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NOVEL METHOD FOR SELECTIVE ESTERIFICATION OF POLYHYDROXY-ANTHRAQUINONES

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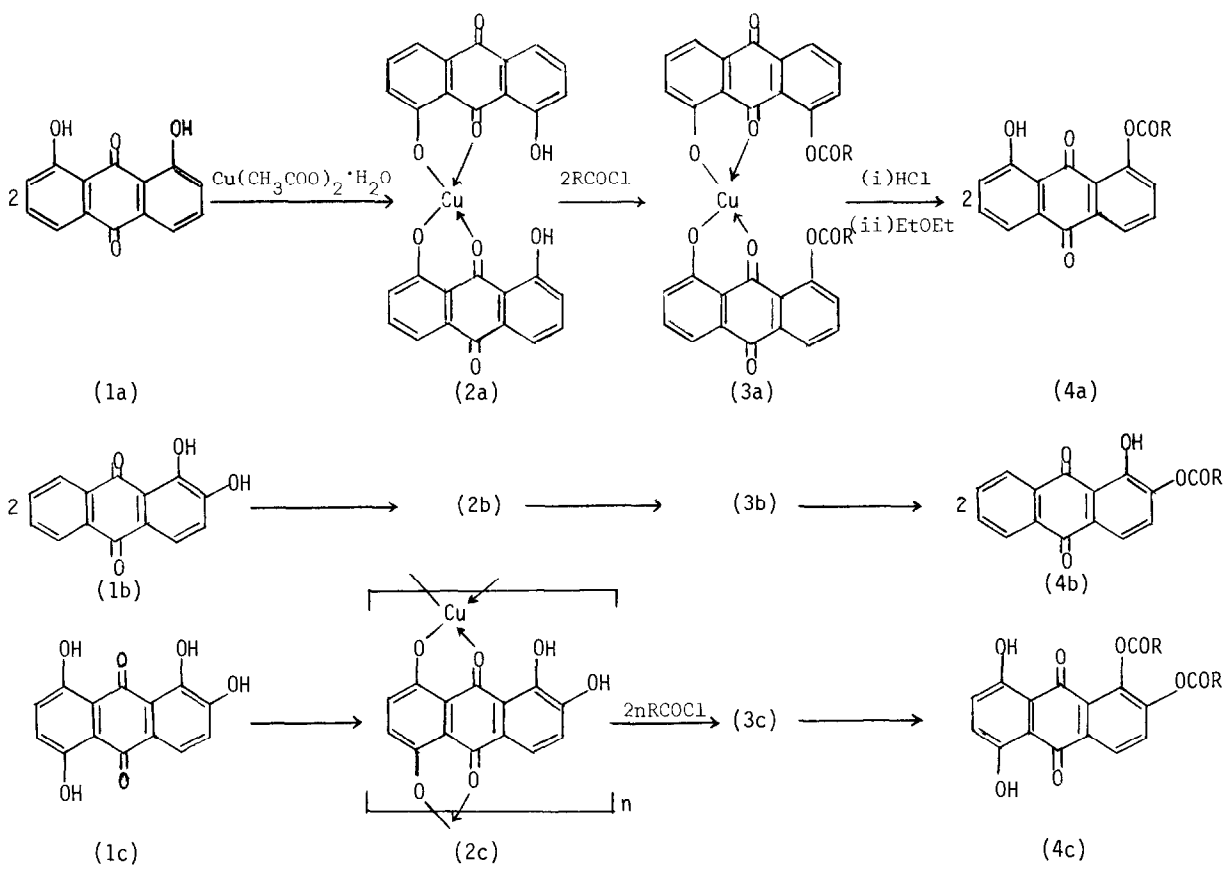
Summary : Polyhydroxy-anthraquinones form mono- and diesters via metal chelation followed by acid hydrolysis of the chelates.

Polyhydroxy-anthraquinones have been the subject of extensive research mainly due to their well-recognized biological importance and the significant biological applications of their esters.[1-4] The mono-esters are attracting attention in view of their potential as laxatives.[5] The synthesis of mono-esters encounters inherent difficulties with regard to selectivity of esterification. An illustrative example is the reported formation of mono-esters of chrysazin with fatty acids in the presence of N,N-dicyclohexylcarbodiimide,[6] which is characterized by lack of selectivity, complexity of the work-up and low yields of the esters obtained.

In this paper we report a novel method for the selective esterification of three of the most important and widely used members of the polyhydroxy-anthraquinone family, chrysazin (1a), alizarin (1b) and quinalizarin (1c) (Scheme 1).

Scheme 1



The method is simple and efficient and is based on the chelating ability of these compounds. The corresponding Cu(II) chelates (2a), (2b) and (2c) were prepared by modification of the procedure described by Coble and Holtzclaw.[7] This comprises the following changes: (a)the reaction is carried out in ethanol at room temperature; (b) a 1:2 mole ratio of ligand to copper(II) acetate is used; (c) the Cu(II) complexes are filtered from the reaction mixture, as soon as they are formed.In this way some hydroxyl groups were protected.

The choice of the metal was dictated by the well-documented lability of its complexes.[8] Subsequent acid hydrolysis of the complexes (dilute HCl acid in the presence of diethylether), after complete esterification of the free hydroxyl groups, afforded the mono-esters (4a) and (4b) and the diester (4c). The esters, thus, prepared and the esterification conditions are listed in Table 1.

Analytical and spectroscopic data of the esters were consistent with the proposed structures.

Table 1. Compounds (4a), (4b) and (4c)

Compound No		R	Yield %	m.p. °C	Esterification conditions
1	4a	$-(CH_2)_2CH_3$	84	133-135	4h/90°C
2		$-(CH_2)_6CH_3$	74	116-117	5h/120°C
3	4b	$-(CH_2)_2CH_3$	80	169-170	3,5h/90°C
4		$-(CH_2)_6CH_3$	76	121-123	4h/120°C
5		$-(CH_2)_{10}CH_3$	73	97-98	5h/120°C
6			65	234-235	72h/reflux
7	4c	$-CH_3$	85	196-197	4h/40°C
8		$-(CH_2)_2CH_3$	71	155-156	5h/90°C
9		$-(CH_2)_6CH_3$	66	99-100	7h/120°C
10		$-(CH_2)_{10}CH_3$	61	94-95	8h/120°C
11			19	254-255	75h/reflux

In all cases, except for 6 and 11, the acid chloride was used in a neat state. In the case of 6 and 11 dry benzene was used as solvent in the presence of pyridine.

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