

Revisiting the Hydroiodination of Propiolic Acid

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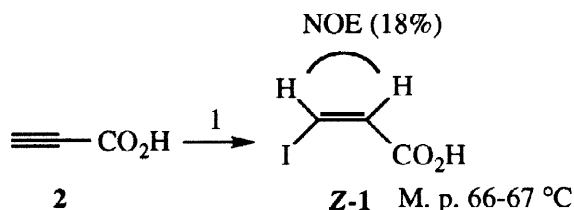
Abstract: Z-3-iodoacrylic acid **Z-1**, that formed by reacting propiolic acid **2** with 57% aqueous HI at 80–85 °C, was efficiently converted into the isomeric acid **E-1** by treatment in the same conditions. © 1998 Published by Elsevier Science Ltd. All rights reserved.

In the course of an ongoing synthetic work, we needed to prepare the pure *E* isomer (*i.e.* **E-1**) of 3-iodoacrylic acid **1**. The more convenient, obvious, way for preparing this useful synthon was to add HI to propiolic acid **2** but, though this hydroiodination process has been mentioned several times in literature,¹ some uncertainty still subsists concerning the exact incidence on its stereoselectivity of the conditions used. Hence, initially reported as giving a mixture of the **E-1** and the **Z-1** isomer,^{1a} the reaction of the acid **2** with aqueous hydroiodic acid was later claimed, without mention of any experimental detail, "to afford pure (*E*)-3-iodoacrylic in ca. 90% yield".^{1g} More recently, the acid **Z-1**, shown previously to be the kinetic product of the addition of HI to propiolic acid **2** in water,^{1c} was obtained in good yield by reacting **2** with excess 57% aqueous HI at 65 °C, whereas the isomeric acid **E-1** was formed by operating at 130 °C in a sealed tube, a result that led the authors to conclude that "temperature is a crucial parameter".¹ⁱ

With the aim to find out conditions permitting to prepare **E-1** on a large scale without recourse to the use of a sealed vessel and, subsidiarily, to shed some light on these contradictory literature data, we decided to re-investigate the **Z-1-E-1** isomerisation.

First, the acid **Z-1** was prepared by heating at ca 80–85 °C in the dark and under an argon atmosphere a solution of the acid **2** in freshly distilled 57% aqueous HI, which afforded a 94/6 mixture (NMR) of, respectively, the acids **Z-1** and **E-1**. Recrystallization of that crude product from hot hexane then afforded pure **Z-1** (91%), the structure of which was confirmed by performing a NOE experiment.

Reagents and conditions: 1- 57% (aqueous) HI (0.2 ml/mmol, 1.5 eq.) added to a solution of **2** in water (0.14 ml/mmol); 80–85 °C, overnight, then cristallization from hot hexane (91%).

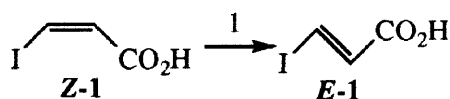


The acid **Z-1** thus obtained was submitted to conditions known to isomerise olefins by a free-radical pathway as, for instance, treatment by a catalytic amount of bromine or iodine, either in water or chloroform, with, or without irradiation of the reaction mixture with an ordinary 150W Philips lamp. Though trace amounts of the **E-1** isomer could be detected in a few cases, it soon became clear that such conditions would be of no practical value and, furthermore, that the inconsistency of some of the aforementioned literature reports could not be due to the accidental formation of iodine atoms during the hydroiodination step.

A solution came into view when we noted in relevant referenced that treatment of **2** by sodium iodide in refluxing AcOH for a few hours furnished uniquely the acid **Z-1**^{2a} whereas stirring **2** with LiI in CF₃CO₂H for 24

hours at *room temperature* afforded a 5/2 mixture of **Z-1** and **E-1**, respectively.^{2b} Given the ionic nature of that hydroiodination, this apparent sensitivity of the stereoselectivity to the strength of the acid medium used is not surprising, and is consonant anyway with results of an earlier kinetic study performed in water.^{1c} Although the temperature seems to be an important factor, the incidence of the HI concentration on the fate of the acid **Z-1** should be crucial as well: the higher the HI concentration, the faster the **Z-1/E-1** isomerisation. In experiments performed by using slight excess of HI, the concentration of this acid will, *necessarily*, drop as the addition reaction progresses: the addition will proceed, overall, under kinetic control, and harsh temperature conditions (130 °C, *vide supra*) will prove necessary to obtain the *E* isomer. Conversely, provided a large excess of HI is used, the concentration will not vary as much and, whatever the temperature used, some *Z-E* isomerisation should take place. It follows that the inconsistency of some reported stereoselectivities could originate from the use of different, unfortunately not defined, 2/57% HI ratios.

Reagents and conditions: 1- 57% (aqueous) HI (0.2 ml/mmol. 1.5 eq.); 85-90 °C, 24 hours.



In fact, heating for 24 hours a solution of the acid **Z-1** in 57% aqueous HI gave quantitatively a 5/95 (NMR) mixture of the acids **Z-1** and **E-1** and, ultimately, a very convenient procedure for preparing **E-1** was secured by reacting **2** with HI as precedently, then treating the resulting crude product with 57% HI, which gave, after crystallization, the pure acid **E-1** in an interesting 81% yield.³

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References and Notes

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- 3- *Protocol for preparing the acid Z-1:* Freshly distilled 57% HI (8.5 ml, 64.24 mmol) was added to the acid **2** (3g, 42.83 mmol), diluted with water (6 ml) and the resulting mixture was heated at ca 80-85 °C (oil bath), under an argon atmosphere. After cooling, the crude reaction mixture was diluted with 1N aqueous HCl (100 ml), and ether (100 ml). The aqueous phase was further extracted with ether (4x50 ml) and the pooled organic extracts were washed with 10% sodium thiosulfate (20 ml), and brine (20 ml). After drying (MgSO₄), the solvents were evaporated in a vacuum to give a white solid (7.95 g), that afforded the pure acid **Z-1** (91%; M. p.: 66-67 °C) by recrystallization from hot hexane. *Protocol for preparing the acid E-1:* Treatment of the acid **2** by HI was performed as precedently and the resulting crude product (**E-1/Z-1**=4/96, by ¹H NMR) was taken up in 57% HI (8 ml). The resulting solution was stirred at 85-90 °C for 24 hours, then worked up as above to give a solid, that proved to be (¹H NMR) a 95/5 mixture of the acids **E-1** and **Z-1**, respectively, and whose recrystallization from CH₂Cl₂/hexane afforded the pure acid **E-1** as white crystals (81%; M. p.: 140-141 °C). Both the acid **E-1** and **Z-1** thus obtained displayed NMR spectra identical to literature data.¹ⁱ