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A FACILE SYNTHESIS OF FUROTROPONE DERIVATIVES BY AN APPLICATION OF CLAISEN REARRANGEMENT

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The reaction of 1,4-dichloro-trans-2-butene with dipotassium salt of 5-hydroxytropolone in presence of 18-crown-6-ether afforded 5-(4-chloro-trans-2-butenyloxy)tropolone and 2,5-di(4-chloro-trans-2-butenyloxy)-tropone which were transformed into furotropone derivatives by dehydrochlorination under the conditions of Claisen rearrangement.

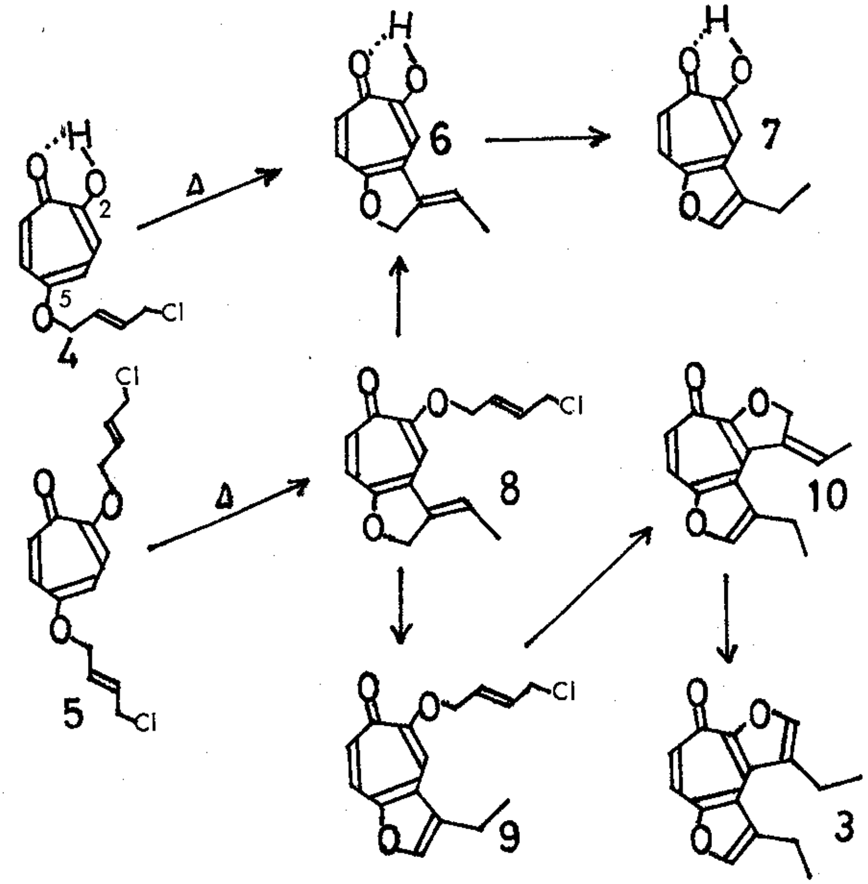
Recently, we have found that several 2-(2-alkenyloxy)tropones can be prepared by a mild condensation of naked tropolonate anion, generated in crown-ether-containing benzene solutions, with corresponding allylhalides,[1)] and this improvement allowed us to extend Claisen rearrangement of troponoids[2)] to some bifunctional derivatives. This paper will be concerned with the condensation of 1,4-dichloro-trans-2-butene (1) and 5-hydroxytropolone (2) and subsequent Claisen type reaction to lead new furotropones, 3,4-diethyldifuro[2,3-b:3,2-d]tropone (3) and intermediary products. It is known that 2-propargyloxytropone is convertible into 2-methylfuro[2,3-b]tropone by thermolysis.[3,4)]

When an anhydrous benzene solution of dipotassium salt of 2 and 18-crown-6-ether (CE) was mixed with a slight excess of 1 and heated to reflux for 4 h, a 1:1-condensate (4), 5-(4-chloro-trans-2-butenyloxy)tropolone, was obtained in 65 % yield after an ordinary work-up. The structure of 4, colorless needles, mp 141-143°C, was deduced from the NMR[δ5):4.04(2H, dd, J=7, 2 Hz), 4.51(2H, dd, J=7, 2 Hz), 4.98(2H, m), 6.85-7.35(5H, AA'BB'-type 4H and OH)] and the IR[ν:3240, 1600, 1545, 1265, 1195 cm^{-1}] spectra. The 1:2-condensate, 2,5-di(4-chloro-trans-2-butenyloxy)tropone (5), colorless prisms, mp 70-71°C, was unstable under aqueous alkalline conditions and its isolation required rather careful work-up. The structure of 5 was also deduced from the NMR[δ:4.07(4H, m), 4.46(2H, m), 4.97(4H, m), 6.21-7.32(4H, m)] and the IR[ν: 1630, 1570, 1240, 1195 cm^{-1}] spectra together with an independent formation from 4.

When 4 was dissolved in o-dichlorobenzene and heated to reflux for 1 h, two crystalline products were obtained: The major product, 6, yellow needles, mp 133-134°C, 56 %, was identified as 3-ethylidene-2,3-dihydrofuro[3,2-c]tropolone on the basis of the NMR[δ:1.80(3H, dt, J=7, 2.5 Hz), 5.13(2H, dq, J=3.5, 2.5 Hz), 6.11(1H, qt, J= 7, 3.5 Hz), 7.00-7.35(4H, m)] and the IR[ν:3200, 1605, 1535, 1450, 1255, 1195 cm^{-1}] spectral evidences, and the minor product, 7, colorless needles, mp 153-154°C, 17 %, as 3-ethylfuro[3,2-c]tropolone[δ:1.32(3H, t, J=8 Hz), 2.66(2H, qd, J=8, 1 Hz), 7.22 (1H, d, J=12 Hz), 7.43(1H, s), 7.49(1H, t, J=1 Hz), 7.75(1H, d, J=12 Hz). ν:3200, 1625, 1595, 1460, 1405 cm^{-1}]. 6 isomerized into 7 by heating in o-dichlorobenzene solution, or even by passage through a silica-gel column.

Similarly, when 5 was refluxed in xylene for 4 h, a rather complicated reaction occurred, and following compounds were isolated by repeated silica-gel column chromatography including an aid of cupric sulfate impregnation. 6(3 %) and 7(6 %) together with 4(3 %) obtained from acidic fractions revealed a deallylation prior to thermal rearrangement. Neutral fractions afforded 3, colorless needles, mp 160-161°C(3 %) [δ:1.29(3H, t, J=8 Hz), 1.30(3H, t, J=8 Hz), 2.88(4H, overlapped qd, J=8, 1 Hz), 6.98(1H, d, J=12 Hz), 7.56(1H, t, J=1 Hz), 7.68(1H, d, J=12 Hz), 7.71(1H, t, J=1 Hz). ν:3000, 1600, 1560, 1510, 1120 cm^{-1}], 8, colorless crystals, mp 156-157°C(2 %)[δ:

1.79(3H, dt, J=7, 2.5 Hz), 4.10(2H, m), 4.53(2H, m), 5.17(2H, dq, J=3.5, 2.5 Hz), 6.00(3H, overlapped m), 7.06-7.35(3H, m). ν:3000, 1630, 1560, 1515, 1200 cm^{-1}], 9, a colorless oil (8 %) [δ:1.33(3H, t, H=8 Hz), 2.64(2H, qd, J=8, 1 Hz), 4.10(2H, m), 4.71(2H, m), 6.04(2H, m), 6.97(1H, s), 7.06(1H, d, J=12 Hz), 7.43(1H, t, J=1 Hz), 7.54(1H, d, J=12 Hz). ν:3000, 1610, 1580, 1530, 1210, 1115 cm^{-1}] and 10, a colorless oil (4.5 %) [δ:1.20(3H, t, J=8 Hz), 1.85(3H, dt, J=7, 2.5 Hz), 2.67(2H, qd, J=8, 1 Hz), 5.16(2H, dq, J=3.5, 2.5 Hz), 5.89(1H, qt, J=7, 3.5 Hz), 6.92-7.66(3H, m). ν:3000, 1600, 1560, 1510, 1120 cm^{-1}].



[Chart 1]

When **8** was heated in xylene, a formation of **6** and **7** was confirmed by the NMR spectroscopic analysis, thus, at least one route to lead deallylation products was ascertained. Neutral fractions of the mixture resulted in the isolation of **3** and **10**. Therefore, the sequence of their formation could be expressed as shown in Chart 1.

It is interesting that the C_5-allyl system is more reactive than C_2-allyl system in the Claisen type [3,3] sigmatropy, and this should be attributable to the thermodynamic stability of the intermediates, i.e., C_2-allyl rearrangement generates a cisoid-1,2-dioxo system which must raise a dipole-dipole interaction.

Finally, we would like to mention that both 3 and 9 should be good precursors to prepare various isoelectronic derivatives of pseudozoathoxanthins6) and paragracines,7) *physiologically active bases of marine origin.*8)

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