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THE SYNTHESIS OF VAFZELIN AND SYNCARPIN, CONSTITUTENTS OF UVARIA AFZELII

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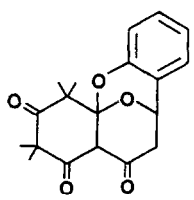
Summary: Efficient syntheses of vafzelin and syncarpin, unusual plant metabolites from Uvaria afzelii, are described.

The genus Uvaria continues to be a source of chemically and biologically interesting compounds.[1] Recent work on U. afzelii has resulted in the isolation and characterization of the unusual metabolites vafzelin (1)[2] and syncarpin (2)[3]. Since vafzelin (1) is a naturally occurring racemate, it had been speculated[2] that it might arise by a simple, nonenzymatic route. We now wish to report an efficient preparation of vafzelin (1) and the closely related metabolite syncarpin (2).



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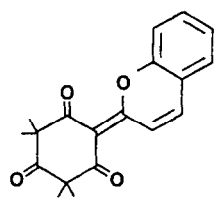

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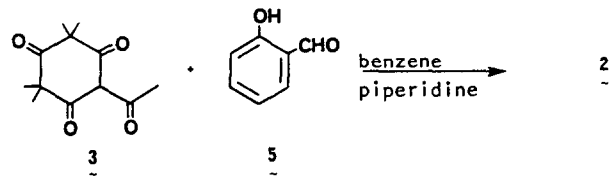
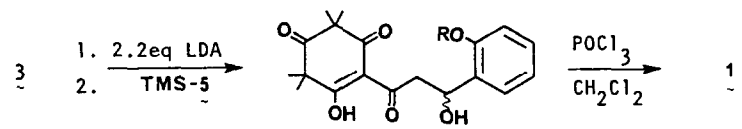
The sequences begin with C-acetylsyncarpic acid (3) which was prepared by the method of Jain and Seshadri.[4] This was used in an aldol condensation with salicylaldehyde. To prepare syncarpin (2), C-acetylsyncarpic acid (3) and salicylaldehyde (5, 1.2 eq.) were dissolved in benzene with a catalytic amount of piperidine. A compensated dropping funnel filled with 3A molecular sieves was placed between the flask and the reflux condenser to aid in water removal and the mixture was heated under reflux for 8 hours. Removal of the solvent by rotary evaporation followed by chromatography (silica gel, 5:1 hexanes:ethyl acetate) gave syncarpin (2) in an 80% isolated yield based on 3. Recrystallization from methanol resulted in syncarpin with an m.p. of 88-89°C.[5]

Vafzelin (1) was prepared in a two-step process. C-acetylsyncarpic acid (3) was first treated with 2.2 eq. of LDA (THF, -78°C) to generate the dianion and one equivalent of the TMS ether of salicylaldehyde 6 was added.[6] Allowing this mixture to warm to 0° and quenching with



3 5 2

1N HCl resulted in a near quantitative yield of 4a and 4b.[7] The resulting aldol products were dissolved in CH_2Cl_2 and treated with one equivalent of $POCl_3$ (rt, overnight). After chromatography (silica gel, 6:1 hexanes:ethyl acetate), vafzelin (1) was obtained in 85% yield based on 3. Recrystallization from n-hexane resulted in 1 (75% yield). This material is identical (MP, TLC, ^1H NMR snd single crystal x-ray lattice parameters) to an authentic sample.[2]



3 → 1

4a R=H
4b R=TMS

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NOTES AND REFERENCES

1. J.R. Cole, S.J. Torrance, R.M. Wiedhopf, J. Org. Chem., 41, 1852 (1976); C.D. Hufford B.O. Oguntimein, Phytochemistry, 18, 2036 (1980); and references therein.

2. C.D. Hufford, B.O. Oguntimein, D. Van Engen, D. Muthard, J. Clardy, J. Am. Chem. Soc., 102, 7365 (1980).

3. C.D. Hufford, B.O. Oguntimein; paper to appear in J. Org. Chem.

4. A.C. Jain, T.R. Seshardri, Proc. Indian Acad. Soc. Sect A, 42, 279 (1955).

5. Syncarpin (2): IR($CHCl_3$) 1730, 1680, 1560 cm^{-1}; UV (dioxane) λ_{max} 445 mm (sh log ε 4.37), 422 (4.53), 400 (4.49), 280 (4.27), 220 (4.57); ^1H NMR ($CDCl_3$) δ 8.-3 (1H, d, J=10Hz), 7.70 (1H, d, J=10Hz), 7.60-7.20 (4H, m), 1.43 (12H, s); ^{13}C NMR 210.6s, 197.1s(2x), 166.8s, 152.6s, 139.8d, 132.9d, 127.5d, 125.8d, 120.9s, 119.6d, 117.7d, 108.6s, 58.2s(2x), 23.1q(4x)

6. Prepared from salicylaldehyde, triethylamine and chlorotrimethylsilane. B.P. 128°C/22mm; ^1H NMR δ 0.27 (9H, s); 6.78-7.86 (4H, m), 10.49 (1H, s).

7. Some hydrolysis always occurs during the acid quench. The ratio of 4a to 4b was determined by ^1H NMR and was dependent upon temperature and duration of the acid wash. Following partition (ether:1N HCl, 0°C) and solvent removal, the mixture was used without further purification. 4b ^1H NMR ($CDCl_3$) 6.82-7.25 (m 4H), 5.42 (m 1H), 3.84 (m 1H), 1.43 (br s 6H) 1.36 (br s 6H).

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