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A NEW SYNTHESIS OF BULLATENONE

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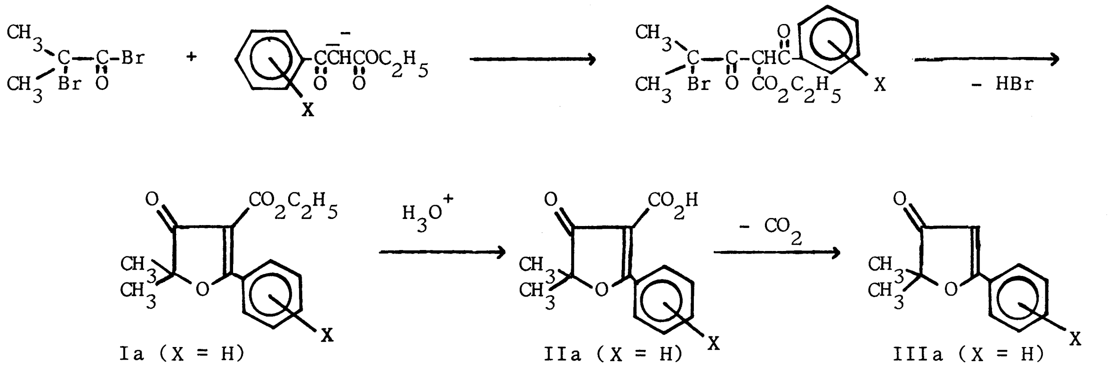
Bullatenone (IIIa) and its homologs substituted at p- and m- positions in the benzene ring have been prepared by the decarboxylative hydrolysis of ethyl 2,3-dihydro-2,2-dimethyl-3-oxo-5-arylfuran-4-carboxylates (I), which were obtained by the reaction of α-bromoisobutyryl bromide and ethyl sodioaroylacetate.

Bullatenone was first isolated by Brandt and his co-workers$^{1)}$ from the essential oil of Myrtus bullata, a shrub endemic to New Zealand. In 1958, Parker, Raphael, and Wilkinson$^{2)}$ have shown its structure to be 2,3-dihydro-2,2-dimethyl-3-oxo-5-phenylfuran (IIIa) by degradative studies and by synthesis from 2-methylbut-3-yn-2-ol in several steps. It involves the process to oxidize 4-methyl-1-phenylpent-2-yne-1,4-diol to 4-hydroxy-4-methyl-1-phenylpent-2-yn-1-one which seems to us undesirable for the purpose of a large scale preparation. We wish to report here a simple and convenient synthesis of bullatenone by the decarboxylative hydrolysis of ethyl 2,3-dihydro-2,2-dimethyl-3-oxo-5-phenylfuran-4-carboxylate (Ia), which can be conveniently obtained by the reaction of α-bromoisobutyryl bromide with ethyl sodiobenzoylacetate.



Ia (X = H)
Ib (X = p-CH_3)
Ic (X = m-CH_3)

IIa (X = H)

IIIa (X = H)
IIIb (X = p-CH_3)
IIIc (X = m-CH_3)

In a typical experiment 4.6 g (0.2 mol) of sodium was added in small pieces with caution to 96 g (0.5 mol) of ethyl benzoylacetate. The mixture was stirred for 2 hr at 60-70°C to come to a complete solution to which 23 g (0.1 mol) of α-bromoisobutyryl bromide was added with stirring at a temperature not exceeding 10°C. The stirring was continued for additional 6 hr at room temperature and for 24 hr at 50°C. The mixture was diluted with 80 ml of water, neutralized with 1 N hydrochloric acid and then extracted with ether. Repeated distillation gave 11.8 g of a fraction, bp 147-154°C/0.07 mmHg, which was shown to contain 79% Ia by glpc (Apiezon Grease L on Chromosorb W column: column temperature, 200°C; carrier gas, N_2, 42 ml/min; retention time, 16 min), yield 36%: IR (cm^{-1}, liquid) 1740 (ketone C=O), 1710 (ester C=O),[3] 1609, 1590 (benzene C=C), 1560 (C=C); NMR (60 MHz, CCl_4) δ 1.33 (t, 3H, J = 7 Hz, $-CO_2CH_2\underline{CH_3}$), 1.47 (s, 6H, 2 CH_3-), 4.23 (q, 2H, J = 7 Hz, $-CO_2\underline{CH_2}CH_3$), 7.4-8.05 (m, 5H, phenyl proton); MS (80 eV) m/e (relative intensity) 260 (M^+, 20), 245 ($M^+ - CH_3$, 2), 215 (29), 173 (25), 128 (40), 105 ($PhCO^+$, 56), 102 (100), 77 (Ph^+, 31). Found: C, 69.13; H, 6.25%. Calcd for $C_{15}H_{16}O_4$: C, 69.22; H, 6.20%.

The treatment of the ester Ia with concentrated hydrochloric acid at room temperature for 30 hr afforded a small amount of the acid IIa, white needles, mp 132-133°C (decomposition): IR (nujol) 3500-2500 ($-CO_2H$), 1750 (ketone C=O),[3] 1660 (carboxyl C=O), 1600, 1585 (benzene C=C), 1550 (C=C); NMR ($CDCl_3$) δ 1.60 (s, 6H, 2 CH_3-), 7.4-8.6 (m, 5H, phenyl proton), 10.1-11.3 (broad s, 1H, CO_2H); MS m/e (relative intensity) 232 (M^+, 82), 188 ($M^+ - CO_2$, 72).

Hydrolysis of Ia with concentrated hydrochloric acid, which was carried out at 70°C for 9 hr, afforded bullatenone in a 58% yield, bp 115-122°C/0.08 mmHg (lit.[2] bp 110°C/1 mmHg), mp 66-67°C (lit.[2] mp 67.5-68.5°C): IR (cm^{-1}, KBr) 1705 (C=O), 1608, 1590 (benzene C=C), 1565 (C=C)[3]; NMR (CCl_4) δ 1.42 (s, 6H, 2 CH_3-), 5.90 (s, 1H, ), 7.3-7.9 (m, 5H, phenyl proton); MS m/e (relative intensity) 188 (M^+, 100), 173 ($M^+ - CH_3$, 37), 105 ($PhCO^+$, 83).

Two homologs of bullatenone substituted in the benzene ring at p- and m- positions have also been synthesized in the similar manners: Ib, bp 172-195°C/0.02 mmHg, yield 36%; Ic, bp 165-173°C/0.02 mmHg, yield 17%; IIIb, mp 68-68.5°C, yield 54%; IIIc, mp 81-81.5°C, yield 63%.

References

1) C. W. Brandt, W. I. Taylor, and B. R. Thomas, J. Chem. Soc., <u>1954</u>, 3245.

2) W. Parker, R. A. Raphael, and D. I. Wilkinson, ibid., <u>1958</u>, 3871.

3) R. E. Rosenkranz, K. Allner, W. v. Philipsborn, and C. H. Eugster, Helv. Chim. Acta, <u>46</u>, 1259 (1963); A. Hoffmann, W. v. Philipsborn, and C. H. Eugster, ibid., <u>48</u>, 1322 (1965).

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