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A GENERAL SYNTHESIS OF ISOTWIST-8-EN-2-ONES FROM o-(3-BUTENYL)PHENOLS

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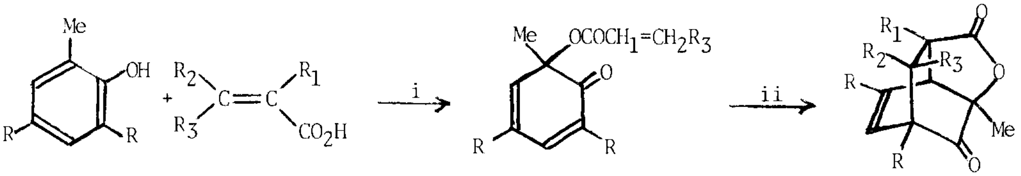
Abstract: Wessely oxidation of o-(3-butenyl)phenols with lead tetraacetate gives 2,4-cyclohexadienone derivatives that on heating undergo intramolecular Diels-Alder reactions to give 3-acetoxyisotwist-8-en-2-ones.

A general method has been devised in these Laboratories for the synthesis of tricyclic lactones of type 1 involving a "modified" Wessely oxidation of ortho-alkyl-substituted phenols with lead tetraacetate in the presence of an excess of an α,β-unsaturated carboxylic acid followed by an intramolecular Diels-Alder reaction (Scheme 1).[1] We now report the application of a related tandem of reactions to the synthesis of isotwist-8-en-2-ones 5,[2] the tricarbocyclic analogues of 1.



R = H or Me

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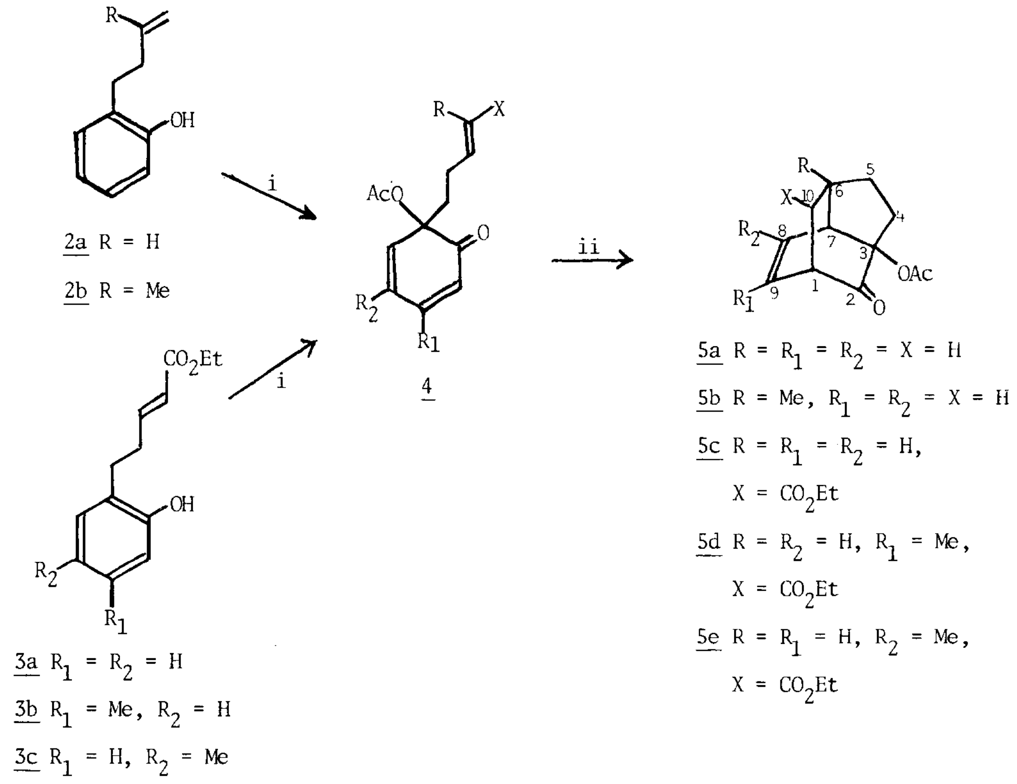
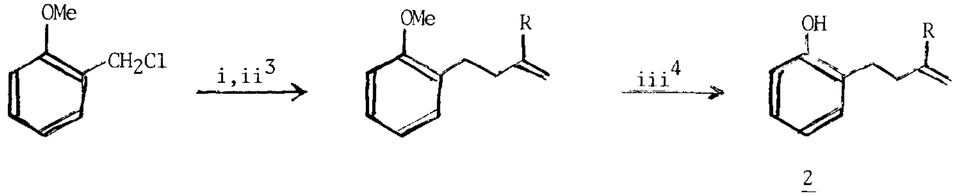
Scheme 1. i, $Pb(OAc)_4/CH_2Cl_2$; ii, Δ.

Conventional Wessely oxidation of o-(3-butenyl)phenols of types 2 and 3 with lead tetraacetate in acetic acid gave 2,4-cyclohexadienones of type 4 which were not isolated but were heated in boiling xylene to give the isotwist-8-en-



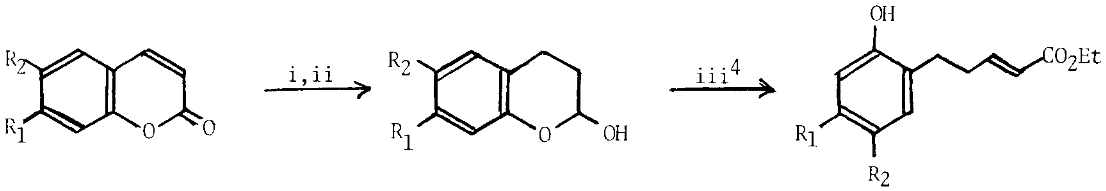
Scheme 2. i, Pb(OAc)$_4$/AcOH; ii, Δ.

2-ones 5. The phenols of type 2 were prepared from o-methoxybenzyl chloride in 50-60% yield (Scheme 3); phenols of type 3 were prepared from the corresponding



Scheme 3. i, Mg/Et$_2$O; ii, CH$_2$=CHRCH$_2$Cl; iii, EtSNa, Δ.

coumarins 6 in 80-90% yield (Scheme 4); the *E* isomers were formed preponderantly, accompanied by small amounts of the *Z* isomers.



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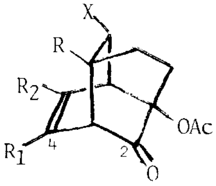
Scheme 4. i, $H_2/Pd/C$; ii, ($\underline{i}$-Bu)$_2$AlH; iii, $Ph_3P{=}CHCO_2Et$.

The infrared, ^1H and ^{13}C nuclear magnetic resonance, and mass spectra of the isotwist-8-en-2-ones 5 were in accord with the structural assignments, as exemplified by the spectra of 5a, m.p. 52.2-53.5°C; λ_{max} ($CHCl_3$) 1750 (sh), 1730 cm^{-1}; $^{H}\delta$ ($CDCl_3$) (250 MHz) 1.37 (ddd, *J* 13, 3, 2 Hz, 1H), 1.47 (ddd, J 12, 9, 2.5 Hz, 1H), 1.64 (ddd, *J* 13, 10.5, 2 Hz, 1H), 1.84 (m, 1H), 1.96 (s, 3H), 2.02 (m, 1H), 2.20 (m, 1H), 2.39 (dddd, *J* 14, 12, 3, 1.5 Hz, 1H), 3.11 (m, 1H), 3.47 (ddd, *J* 6. 4.5, 2 Hz, 1H), 6.12 (ddd, *J* 8, 6, 1.5 Hz, 1H), 6.21 (ddd, *J* 8, 6.5, 2 Hz, 1H); $^{C}\delta$ ($CDCl_3$) 21.7 (q), 28.9 (t), 29.8 (t), 31.2 (t), 34.3 (d), 46.3 (d), 47.4 (d), 84.4 (s), 129.8 (d), 131.7 (d), 169.9 (s), 208.2 (s); m/e (rel abund) 206 (19), 164 (35), 136 (78), 118 (86). There are two possible regiochemical courses for the Diels-Alder reactions - that in Scheme 2 leading to products of type 5 and another giving rise to twist-4-en-2-ones of type 7. That the former course is pursued, as in the case of the analogous lactone formation in Scheme 1, is established by detailed analysis of the nuclear magnetic resonance spectra and in the case of 5a by the demonstration that hydrolysis to the corresponding α-ketol followed by oxidative cleavage of the latter function with periodic acid gives the keto acid 8 (λ_{max} 1750, 1710 cm^{-1}) rather than 9.



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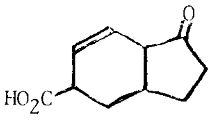

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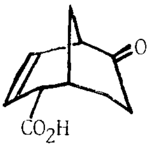

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The yields of the isotwist-8-en-2-ones 5 from the phenols 2 and 3 are 20-30%; however, this disadvantage is offset by the brevity of the synthetic sequence. Related syntheses of isotwist-8-en-2-ones and twist-4-en-2-ones and analogous compounds utilizing intramolecular Diels-Alder reactions of 2,4-cyclohexadienones have been reported previously; in these the dienones were generated by C-alkylation of phenols[6] or pyrolysis of fulvene 5,6-epoxides.[7] The present synthesis differs from these in providing tricyclic ketones bearing an acetoxy substituent, a feature that can be of advantage for further synthetic elaborations.

Acknowledgement

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References and Notes

1. D.J. Bichan and P. Yates, J. Am. Chem. Soc., 94, 4773 (1972); Can. J. Chem., 53, 2054 (1975); P. Yates and H. Auksi, J. Chem. Soc., Chem. Commun., 1016 (1976); Can. J. Chem., 57, 2853 (1979).
2. Isotwistane is tricyclo[4.3.1.0^{3,7}]decane or octahydro-1,5-methano-1*H*-indene; the numbering used corresponds to that for the former formal designation and is given in 5.
3. M. Oki and H. Iwamura, Bull. Chem. Soc. Jpn., 33, 681 (1960).
4. *Cf*. G.I. Feutrill and R.N. Mirrington, Aust. J. Chem., 25, 1719 (1972).
5. *Cf*. L.D. Bergel'son, E.V. Dyatlovitskaya, and M.M. Shemyakin, Izv. Akad. Nauk SSSR, Ser. Khim., Engl. Transl., 1904 (1964).
6. H. Greuter and H. Schmid, Helv. Chim. Acta, 55, 2382 (1972).
7. F. Näf, R. Decorzant, and W. Thommen, Helv. Chim. Acta, 60, 1196 (1977).

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