

The Reaction of (E)-2,4-Pentadienoic Acid with Aqueous Bromine Re-evaluation of the product

Yurngdong Jahng and Jin-II Kim

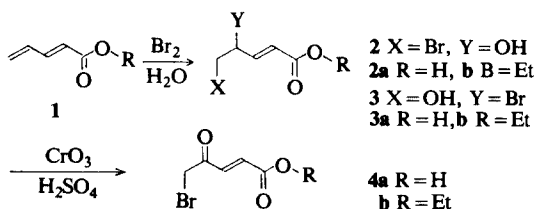
College of Pharmacy, Yeungnam University, Gyongsan 713-749, Korea
(Received August 12, 1989)

Abstract □ The reaction of (E)-2,4-pentadienoic acid with aqueous bromine was reinvestigated to affirm the formation of (E)-5-bromo-4-hydroxy-2-pentenoic acid, whose structure was confirmed by the spectroscopic methods as well as the chemical modification.

Keywords □ (E)-2,4-pentadienoic acid, ethyl (E)-2,4-pentadienoate, (E)-5-bromo-4-hydroxy-2-pentenoic acid, and ethyl (E)-5-bromo-4-hydroxy-2-pentenoate.

As a part of our efforts to prepare analogs of mevinolin, antihypercholesterolemic agent, we need ethyl (E)-5-bromo-4-oxo-2-pentenoate (**4b**). On the literature, the prerequisite 5-bromo-4-hydroxy-2-pentenoic acid (**2a**) was prepared with controversial results from the reaction of 2,4-pentadienoic acid (**1**) and aq. bromine. Early report on the reaction of 2,4-pentadienoic acid and aq. bromine showed the formation of 4-bromo-5-hydroxy-2-pentenoic acid (**3a**).¹⁾ From the same reactants and condition, Ingold *et al.* claimed the formation of 5-bromo-4-hydroxy-2-pentenoic acid (**2a**) without any spectral proof.²⁾

In this paper, we wish to report our studies on this reaction under various bromohydrin forming conditions. The electrophilic reaction of aq. bromine to the double bond affords a bromonium ion, which then undergoes nucleophilic ring opening by H₂O to provide corresponding bromohydrin. This nucleophilic ring opening-attack occurs at the carbon, where the more stable carbocation can be formed.³⁾ Since the electron density on the 4,5-double bond is higher than the density on the 2,3-double bond, the bromonium ion is formed at the 4,5-double bond, which can be attacked by hydroxide ion at C₄.⁴⁾ On this theoretical basis, we reinvestigated this reaction by treating (E)-2,4-pentadienoic acid with either eq. bromine or NBS in aq. DMSO to find the formation of (E)-5-bromo-4-hydroxy-2-pentenoic acid (**2a**) with 80% of yield. This structure was verified by ¹H and ¹³C NMR. The reaction of ethyl (E)-2,4-pentadienoate with NBS in aq. DMSO also afforded ethyl (E)-5-bromo-4-



hydroxy-2-pentenoate (**2b**) in good yield. From none of these reactions, we could not find any evidence of the formation of 4-bromo-5-hydroxy derivatives (**3**). On the other hand, Jones's oxidation of these bromohydrins gave (E)-5-bromo-4-oxo-2-pentenoic acid and ethyl (E)-5-bromo-4-oxo-2-pentenoate, respectively,⁵⁾ which could be the additional evidence of the above results.

EXPERIMENTAL

Melting points were determined on Yanaco micro melting point apparatus and uncorrected. Infrared spectra were obtained on a Perkin-Elmer 280 B spectrophotometer in KBr, except where noted. Nuclear magnetic resonance spectra were obtained on a Bruker AM-300 (300 MHz for ¹H NMR and 75 MHz for ¹³C NMR) spectrometer and chemical shifts are reported in parts per million downfield from tetramethylsilane. All solvents were reagent grade and used directly without further purification.

(E)-5-bromo-4-hydroxy-2-pentenoic acid (**2a**)

To a solution of 4.9g (0.05 mol) of (E)-

2,4-pentadienoic acid⁶⁾ in 160 ml of H₂O contained 4.2g of NaHCO₃ was added dropwise 2.8 ml of Br₂ with stirring over 4h. at room temperature. The reaction mixture was then allowed to be stirred for an additional hour and acidified to pH 2 with c-H₂SO₄. Work-up as usual afforded 5.28g (91%) of colorless oil, which was allowed to be crystallized from ether to give white crystals: mp 88-89 °C (lit.²⁾ 92-93 °C). The unpublished spectral data of this compound are as follows: ¹H NMR (300 MHz, CDCl₃) δ 3.50 (2H, d, J=6.7 Hz), 4.61 (1H, m), 6.15 (1H, dd, J=16.0, J=1.50 Hz), 7.00 (1H, dd, J=16.0, J=5.0 Hz), 7.30 (1H, s), and 11.40 (1H, s); ¹³C NMR (75 MHz, CDCl₃) δ 32.5, 70.2, 122.6, 145.0, 165.6; IR (KBr) 3500-2500 (br), 1660 (C=O) cm⁻¹.

Ethyl (E)-2,4-pentadienoate

The solution of 9.8g (0.1 mol) of (E)-2,4-pentadienoic acid in 50 ml of absolute EtOH was refluxed for 8 h. with 5 ml of conc. sulfuric acid. The reaction mixture was poured into cold 10% NaHCO₃ solution and extracted with ether. The combined organic layers were dried over MgSO₄ and removed the solvent to afford pale yellow liquid, which was distilled under reduced pressure to give 2.66g (22%) of colorless liquid: bp 53-55 °C/15 mmHg (lit.⁷⁾ bp 53-55 °C/19 mmHg). Unpublished spectral data of this compound are as follows: ¹H NMR (300 MHz, CDCl₃) δ 1.30 (3H, t, J=6.7 Hz), 4.20 (2H, q, J=6.7 Hz), 5.41 (1H, dd, J=9.7 Hz, J=2 Hz), 5.54 (1H, dd, J=16 Hz, J=2 Hz), 5.80 (1H, d, J=16 Hz), 6.44 (1H, dt, J=16 Hz, J=9.7 Hz), 7.20 (1H, dd, J=16 Hz, J=9.7 Hz); IR (thin film) 1720 (C=O), 1640 cm⁻¹.

Ethyl (E)-5-bromo-4-hydroxy-2-pentenoate (2b)

The mixture of 15.93g (0.13 mol) of ethyl (E)-2,4-pentadienoate and 23.1g (0.13 mol) of NBS in 150 ml of distilled water was stirred for 15 h.⁸⁾ The reaction mixture was extracted with CH₂Cl₂ and combined organic layers were washed with brine. After drying over anhyd. MgSO₄, solvents was evaporated. Resulting liquid was chromatographed on silica gel, eluting with CCl₄: EtOAc (4:1). The early fractions afforded 21.36 g (76%) of pale yellow liquid: ¹H NMR (300 MHz, CDCl₃) δ 1.30 (3H, t, J=6.7 Hz), 3.48 (1H, s, OH), 4.21 (2H, q,

J=6.7 Hz), 4.55 (1H, dt, J=3.5, J=1.5 Hz), 6.15 (1H, dd, J=14.0, J=1.65 Hz), 6.90 (1H, dd, J=14.0, 4.65 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 14.0, 36.7, 60.6, 70.0, 122.6, 145.6, and 166.1; IR (thin film) 3450 (br), 2990, 1710, 1650, 1370, 1300, 1175, 1040, 980, 870, and 720 cm⁻¹.

ACKNOWLEDGEMENT

The sincere appreciations will be given to Korea Science Foundation for the support of this study (# 883-0308-003-2).

LITERATURE CITED

- Muskat, I.E. and Hudson, L.: Studies of conjugated systems. IX. The addition of hypochlorous and hypobromous acids to vinylacrylic acid. *J. Am. Chem. Soc.* **53**, 3179 (1931).
- Ingold, C.K., Pritchard, G.J. and Smith, H.G.: The modes of addition to conjugated unsaturated systems. Part VI. Addition of halogens and hydrogen halides to conjugated unsaturated carboxylic acids and esters. *J. Chem. Soc.*, 79 (1934).
- Morrison, R.T. and Boyd, R.W.: "*Organic Chemistry*", Allyn & Bacon, Inc., 5th. ed., p. 323 (1987).
- Fleming, I.: "*Frontier Orbitals and Organic Chemical Reactions*", John Wiley & Sons, New York p. 121 (1972).
- The complete details for the preparation and properties will be furnished in a future publication.
- Jessup, P.J., Petty, C.B., Roos, J. and Overman, L.E.: 1-N-Acylamino-1,3-dienes from 2,4-pentadienoic acid by the Curtius rearrangement, *Org. Syn.* **59**, 1 (1980).
- Sundberg, R.J. Bukowick, P.A. and Holcombe, F.: The preparation of esters of 4-alkyl-2,4-pentadienoic acids by the phosphonate modification of the Wittig reaction, *J. Org. Chem.* **32**, 2938 (1967).
- The same result was obtained by treating the starting materials with NBS in either aq. DMSO or ether.