Tetrahedron Vol. 41, No. 15, pp. 3029 to 3032, 1985
Printed in Great Britain.

0040-4020/85 $3.00+.00

ACID CATALYSED NOVEL REARRANGEMENT OF BICYCLIC DIENONE

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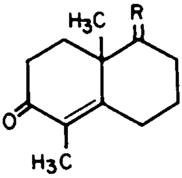
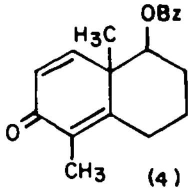
(*Received in USA* 10 *January* 1985)

Abstract-The dienone (4) on heating with methanolic hydrochloric acid underwent ring cleavage yielding the aromatic ketal (6) which on acid hydrolysis produced the aldehyde (7). Similar treatment of the dienone (4) with acetic anhydride and p-toluenesulfonic acid furnished the ester (8) which on alkaline hydrolysis afforded the dimeric product (10). The structure of the products (6), (7), (8) and (10) are defined on the basis of the spectral evidence.

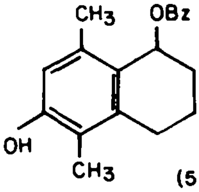
The rearrangement of cyclohexadienone to phenol is now a well documented reaction[1,2]. Particular attention has been paid to the steroidal dienones to prepare aromatic steroids[3,4]. In connection with our interest on acid-catalysed molecular rearrangements[5,6], the reaction of the dienone (4) with methanolic hydrochloric acid was investigated with the hope of obtaining the phenolic product (5) which appears to be an important synthon for the synthesis of sesquiterpenes like rishitinal[7] and Occidol[8]. The dienone (4) underwent aromatization along with an unexpected ring cleavage and the present paper describes the structure of the product obtained.



(1) R = O
(2) R = $<^{OH}_{H}$, (3) R = $<^{OBz}_{H}$



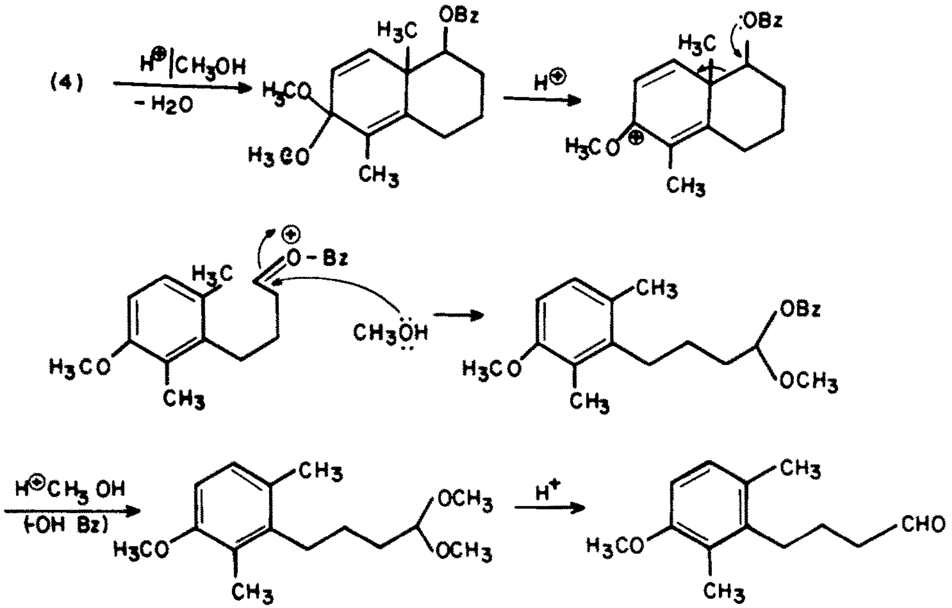
(4)



(5)

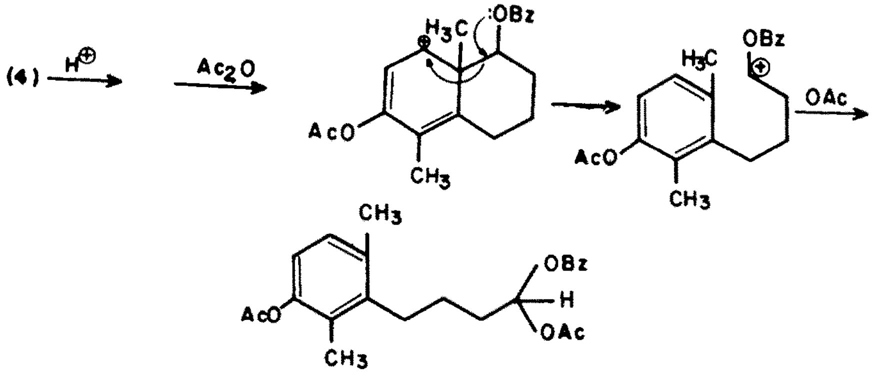
The condensation of the commercially available 2-methyl-1,3-cyclohexadione with 1-chloro-3-pentanone catalysed by p-toluenesulfonic acid monohydrate afforded the bicyclic enone (1) whose alternative synthesis has been reported[9]. The alcohol (2), prepared from the enone (1) by the published procedure[9], was converted to its benzoyl derivative (3) and this on heating with 2,3-dichloro-5,6-dicyano-benzoquinone (DDQ) in dioxane[10] yielded the dienone (4) which on treatment with HCl in MeOH gave pure and only isolable product in 79% yield whose spectroscopic properties indicated a structure far removed from the desired product (5). The rearrangement product was assigned aromatic ketal structure (6) on the following considerations. Its IR spectrum exhibited the absence of the characteristic absorption for the hydroxyl, and ester group. The ^{1}H NMR spectrum showed signals for two methyl groups attached directly to aromatic nucleus (δ2.26 and δ2.30), three methoxy groups δ 3.36(6H) and δ3.82(3H) and two aromatic protons(δ6.63 and δ6.96). Thus the structure (6) is entirely consistent with spectroscopic data recorded. In the mass spectrum of the ketal (6) the parent ion was not observed but the m/z values displayed at 220 and 180 indicated the fragments produced after splitting of the parent molecule. Mechanistically the course of the events outlined in Scheme I seems plausible. Heating the ketal (6) with aqueous HCl yielded the aldehyde (7) in satisfactory yield which was found very unstable as noted by its rapid change of color from yellow to red.

However, the spectroscopic data of the aldehyde (7) and an elemental analysis of its 2,4-dinitrophenylhydrazone derivative confirmed its identity.



Scheme I

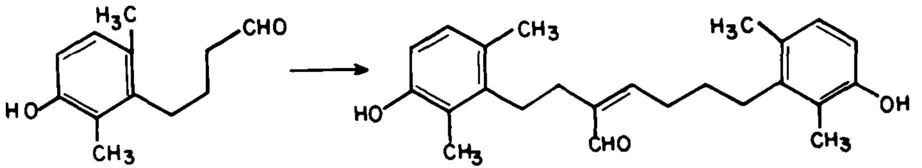
As the desired product (5) was not obtained an alternative attempt was made to aromatize the dienone (4) by heating with AC$_2$O and p-toluenesulfonic acid. This operation afforded the major product in 70% yield which was assigned structure (8) on the basis of its spectroscopic properties. Its IR spectrum showed absorption for the ester carbonyl at 1770 and 1730 cm^{-1} . The ^{1}H NMR spectrum exhibited signals for two methyl group attached to aromatic nucleus, two acetyl groups, two aromatic protons and one methine protons (δ 6.54-6.99) and five proton multiplet for benzoate group (δ 7.51-8.09). Its mass spectrum had weak molecular ion peak M$^+$ at 398 but displayed intense m/z values at 356, 296 and 216 which are the fragments that can be expected after splitting the ester (8). The transformation of the dienone (4) into the aromatic ester (8) can be rationalized by a possible mechanism outlined in Scheme II.



(8)

Scheme II

Hydrolysis of the aromatic ester (8) by heating with dilute HCl and tetrahydrofuran or by heating with aqueous HCl yielded a mixture of products from which no characterizable products could be isolated. The experiment was repeated under various conditions but all were uniformly unsuccessful. Alkaline hydrolysis of the ester (8) that afforded a material in excellent yield was not the desired aldehyde (9) but was identified as dimeric product (10) on the basis of its spectroscopic properties. The IR spectrum exhibited the presence of the hydroxyl and carbonyl group. The ^1H NMR spectrum had signals for four methyl groups, four aromatic and one vinyl protons in the region δ 6.55-6.84 (5H), two phenolic hydroxyl and one aldehyde groups. The region δ 1.51-1.82 and δ 2.32-2.72 contained two and eight protons respectively. This led us to assume that the aldehyde (9) initially formed during the alkaline hydrolysis of aromatic ester (8) underwent aldol condensation affording the dimeric product (10).



(9) (10)

In summary,the aromatization followed by ring scission of the dienone (4) led us to the conclusion that the nature of the rearrangement of the dienone by acid depends upon the structural features[11] and substituent in the vicinity of the dienone system as well as upon the reaction condition[12]. It is worthwhile to mention that some bicyclic δ -hydroxy enones on treatment with acid also undergoes aromatization alone with skeletal transformations[13,14].

EXPERIMENTAL[15]

5,9-Dimethyl-$\Delta^{5,10}$-Octalin-1,6-dione(1)

A solution of 2-methyl-1,3-cyclohexadione (12.62 g), freshly distilled 1-chloro-3-pentanone(18.42 g) and p-toluenesulfonic acid monohydrate (614 mg) in dry C_6H_6 (500 ml) was heated under reflux for 28 h, removing the water formed with a Dean-Stark water separator. The solution was cooled, washed with a solution of $NaHCO_3$ (5%), brine, dried and evaporated. The residue on distillation b. p. 125-132° (bath)/0.25 mm., afforded a yellow oil which solidified on standing. Trituration with Et_2O-hexane gave the dione (1) (14.71 g, 76.5%), m.p. 35-36°)(Reported[9]. 39-40°) IR: 1722, 1672 and 1628 cm^{-1}; δ 1.73 (3H, s, 5-CH_3) and 1.37 (3H, s, 9-CH_3), m/z 192 (M^+). (Found: C,74.88; H, 8,22. Calc. for $C_{12}H_{1\epsilon}O_2$: C, 74.97; H, 8.39%).

1β-Benzoyl-5,9-dimethyl- $\Delta^{5,10}$ -Octalin-6-one (3).

A solution of the alcohol (2) (970 mg) in pyridine (5 ml) and benzoyl chloride (1.51 g) was stirred for 20 h at room temperature. The reaction mixture was diluted with water and then extracted with Et_2O. The organic layer was washed with dilute HCl, aqueous $NaHCO_3$, brine, dried and evaporated to leave a solid material which on crystallization from Et_2O-hexane yielded the benzoate (3) (1.21 g, 90%), m.p. 70-72°(from Et_2O-hexane), IR: 1710, 1660 and 1270 cm^{-1}, δ 1.40 (3H, s, 9-CH_3), 1.80 (3H, s, 5-CH_3), 4.84 (1H, m, 1-H) and 7.25-8.22 (5H, m. aromatic protons), m/z 298 (M^+) and 176 (M^+-PhCOOH). (Found: C, 76.59; H, 7.48. Calc. for $C_{19}H_{20}O_3$: C, 76.48; H, 7.43%).

1β-Benzoyl-5,9-dimethyl-7-hexanal-6-One (4)

To a solution of the benzoate (3) (898 mg) in freshly distilled dry dioxane (100 ml) was added DDQ (1.21 g) and the resulting solution was refluxed under N_2 for 72 h. The reaction mixture was cooled, filtered and concentrated to yield a dark oily material which was chromatographed over silica gel. Evaporation of Et_2O-hexane (85:15) elute afforded the dienone (4) (701 mg, 79%), m.p. 63-65°(from Et_2O-hexane), UV: 245 mμ (ξ 11400), IR: 1735, 1645, 1630 and 1275 cm^{-1}, δ1.42 (3H, s, 9-CH_3), 1.92 (3H, s, 5-CH_3), 6.32 (1H, d, J=9 Hz), 6.84 (1H, d, J=0 Hz) (vinyl protons) and 7.42- 8.24 (5H, aromatic protons), m/z 296 (M^+) and 174 (M^+) and 174 (M^+ -PhCOOH). (Found: C, 77.04; H, 6.85. Calc. for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80%).

2.4-Dimethyl-e(1,1-dimethoxybutan-4-yl)ansiole (6)

To the dienone (4) (590 mg) dissolved in MeOH (15 ml), aqueous HCl (10 ml, 10%) was added and the solution was heated under reflux for 1 h, the progress of the reaction being monitored by TLC. The reaction mixture was diluted with water and extracted with Et_2O. The organic extract was washed, dried and evaporated to yield a thick oily material which on being purified by preparative TLC with hexane: Et_2O (80: Et_2O) as eluent, yielded the ketal (6) (352 mg, 70%), δ1.26-1.84 (4H,m) 2.26 (3H, s, CH_3), 2.30 (3H, s, CH_3), 2.66 (2H, t, J=9 Hz, benzyl protons), 3.36 (6H, s, 2 OCH_3), 3.82 (3H, s, OCH_3), 4,44 (1H, t, methine proton), 6.63 (1H, d, J=6 Hz) and 6.96 (1H, d, J=6 Hz) (aromatic protons), m/z 220 (M^+ -CH_3OH) and 188 (M^+ -2 CH_3OH). (Found: C, 71.45; H, 9.63 Calc. for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59%).

2, 4- Dimethyl-3(1-Oxobutan-4-yl) anisole (7)

The ketal (6) (250 mg) dissolved in tetrahydrofuran (15 ml) was treated with dilute HCl (3ml, 10%) and heated for 3 h. The reaction mixture after dilution with water was extracted with Et_2O. The organic extract was washed, dried and evaporated to obtain an oily material which was chromatographed over aluminia. Evaporation of Et_2O -hexane (30: 70) elute afforded the aldehyde (7) (140 mg, 68%), IR: 2700 and 1710 cm^{-1}, δ 1.32-1.92 (4H, m), 2.23 (3H, s, CH_3), 2.26 (3H, s, CH_3), 2.68 (2H, t, J=9 Hz) (benzyl protons), 3.78 (3H, s, OCH_3), 6.64 (1H, d, J=9 Hz), 6.98 (1H, d, J=9 Hz) (aromatic protons) and 9.82 (1H, t, J=9 Hz, CHO), m/z 206 (M^+) and 177 (M^+ - CHO). Its 2,4 -DNP derivative, yellow solid, m.p. 180-182°(from MeOH). (Found: C, 59.11; H, 5.78; N, 14.56. Calc. for $C_{19}H_{22}O_5N_4$: C, 59.06; H, 5.74; N. 14.50%).

2,4-Dimethyl-3(1-benzoyl-1-acetyl-butan-4-yl)-1-acetoxy benzene (8)

To the dienone (4) (600 mg) dissolved in AC_2O (20 ml), p-toluenesulfonic acid (50 mg) was added and heated at 120°for 1 h. The resulting deep red material, completely free from the starting material as evidenced by TLC, was diluted with water and extracted with Et_2O. The organic extract was washed, dried and evaporated to afford an oily material which on being purified by preparative TLC |hexane: Et_2O (70:30) | as eluent yielded the ester (8) (478 mg, 70%), IR: 1770, 1730 and 1270 cm^{-1}, δ2.23 (3H, s, CH_3), 2.26 (3H, s, CH_3), 2.06 (6H, s, OAc), 6.54-6.99 (3H, m) (aromatic and methine protons) and 7.51-8.09 (5H, benzoate protons), m/z 398 (M^+), 356 (M^+ $-CH_2=CO$), 296 (M^+ $-CH_2=CO-CH_3COOH$), 276 (M^+ - PhCOOH) and 216 (M^+ - $PhCOOH-CH_3COOH$). (Found: C, 69.33; H, 6.62.Calc. for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58%).

Dimeric product (10)

To a solution of the ester (8) (400 mg) in MeOH (25 ml) was added aqueous KOH (5 ml, 10%) and heated under reflux for 3 h. The reaction mixture was cooled, diluted with water, and extracted with $CHCl_3$. The organic extract was washed, dried and evaporated to obtain the dimeric product (10) (358 mg, 98%), m.p. 143-144°(from CH_3COCH_3), IR: 3460, 1695 and 800 cm^{-1}; δ(CD_3COCD_3) 1.52-1.8 (m, 2H), 2.16 (s, 3H) 2.23 (3H, s), 2.26 (6H,s) (four CH_3), 2.32-274 (m, 8H), 6.55-6.84 (5H,m, aromatic and vinyl protons), 7.81 (2H,s, OH, exchangeable by D_2O) and 9.55 (1H, s, CHO), m/z 366 (M^+) (Found: C; 78.68; H, 8.27. Calc. for $C_{24}H_{30}O_3$: C, 68.65; H, 8.25%).

ACKNOWLEDGEMENTS

We express our gratitude and thanks to Prof. D.S. Caine and his collaborators, specially Mr. Charles Harrison for helpful suggestions, to Dr. P. de Mayo, Canada and M.E. Alonso, Venezuela for helpful discussions, to Dr. S.K. Wong and Mr. D. Hairsine the University of Western Ontario, Canada for mass spectral measurements of the compound (8). Partial financial help (Project S1-1166) from Consejo Nacional de Investigaciones Científicas y Tecnológicas (CONICIT) is gratefully acknowledged.

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