CHEMISTRY LETTERS, pp. 627-630, 1977. Published by the Chemical Society of Japan

THIELE ACETYLATION OF p-TROPOQUINONE, AN ABNORMAL RING CONTRACTION

Masahiro HIRAMA and Shô ITÔ

Department of Chemistry, Tohoku University

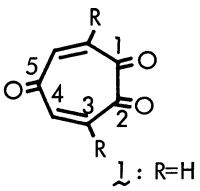
Sendai 980

Thiele type acylation reaction of p-tropoquinone 1, a novel nonbenzenoid quinone, in the presence of sulfuric acid, resulted in the unexpected ring contraction to a benzaldehyde derivative 2, in addition to a tropone 3. It was proved in this reaction that acetoxyl group attacked C_3 exclusively and that the carbon became aldehydic. In the reaction catalyzed by BF_3, regioselectivity of the nucleophilic attack was reduced to 4:1 (C_3:C_4) yielding 9, 10, and 11, all seven-membered ring compounds. Plausible mechanisms for the all reaction pathways are proposed.

In the previous paper[1], we have reported the Michael-type addition reactions of p-tropoquinone which has been synthesized recently by us.[2] In these reactions, nucleophilic attack occurs at C_4, the position of the lower π-electron density, rather than at C_3. Another reaction of this type is Thiele acetylation reaction, which has extensively been investigated in benzenoid series because of the mechanistic interest as well as of the synthetic importance.[3] This reaction also occurred with p-tropoquinone in the presence of sulfuric acid or boron trifluoride but in different ways from the other nucleophiles.

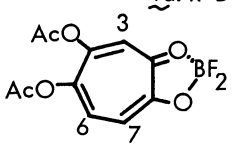
p-Tropoquinone 1 reacted with freshly distilled acetic anhydride at room temperature in the presence of 5% of conc. sulfuric acid and after 14 hr afforded the 6-membered pentacetate 2, colorless prisms, mp 152.5-154°, in 22% yield along with the 7-membered triacetate 3,[4] colorless prisms, mp 111-112° (7% yield).[5] While structure of 3 was deduced by its derivation from 3,5-dihydroxytropolone 4,[6,7] that of 2 was determined as follows: 2 was hydrolyzed with 6N-sulfuric acid in methanol to 2,3,6-trihydroxybenzaldehyde 5, bright yellow prisms, mp 170-180° (dec.), quantitatively. Compounds 2 and 5 being different from 2,3,4-trihydroxybenzaldehyde 6[8] and its pentacetate 7, colorless cryst., mp 137-138°, respectively, their structures were deduced by spectral analyses.[9] 6 and 7 are absent in the reaction mixture.

In order to clarify the reaction pathway leading to 2, the following reactions were carried out. The triacetate 3 isomerized to 8, colorless prisms, mp 127-128.5° (ca. 40%),[10] but not to 2 under the same acetylation condition (15 hr). Thus, 3 is not involved in the pathway. Although fuming sulfuric acid (30% SO_3) (in place of conc. sulfuric acid) caused no change in the yield of products, addition of acetic acid (20%) to the solution increased the yield of 2 to 36%, suggesting the necessity of a proton source in the reaction. Furthermore, the deuterated pentacetate 2d was obtained through the reaction with tropoquinone-3,7-d_2 1d, prepared from tropolone-3,5,7-d_3.[12] 2d and its hydrolysis product 5d were found to contain two deuterium atoms solely at C_4 and aldehydic positions, revealing that the aldehydic carbon originated from C_3 of 1. Thus, it was revealed that nucleophilic attack occurred only at C_3 position in this acetylation reaction in contrary to the other Michael addition of 1.

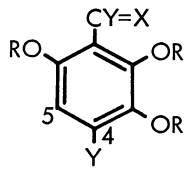


1 : R=H

1d: R=D



10

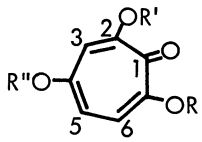


2 : R=Ac, X=$(OAc)_2$, Y=H

2d: R=Ac, X=$(OAc)_2$, Y=D

5 : R=H, X=O, Y=H

5d: R=H, X=O, Y=D

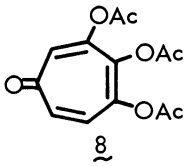


3 : R=R'=R"=Ac

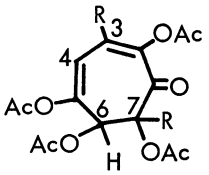
4 : R=R'=R"=H

9 : R=BF_2, R'=R"=Ac

or R=R"=Ac, R'=BF_2



8

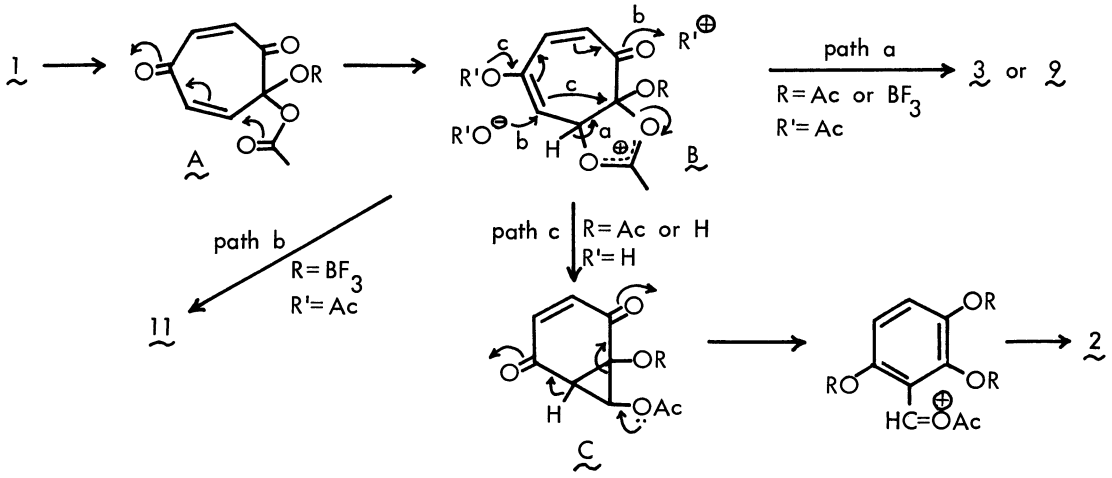


11 : R=H

11d: R=D

The acetylation (r.t., 4-19 hr) in the presence of boron trifluoride etherate (1-1.2 equivalent) is also somewhat abnormal, although no ring contraction was observed. The products obtained were the acetates 9 (38%), colorless prisms, mp 140.5-142°, 10 (14%), colorless needles, dp 156-160° and 11 (18%), colorless cryst., mp 123-126°. The boron-containing products 9 and 10 resisted to the acidic and alkaline hydrolysis. Structure of 9 was established by i) its conversion with $Cu(OAc)_2$ to the corresponding copper complex and subsequent acid hydrolysis to 4 and ii) its quantitative formation from 3 by the treatment with BF_3 etherate (room temperature), while structure of 10 rests on its spectral analysis (Table).[13] Tetracetate 11 was gradually converted to 9 (22 hr, 27%) under the acetylation condition; hence the positions of three acetoxyl groups are obvious. The position of the fourth acetoxyl group was determined spectroscopically with aid of the deuterated product 11d, PMR of which lacks H_3 and H_7 signals and changes H_4 and H_6 to AB type. Thus, in this reaction, attack of acetoxyl group occurred at C_3 and C_4 of 1 in the ratio of ca. 4:1 assuming that 11 was formed by the former process.

The nucleophilic attack in these acetylation reactions shows a sharp contrast to the other conjugate addition reactions.[1] The attack at C_3 must have been caused by the interaction of electrophiles (H^+ or Ac^+ or BF_3) with one of the carbonyl oxygens. O_2 rather than O_5 should have the preferential interaction because of strong dipole-dipole interaction between two adjacent carbonyl groups. This facilitates the nucleophilic attack at C_2 and C_4. The former attack is reminiscent of the formation of hydrate and hemiacetals.[2] While 10 results from the latter attack, the rest of the products is rationalized as shown below as being derived from



the former process yielding intermediate A, followed by its conversion to the bicyclic intermediate B. This kind of cyclization would be facilitated for angular groups such as acetoxyl more than for monoatomic or linear groups as chloride or azido group. Pathway c to 2 would involve rather unusual ring contraction via homo-p-benzoquinone intermediate C, while paths a and b are straightforward.

Table

2 : m/e 323 (M-59), 280, 238, 196, 154 (b.p.); δ 2.04 (6H, s), 2.25 (3H, s), 2.34 (6H, s), 7.03 (d, 9.0, H_5), 7.28 (d, 9.0, H_4), 7.96 (s, -C<u>H</u>$(OAc)_2$); ν 1775 sh, 1763, 1619, 1607, 1490, 1375, 1240, 1201, 1181 cm^{-1}; λmax (CH_2Cl_2) 270 (log ε 3.11), 274.5 nm (3.11).

3 : m/e 280 (M^+), 238, 196, 154 (b.p.), 126, 43; δ 2.29 (3H, s), 2.34 (6H, s), 6.88 (dd, 10.2, 2.3, H_5), 7.16 (d, 2.3, H_3), 7.24 (d, 10.2, H_6); ν 1768, 1759, 1593, 1513, 1365, 1187, 1163, 1119 cm^{-1}; λmax 234.5 (log ε 4.48), 322.5 nm (3.99).

4 : m/e 154 (M^+, b.p.), 126, 110, 108, 80, 52; δ (acetone-d_6) 5.5 (3H, OH), 6.84 (dd, 11.3, 2.6, H_5), 7.22 (d, 2.6, H_3), 7.39 (d, 11.3, H_6); ν 3250, 1623, 1590, 1416, 1182, 961, 892 cm^{-1}; λmax 248 (log ε 4.45), 270 (4.02), 330.5 (3.79), 378 (sh, 3.84), 388 nm (3.87).

5 : m/e 154 (M^+, b.p.), 153, 136, 125, 108, 107, 80, 79; δ (acetone-d_6) 6.25 (d, 8.7, H_5), 7.00 (d, 8.7, H_4), 10.33 (s, -C<u>H</u>O); ν 3427, 3112, 1640, 1621, 1580, 1474, 1255, 935, 795, 728 cm^{-1}; λmax (EtOH) 238 (log ε 3.80), 279 (4.02), 390 nm (3.48).

8 : m/e 280 (M^+), 238, 196, 154 (b.p.), 126; δ 2.02, 2.09, 2.29 (each 3H, s), 6.62 (1H, m), 6.74 (2H, m); ν 1775 sh, 1764, 1630, 1583, 1440, 1425, 1394, 1370, 1262, 1248, 1200, 1179, 1122, 1090 cm^{-1}; λmax 225 (sh, log ε 4.31), 239 (4.39), 251 (sh, 4.25), 258 (sh, 4.17), 302 (sh, 3.86), 314.5 nm (3.94).

9 : m/e 286 (M^+), 267, 244, 224, 202 (b.p.), 182, 174, 154, 43; δ 2.40, 2.42 (each 3H, s), 7.40 (dd, 12.1, 2.6, H_5), 7.65 (d, 2.6, H_3), 7.88 (d, 12.1, H_6); ν 1781 sh, 1775, 1611, 1593, 1445, 1418, 1135 cm^{-1}; λmax 243.5 (log ε 4.53), 308 (sh, 3.79), 323 (3.93), 356 (sh, 3.79), 368 nm (3.82).

10 : m/e 286 (M^+), 267, 244, 224, 202, 182, 174, 154, 43 (b.p.); δ (acetone-d_6) 2.39, 2.42 (each 3H, s), 7.96 (d, 11.8, H_6 or H_7), 8.06 (s, H_3), 8.30 (1H, d, 11.8, H_7 or H_6); ν 1791, 1772, 1609, 1438, 1374, 1350, 1186 cm^{-1}; λmax 240 (log ε 4.47), 310 (sh, 3.89), 324.5 (4.00), 358 (3.81), 371 nm (sh, 3.75).

11 : m/e 340 (M^+), 298, 280, 256, 238, 214, 196, 172, 154, 126, 78, 43 (b.p.); δ 2.07, 2.18 (each 3H, s), 2.23 (6H, s), 5.49 (dd, 1.8, 1.5, H_6), 5.95 (dd, 9.2, 1.8, H_4), 6.03 (d, 1.5, H_7), 6.43 (d, 9.2, H_3); ν 1776, 1751, 1693, 1667, 1369, 1218, 1192 cm^{-1}; λmax ca. 240 (sh, log ε 3.51), 302 nm (3.77).

References and Notes

1) M. Hirama and S. Itô, Tetrahedron Lett., 2339 (1976).

2) S. Itô, Y. Shoji, H. Takeshita, M. Hirama, and K. Takahashi, ibid., 1075 (1975).

3) J.F.W. McOmie and J.M. Blatchly, "Organic Reactions", Ed. by W.G. Dauben, Vol. 19, p. 199, John Wiley, New York (1972); K.T. Finley, "The Chemistry of the Quinonoid Compounds", Ed. by S. Patai, p. 877, John Wiley, London (1974) and references cited therein.

4) In some cases, 3 was not isolated but the yield of 2 did not change greatly.

5) All new compounds described gave correct elemental analyses and or parent ion peaks in their mass spectra. Spectral data which are shown in Table refer to the following conditions unless otherwise stated: UV (λ), MeOH solution; IR (ν), KBr disk; NMR (δ), $CDCl_3$ solution.

6) Y. Kitahara, Sci. Repts. Tohoku Univ., Ser. I, 39, 275 (1956).

7) 3 was obtained by heating 4 at 110° with acetic anhydride. The location of the acetoxyl groups was based on their chemical shifts (Table), those of 2,5-diacetoxytropone (δ 2.29, 2.33) and of 2,7-diacetoxytropone (2.34 (2 Me)) being taken into consideration.

8) H. Gross, A. Rieche, and G. Matthey, Chem. Ber., 96, 308 (1963). This compound was easily acetylated to the corresponding pentacetate with acetic anhydride in the presence of conc. sulfuric acid.

9) Aromatic protons in 2 and 5 were assigned on the basis of substituent effect on the chemical shift of benzene (cf. L.M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd Ed., p. 201, Pergamon Press, London (1969)). Trimethoxybenzaldehyde derived from 5 is also useful for the purpose: Calculated chemical shifts of H_4 (δ 6.93) and H_5 (6.59) are in good agreement with experimental results (δ (CCl_4) 6.96, 6.54 (each 1H, d, J=9.2)).

10) 8 was spectral properties similar to 3 (cf. 7) except for IR and NMR (shown in Table) and is easily hydrolyzed to 4. NMR spectra of 3 and 8 in C_2Cl_4 are not dependent on temperature at 40-100°. These facts and facile acylotropic rearrangement of tropolone acetates[11] support the structure of 8.

11) S. Masamune, M. Yasunami, and K. Takase, Chem. Commun., 283 (1973). V.I. Minkin, L.P. Olekhnovich, Y.A. Zhdanov, Z.N. Budarima, and V.P. Metlushenko, Tetrahedron Letters, 563 (1974).

12) S. Itô, J. Tsunetsugu, T. Kanno, H. Sugiyama, and H. Takeshita, ibid., 3659 (1965).

13) PMR spectrum of 10 shows an AB pattern and a singlet. It is common in PMR spectra of troponoids that 5-bond coupling is not observed, while 4-bond coupling constant is ca. 2 Hz.

(Received March 7, 1977)