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PRENYLATIONS OF BUT-2-ENOLIDES: SYNTHESES OF ROSEFURAN AND RELATED NATURAL FURANS

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3-Substituted furanosesquiterpenes possessing the basic farnesane carbon skeleton are widely distributed in Nature.[1] In spite of considerable effort, relatively few simple and general methods are available for the synthesis of these molecules.[2] In connection with synthetic studies amongst the furano-butenolide sesquiterpenoids found in *Eremophila freelingii*,[3] we have investigated the suitability of regioselective prenylations of but-2-enolides as a synthetic entry to this class of compound. In this Letter, we report new syntheses of rosefuran (8a), an important odoriferous compound of Bulgarian rose oil,[4] sesquirosefuran (8b) which is found in *Actinodaphne longifolia*,[5] and the related compounds (3), (9), and (11).

The lithium enolate of 2-methylbut-2-enolide was first prepared at -78° by slow addition of the butenolide (1 equiv.) to a 1:1 complex of lithium diisopropylamide (1.1 equiv.) and hexamethylphosphoramide (1.1 equiv.) in tetrahydrofuran.[6] The mixture was stirred for 0.5h., and then a solution of dimethylallyl bromide (1.2 equiv.) in tetrahydrofuran was introduced. The temperature was raised to 0° during 1h., and the reaction was then quenched by the addition of excess saturated ammonium chloride solution. Chromatography separated the α- and γ-prenyl-substituted butenolides, (1a) and (2a) respectively (65%), present in the crude reaction mixture in the proportion 3:2; the proportion of (1a) and (2a) was not affected when the prenylation was carried out at temperatures between -78° and 0°, rather than at -78°. In a similar manner, treatment of the enolate of 3-methylbut-2-enolide with geranyl bromide, led to a 3:2 mixture of the prenylogues (1b) and (2b). The 2-methyl-4-prenylbut-2-enolide moiety (viz.2) is present in freelingnite (2c), which we have earlier isolated from *E.freelingii*,[3b] and comparative spectral data between synthetic (2*b*) and natural freelingnite fully endorse the structure assigned to the butenolide moiety of the natural metabolite. Reduction of (2*a*), ν_{max} 1760cm^{-1}, τ 2.9m (:C$\underline{H}$.CH OCO), 4.9t(*J*~7,:C$\underline{H}$ CH_2), 5.12t(*J*~7, $CH_2C\underline{H}$ O CO), 7.6m ($C\underline{H}_2$.CH:), 8.08m(:CMe.Co) 8.18(Me), 8.26(Me), using di-isobutylaluminium hydride (THF at -30°)[7] led (96%) to furan (3), a pale yellow oil, ν_{max} 1643, 1510 cm^{-1}, τ 2.87 (α-H), 4.12 (β-H), 4.66t (*J*~7, :C$\underline{H}$.CH_2), 6.71d (*J*8,:CH.$C\underline{H}_2$), 8.02 (Me), 8.24 (Me), 8.32 (Me).

Prenylations of the lithium enolate of 3-methylbut-2-enolide, using both dimethylallyl and geranyl bromides led (60%) also to mixtures (1:2) of α- and γ-prenyl-substituted butenolides, (4) and (5), which were accompanied by the bis-prenylated derivatives (6) and (7). Efforts to suppress the bis-prenylations, by using an excess of butenolide over prenylating agent, and to alter the distribution of α- and γ-substituted products, by carrying out the reactions in the presence of Cu(I) salts,[8] were singularly unsuccessful. Reduction of the but-2-enolides (5*a*) and (5*b*) with di-isobutylaluminium hydride then led to rosefuran (8*a*; 80%) and sesquirosefuran (8*b*; 85%) respectively, which displayed p.m.r. spectral data identical to those recorded for the natural products.[9]

The reactions between the anion derived from but-2-enolide itself, and the prenyl bromides above, occurred exclusively at the α-position,[10] but led to mixtures of mono- and bis-prenylated derivatives (9) and (10) respectively, in low conversions (~30%). By contrast, metalation of *O*-methyl 2-methyltetronic acid followed by prenylation with dimethylallyl bromide gave high yields (~85%) of the product (11) resulting from γ-addition; only small amounts (~5%) of the corresponding α-addition product were detected in crude reaction mixtures.

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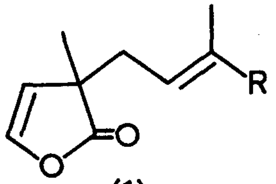

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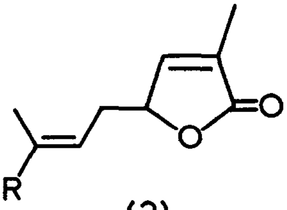

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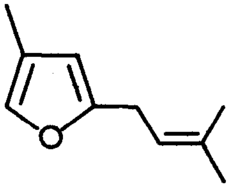

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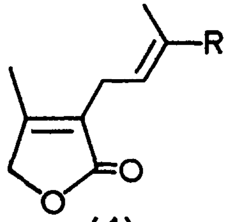

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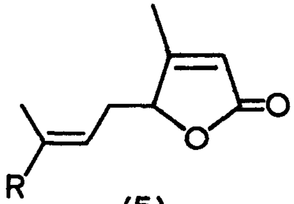

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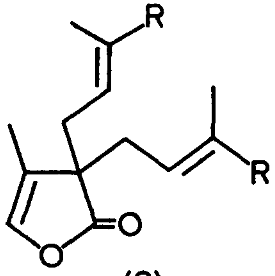

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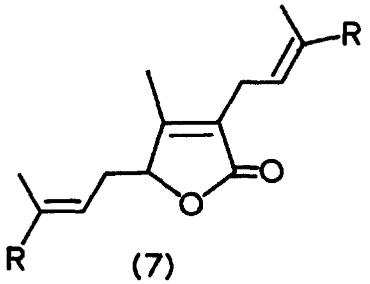

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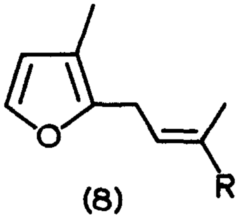

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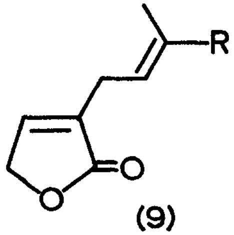

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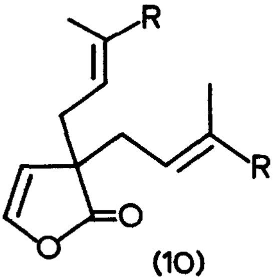

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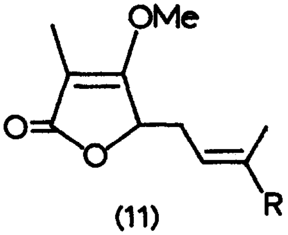
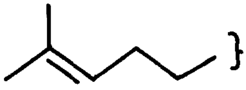
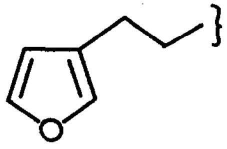


(11)

a R = Me ; b R =  ; c R = 

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