# Novel Base-induced Ring Transformation of 1,2-Benzisoxazole-3-acetic Acid Esters into 2*H*-Azirines or Benzofurans

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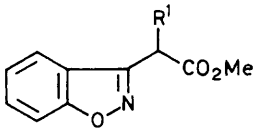
Treatment of α-mono-substituted 1,2-benzisoxazole-3-acetic acid esters (**1**) with strong bases caused a ring transformation to afford 2*H*-azirines (**2**) or 3-imino-2,3-dihydrobenzofurans (**3**).

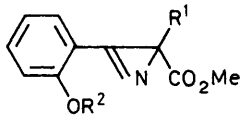
During our studies, we have paid much attention to the high nucleophilicity of the α-methylene carbon of 1,2-benzisoxazole-3-acetic acid derivatives.[1] As an extension of these studies, we now report the novel ring transformation of α-mono-substituted 1,2-benzisoxazole-3-acetic acid esters (**1**) with strong bases to give 2*H*-azirines (**2**) or 3-imino-2,3-dihydrobenzofurans (**3**).

The esters (**1**) were treated with an equimolar amount of NaH or Bu$^t$OK in dimethylformamide for 30 min at room temperature. An aqueous solution of ammonium chloride was added to the reaction solution at 0 °C, and the mixture was extracted with diethyl ether. After evaporation of the solvent, the residue was purified by means of recrystallization or column chromatography. Compounds (**1a—d**) having an alkyl, benzyl, phenylthio, or phenoxy group as an α-substituent gave 2*H*-azirine derivatives [(**2a**):† 90% yield, m.p. 107—109 °C; (**2b**): 65%, m.p. 74—77 °C; (**2c**): 60%, m.p. 112—114 °C; (**2d**): 91%, oil]. On the other hand, α-amino-substituted compounds (**1e**) and (**1f**) gave 3-imino-2,3-



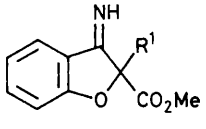
(**1**)

**a**; $R^1 = CH_2Ph$
**b**; $R^1 = Me$
**c**; $R^1 = SPh$
**d**; $R^1 = OPh$
**e**; $R^1 = NMe_2$
**f**; $R^1$ = morpholino



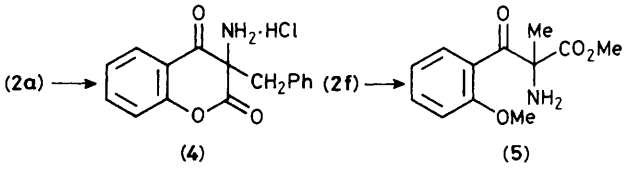
(**2**)

**a**; $R^1 = CH_2Ph$, $R^2 = H$
**b**; $R^1 = Me$, $R^2 = H$
**c**; $R^1 = SPh$, $R^2 = H$
**d**; $R^1 = OPh$, $R^2 = H$
**e**; $R^1 = R^2 = CH_2Ph$
**f**; $R^1 = R^2 = Me$

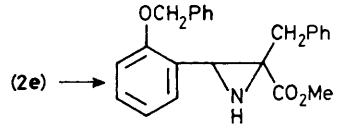


(**3**)

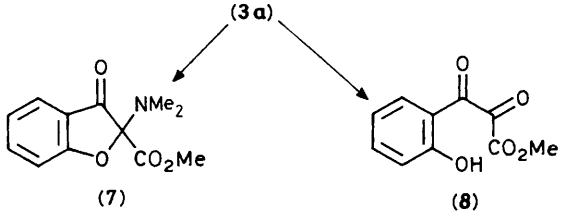
**a**; $R^1 = NMe_2$
**b**; $R^1$ = morpholino



(**4**) (**5**)



(**6**)



(**7**) (**8**)

† All new compounds described in this paper gave satisfactory spectral ($^1$H n.m.r., i.r., and mass) and analytical data.

dihydrobenzofuran derivatives [(**3a**): 76%, m.p. 119—121 °C; (**3b**): 66%, m.p. 136—137 °C]. The structures of compounds (**2**) and (**3**) were deduced from elemental and spectral analyses and chemical transformations.

I.r. spectra of compounds (**2**) showed the characteristic band due to the azirine C=N bond[2] at around 1760 $cm^{-1}$ [*e.g.*, (**2a**): ν(KBr) 3250 (OH), 1760 (C=N), 1725 $cm^{-1}$ (C=O)].

Acid catalysed hydrolysis of azirines to α-amino ketones is well established. Treatment of compound (**2a**) with hydrochloric acid in methanol gave 3-amino-3-benzylchroman-2,4-dione hydrochloride (**4**) (m.p. 143—145 °C) which was considered to be formed by recyclisation of the initially formed amino keto ester. Under similar conditions, compound (**2f**) which was prepared by methylation of the phenolic OH of (**2b**) gave the expected amino keto ester (**5**) in quantitative yield as an oily product [ν(film): 3400 and 3330 ($NH_2$), 1740 and 1680 $cm^{-1}$ (C=O)].

Furthermore, reduction of (**2e**), which was prepared by benzylation of (**2a**), with $NaBH_4$ gave the corresponding dihydro derivative (**6**) (m.p. 110—112 °C) in 60% yield.

Meanwhile, mild hydrolysis of (**3a**) with oxalic acid in methanol–water gave the corresponding 3(2*H*)-benzofuranone (**7**) (m.p. 120—121 °C) in quantitative yield. The $^{13}C$ n.m.r. spectral data of (**7**) [δ($CDCl_3$): 103.8 (2-C), 192.9 (3-C), 119.0 (3a-C), 122.4 and 125.2 (4-C, 5-C), 139.4 (6-C), 113.4 (7-C), 164.7 (7a-C), 39.0 (N–$CH_3$), 53.9 (O–$CH_3$), 172.3 (–CO–O)] are similar to the reported data[3] for 2-methoxy-2-(4-methoxybenzoyl)-3(2*H*)-benzofuranone.

Furthermore, hydrolysis of (**3a**) with hydrochloric acid in methanol at room temperature afforded the diketo ester (**8**) (m.p. 109 °C) in 40% yield. Thus the evidence described above substantiates the structures of compounds (**2**) and (**3**).

A plausible mechanism for the ring transformation of compounds (**1**) to 2*H*-azirines (**2**) may involve the Neber-like rearrangement of the initially formed α-carbanion of (**1**). In the case of the α-amino derivatives (**1e**), (**1f**), it is assumed that the initially formed azirines, which could not be isolated, may undergo further cleavage of the azirine C–N bond followed by recyclisation to give benzofurans (**3**).

The present azirine formation from (**1**) is the first example of the Neber-like rearrangement which involves a phenoxide as a leaving group.

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## References

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