided not a trace of alcohol 3 as evidenced by the lack of the C(16) methine proton in the high field NMR spectrum of the crude product. There was obtained a 60% yield of a crystalline compound,

mp 163-164°C, which was initially assigned structure 5⁵ on the basis of NMR (220 MHz) data. The stereochemical features of 5 were unambiguously established by single-crystal X-ray analysis. The molecular structure of compound 5 reveals the presence of the C(7), C(11) oxygen bridge.



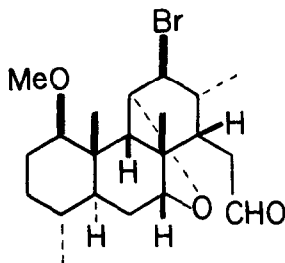
A similar rearrangement was observed upon treatment of epoxide 2 with a catalytic amount of concentrated hydrochloric acid in aqueous acetone at room temperature. Workup gave rise in 92% yield to a crystalline substance, mp 146-147°C, which has been assigned structure 6⁵ on the basis of spectral data [IR (CHCl₃) 3590, 3410, 2710, 1716 cm⁻¹; NMR (300 MHz) CDCl₃ δ 9.85 (t, 1H, J = 1.5 Hz, -CHO), 4.10 (s, 1H, C(11) H), 3.72 (d, 1H, J = 5 Hz, C(7) H), 3.33 (s, 4H, -OCH₃, C(12) H), 3.18 (dd, 1H, J = 4.8 Hz and 10.5 Hz, C(1) H), 2.50 (s, 1H, C(9) H)]. Examination of



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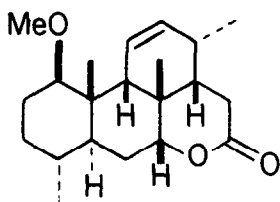
a Dreiding model of epoxide 2 indeed reveals the close proximity of the C(7) oxygen atom to the C(11) carbon atom.

Further experimentation has revealed that the rearrangements observed above are indeed general in the context of 9 β -picras-11-en-16-one derivatives. For example, irradiation (sun lamp) of 1 in aqueous acetone containing N-bromoacetamide afforded (75%) bromo aldehyde 7,⁵ mp 115-118°C (dec) [IR (CHCl₃) 2710, 1717 cm⁻¹].

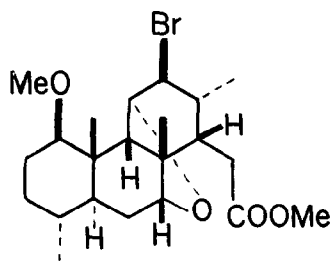


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Similar exposure of (1 β ,9 β)-1-methoxypicras-11-en-16-one (8)⁶ to N-bromoacetamide in aqueous acetone provided after esterification (CH₂N₂) of the resultant bromo acid a 65% yield of bromo ester 9.⁵



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References and Notes:

1. On leave from the University of Pavia, 1979-1980.
2. P.A. Grieco, S. Ferrino and G. Vidari, *J. Am. Chem. Soc.*, **102**, 0000 (1980).
3. Z. Valenta, S. Papadopoulos and C. Podesva, *Tetrahedron*, **15**, 100 (1961); Z. Valenta, A.H. Gray, D.E. Orr, S. Papadopoulos and C. Podesva, *Tetrahedron*, **18**, 1433 (1962); R.M. Carman and A.D. Ward, *Aust. J. Chem.*, **15**, 805 (1962).
4. G.B. Payne and P.H. Williams, *J. Org. Chem.*, **26**, 651 (1961); G.B. Payne, P.H. Deming, and P.H. Williams, *J. Org. Chem.*, **26**, 659 (1961).
5. All new compounds have been fully characterized including combustion (C, H) analysis.
6. The preparation of 6 follows from previously published work [P.A. Grieco, S. Ferrino, G. Vidari and R.C. Haltiwanger, *Tetrahedron Letters*, 1619 (1980)] and will be reported in due course.
7. Compound 5 crystallizes in space group $P2_1/n$ with $a = 11.997(2)$, $b = 10.753(2)$, $c = 16.056(3)$ Å, and $\beta = 109.86(2)^\circ$ at -182°C ; $D_{\text{calc}} = 1.243$ gm/cm³ for $Z = 4$. A continuous $\theta - 2\theta$ scan at a rate of $3^\circ/\text{min}$ over a range of 2° + dispersion and 5 sec background counts was used to collect the 2534 unique amplitudes on a Picker goniostat. The structure was solved by direct methods and refined by full-matrix least squares to yield final residuals of $R(F) = 0.067$ and $R_w(F) = 0.059$.

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