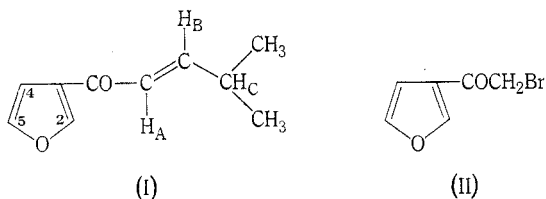


## THE SYNTHESIS OF ISOEGOMAKETONE\*

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The furano monoterpene, isoegomaketone (I), was isolated together with perilla ketone from the seeds of *Perilla frutescens* Britton var. *crispa* by Ito.<sup>1</sup> Recent studies in these laboratories<sup>2</sup> on the structure and synthesis of furano terpenes have now led to the synthesis of isoegomaketone.

Furantetracarboxylic acid was prepared from sodio ethyl oxalacetate as described in the literature.<sup>3</sup> It was found that decarboxylation to 3-furoic acid<sup>4</sup> was most satisfactory when quantities of about 30 g were used. Copper chromite was found to be preferable to copper powder for this reaction. 3-Acetylfuran was obtained in considerably higher yield than reported<sup>5</sup> from the reaction of 3-furoic acid with methyllithium. This ketone was readily converted to 3-( $\alpha$ -bromoacetyl)furan (II) with bromine in carbon disulphide. Reaction of (II) with triphenyl phosphine gave the phosphonium salt which on treatment with base gave the stable phosphorane. The Wittig reaction of the phosphorane with isobutyraldehyde gave isoegomaketone (I), together with a small quantity of an impurity. Its physical data and the melting point of the 2,4-dinitrophenylhydrazone derivative agreed with the values in the literature.<sup>1</sup> In particular, the structure was confirmed by the n.m.r. spectrum. This showed the presence of two methyl groups at a tertiary position at  $\tau$  8.9 (doublet).  $H_C$  appeared at  $\tau$  7.5.  $H_A$  absorbed at  $\tau$  3.6 and the coupling constant ( $J_{AB}$  16 c/s) confirmed the *trans* configuration about the double bond.  $H_B$  appeared at  $\tau$  2.97 and the furan protons at  $\tau$  3.22, 2.58, and 2.0. The infrared spectrum showed the presence of the conjugated carbonyl group (1670, 1625  $\text{cm}^{-1}$ ).



### Experimental

Melting points are uncorrected. Infrared spectra were determined using a Perkin-Elmer Infracord 237. N.m.r. spectra were measured in  $\text{CDCl}_3$  solutions using a Varian DP60 spectrometer with tetramethylsilane as internal standard. Microanalyses were done by the Australian Microanalytical Service, Melbourne.

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<sup>2</sup> Massy-Westropp, R. A., Reynolds, G. D., and Spotswood, T. M., *Tetrahedron Lett.*, in press.

<sup>3</sup> Grüssner, A., Hardmeier, E., Reichstein, T., and Schindler, K., *Helv. Chim. Acta*, 1933, **16**, 276.

<sup>4</sup> Conley, J. B., King, W. H., and Smith, H. A., *J. Am. Chem. Soc.*, 1951, **73**, 4633.

<sup>5</sup> Gronowitz, S., and Sorlin, G., *Arkiv. Kemi*, 1962, **19**, 515.

*3-( $\alpha$ -Bromoacetyl)furan*

A solution of 3-acetylfuran (1.1 g, m.p. 51° (lit.<sup>5</sup> m.p. 51–52°)) in carbon disulphide (30 ml) was cooled to 5°. Bromine (1.6 g) in carbon disulphide (20 ml) was added dropwise with stirring over a period of 10 min. After stirring for a further 60 min at 5° the solvent was removed under reduced pressure at room temperature to yield a colourless oil which darkened rapidly on standing. To reduce decomposition most of the carbon disulphide was removed, ether added, and the solution washed with sodium carbonate solution. The solution was dried and the ether removed to give 3-( $\alpha$ -bromoacetyl)furan as a colourless oil (1.76 g, 92%), b.p. 70°/5 mm. Crystallization from light petroleum (b.p. 50–65°) gave colourless needles, m.p. 36–37°.  $\nu_{\max}$  3140, 1560, 1510, 1160, 875  $\text{cm}^{-1}$  (furan), and 1675  $\text{cm}^{-1}$  (carbonyl) (Found: C, 38.5; H, 2.9. Calc. for  $\text{C}_6\text{H}_5\text{BrO}_2$ : C, 38.1; H, 2.7%).

*Phosphonium Salt*

3-( $\alpha$ -Bromoacetyl)furan (1.76 g) in benzene (7 ml) was added to triphenylphosphine (2.74 g) in benzene (7 ml) over 20 min. The product was collected after 60 min and washed with benzene. Recrystallization from ethyl acetate/methanol (2:1) gave the pure *phosphonium salt* (2.9 g, 70%), m.p. 275° (Found: C, 63.7; H, 4.4; Br, 17.9.  $\text{C}_{24}\text{H}_{20}\text{BrO}_2\text{P}$  requires C, 63.9; H, 4.4; Br, 17.7%).

*Preparation of the Phosphorane*

A solution of sodium ethoxide, prepared from sodium (0.1 g) and ethanol (2 ml), was added during 30 min to a stirred suspension of the phosphonium salt (0.9 g) in ethanol (4 ml) under nitrogen. The suspension dissolved and sodium bromide precipitated. After 30 min water (8 ml) was added and the mixture stirred for 12 hr. The product was collected, washed with water until free of bromide ions, and then dried at 60–80°. The *phosphorane* (0.65 g, 88%) was a colourless solid, m.p. 204° (from aqueous methanol) (Found: C, 77.7; H, 5.4.  $\text{C}_{24}\text{H}_{19}\text{O}_2\text{P}$  requires C, 77.8; H, 5.1%).

*Isoegomaketone*

A mixture of phosphorane (0.5 g), isobutyraldehyde (0.4 g), and benzene (5 ml) was stirred under reflux in an atmosphere of nitrogen for 6 hr. The solution was cooled to 20° and light petroleum (5 ml) added. This solution was allowed to stand for 2 hr, and the triphenyl phosphine oxide removed by filtration. Removal of the solvent from the filtrate gave a pale yellow oil (0.4 g) which was chromatographed on silica gel (B.D.H., 40 g). Elution with 50% ether/light petroleum (b.p. 50–65°), gave isoegomaketone (0.15 g, 68%) as a colourless oil together with a small quantity of an impurity. The pure ketone had b.p. 70°/1 mm.  $\nu_{\max}$  3140, 1670, 1625, and 980  $\text{cm}^{-1}$ . The n.m.r. spectrum showed the following absorptions. Methyl groups,  $\tau$  8.9 ( $J$  7 c/s) (doublet),  $\text{H}_C$  multiplet at  $\tau$  7.5,  $\text{H}_A$  doublet at  $\tau$  3.6 ( $J_{AB}$  16 c/s),  $\text{H}_B$  quartet at  $\tau$  2.97 ( $J$  8 c/s),  $\text{H}_2$  doublet at  $\tau$  2.0,  $\text{H}_4$  doublet at  $\tau$  3.22, and  $\text{H}_5$  doublet at  $\tau$  2.58. The 2,4-dinitrophenylhydrazone was prepared by Shine's method<sup>6</sup> and chromatographed on bentonite/kieselguhr (4:1) using chloroform as eluant.

The 2,4-dinitrophenylhydrazone crystallized from methanol as a red solid, m.p. 178° (lit.<sup>1</sup> m.p. 179–180°) (Found: C, 56.0; H, 4.8. Calc. for  $\text{C}_{16}\text{H}_{16}\text{N}_4\text{O}_5$ : C, 55.8; H, 4.7%).

<sup>6</sup> Shine, H. J., *J. Org. Chem.*, 1959, **24**, 1790.