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A NEW METHOD FOR THE ANNELATION OF PHENOLS[1]

Lloyd J. Dolby and Ellis Adler[2]

Department of Chemistry, University of Oregon

Eugene, Oregon 97403

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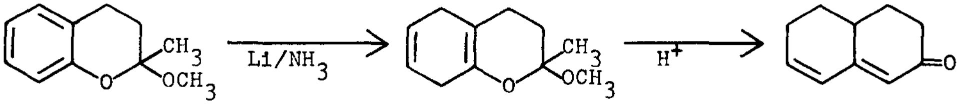
The recently developed synthesis of 2-methoxy-2-methylchromans[3] makes these materials attractive intermediates for the synthesis of reduced naphthalene and phenanthrene compounds. Thus the condensation of phenol with 2-methoxybutadiene[4] affords 2-methoxy-2-methylchroman 1 in 82% yields and Birch reduction followed by hydrolysis and cyclization gives 4,4a,5,6-tetrahydro-2-(3H)-naphthalenone 3 in 47% yield based on the chroman.

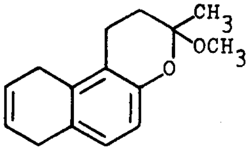


1 2 3

In this instance, Birch reduction of 2-methoxy-2-methylchroman using lithium in tetrahydrofuran, t-butanol, and liquid ammonia afforded the 5,8-dihydro-2-methoxy-2-methylchroman 2 in 82% yield. The structure was supported by the expected spectroscopic properties: ir (CCl_4) 1720 cm^{-1}; pmr (CCl_4) δ 1.32 (s, 3H), 1.4-2.2 (m, 4H), 2.58 (broad, 4H), 3.15 (s, 3H), and 5.55 (m, 2H). Hydrolysis of the ketal function, cyclization, and double bond isomerization could be accomplished in a single step by treatment of 2 with hydrochloric acid in aqueous dioxane to give the hexalone 3 in 57% yield. Alternatively, the hexalone was obtained in comparable yield by mild acid hydrolysis followed by cyclization with methanolic sodium methoxide. The hexalone was identified by comparison of its properties with those previously reported.[5] To further

Mild hydrogenation of the mixture of dihydro and tetrahydrochromans followed by hydrolysis afforded only the diketone 11 which was always obtained as a mixture of diastereomers.[6] Thus this sequence is useful for preparing 8-methyl-4,4a,5,6,7,8-hexahydro-2(3H)-naphthalenone derived by cyclizing 11.

Birch reduction of chroman 6 using 5 g-atoms of lithium per mole of chroman afforded predominantly a dihydro compound, mp 88-89°; assigned structure 12.



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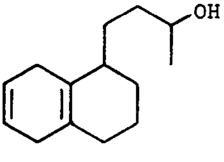
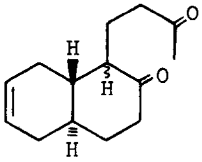
The pmr spectrum showed a three proton singlet at δ 1.45 ascribed to the methyl group and a second three proton singlet at δ 3.15 for the methoxy group. The vinyl protons appeared as an apparent triplet (J = 1.5 Hz) at δ 5.79 and the two aromatic protons gave an AB quartet δ 6.42 and 6.65 (J = 8.5 Hz). The ultraviolet spectrum showed λ_{max}^{EtOH} 277 (ϵ 1,570) 287 (1,520).

Birch reduction of chroman 6 using 16 g-atoms of lithium per mole of chroman gave a complex mixture of reduction products. Hydrolysis of the reduction products with dilute acid afforded a mixture from which two compounds, 13 and 14, were isolated in the yields indicated.

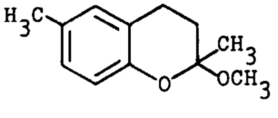


13 (13%)



14 (54%)

The compounds were obtained as oils and the structures are based on spectroscopic evidence. Cyclization of the hydrolysis mixture with sodium methoxide in methanol afforded a mixture, bp ca 125° (0.15 mm), which deposited crystalline anti-trans-4,4a,4b,5,8,8a,9,10-octahydro-2-(3H)-phenanthrenone (15), mp 88-89°, in 36% yield upon dilution with pentane. The location of the isolated double bond is assigned partly on the basis that the unsubstituted ring is more readily reduced leaving a 6,7 double bond. The spectral properties are in accord with test the utility of this sequence the chromans shown below were prepared in yields from 66 to 93% by condensation of the appropriate phenol with 2-methoxybutadiene.



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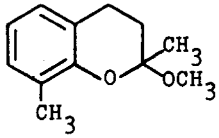

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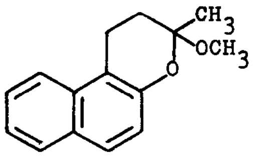

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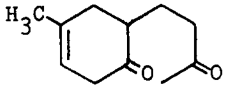
Both the Birch reduction of chroman 4 and subsequent hydrolysis proceeded in better than 90% yield to give the unsaturated diketone 7. Cyclization in either acid or base afforded hexalone 8 in 50% yield as a mixture of stereoisomers. The spectra are in accord with the assigned structure: ir, $\bar{\nu}_{max}^{CCl_4}$ 1680, 1630, and 1595 cm^{-1}; uv λ_{max}^{EtOH} 278 nm (ϵ 22,900). The pmr spectrum showed two methyl doublets: δ 1.08 and 1.12 (J = 7 Hz) in the ratio of 3:1 for the two diastereomers.



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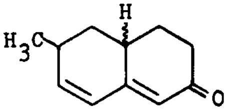

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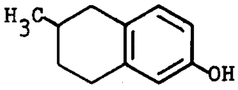

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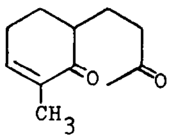
Treatment of the Birch reduction product with refluxing hydrochloric acid in dioxane yielded 6-methyl-5,6,7,8-tetrahydronaphthol (9), mp 85-85.5°, in 63% yield.

The Birch reduction of chromans 5 and 6 proved to be more difficult. Reduction of chroman 5 using 20 g-atoms of lithium per mole of chroman afforded a mixture of dihydro and tetrahydrochromans which could be hydrolyzed to a mixture of ketones 10 and 11 in a ratio of 2:1.



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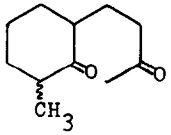

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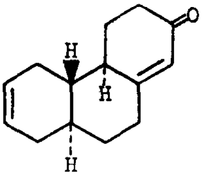
the proposed structure: ir, $\bar{\nu}_{max}^{CCl_4}$ 1685 and 1630 cm^{-1}; pmr (CCl_4) δ 0.8-2.8 (complex multiplets, 15H) and 5.6-5.9 (multiplet, 3H); uv λ_{max}^{EtOH} 237 nm (ϵ 18,500).



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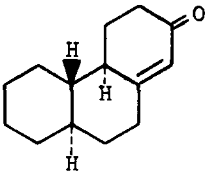

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The structure and stereochemistry of the compound was confirmed by reduction of the isolated double bond to give *anti*-*trans*-4,4a,4b,5,6,7,8,8a,9,10-decahydro-2(3H)-phenanthrenone (**16**), mp 70-72° (lit.[7] mp 73°), the 2,4-dinitrophenylhydrazone showed mp 203-205° (lit.[7] mp 195-196°).

REFERENCES AND NOTES

1. The authors gratefully acknowledge financial support from the National Institute of Arthritis and Metabolic Diseases of the Public Health Service, Grant AM 18176, and a Public Health Service Career Program Award (1-K3-NB-28, 105) from the National Institute of Neurological Diseases and Blindness.
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