β-Lactone Formation in a Halogeno-lactonization Reaction

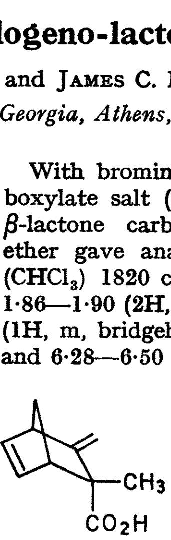
By WILLIAM E. BARNETT* and JAMES C. MCKENNA
(*Chemistry Department, University of Georgia, Athens, Georgia* 30601)

Summary The first example of β-lactone formation resulting from halogeno-lactonization of a βγ-unsaturated acid is reported.

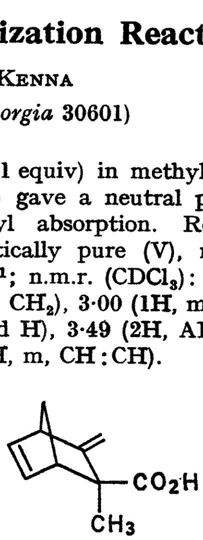
In connection with a recent total synthesis of teresantalol,[1] it was necessary to separate the mixture (40:60) of *endo*- and *exo*-acids, (I) and (II). Halogeno-lactonization reactions[2] have been employed for mixtures of similar but simpler norborn-5-enyl acids,[3,4] the *endo*-acid usually reacting to produce a neutral γ-lactone while the *exo*-acid remained in the aqueous layer as the carboxylate salt. However, in the acid (II) there is an extra double bond which is stereochemically accessible to the carboxyl group so that this *exo*-acid might be able to form a halogeno-lactone. From bromolactonization of the acid mixture only a trace of base-soluble matter was recovered, indicating that indeed both acids had reacted to produce neutral products. The i.r. spectrum of the crude neutral material had two carbonyl bands, 1792 and 1820 cm^{-1}, suggesting the formation of a γ-lactone and a β-lactone. It was not possible to isolate the β-lactone from this unstable mixture.

It seemed probable that the *exo*-acid (II) was the precursor of the β-lactone and attempts were made to isolate pure (II) in order to test this possibility. Esterification of mixtures of (I) and (II) followed by hydrolysis with limited amounts of base gave acid mixtures containing a greater proportion of (II), but the rates of hydrolysis of the *exo*- and *endo*-esters were not sufficiently different to permit an effective separation by this procedure. A very efficient method for the separation of the isomers involved iodolactonization with an amount of iodine required to consume only the *endo*-isomer. Under these conditions iodolactone (III)[1] was precipitated and pure *exo*-acid (II)† could be recovered by acidifying the bicarbonate layer, i.r. (CCl_4): 1699 cm^{-1} (CO_2H); n.m.r. ($CDCl_3$): δ 1·27 (3H, s), 1·70—1·76 (2H, m), 3·19 (2H, broad singlet), 5·03 (1H,s), 5·13 (1H, s), and 6·16 (2H, m).

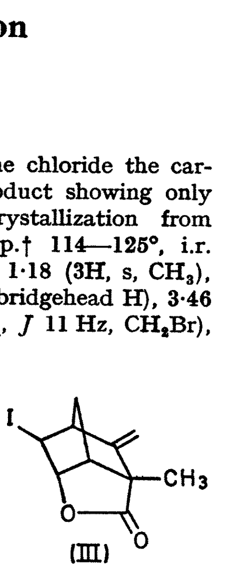
With bromine (1 equiv) in methylene chloride the carboxylate salt (IV) gave a neutral product showing only β-lactone carbonyl absorption. Recrystallization from ether gave analytically pure (V), m.p.† 114—125°, i.r. ($CHCl_3$) 1820 cm^{-1}; n.m.r. ($CDCl_3$): δ 1·18 (3H, s, CH_3), 1·86—1·90 (2H, m, CH_2), 3·00 (1H, m, bridgehead H), 3·46 (1H, m, bridgehead H), 3·49 (2H, ABq, *J* 11 Hz, CH_2Br), and 6·28—6·50 (2H, m, CH:CH).



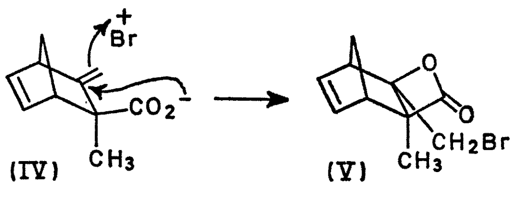
(I)



(II)



(III)



Few investigations concerning the bromolactonization reaction have been reported, presumably because no advantages or differences with the more commonly used iodolactonization reaction were found or expected. In a study[5] of the iodolactonization reaction, van Tamelen generalized that βγ-unsaturated acids form only γ-lactones or products which are not lactones. Subsequent work[6] has tended to support this generalization. Indeed, we have not been able to detect any β-lactone from the iodination of (IV). Our discovery of (V)‡ resulting from bromination of (IV) suggests that there may be a dramatic difference between the iodolactonization and bromolactonization of conformationally rigid βγ-unsaturated acids.

---

† The melting point varies, depending on the rate of heating; n.m.r. seems to be the best criterion for purity.

‡ An α-chloro-β-lactone and an α-bromo-β-lactone have been isolated from the bromination of an αβ-unsaturated acid (dimethylmaleic acid). These are apparently the only other β-lactones arising from a halogeno-lactonization reaction. D. S. Tarbell and P. D. Bartlett, *J. Amer. Chem. Soc.*, 1937, **59**, 407.

We thank the Office of General Research at the University of Georgia and the Petroleum Research Fund administered by the American Chemical Society for support of this work.

(*Received, March* 16*th*, 1971; *Com.* 308.)

---

[1] W. E. Barnett and J. C. McKenna, *Tetrahedron Letters*, 1971, 227.

[2] H. O. House, "Modern Synthetic Reactions," Benjamin, New York, 1965, p. 143.

[3] S. Beckmann and H. Geiger, *Chem. Ber.*, 1959, **92**, 2411.

[4] J. A. Berson and A. Remanick, *J. Amer. Chem. Soc.*, 1961, **83**, 4947.

[5] E. E. Van Tamelen and M. Shamma, *J. Amer. Chem. Soc.*, 1954, **76**, 2315.

[6] J. Klein, *J. Amer. Chem. Soc.*, 1959, **81**, 3611.