Tetrahedron Letters, Vol.22, No.34, pp 3273 - 3274, 1981
Printed in Great Britain

0040-4039/81/343273-02$02.00/0

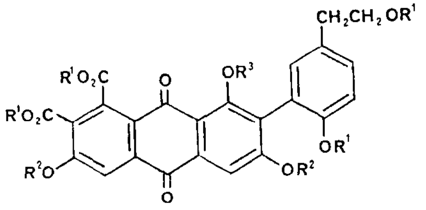
SYNTHESIS OF THE XANTHOLACCAIC ACID B SYSTEM

Donald W. Cameron*, Geoffrey I. Feutrill and Patrick Perlmutter
Department of Organic Chemistry, University of Melbourne, Parkville, Vic., 3052, Australia.

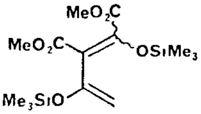
Summary. The xantholaccaic acid B system has been synthesized for the first time by successive regiospecific Diels-Alder reactions.

This communication reports the synthesis of a derivative of xantholaccaic acid B (1), the major water-soluble pigment of the Australian lac insect *Austrotachardia acaciae* Maskell.[1] This insect and the related Indian species *Laccifer lacca* Kerr, elaborate a series of aryl-substituted polyhydroxyanthraquinone carboxylic acids which are among the most complex natural anthraquinones and which form the basis of the lac dyestuffs.[2] Structural elucidation of the acids was complicated by their high polarity, they were most effectively handled as methyl ester methyl ether derivatives[3,4] and their structures have not hitherto been confirmed by synthesis or degradation to known compounds. In our recent report of the occurrence of xantholaccaic acid B in *A. acaciae* the structure of the hexamethyl derivative (2) was determined by X-ray diffraction.[1]

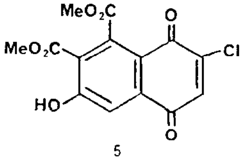
In other work we have described a highly convergent methodology for the synthesis of less complex anthraquinones.[5] This has now been developed to obtain the first synthesis of the xantholaccaic acid system. The synthesis involved sequential Diels-Alder additions of appropriately substituted butadienes to 2,6-dichlorobenzoquinone, utilizing the regiochemical control generally observed in cycloadditions to haloquinones.[5] Diene (3) was prepared from the tautomeric diketo diester (4) which was itself readily available through acylation (72%) of methyl acetoacetate with methyl oxalyl chloride. Treatment of (4) with *N*,*O*-bis(trimethylsilyl)-acetamide in benzene then gave (3) (90%) (δ 0.14, 0.20, 2 x $OSiMe_3$; 3.68, 3.72, 2 x OMe; 4.62, d, *J* 1Hz, =CH; 4.81, d, *J* 1Hz, =CH). Reaction of (3) with 2,6-dichlorobenzoquinone in a sealed tube at 90°, followed by aromatization of the initial adduct on silica, gave the napthoquinone (5) (35%), m.p. 210.5°, as the only tractable product. Its ^1H n.m.r. spectrum consisted of five singlets, δ 3.77, 3.90 (2 x OMe); 7.25, 7.73 (H2, H8); 11.95 (OH).



	R^1	R^2	R^3
1	H	H	H
2	Me	Me	H
12	Me	H	H
13	Me	Me	Me



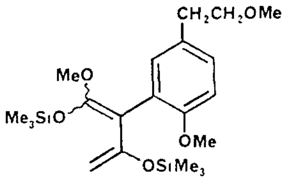
3



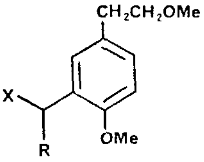
5

$MeCOCH(CO_2Me)COCO_2Me$

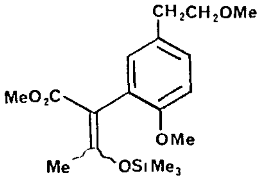
4



6



	R	X
7	H	Cl
8	H	CN
9	Ac	CN
10	Ac	CO_2Me



11

The aryl-substituted ring of the xantholaccaic acid system was introduced by means of the diene (6). Its synthesis relied on earlier preparations of 1,1,3-trioxygenated butadienes from β-keto esters.[6] Mild chloromethylation of *p*-methoxyphenethyl methyl ether ($HCHO/ZnCl_2/HCl$) gave the product (7) (54%). This underwent quantitative conversion to the nitrile (8) ($NaCN/Me_2SO$). Successive acylation (NaOEt/AcOEt) (92%) and methanolysis (90%) of the resulting nitrile (9) then gave the aryl acetoacetate (10). Treatment of (10) with *N,O*-bis(trimethylsilyl)acetamide in benzene gave the silyl enol ether (11) as a 1:1 mixture of (*E*)- and (*Z*)- isomers (97%), b.p. 85°/0.8 mm. The presence of the two isomers was apparent from the ^1H n.m.r. spectrum, in particular singlet resonances for the trimethylsilyl (δ -0.04, 0.30) and for the *C*-methyl groups (1.75, 2.37). Generation of the enolate of (11) with lithium diisopropylamide in tetrahydrofuran at -78° followed by addition of trimethylchlorosilane (-78 to 0°) and evaporation of the solvent at 0° gave (6) (δ 0.2, 0.4, 2 x $OSiMe_3$; 2.8, br t, *J* 7Hz, $ArCH_2$; 3.4, 3.6, 2 x OMe; 3.7, obscured t, *J* 7Hz, CH_2O; 3.8, OMe and =CH; 4.2, =CH; 6.9, m, 3 x ArH). This product was appreciably unstable even at 0° and was used without purification.

Treatment of the quinone (5) with excess of diene (6) in tetrahydrofuran at 0°, and aromatization of the adduct as before, gave the anthraquinone (12) (81%), m.p. 202-202.5°. Methylation of (12) with methyl iodide (Ag_2O in dimethylformamide) gave the heptamethyl derivative of xantholaccaic acid B (13) (84%) identical in all respects with an authentic sample.[1]

All new compounds reported in this work, with the exception of the labile dienes (3) and (6), gave satisfactory combustion analyses; all gave satisfactory spectroscopic data. We are grateful to the Australian Research Grants Committee for financial support.

References

1. D.W. Cameron, G.I. Feutrill, A.F. Patti, C.L. Raston, W.D. Raverty and A.H. White, Aust. J. Chem., 1978, 31, 2651.
2. R.H. Thomson, "Naturally Occurring Quinones", 2nd Edition (Academic Press : London 1971).
3. R. Burwood, G. Read, K. Schofield and D. E. Wright, J. Chem. Soc. C., 1967, 842.
4. N.S. Bhide, E.D. Pandhare, A.V. Rama Rao, I.N. Shaikh and R. Srinivasan, Indian J. Chem., 1969, 7, 987.
5. D.W. Cameron, G.I. Feutrill, P.G. Griffiths and D.J. Hodder, J. Chem. Soc. Chem. Commun., 1978, 688.
6. T.H. Chan and P. Brownbridge, J. Am. Chem. Soc., 1980, 102, 3534; D.W. Cameron, C. Conn, and G.I. Feutrill, Aust. J. Chem., 1981, 34, in press.

(Received in UK 15 June 1981)