

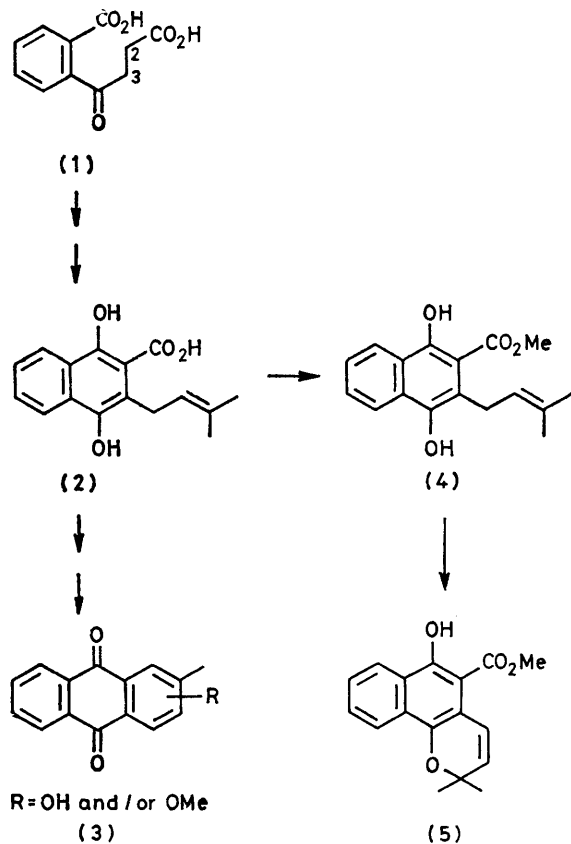
**2-Methoxycarbonyl-3-prenyl-1,4-naphthoquinone, a Metabolite related
to the Biosynthesis of Mollugin and Anthraquinones in
Galium mollugo L.**

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Summary The structure of 2-methoxycarbonyl-3-prenyl-1,4-naphthoquinone, isolated from *Galium mollugo* plants, has been elucidated by spectroscopic methods, synthesis, and derivatisation.

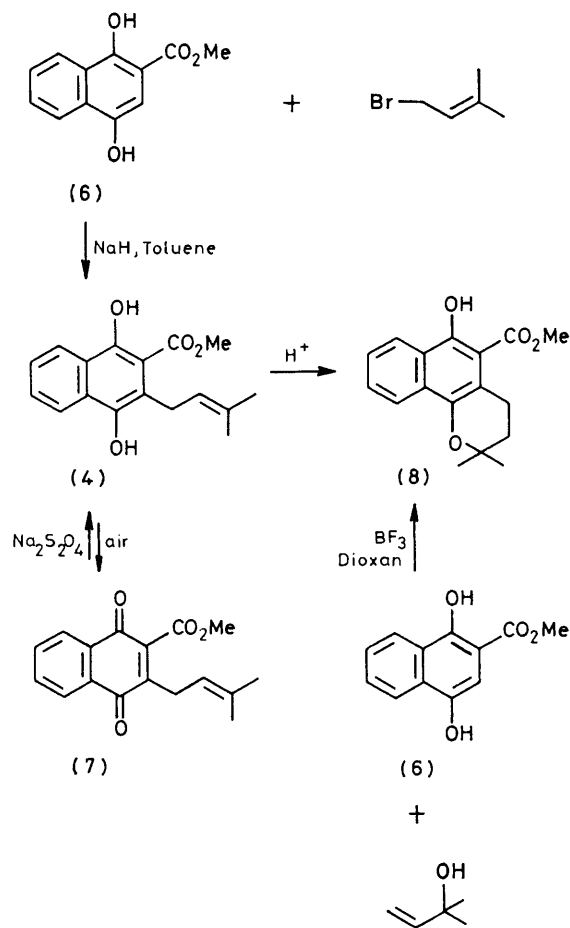
1,4-DIHYDROXY-3-PRENYL-2-NAPHTHOIC ACID (**2**) has been repeatedly postulated^{1,2} as an intermediate in the biosynthesis of anthraquinones (**3**) and mollugin (**5**). Compound (**2**) is likely to be a branch point in the biosynthetic pathway leading to (**3**) and (**5**) (Scheme 1). During investigations on the biosynthesis of anthraquinones in intact plants and cell suspension cultures³ of *Galium mollugo* we detected a new natural product (**7**). This compound is structurally related to the metabolites assumed^{1,2} to be involved in the biosynthetic sequence leading from 4-(2-carboxyphenyl)-4-oxobutanoic acid (**1**) to mollugin (**5**) and anthraquinones (**3**) and its natural occurrence supports the current concept⁴ of their biosynthesis. It also confirms evidence obtained from tracer studies^{1,2} indicating that prenylation occurs at a position corresponding to C-3 rather than C-2 of (**1**) (Scheme 1). The latter mechanism has been shown to be involved in menaquinone⁵ and catalpalactone⁶ biosynthesis. Finally the co-occurrence of 2-methoxycarbonyl-3-prenyl-1,4-naphthoquinone (**7**) and mollugin (**5**) suggests that in the biosynthesis of mollugin (**5**) esterification is likely to precede chromen ring formation.



SCHEME 1.

Galium mollugo L. plants were grown in our botanical garden from seeds obtained from the botanical garden in Tübingen, West Germany. The root system (314 g) of a plant (5 years old) was harvested in November and extracted

with Me_2CO . The lipophilic portion of the extract was fractionated [silica gel column, light petroleum (b.p. 40–60 °C)–MeOH, 30:1] and a yellow crystalline compound was isolated; yield 5.0 mg, m.p. 43 °C (hexane). The spectral data [λ_{max} (MeOH) 338 (log ϵ 3.48), 262 sh (4.10), 252 (4.26), and 246 (4.27) nm; ν_{max} (KBr) 1737, 1663, 1652, 1620, and 1588 cm^{-1} ; ^1H n.m.r. (CDCl_3 vs. Me_4Si) δ 1.71 (3H, s), 1.74 (3H, s), 3.33 (2H, d), 3.96 (3H, s), 5.10 (1H, t), 7.75 (2H, m), and 8.10 (2H, m); m/z 284 (M^+ , 21%), 269 ($M^+ - \text{Me}$, 30%), 252 ($M^+ - \text{MeOH}$, 49%), and 237 ($M^+ - \text{MeOH} - \text{Me}$, 100%)] suggested structure (**7**) for this compound. This was confirmed by synthesis (Scheme 2). The anion (NaH) of methyl 1,4-dihydroxy-2-naph-



SCHEME 2.

thoate (**6**) and 3-methylbut-2-enyl bromide were refluxed for 3 h in dry toluene. The product (**4**) was isolated following addition of $\text{Na}_2\text{S}_2\text{O}_4$; yield 24%, m.p. 89 °C (hexane); λ_{max} (MeOH) 372 (log ϵ 3.78), 317 (3.57), 264 (4.43), and 220 (4.61) nm; ν_{max} (KBr) 3520 and 1626 cm^{-1} ; ^1H n.m.r. ($\text{CD}_3\text{-SOCD}_3$ vs. Me_4Si) δ 1.81 (3H, s), 1.89 (3H, s), 3.73 (2H, d), 4.04 (3H, s), 5.27 (1H, t), 7.71 (2H, m), 8.34 (2H, m), 8.84 (1H, s), and 9.92 (1H, s); m/z 286 (M^+ , 31%), 254 ($M^+ - \text{MeOH}$, 100%), and 239 ($M^+ - \text{MeOH} - \text{Me}$, 71%). This synthetic sample (**4**) was oxidized (air) to the quinone (**7**),

and its u.v. and i.r. spectra were superimposable with those of the isolated material. Reduction ($\text{Na}_2\text{S}_2\text{O}_4$) of the isolated material gave (4) which on acid treatment was converted into (8). The chroman (8) was identical with a sample obtained from (6) and 2-methylbut-3-en-2-ol in the presence of BF_3 and dioxan (Scheme 2). The physical data for both chroman samples were identical (u.v., i.r., m.s., ^1H n.m.r.) with those reported for (8) and synthesised by a different

approach.⁷ Thus the isolated natural material is 2-methoxy-carbonyl-3-prenyl-1,4-naphthoquinone (7).

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