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# OPTICALLY ACTIVE GOSSYPOL FROM THESPESIA POPULNEA

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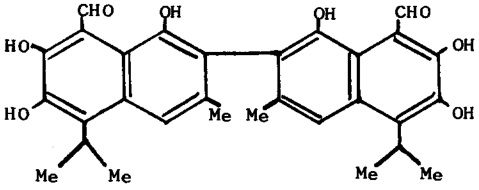
*Thespesia populnea* is a common tree in Africa, Asia, and the Pacific Islands. In Ceylon extracts of the bark have been used for the treatment of certain allergic conditions such as asthma. Previous chemical investigations of the plant have been reported by Seshadri *et al.* who isolated kaempferol and herbacetin and their glycosides from the flowers (1).

We have reinvestigated this species and by light petroleum (b.p. 56-70°) extraction of both the bark and the flowers have obtained a yellow phenol in 1.25% yield from the bark and 0.4% yield from the flowers. After initial crystallisation from aqueous acetone the phenol appeared to be homogeneous by paper and thin-layer chromatography in several solvents but was readily separated into two fractions by crystallisation from chloroform.

The nature of the fraction (about one third of the total crystalline extract) less soluble in chloroform was revealed by its mass and N.M.R. spectra. The former showed a small parent ion peak at mass number 518 and peaks corresponding to the loss of one and two (base peak) molecules of water. The N.M.R. spectrum was simple and showed peaks corresponding to 15 protons as follows: doublet (6H), $\tau$ 8.45 (J, 7 c.p.s.); broad based singlet (4H), $\tau$ 7.83; multiplet (1H), $\tau$ 6.1 (J, 7 c.p.s.); singlet (1H) $\tau$ 3.4-3.75 depending on concentration; singlet (1H) $\tau$ 3.7; singlet (1H) $\tau$ 2.2; singlet (1H) $\tau$ -1.1. After deterium exchange the peak at 7.83 $\tau$ became narrower at the base and its intensity was reduced by one quarter and the two peaks *ca.* 3.7 $\tau$ disappeared. The above data strongly indicated a symmetrical aromatic system with six hydroxy, two methyl, two isopropyl and two aldehyde groups as substituents, and together with the molecular weight and analytical data suggested that our material was gossypol (I). A comparison of the properties (including numerous colour tests) of the extractive with those of gossypol (2) confirmed this suggestion beyond doubt.



I

The chloroform soluble fraction of the extract appeared to be identical with the gossypol on chromatographic, spectroscopic and colour test criteria and its nature as optically active gossypol became apparent when its solution was shown to be strongly dextrorotatory. The active form was purified by crystallisation from aqueous acetone or acetone from which it separated with acetone of crystallisation. From pure acetone active gossypol separates either as deep yellow stout prisms or as a bright yellow powder (square prisms under the microscope) and either form can be obtained by appropriate seeding of the super-saturated acetone solution. From aqueous acetone large elongated plates separate. The above forms all have an indistinct m.p. 170-180° (Kofler) associated with loss of acetone. The acetonates dissolve readily in boiling light petroleum (b.p. 100-120°) and then after a few minutes unsolvated active gossypol separates as a bulky mass of pale yellow needles from the boiling solution. The m.p. of this form is 181-183° (Kofler). The rotatory properties of pure active gossypol are: $[\alpha]_D^{19}$ + 445 ± 10° (C 0.15 in chloroform) o.r.d. $[\phi]$ + 22,200 pk. (412 mµ); -49,000 tr. (360 mµ); +24,400 pk. (285 mµ); -21,600 inf. (278 mµ); -44,400 sh. (273 mµ); -67,800 tr. (255 mµ); -59,500 pk. (250 mµ); -89,200 tr. (238 mµ); +56,700 pk. (217 mµ) in methanol.

Appropriate experiments have shown that in common solvents except acetone inactive gossypol is appreciably less soluble than the active form and only from acetone containing solutions have we been able to concentrate the active form in the presence of the racemate. Furthermore, we have been unable to prepare from active gossypol the acetic acid solvate commonly used to isolate gossypol from cotton-seed oil.

The active phenol readily gave the orange dianilino derivative characteristic of gossypol, it had $[\alpha]_D$ + 2740°. Again comparison showed that the active derivative is appreciably more soluble in common solvents than the racemate. The m.p.s of these derivatives were very sensitive to the rate and method of heating (as also are the m.p.s of the various forms of gossypol itself) thus the active dianilino derivative had m.p. (capillary) 295° (decomp.), (Kofler) soften 220° orange liquid at 226°; inactive derivative m.p. (capillary) 300-302° (decomp.) lit. 302-303°, (Kofler) softens 230° orange liquid at 242°.

As far as we are aware this is the first report of gossypol occurring elsewhere than in Gossypium species, and the active form would seem to be the first natural β-β' dinaphthyl derivative showing optical activity due to restricted rotation.

## Acknowledgement

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## References

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