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# A PARTIAL SYNTHESIS OF PICRASIN B AND $\Delta^2$-PICRASIN B[1]

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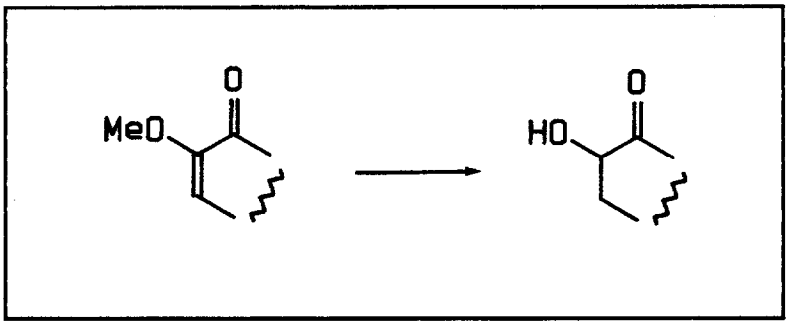
Abstract. The regioselective reductive demethylation of the O-methyldiosphenol functionality in the A ring of quassin (3) with chlorotrimethylsilane and sodium iodide furnished picrasin B (1). Swern oxidation of 1 furnished $\Delta^2$-picrasin B (2), and O-methylation of 2 regenerated quassin (3).

In connection with an enantioselective total synthesis[2] of picrasin B (1) and $\Delta^2$-picrasin B (2), we required authentic samples of these quassinoids[3] first isolated by Takemoto[4] and Polonsky.[5] In undertaking a partial synthesis of these quasssinoids from quassin (3), we sought a regioselective reduction and demethylation of the O-methyldiosphenol in the A ring of 3 in order to procure the α-ketol and diosphenol functionality characteristic of 1 and 2, respectively. In the former case, a direct method for the reductive demethylation of an O-methyldiosphenols to an α-ketols was not available, but the ability of iodotrimethylsilane to undergo 1,4-additions to α,β-unsaturated ketones,[7] to effect the demethylation of methyl ethers,[8] and to promote the reduction of α-haloketones[9] suggested that this reagent might achieve this overall conversion. It also seemed likely that iodotrimethylsilane would differentiate between the two O-methyldiosphenol groups in quassin (3) in favor of the O-methyldiosphenol in the A ring lacking a β-methyl substituent.[10] We report a partial synthesis of 1 and 2 that employed an unexpected but selective reductive demethylation of quassin (3).



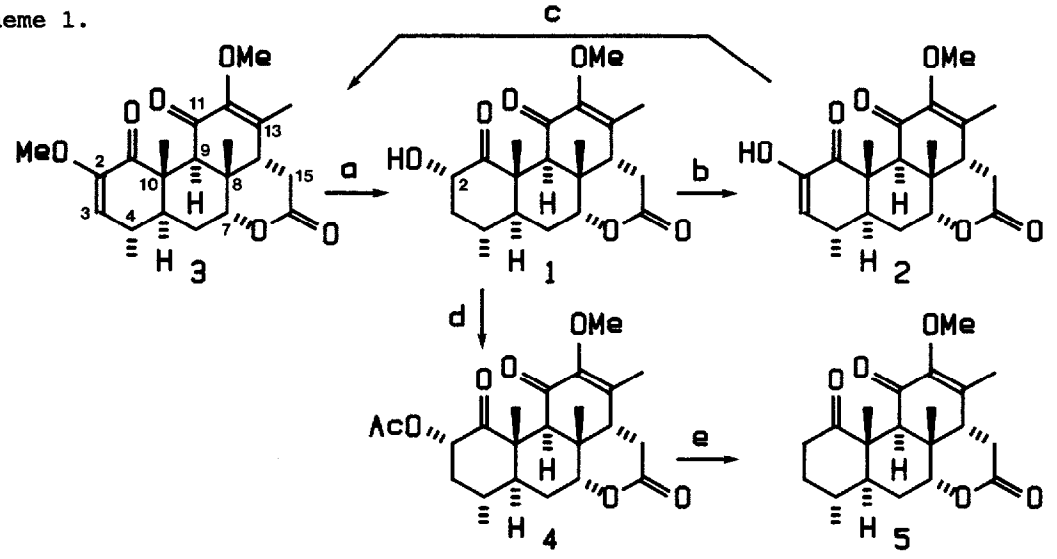
Exposure of quassin (3) to 3.5 equivalents of chlorotrimethylsilane and 3.5 equivalents of sodium iodide[11] in acetonitrile at 25°C furnished picrasin B (1) in 42% yield as shown in Scheme 1. Although we could not secure an authentic sample of 1, all spectral data was in accord with published information for this structure. The $^1$H NMR spectrum of 1 displayed a characteristic multiplet at δ 4.78-4.93 for $H_{2\beta}$ and a single methoxy signal at δ 3.67 as well as the absence of the vinylic $H_3$ signal at δ 5.31 (d, J=2.5 Hz). Swern oxidation[12] of the α-ketol functionality in 1 furnished $\Delta^2$-picrasin B (2), and O-methylation of 2 regenerated quassin (3) thereby securing the structural assignments in this series. Furthermore, conversion of 1 to the α-acetoxyketone 4 and the reduction of 4 using zinc in acetic acid[13] secured 2-deoxypicrasin B (5) that was identical to material prepared by an enatioselective synthesis[2] from R-(-)-enantiomer of the Wieland-Miescher ketone.

We observed that the reduction of quassin (3) by iodotrimethylsilane in $CH_3CN$ proceeded with the rapid formation of a dark brown color consistent with the presence of iodine, that the reduction in the presence of $CD_3CN$ led to no deuterium incorporation, and that the reduction in the presence of 0.5 equivalents of water successfully produced picrasin B (1). In addition, the reduction of quassin (3) produced both the α-ketol 1 and a 9% yield of the α-methoxyketone 9. The mechanism of this reduction presumably involved the 1,4-addition of iodotrimethylsilane to the O-methyldiosphenol functionality in the A ring to provide the intermediate β-iodo trimethylsilyl enol ether 6 in Scheme 2. The C-13 methyl group in 3 retarded addition to the O-methyldiosphenol functionality in the C ring. Hydrogen iodide, produced by the adventitious hydrolysis of iodotrimethylsilane in experiments conducted in $CH_3CN$ or $CD_3CN$ alone, provided the reducing agent for the conversion of 6 to the enol ether 7.[14] Further demethylation of the C-2 methoxy group and hydrolysis of the trimethylsilyl enol ethers 7 or 8 furnished the products.

The experimental procedure for the preparation of picrasin B (1) is as follows. To 299 mg (0.77 mmol) of quassin (3) (Pfaltz and Bauer, purified) in 10 mL of acetonitrile at 25°C was added 404 mg (2.7 mmol) of sodium iodide followed by 342 μL (2.7 mmol) of chlorotrimethylsilane. The mixture was

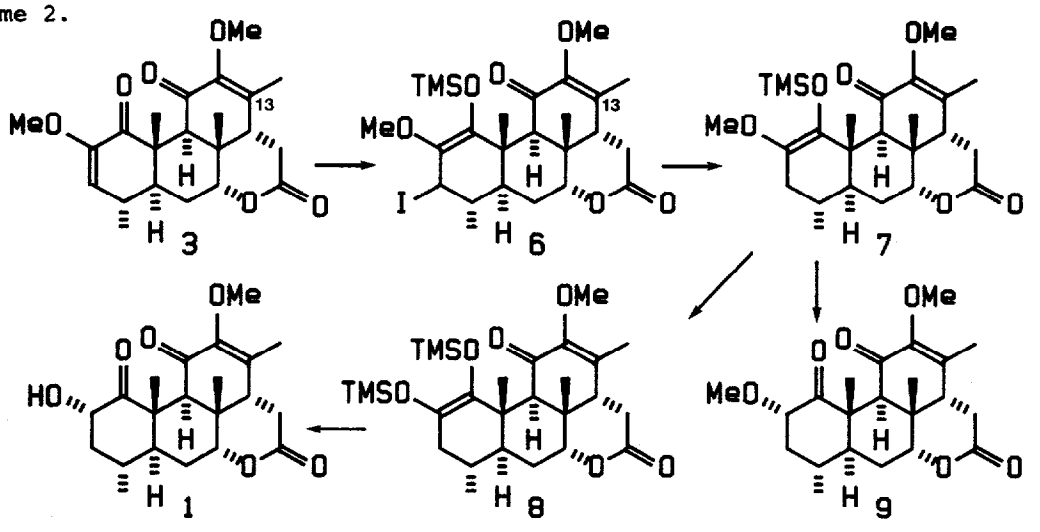
stirred for 18 h and quenched by the addition of 5% aqueous sodium thiosulfate solution. The mixture was diluted with EtOAc and washed successively with water and brine. The organic layer was dried and chromatographed on silica gel using 2:1 ethyl acetate-hexane to afford 120 mg (42%) of 1, having all spectral data in accord with published values, and 28 mg (9%) of 9.[15]

Scheme 1.




a, TMSCl, NaI, $CH_3CN$, 25°C; b, DMSO, TFAA followed by $Et_3N$; c, NaH, MeI; d, $Ac_2O$, Py; e, Zn, HOAc, reflux.

Scheme 2.



## Acknowledgement

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15. Spectral data for α-methoxyketone 9: IR (TF) 1720, 1670, 1630 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 0.94 (d, J=6.5 Hz, 3, C-4 $CH_3$), 1.21 (s, 3, C-8 $CH_3$), 1.46 (s, 3, C-10 $CH_3$), 1.91 (s, 3, C-13 $CH_3$), 2.99 (dd, J=6 and 18 Hz, 1, C-15β H), 3.30 (s, 1, C-9α H), 3.42 (s, 3, C-2 $OCH_3$), 3.66 (s, 3, C-12 $OCH_3$), 4.28 (t, J=2 Hz, 1, C-7β H), 4.50 (dd, J=7 and 11 Hz, 1, C-2β H); exact mass spectrum calcd for $C_{22}H_{30}O_6$ 390.2043, found 390.2041.

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