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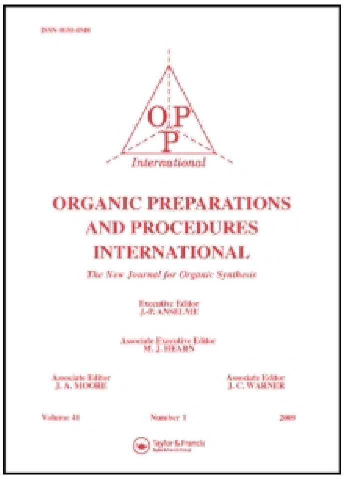

Organic Preparations and Procedures International

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

CONVENIENT SYNTHESIS OF 2,3-DIHYDROXY-2-METHYLPROPANAMIDE *via* 2,3-EPOXY-2-METHYLPROPANAMIDE

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To cite this Article Pilichowski, J. F. , Mailhot, G. and Bolte, M.(1994) 'CONVENIENT SYNTHESIS OF 2,3-DIHYDROXY-2-METHYLPROPANAMIDE *via* 2,3-EPOXY-2-METHYLPROPANAMIDE', Organic Preparations and Procedures International, 26: 5, 551 — 554

To link to this Article: DOI: 10.1080/00304949409458054

URL: http://dx.doi.org/10.1080/00304949409458054

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CONVENIENT SYNTHESIS OF 2,3-DIHYDROXY-2-METHYLPROPANAMIDE *via* 2,3-EPOXY-2-METHYLPROPANAMIDE

Submitted by
(11/03/93)

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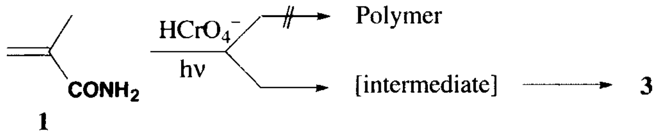
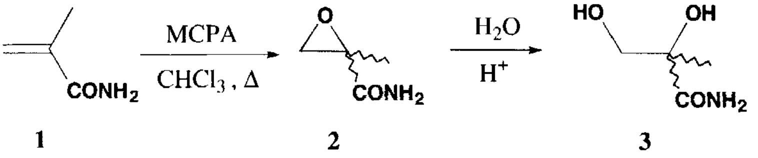
In the course of an investigation of the photopolymerization of methacrylamide (**1**) in the presence of chromium in aqueous solution, unexpected results were obtained.[1] Even though the experimental conditions were similar to those used for acrylamide,[2] no polymerization occured; instead, only one product could be isolated.



Irradiation of **1** (M < [**1**] < 10^{-4}M in water, $HCrO_4^-$ as photoinitiator, λ_{irr} = 365, 436 nm) led to only one product detected by HPLC. After work-up[3] of the reaction mixture, another new compound was obtained. Although the chemical behavior and analytical data (UV, IR and NMR spectra) fitted well with 2,3-dihydroxy-2-methylpropanamide (**3**), a comparison with an authentic sample was deemed useful. At the same time, epoxy derivative **2** a possible intermediate in the photoreaction,[4] was also synthesized. To our knowledge, in spite their simple structure, these two products have not been previously reported. There exists an extensive literature on the epoxidation of olefins, especially with peracids.[5] Actually, the reaction is not easy with alkenes bearing electron-withdrawing groups.[6] For example, the reaction of acrylonitrile with hydrogen peroxide leads to 2,3-epoxypropanamide in only 25% yield.[7] Although Emmons and Pagano claimed[8] peroxytrifluoroacetic acid to be efficient (84% in the case of methylmethacrylate), we chose *m*-chloroperbenzoic acid (MCPA) as the most convenient reagent, even if slight modifications of the standard method[9] appeared to be necessary (reaction time, heating, etc. see Experimental Section).

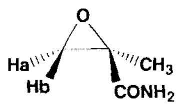
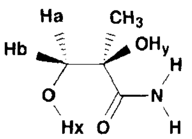


Thus, oxidation of methacrylamide with MCPA led to 2,3-epoxymethacrylamide in moderate yield (*ca* 22%). The progress of the reaction was monitored by TLC[10] and NMR; it was stopped just after the appearance of aromatic peaks in the NMR spectrum (58% completion). Treatment of the crude mixture with aqueous sodium hydroxide followed by liquid chromatography (silica gel), afforded the expected epoxide **2**. Its ^1H NMR spectrum (400 MHz) shows an AB spectrum (CH_2) both in D_2O (J = 5.0 Hz) and $CDCl_3$ (J = 5.4 Hz), beside the amide protons as a broad resonance (δ 6.05-6.35, $CDCl_3$, 25°). The acid-catalyzed hydrolysis of the epoxide ring proceeded readily to give the diol **3**. Proton NMR analysis shows non-equivalence in the CH_2 group. Coupling across oxygen atom, beside double resonance for the amide moiety, suggests a somewhat rigid intramolecular chelated conformation. ^{13}C NMR and mass spectra confirm the structures. From this synthesis, it can be conclued that the dihydroxy derivative **3** is the product isolated after the photoreaction. On the contrary, epoxide **2** is not the intermediate, the possible structure of which being that of a cyclic chromate ester. Related suggestions have been already put forward regarding the oxidation of olefinic compounds with chromyl salts.[11] No attempt was made to generalyze the synthetic method for production of other glycols of type **3**.

EXPERIMENTAL SECTION

Mps were determined in capillary tubes using a Buchi SMP-20 apparatus and are uncorrected. The IR spectra were obtained using a Nicolet FT-IR 20SX spectrophotometer. The NMR spectra were recorded with a Bruker AC 400 instrument refered to TMS or internal solvent. Mass spectra and elemental analyses were obtained from "Service Central d'Analyse", CNRS, Vernaison, France.

TABLE. ^{1}H NMR Data of Compounds **2** and **3**^{a}

		$CDCl_3$	D_2O	DMSO-d_6
	CH_3	1.58 (s)	1.75 (s)	
	Ha (or b)	2.64 (d, J = 5.4)	3.19 (d, J = 5)	
	Hb (or a)	2.91 (d, J = 5.4)	3.23 (d, J = 5)	
	NH_2	6.05-6.35 (m)		
	CH_3		1.44 (s)	1.18 (s)
	Ha (or b)		3.64 (d, J = 11.6)	3.31 (dd, Jab = 10.8, Jax = 5.2)
	Hb (or a)		3.89 (d, J = 11.6)	3.51 (dd, Jab = 10.8, Jbx = 6.7)
	OHx			4.70 (t, J ≈ 6)
	OHy			5.01 (s)
	NH			7.07 (s)
	NH			7.49 (s)

a) 5-10 per cent [w/v] concentrations.

2,3-Epoxy-2-methylpropanamide (2).- A solution of MCPA (10g, 32 mmol, Merck, 55% purity) in $CHCl_3$ (150 mL) was dried over $MgSO_4$. After filtration, the solution was added dropwise to a solution of methacrylamide (2.47g, 29 mmol) in the same solvent (50 mL), maintained at 5° under magnetic stirring. The temperature of the mixture was raised to 25° (3 hr) then to 60° (1.5 hr). The solution was cooled and washed with aqueous 0.5N NaOH until no more acidic material was extracted. The aqueous phase was extracted continuously with $CHCl_3$. The combined organic layers were dried and the solvent was evaporated. The crude mixture (*ca* 1.3g) was chromatographed on silica gel, using $CHCl_3$ as eluent, to give 0.57g (22%)[12] of the desired product, as colorless flocculent material, mp. 76-77°. TLC: Rf ≈ 0.4 (silica gel sheet, eluent EtOH/$CHCl_3$ (10/90, v/v)). IR (KBr): 3390, 3200 (NH); 1665 (C=O) cm^{-1}. ^{13}C-NMR ($CDCl_3$): 16.9, 54.1, 55.9, 173.6. GC–MS (EI): m/z 101(<1), 84(20), 71(20), 58(32), 44(92), 43(100).

*Anal.*Calcd. for C4H7NO2: C, 47.51; H, 6.98; N, 13.86. Found: C, 47.47; H, 7.06; N, 13.55

2,3-Dihydroxy-2-methylpropanamide (3).- To a solution of **2** (101 mg, 1 mmol) in water (6 mL) was added two drops of formic acid. The temperature of the mixture was raised to 75-80° (int.) and maintained for 15 hr. The solution was concentrated under vaccum to provide a solid residue which was washed with CHC13 (3 x *ca* 2 mL, discarded). The resulting product was dried under vacuum to give 2,3-dihydroxy-2-methylpropanamide as a white powder, in nearly quantitative yield, mp. 104-105°. The purity was checked by NMR. IR (KBr): 3450, 3240, 3100 (OH, NH), 1670 (C=O) cm^{-1}. ^{13}C-NMR (D_2O): 20.8, 66.6, 75.5, 179.9. GC–MS (EI): m/z 119(<1), 101(<1), 89(16), 75(96), 44(52), 43(100).

Anal. Calcd. for $C_4H_9NO \bullet 0.5\ H_2O$: C, 37.50; H, 7.86; N, 10.94. Found: C, 37.88; H, 7.68; N, 11.25

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12. If the unreacted methacrylamide is taken into account, the yield is 38%.

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