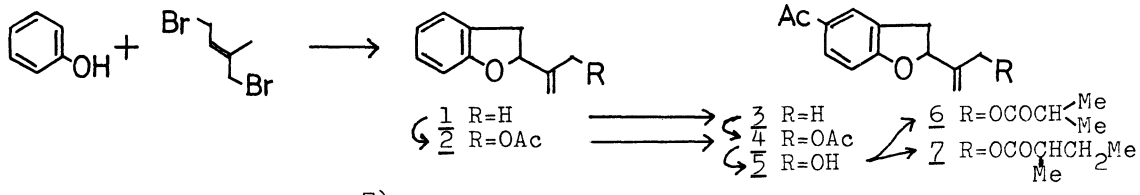
CHEMISTRY LETTERS, pp. 253-254, 1978. Published by the Chemical Society of Japan

THE SYNTHESIS OF dl-5-ACETYL-2-(1-HYDROXYMETHYLVINYL)-2,3-DIHYDROBENZOFURAN AND ITS ESTERS

Yoshiyuki KAWASE, Seiji YAMAGUCHI, Seizô KONDÔ, and Keiko SHIMOKAWA
Department of Chemistry, Faculty of Science, Toyama University, Gofuku, Toyama 930

dl-Tremetone, synthesized conveniently from phenol in two steps, was oxidized by selenium dioxide in acetic anhydride to give dl-5-acetyl-2-(1-acetoxymethylvinyl)-2,3-dihydrobenzofuran, which was hydrolized to dl-form of the natural alcohol. The dl-alcohol was further esterified to dl-forms of the two natural esters.

The structure of tremetone was determined to be l-3[1] and the synthesis of dl-3[2,3] and l-3[4] was also reported. Recently, the compound hydroxylated in the isopropenyl side chain of 3, that is 5-acetyl-2-(1-hydroxymethylvinyl)-2,3-dihydrobenzofuran[5] (l-5), and its two esters[6] (6 and 7) have been isolated from the natural sources. The structure of l-5 was determined by chemical and spectroscopical methods, and those of 6 and 7 were by spectroscopy. We studied a convenient method for the synthesis of dl-3, which was converted to dl-5 and then to dl-6 and dl-7.



It was reported by Nickl[7] that the reaction of isoprene dibromide and sodium with phloroacetophenone gave 2-isopropenyl-2,3-dihydrobenzofuran derivative. The reaction was applied to phenol to give dl-2-isopropenyl-2,3-dihydrobenzofuran (dl-1) [bp 67-76°C/2 mmHg, yield 42.9%], the spectral data of which are identical with those of the authentic sample.[2] The acetylation of dl-1 with acetic acid and trifluoroacetic anhydride at room temperature gave dl-3 [bp 120-127°C/2 mmHg, yield 34%, ν_{CO} 1670 cm^{-1}, $\delta(CCl_4)$ 1.80(3H, broad, $-C<^{CH_3}_{CH_2}$), 2.45(3H, s, $-COCH_3$), 3.20(2H, m, 3-H), 5.11(3H, m, $>C=CH_2$ and 2-H), 6.83(1H, d, J=10 Hz, 7-H), 7.83(2H, m, 4- and 6-H), λ_{max}^{EtOH} 226, 280, 287sh nm, Anal. C, 76.96; H, 6.74%]. The spectral data are identical with the reported.[1,3] The dl-3 was converted by the action of selenium dioxide in acetic an-

hydride at 130° to *dl*-5-acetyl-2-(1-acetoxymethylvinyl)-2,3-dihydrobenzofuran (*dl*-4) [bp 120-135°C/4 mmHg, yield 5.4%, ν_{CO} 1740, 1670 cm^{-1}, δ(CCl_4) 1.97(3H, s, $-COCH_3$), 2.43(3H, s, $-COCH_3$), 3.27(2H, m, 3-H), 4.67(2H, broad, $>CH_2$), 5.23(3H, m, $>C=CH_2$ and 2-H), 6.75(1H, d, J=9 Hz, 7-H), 7.73(2H, m, 4- and 6-H), λ_{max}^{EtOH} 226, 279, 287sh nm, Anal. C, 69.31; H, 6.25%]. The NMR spectrum is identical with that reported for the compound derived from natural *l*-5. The *dl*-4 was also prepared in better yield from *dl*-1 by the action of selenium dioxide in acetic anhydride to give *dl*-2-(1-acetoxymethylvinyl)-2,3-dihydrobenzofuran (*dl*-2) [bp 100-115°C/4 mmHg, yield 15.6%, ν_{CO} 1740 cm^{-1}, δ(CCl_4) 1.97(3H, s, $-OCOCH_3$), 3.23(2H, m, 3-H), 4.65(2H, broad, $-CH_2-O-$), 5.23 (3H, m, $>C=CH_2$ and 2-H), 6.67-7.33(4H, m, arom-H), λ_{max}^{EtOH} 223, 279, 286sh nm, Anal. C, 71.49; H, 6.53%], which was acetylated with acetic acid and trifluoroacetic anhydride to *dl*-4 [yield 46.7%]. The alkaline hydrolysis of *dl*-4 gave *dl*-5 [bp 103-105°C/3 mmHg, yield 18.8%, ν 3350(OH), 1665 cm^{-1}(CO), δ($CDCl_3$) 2.53(3H, s, $-COCH_3$), 3.07(1H, s, -OH), 3.37(2H, m, 3-H), 4.27(2H, broad, $-CH_2OH$), 5.30(3H, m, $>C=CH_2$ and 2-H), 6.81(1H, d, J=9 Hz, 7-H), 7.81(2H, m, 4- and 6-H), λ_{max}^{EtOH} 227, 280, 288sh nm, Anal. C, 71.26; H, 6.62%]. The spectral data are identical with the reported.[5] The *dl*-5 was then esterified with acid chlorides and pyridine to give the esters, *dl*-6 [bp 134-136°C/1 mmHg, yield 81.5%, ν_{CO} 1735, 1675 cm^{-1}, δ(CCl_4) 1.15(6H, d, J=6 Hz, $-CH<^{CH_3}_{CH_3}$), 2.45(3H, s, $-COCH_3$), 2.50(1H, m, J=6 Hz, $-CH<^{CH_3}_{CH_3}$), 3.30(2H, m, 3-H), 4.63(2H, broad, $-CH_2-O-$), 5.30(3H, m, $>C=CH_2$ and 2-H), 6.75(1H, d, J=9 Hz, 7-H), 7.75(2H, m, 4- and 6-H), λ_{max}^{EtOH} 225, 279, 288sh nm, Anal. C, 70.67; H, 6.73%] and *dl*-7 [bp 128-134°C/1 mmHg, yield 73.2%, ν_{CO} 1735, 1675 cm^{-1}, δ(CCl_4) 0.93(6H, m, $-CH<^{CH_2-CH_3}_{CH_3}$), 1.48(2H, m, $-CH<^{CH_2-CH_3}_{CH_3}$), 2.33(1H, m, $-CH<^{CH_2-}_{CH_3}$), 2.43(3H, s, $-COCH_3$), 3.27(2H, m, 3-H), 4.60(2H, broad, $-CH_2-O-$), 5.28(3H, m, $>C=CH_2$ and 2-H), 6.73(1H, d, J=9 Hz, 7-H), 7.72(2H, m, 4- and 6-H), λ_{max}^{EtOH} 225, 279, 287sh nm, Anal. C, 71.25; H, 7.46%], respectively, the NMR data of *dl*-6 and *dl*-7 are identical with the reported.[6]

References

1) W.A. Bonner, J.I. DeGraw, Jr., D.M. Bowen, and V.R. Shah, Tetrahedron, 17, 417 (1961); W.A. Bonner and J.I. DeGraw, Jr., ibid., 18, 1295 (1962).

2) J.I. DeGraw, Jr. and D.M. Bowen, ibid., 19, 19 (1963).

3) F. Bohlmann and U. Bühmann, Chem. Ber., 105, 863 (1972).

4) D.M. Bowen, J.I. DeGraw, Jr., V.R. Shah, and W.A. Bonner, J. Medical Chem., 6, 315 (1963).

5) G.V. López and B.R. González, Anal. Quim., 67, 879 (1971).

6) F. Bohlmann and C. Zdero, Tetrahedron Lett., 1970, 3575.

7) J. Nickl, Chem. Ber., 91, 553 (1958).

(Received December 22, 1977)