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ELECTROSYNTHESIS OF γ-ASARONE

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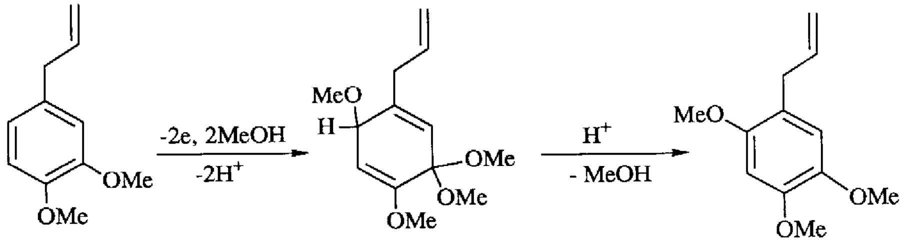
Abstract: γ-Asarone is synthesised in high yield, and conveniently, by anodic methoxylation of methyl eugenol, at constant current. The method is extremely simple and inexpensive.

2,4,5-Trimethoxyallylbenzene (1) is one of the rarer natural allylbenzenes. It was isolated for the first time from *Caesulia axillaries* and named γ-asarone.[1] The back and wood of *Aniba hostmanniana*, an arboreous species of *Lauraceae* contain essential oils composed of *ca*. 95% of (1).[2] The only reported[3] synthesis of (1) is based on the general sequence of reactions: dimethoxyphenol → allyl dimethoxyphenyl ether → allyldimethoxyphenol → trimethoxyallylbenzene, and the overall yield is less than 30%.

Here we report a new synthesis of γ-asarone, via the anodic oxidation of methyl eugenol (2) at a platinum electrode in alkaline methanol solution and under controlled current conditions. The average yield, from several experiments, is 80% and the simplicity and low cost clearly show the advantage of this method as compared with the one previously described.[3] This synthesis is another application of anodic methoxylation, a well established method which has been widely used.[4]

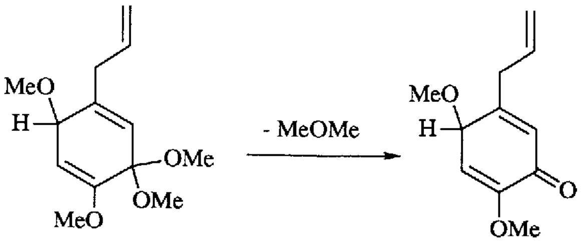
General Procedure: The electrolyses were performed in an undivided cell using a Pt foil anode (2.5 x 3.5 cm) and a W wire as cathode. A solution of methyl eugenol (2.8 mmoles) in MeOH (60 ml) containing $NaClO_4$ (6.0 mmoles) and NaOH (30.0 mmoles) was electrolyzed at room temperature (50 mA, 0.0057 Acm^{-2} 3F/mol). After completion, MeOH was removed under reduced pressure [because of the possible formation of explosive perchlorates the mixture should never be taken completely to dryness]. Water added to the residue, the mixture acidulated with hydrochloric acid until pH4 and extracted with ether. After concentrating under vacuum, γ-asarone was isolated by column chromatography (SiO_2, Hex-EtOAc 3:2) and fully characterised; spectral data were according to the literature[2]. When 5.6 mmoles of (2) were used, under otherwise similar conditions, γ-asarone was obtained in lower yield (55%).

The reaction probably proceeds through an intermediate (3) which during acid work-up originates product (1). This type of intermediate was observed during the anodic oxidation of dimethoxybenzenes.[5]



(2) (3) (1)

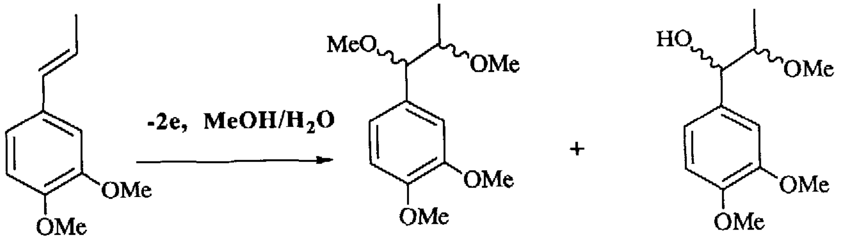
Intermediate (3) was isolated by work-up under alkaline conditions and characterised by ^{1}H n.m.r. When analysed by g.c./m.s. (3) gave a peak the at highest mass *m/z* 194 instead of the expected 240. This is probably due to a fragmentation, in which a molecule of dimethyl ether is lost, and (3) yields (4).



(3) (4)

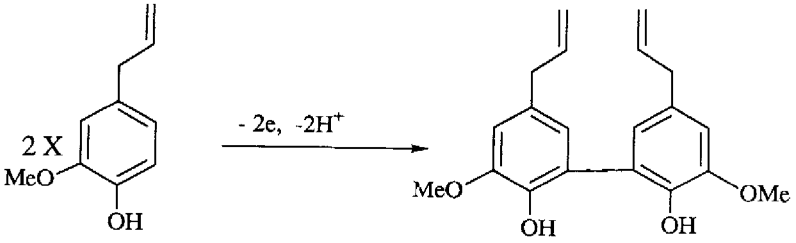
The γ-asarone obtained was isomerized in alkaline solution quantitatively[3] into a 5:1 mixture of (E)- and (Z)-2,4,5-trimethoxypropenylbenzenes; the (E) isomer is important as a precursor in a synthesis of magnosalicin.[6]

As the alkaline isomerization of γ-asarone showed to be very time consuming, attempts to prepare (E)-2,4,5-trimethoxypropenylbenzene via anodic oxidation directly from methyl isoeugenol (5) were made. However no nuclear methoxylation product could be isolated. In a typical experiment, the electrolysis of a solution of (5) (5.7 mmoles) in MeOH (60 ml) containing $NaClO_4$ (6.0 mmoles) and NaOH (26.0 mmoles) at room temperature (80 mA, 0.0091 A cm^{-2}, 2 F/mol), after work-up as described for methyl eugenol (2), afforded two products derived from the side-chain methoxylation of (5): 1,2-dimethoxy-1-(3,4-dimethoxyphenyl) propane (6) (2.85 mmoles, 50%, erythro/threo, 2.5:1) and 1-(3,4-dimethoxyphenyl)-2-methoxy-1-propanol (7) (1.14 mmoles, 20%, erythro/threo, 2:1). Both structures were assigned based on g.c./m.s., i.r. and $^{1}H/^{13}C$ n.m.r. measurements.



(5) (6) (7)

Eugenol (8) when oxidized under similar conditions as for (2), but to 1 F/mol afforded dehydrodieugenol (9)[7] in almost quantitative yield. This electrochemical dimerization has been reported[8] but substituting $NaClO_4$ for $LiClO_4$ enabled us to use solutions with eugenol concentrations of up to 0.1 M which is ten times the one originally employed. With $LiClO_4$ and 0.1 M solutions of eugenol the lithium salt of (9) is formed on the electrode impeding the passage of current.



(**8**)   (**9**)

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