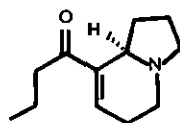


ALTERNATIVE TOTAL SYNTHESIS OF ELAEOCARPUS ALKALOIDS[†]

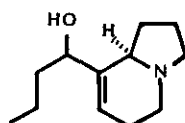
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Abstract—An alternative synthesis of Elaeocarpus alkaloids using 1,3-dipolar cycloaddition of Δ^1 -pyrrolin-1-oxide with the enone to give the isoxazolidine as a key intermediate is described.

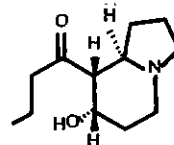
Recently we have published¹⁻³ the stereoselective synthesis of carbapenem antibiotics, thienamycin and its derivatives, by the application of 1,3-dipolar cycloaddition of nitrile oxides with crotonic ester as a key reaction. As an extension of our work on this cycloaddition reaction, we have investigated an alternative synthesis of Elaeocarpus alkaloids, such as elaeokanine A (1), B (2), and C (3), isolated by Johns et al.⁴ from the leaves of Elaeocarpus species. These alkaloids are known to possess a characteristic trans-indolizidine ring system, and several synthetic methods for them have been reported⁵⁻¹² to date. Our synthesis of Elaeocarpus alkaloids began with the preparation of an isoxazolidine as a key intermediate which was obtained by 1,3-dipolar cycloaddition of a nitron^{1,3} with an enone. Thus, the requisite enone (8) was prepared as follows. 3-Butyn-1-ol (4) was converted into its tetrahydropyranyl ether (THP) (5), whose alkylation with *n*-butyraldehyde in the presence of *n*-butyllithium afforded the acetylenic alcohol (6) in 82% yield from 4. Reduction of (6) with lithium aluminium hydride in tetrahydrofuran gave rise to trans-olefin (7), which was then oxidised with manganese dioxide to



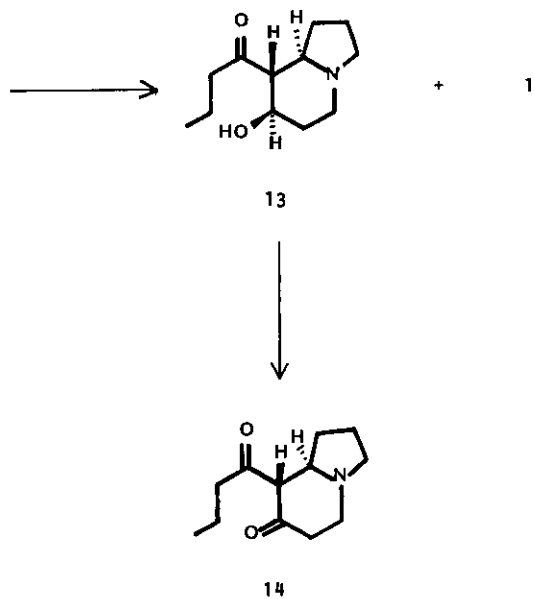
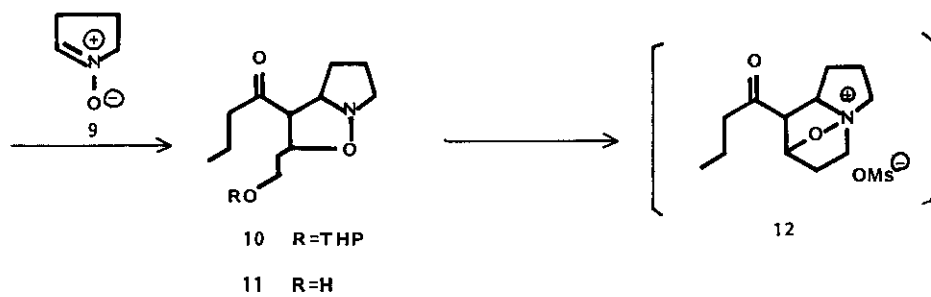
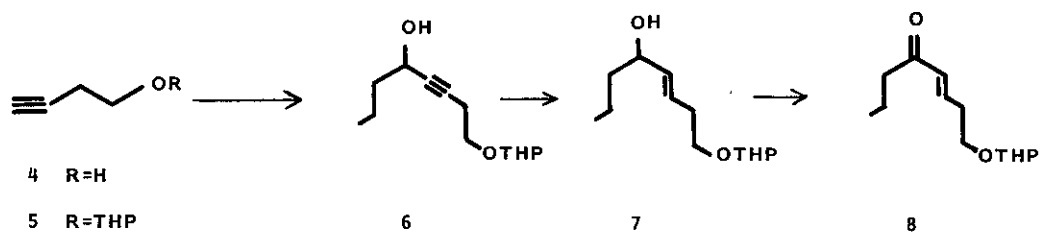
1



2



3



furnish the trans-enone (8) in 50 % yield from (6). 1,3-Dipolar cycloaddition of (8) with Δ^1 -pyrrolin-1-oxide (9) was carried out in refluxing chloroform to yield the stereoisomeric mixtures of adducts (10) in 88 % yield. After the deprotection of tetrahydropyranyl ether of (10) with 10 % aqueous hydrochloric acid in tetrahydrofuran, the resulting primary alcohol (11) was converted to quaternary salts (12) by mesylation, which without purification was treated with zinc powder in 50 % aqueous acetic acid to afford the β -hydroxy ketone (13) as a major product¹⁴ in 26 % yield from (10). The stereochemical assignment was deduced from its spectral data¹⁵ and the formation of (13) suggested that the epimerisation at the C₄-position of (11) occurred during its conversion into (13). Finally the β -hydroxy ketone (13) was oxidised to the diketone (14)¹⁶ whose structure was unambiguously supported by its spectral data^{17,18}. Since the conversion of (14) to elaeokanine C has already been reported⁴, this synthesis constitutes a formal synthesis of elaeokanine C. Furthermore, 1,3-dipolar cycloaddition of the cis-enone with Δ^1 -pyrrolin-1-oxide is under investigation.

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14 Elaeokanine A was also obtained as a minor product in ca. 5 % yield from (10), probably arising from elaeokanine C by dehydration.

15 IR ν_{\max} (CHCl₃) : 1705 cm⁻¹ ; NMR (CDCl₃) 0.90 (3H, t, J = 7 Hz, 13-Me), 1.60 (2H, tq, J = 7 and 7 Hz, 12-CH₂), 2.54 (2H, t, J = 7 Hz, 11-CH₂), 2.25 (1H, dd, J = 10 and 10 Hz, 8-H), 3.87 (1H, dt, J = 5 and 10 Hz, 7-H) : MS m/e 211(M⁺).

16 IR ν_{\max} (CHCl₃) 1720 - 1690 cm⁻¹ (broad) [lit¹⁰, 1720 - 1680 cm⁻¹] : MS m/e 209 (M⁺), 208, 190, 181, 166, 164, 152, 139, 138 (base peak), 136, 120.

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