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STABILITIES OF SOME SANTONIN DERIVATIVES

W. Cocker and T. B. H. McMurry,
University Chemical Laboratory, Trinity College, Dublin.
M. A. Frisch, T. McAllister and H. Mackle,
Department of Chemistry, The Queen's University of Belfast.

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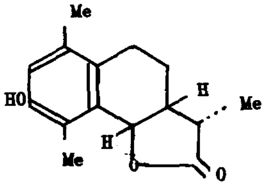
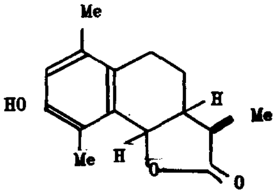
Conversion, in high yield, of (-)α-[I;6,7α(H)], and (+)α-desmotroposantonin (D.T.S.)[II;6,7β(H)] respectively to (-)β-[II;6,7α(H)], and (+)β-D.T.S.[I;6,7β(H)] takes place on refluxing in xylene with anhydrous K_2CO_3.(1) β-Santonin (III;R=βMe] is likewise converted to santonin [III;R=αMe],(2) and also on treatment with potassium tert. butoxide in tert. butanol/benzene.(3) Similarly 6α(H)-santonin [IV;R=αMe] is transformed(4,5) into 6,11α(H)-santonin [IV;R=βMe]. We now know(6) that (+)β-D.T.S.[I;6,7β(H)] is equilibrated with (-)α-D.T.S.[I;6,7α(H)] when either compound is treated with hydrogen chloride in dioxan. The equilibrium mixture consists largely of acidic products, but of the two lactones (+)β-D.T.S. predominates.

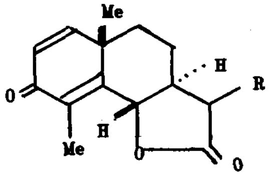
These transformations, carried out in solution, suggest that the order of thermodynamic stabilities is santonin > β-santonin; 6,11α(H)-santonin > 6α(H)-santonin; β-D.T.S. > α-D.T.S. This order is also indicated by the results of heat of combustion and heat of solution measurements given in the table below for the santonins, their methyl ethers, and the acetates of the desmotropo compounds. These derivatives were used because of their lower m.ps. in preference to the phenols themselves. Enthalpy data measure thermochemical rather than *thermodynamic* stability but it is unlikely that the standard molar entropies of each pair of isomers differ significantly.



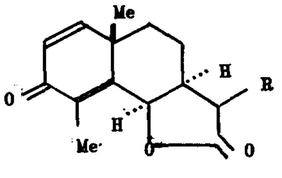
I



II



III



IV

In the cases of the *cis* lactones, the order of stabilities is difficult to reconcile with the configurations shown in formulae, these being based upon the configuration of santonin recently elucidated by X-ray diffraction measurements.(7)

TABLE

Compound	K.cal/mole			
	$-H_C$	$-H_f(s)$	E(soln)	$-H_f$(soln)
Santonin	1884.40±0.54	141.22±0.54	+0.44	140.78±0.5
β-Santonin	1885.23±0.43	141.39±0.43	+0.01	140.38±0.4
6α(H)- "	1885.80±0.36	139.82±0.36	-1.09	140.91±0.4
6,11α(H)- "	1881.47±0.56	144.15±0.56	+0.09	144.06±0.6
(-)α-D.T.S.*	2073.95±0.64	208.08±0.64	-0.36	208.44±0.6
(+)β-D.T.S.*	2071.88±0.43	210.15±0.43	-1.06	211.21±0.4
(-)α-D.T.S.†	2031.24±0.52	156.74±0.52	+1.54	155.20±0.5
(+)β-D.T.S.†	2028.27±0.45	159.71±0.45	+0.33	159.38±0.5

(* as acetate † as methyl ether)

E(soln) refers to measurements made on 0.01 molar solutions in $CHCl_3$ at 25°C.

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