A Novel Synthesis of Protoanemonin by the Catalytic Vapour-phase Oxidation of Silvan

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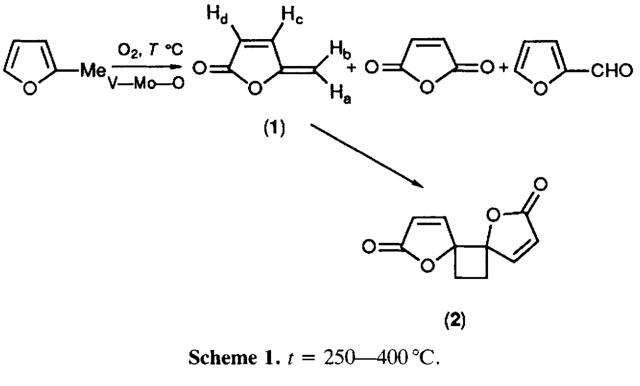
The vapour-phase oxidation of 2-methylfuran (silvan) in air over vanadium–molybdenum oxide catalysts under specific conditions was unexpectedly found to afford 5-methylenefuran-2(5*H*)-one (protoanemonin) which is otherwise difficult to obtain.

The catalytic vapour-phase oxidation of furan, 2-furaldehyde, and 5-methyl-2-furaldehyde in air over vanadium–molybdenum oxide catalysts has been used to prepare maleic anhydride and 2-furoic, fumaric, maleic, and other acids.[1] It is also known that the partial oxidation of 2-methyfuran (silvan) yields solely maleic anhydride[2] under conditions favourable for the synthesis of maleic anhydride from furan over a modified V–Mo–P–O catalyst. Recently, we have shown that furan-2,5-dialdehyde can be obtained in up to 60% yield during the oxidation of 2,5-dimethylfuran and 5-methyl-2-furaldehyde over V–Mo–O catalysts.[3] Moreover, it has been shown that using the same method for 2-methyl-5-t-butylfuran oxidation one can obtain 5-t-butyl-2-furaldehyde.[4] This communication describes the vapour-phase oxidation of silvan in air over vanadium–molybdenum oxide catalysts (individual oxides V_2O_5 and MoO_3, and V–Mo–O catalysts with atomic ratios V : Mo 3 : 1, 1 : 1, and 1 : 3) at 250—400 °C, with a contact period of 0.3—1.3 s, and molar ratio silvan : O_2 1 : 50—250. The study was carried out using the microcatalytic pulse technique[5] over the powdered catalysts and in a flow reactor in the presence of V–Mo–O catalysts supported by an inert carrier.

Unexpectedly silvan was found to give 5-methylenefuran-2(5*H*)one (protoanemonin) (**1**) as the main product (under certain conditions) of partial oxidation (maleic anhydride and 2-furaldehyde are also formed) (see Table 1 and Scheme 1).

Table 1. Vapour-phase oxidation of silvan over V–Mo–O catalysts (350 °C, contact period 0.5 s)

Catalyst (V : Mo)	Conversion/%	Reaction products, yield/% Protoanemonin	Maleic anhydride	2-Furaldehyde
3 : 1	91	43	24	2
1 : 1	94	29	18	2
1 : 3	71	27	24	11
V_2O_5	63	26	15	2
MoO_3	62	10	8	18



Scheme 1. t = 250—400 °C.

The optimal catalyst for the preparation of protoanemonin contained vanadium and molybdenum ions in the ratio 3 : 1. This catalyst, according to *X*-ray powder diffraction data,[6] is a mixture of two phases: (i) a solid solution of MoO_3 in V_2O_5 and (ii) V_2MoO_8. As shown by ESR data,[7] this catalyst contains the highest proportion (of the samples used) of vanadium(4+) ions having vanadyl co-ordination ($[V{=}O]^{2+}$). Using this catalyst (V : Mo 3 : 1), protoanemonin was obtained in 43% yield (selectivity 47%) at 350 °C, contact period 0.5 s, molar ratio silvan : oxygen 1 : 200.

Protoanemonin is a valuable biologically active compound possessing antibacterial,[8—12] antitumour,[13] and antimutagenic[14] activities. The known routes to protoanemonin are based either on its isolation from exotic *Ranunculus* and *Anemone* plants[8—10,15,16] or on multistage syntheses starting from 2-acetyl-2-bromo-propionic acid,[17] levulic acid,[18,19] α-angelicalactone,[20] or ranunculin.[21] Thus, our results are of interest from both the theoretical (unusual transformation of silvan) and practical (protoanemonin preparation) viewpoint.

A typical procedure for the synthesis of protoanemonin (**1**) by the catalytic oxidation of silvan is as follows. The catalyst† (15 cm^3) was heated to 350 °C in a U-shaped stainless steel reactor (15 mm in diameter). Air (110 dm^3 h^{-1}) was bubbled through a carburator with silvan at ambient temperature, so that the catalyst came into contact with a mixture of air and silvan vapour (rate of silvan flow 0.4 g h^{-1}). The catalysate was collected in traps cooled with a mixture of acetone and solid CO_2. The aqueous layer was extracted with ether. The combined organic layer was dried with $MgSO_4$, the solvent and unreacted silvan were removed by distillation, and vacuum distillation of the residue afforded protoanemonin as a viscous yellow liquid, b.p. 40—43 °C/1 mmHg (lit.[17] b.p. 45 °C/1 mmHg), yield 43% (selectivity 47%).

When protoanemonin was allowed to stand in air at room temperature it underwent a characteristic[17] spontaneous dimerization to *trans*-1,7-dioxadispiro[4.0.4.2]dodeca-3,9-diene-2,8-dione [anemonin (**2**), white crystals, m.p. 151—153 °C (lit.[18,19] m.p. 150—153 °C)]. This dimerization can be prevented by the addition of small amounts of hydroquinone to dilute solutions (1—10%) of protoanemonin in H_2O, $CHCl_3$, or CH_2Cl_2.‡

Attempts to prepare protoanemonin from silvan using the available homogeneous oxidation methods were unsuccessful. These included phase-transfer catalysed (PTC) oxidation with oxygen in the presence of strong bases or using cobalt—

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† *Preparation of catalyst.* 3.43 g $(NH_4)_2MoO_4$ and 4.85 g NH_4VO_3 were dissolved in 1 dm^3 of hot water (80 °C). The solution was evaporated on a water bath to *ca.* 100 ml volume, then 30 cm^3 of corundizium (α-Al_2O_3) beads [diameter 2—4 mm, Brunauer–Emmett–Teller (BET) surface area *ca.* 0.1 m^2 g^{-1}], were added and the mixture was evaporated to dryness, dried at 100 °C for 2 h, and calcined at 470 °C for 7 h. Thus, the vanadium–molybdenum catalyst (V : Mo 3 : 1) on a corundizium support (10 wt.%) was obtained.

‡ ^1H NMR and MS data of (**1**) and (**2**) were consistent with the proposed structures.

manganese bromide catalysts, free-radical oxidation with organic peroxides initiated by UV irradiation, or cobalt(II) catalysts as well as oxidation with other reagents such as SeO_2, polymer-supported CrO_3, or $NaIO_4$ under PTC conditions. The failure of these methods indicates the specificity of the oxidative transformation of silvan over vanadium–molybdenum oxide catalysts described above.

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