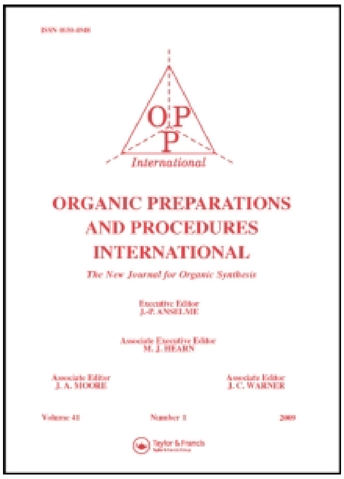


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

A SIMPLE PREPARATION OF TRAUMATIC LACTONE. A PROSTANOID SYNTHON

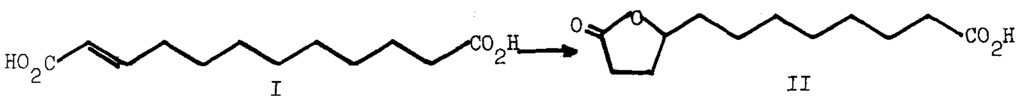
V. B. Deodhar[a]; V. S. Dalavoy[a]; U. R. Nayak[a]
[a] National Chemical Laboratory, Poona, INDIA

To cite this Article Deodhar, V. B. , Dalavoy, V. S. and Nayak, U. R.(1977) 'A SIMPLE PREPARATION OF TRAUMATIC LACTONE. A PROSTANOID SYNTHON', Organic Preparations and Procedures International, 9: 3, 155 — 157
To link to this Article: DOI: 10.1080/00304947709356873
URL: http://dx.doi.org/10.1080/00304947709356873

A SIMPLE PREPARATION OF TRAUMATIC LACTONE†. A PROSTANOID SYNTHON

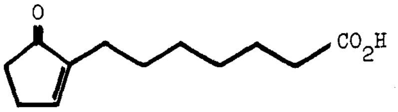
Submitted by V. B. Deodhar, V. S. Dalavoy and U. R. Nayak*
(6/30/77)
National Chemical Laboratory
Poona, INDIA

The importance of traumatic lactone(II) has recently been demonstrated[1] by its conversion with polyphosphoric acid, to the versatile prostaglandin synthon III. The reported conversion[1] of traumatic acid (I) to traumatic lactone(II) in 55% by heating with dilute H_2SO_4 (concentration unspecified) has proved to be quite unsatisfactory. This transformation (I → II) has been achieved by treatment of molten I[2] with p-toluenesulfonic acid; the product was isolated as its methyl ester.



I

II



III

EXPERIMENTAL

All mps and bps are uncorrected. Light petroleum refers to the fraction, bp. 60-60°. The following instruments were used for spectral/analytical data: Perkin-Elmer Infracord model 137-E (IR); Varian Associates T-60 spectrometer (PMR: TMS as internal standard); CEC mass spectrometer model 21-110B (mass; 70 eV, direct inlet system). "Aerograph" model A-350-B (10% silicone SE-30 on chromosorb W of 60-80 mesh, H_2 as carrier gas; temp. 200°).

Methyl ester of traumatic lactone.- Traumatic acid[2] (22.8 g, 0.1 mole) and p-toluenesulfonic acid (2.28 g) were mixed in a flask fitted with an air condenser and heated in an oil bath at 200 ± 5° (silica gel guard tube). After 6 hrs (optimized), the reaction mixture was cooled treated with dry methanol (220 ml) and left overnight at room temperature for 16 hrs. The product was isolated in the usual manner and the crude ester (24.5 g) (TLC: solvent 10% EtOAc in C_6H_6, 2 major spots) was chromatographed on SiO_2 gel (gr. II, 650 g, 92 x 4.5 cm) with TLC monitoring of fractions.

Fraction 1	light petroleum	500 ml x 4	0.24 g	mixture
Fraction 2	C_6H_6	500 ml x 2	1.03 g	mixture
Fraction 3	C_6H_6	500 ml x 2	2.24 g	pure; nonconjugated isomer of I (dimethyl ester)
Fraction 4	10% EtOAc in C_6H_6	500 ml x 6	14.34 g	pure II as methyl ester
Fraction 5	50% EtOAc in C_6H_6	500 ml x 6	3.20 g	pure II as methyl ester

<u>Fractions 4 and 5</u> were mixed and distilled to furnish the methyl ester of traumatic lactone as a colorless liquid (solidifies in the refrigerator), bp. 178-180°/0.5 mm (15.6 g, 65%); IR (smear): ν_{max} 1770, 1730 and 1180 cm^{-1}; nmr (CCl_4): δ 3.60 (s, 3H, $COOC\underline{H}_3$), 4.30 (br m, 1H, $-O-\underset{CH_2}{C\underline{H}}-CH_2$); Mass: m/e 242 (0.2%), 211 ($M-OCH_3$, 7%), 85 (100%).[3]

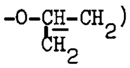
<u>Anal</u>. Calcd. for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15.

Found: C, 65.06; H, 8.90.

<u>Fraction 3</u> was colorless liquid, bp. 130-133°/0.5 mm (2.06 g, <u>ca</u> 8%); IR (smear): ν_{max} = 1730, 1639 and 970 cm^{-1}; nmr(CCl_4): δ 3.60 (s, 6H, 2 x $COOC\underline{H}_3$), 5.33 (br m, 2H, $H_2C-C\underline{H}=C\underline{H}-CH_2$); Mass: m/e M^+ 256 (24%), 692 (100%).

<u>Anal</u>. Calcd for $C_{14}H_{24}O_4$: C, 65.59; H, 9.44.

Found: C, 65.53; H, 9.48.

The ester (4.84 g 0.02 mole) and a 10% aqueous alcoholic potassium hydroxide solution (40 ml) were refluxed for 4 hrs. Most of the ethanol was removed under reduced pressure and the residue was diluted with water (100 ml) and extracted with ether to remove any neutral material. The alkaline aqueous layer was acidified with hydrochloric acid (Congo red), extracted with ether (100 ml x 3), washed with water, dried and the solvent removed. Distillation of the residue yielded 3.34 g (73%) of II as a colorless liquid, bp. 195-198°/0.4 mm which solidified, mp. 48-50°, lit.[1] bp. 190-195°/0.4 mm, IR ($CHCl_3$): ν_{max} 3200, 2680, 1770, 1705 and 1180 cm^{-1}; nmr ($CDCl_3$): δ 4.43 (broad m, 1H,  $-O-\underset{CH_2}{\underline{CH}}-CH_2$).

Anal. Calcd. for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83.

Found: C, 63.36; H, 9.17.

Esterification of II with CH_2N_2 gave a product identical (TLC, IR, PMR) with the ester described earlier.

REFERENCES

† The trivial name traumatic lactone has been adopted for dodecan-4-olide-12-oic acid, the lactone acid II (R = H) derived from traumatic acid I.

†† Communication No. 2114, National Chemical Laboratory, Poona.

1. S. B. Thakur, K. S. Jadhav and S. C. Bhattacharyya, Indian J. Chem., 12, 893 (1974).
2. A. S. C. Prakasa Rao, U. R. Nayak and S. Dev, Synthesis, 608 (1975).
3. Absence of the δ-lactone (expected base peak m/e 99) is borne out by the negligible abundance (ca 0.2%) of this ion. See e.g. H. Budzikiewicz, C. Djerassi and D. H. Williams (ed.) "Mass spectrometry of Organic Compounds" Holden Day, San Francisco, p. 206 (1967) and J. W. Wheeler, G. M. Happ, J. Araujo and J. M. Pasteels, Tetrahedron Letters, 4635 (1972).