The Synthesis of Sinigrin

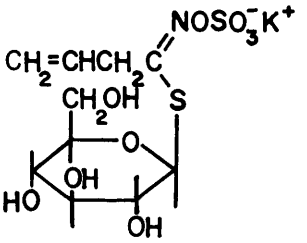
By M. H. BENN and M. G. ETTLINGER

[*Department of Chemistry, University of Alberta in Calgary, Calgary, Alberta, Canada* (*M.H.B.*)]

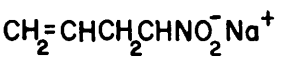
SINIGRIN (potassium myronate), the glucosidic precursor of the volatile, pungent allyl mustard oil, was isolated in 1839[1] from seeds of black mustard, *Brassica nigra* Koch. First of the

[1] A. Bussy, *Compt. rend.*, 1839, **9**, 815; *J. Pharm.*, 1840, **26**, 39.

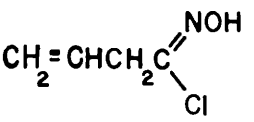
mustard oil glucosides to receive detailed analysis,[2] it became the textbook example of its class. The structure (I) proposed and established for sinigrin in 1956[3] has been confirmed by *X*-ray crystallographic analysis.[4] We can now report the first synthesis of sinigrin.



(I)



(II)



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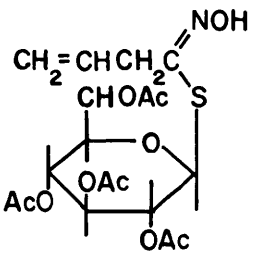
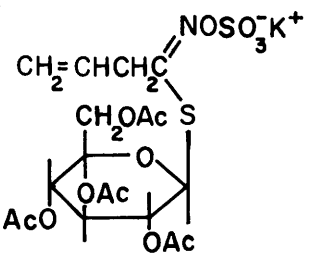


(IV)



(V)

But-3-enyl bromide was treated with sodium nitrite and urea in dimethyl sulphoxide[7] to give 4-nitrobut-1-ene (b.p. 144°/670 mm., n_D^{26} 1·4305), which was converted into the sodium salt (II) with sodium ethoxide. Addition of the salt (II) to a lithium chloride–hydrochloric acid mixture at 0° yielded[6] but-3-enohydroxamoyl chloride (III), which was condensed directly with tetra-acetyl-β-D-glucopyranosyl mercaptan and triethylamine[5] to give the thiohydroximic acid (IV) [m.p. 164—165°, considerably higher than reported[8] for material from enzymatic hydrolysis of tetra-acetylsinigrin; $[\alpha]_D^{26} - 13°$ (*c*, 0·14 in $CHCl_3$)]. Sulphonation of the intermediate (IV) with

The general route from hydroxamoyl chlorides to mustard oil glucosides, which was used for synthesis[5] of sinalbin, the other classical mustard oil glucoside, served also to reach sinigrin. However, the required hydroxamoyl chloride was obtained not from the corresponding aldoxime as usual but from the nitro-compound, by a reaction that Kornblum and Brown recently noted.[6]

[2] See F. Challenger, "Aspects of the Organic Chemistry of Sulphur," p. 115, Butterworths, London (1959) and A. Kjær, *Fortschr. Chem. org. Naturstoffe*, 1960, **18**, 122.
[3] M. G. Ettlinger and A. J. Lundeen, *J. Amer. Chem. Soc.*, 1956, **78**, 4172.
[4] J. Waser and W. H. Watson, *Nature*, 1963, **198**, 1297.
[5] M. H. Benn, *Canad. J. Chem.*, 1965, **43**, 1.
[6] N. Kornblum and R. A. Brown, *J. Amer. Chem. Soc.*, 1965, **87**, 1742.
[7] N. Kornblum, H. O. Larson, R. K. Blackwood, D. D. Mooberry, E. P. Oliveto, and G. E. Graham, *J. Amer. Chem. Soc.*, 1956, **78**, 1497.
[8] Z. Nagashima and M. Uchiyama, *J. Agric. Chem. Soc. Japan*, 1959, **33**, 1068; M. Uchiyama, *ibid.*, 1963, **37**, 543.

pyridine–sulphur trioxide, followed by treatment with potassium hydrogen carbonate, gave tetra-acetylsinigrin (V), m.p. 193—195°, $[\alpha]_D^{26}$ — 16° (*c*, 0·14 in H_2O),[9] which on deacetylation with methanolic ammonia[9] afforded pure, crystalline sinigrin (I), m.p. 125—127°, $[\alpha]_D^{28}$ — 17° (*c*, 0·2 in H_2O). Both the synthetic tetra-acetate and sinigrin were identical with samples of natural origin.

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[9] O.-E. Schultz and W. Wagner, *Arch. Pharm.*, 1955, **288**, 525; A. Kjær, R. Gmelin, and R. B. Jensen, *Acta Chem. Scand.*, 1956, **10**, 432.