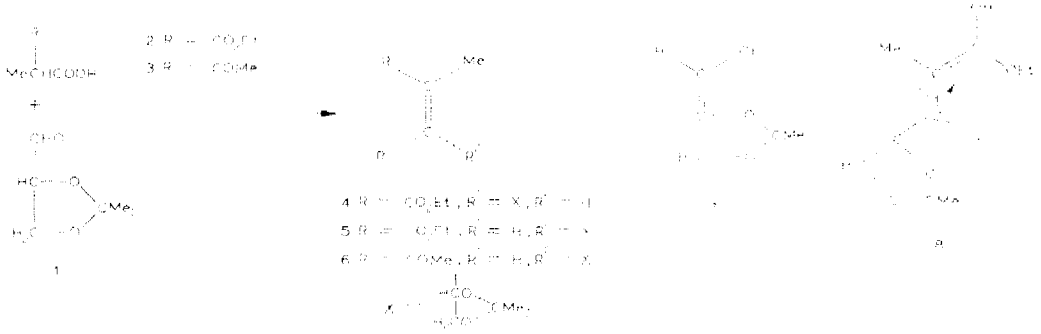
*Carbohydrate Research*, 115 (1983) 250–253
Elsevier Science Publishers B.V., Amsterdam Printed in The Netherlands

## Note

# Configurational reassignment of some derivatives of 2-*C*-methylpent-2-enonic acids*

FIDEL J. LOPEZ APARICIO, ISIDORO IZQUIERDO CUBERO**, AND MARIA D. PORTAL OLEA
*Department of Organic Chemistry, University of Granada, Granada (Spain)*
(Received July 16th, 1982; accepted for publication, November 24th, 1982)

We reported recently[2] the Knoevenagel–Doebner condensation of 2,3-*O*-isopropylidene-D-glyceraldehyde (**1**) and either monoethyl methylmalonate (**2**) or α-methylacetoacetic acid (**3**) to give **4**, its *trans* isomer **5**, and **6**, and assigned the D configuration to each. This assignment was erroneous for **4** and **5**, and a recent investigation[3] has revealed that they were DL mixtures. The formation of the D and L isomers of **4** and **5** can be explained either by partial racemisation of **1** (through the enolic form **7**) prior to its reaction with **2**, or by racemisation of **4** and **5** (through the vinylogous enolic form **8**), under the basic reaction-conditions.



We have now studied the optical stability of **1** and **5** (D isomer) under the Knoevenagel–Doebner reaction conditions. Compounds **4** and **5** (D isomer) were synthesised by a method that ensured that no racemisation occurred.

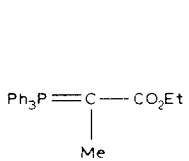
The $[\alpha]_D$ value of **1** decreased from +28° in pyridine–piperidine at room temperature to +5° during 24 h, and to 0° in 4 days, whereas the $[\alpha]_D$ value of a solution of **5** in the same solvent remained at +18° during 4 days. Thus, the second

*Branched-chain Sugars, Part V. For Part IV, see ref. 1.
**To whom correspondence should be addressed.

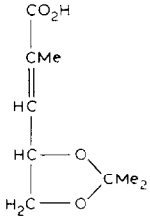
0008-6215/83/$ 03.00 

of the two enolisation processes noted above must be rejected and the racemisation of **1**, or reaction intermediates, must be involved in the formation of D and L isomers of **4** and **5**.

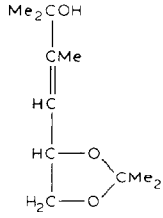
That **4** and **5** were mixtures of their D and L forms was demonstrated by the syntheses from **1** and (1-ethoxycarbonylethylidene)triphenylphosphorane[4] (**9**) of **4** (traces) and **5** (73%) having $[\alpha]_D$ values of $+64.5°$ and $+21°$, respectively, in contrast to the values of $+7.5°$ and $+3°$ previously reported[2].



9

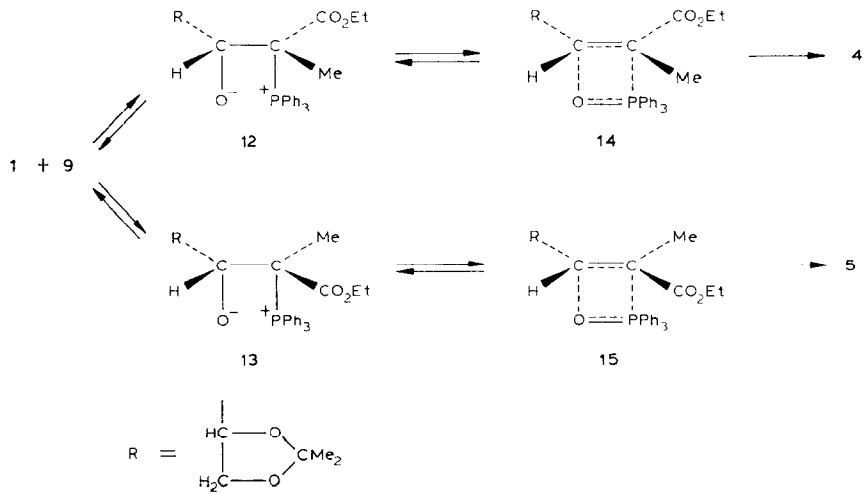


10



11

Hydrolysis of **5** (D isomer) to the corresponding acid **10** followed by reaction with methyl-lithium afforded **6** together with a compound identified as *trans*-1,3,4-trideoxy-5,6-*O*-isopropylidene-2,3-di-*C*-methyl-D-*glycero*-hex-3-enitol (**11**) from its spectroscopic data. Compound **6** had $[\alpha]_D$ $+28°$ (*cf.* $+36°$ previously reported[2]), indicating that little or no racemisation had occurred in the reaction of **1** and **3**. This fact may be explained by the lower reactivity of **1** and **2** in comparison with that of **1** with **3**. Thus, racemisation of **1** takes place before the condensation reaction occurs. The formation of **11** must be the result of the reaction of **6** with methyl-lithium.



The high stereoselectivity in the reaction of **1** with **9** may be explained by the overlap between the $\pi$ orbitals of the carbonyl group and the incipient carbon–carbon double-bond stabilising the transition states **14** and **15**. This overlap is possible only if the carbonyl group is coplanar with the developing double-bond, and this coplanarity must be disfavoured in **14** by the interaction of the bulky dioxolane ring with the ethoxycarbonyl group, so that the activation energy required for the formation of **4** from **12** will be greater than that for the formation of **5** from **13**. These findings accord with those in the literature[5].

## EXPERIMENTAL

*General.* — Melting points were determined with a Reichter hot-plate microscope, and are uncorrected. The general methods have been described elsewhere[2].

*Reaction of 2,3-O-isopropylidene-D-glyceraldehyde* (**1**) *with (1-ethoxycarbonylethylidene)triphenylphosphorane* (**9**). — To a solution of the ylid[4] **9** (8 g, 22.1 mmol) in dry dichloromethane (20 mL) at room temperature was added, dropwise, a solution of **1** (3 g, 23 mmol, $[\alpha]_D$ +28 → 0 (4 days) (*c* 1.6; pyridine–piperidine, 9.5:0.5)) in the same solvent (10 mL). The mixture was stored overnight, and then concentrated, diluted with light petroleum (100 mL), filtered from triphenylphosphine oxide, cooled at ~5° for 2 h, filtered again, and concentrated. The residue was subjected to column chromatography (ether–hexane, 1:5) to give, first, a mixture of triphenylphosphine oxide and a product that was identified, after column chromatography (ether–hexane, 1:7), as ethyl *cis*-2,3-dideoxy-4,5-*O*-isopropylidene-2-*C*-methyl-D-*glycero*-pent-2-enonate (**4**, 32 mg), $[\alpha]_D$ +64.5° (*c* 2.6, chloroform), having spectroscopic data in accord with those reported[2].

Eluted second was ethyl *trans*-2,3-dideoxy-4,5-*O*-isopropylidene-2-*C*-methyl-D-*glycero*-pent-2-enonate (**5**; 3.6 g, 73%), $[\alpha]_D$ +21° (*c* 1.4, chloroform) and +18° (*c* 2, pyridine), having spectroscopic data in accord with those reported[2].

trans-*2,3-Dideoxy-4,5-O-isopropylidene-2-C-methyl*-D-glycero-*pent-2-enonic acid* (**10**). — A suspension of **5** (3.5 g, 16 mmol) in 2M sodium hydroxide (10 mL) was heated under reflux for 30 min. T.l.c. then revealed that **5** had disappeared. The mixture was saturated with sodium chloride and cooled to 5°, acidified with conc. hydrochloric acid, and extracted with ether (10 × 10 mL). The combined extracts were concentrated and the residue (2.6 g) was distilled at 170° (bath) 0.1 mmHg, to yield **10** (2.1 g, 70%), which crystallised on storage; m.p. 53–55°, $[\alpha]_D$ +20° (*c* 1.15, chloroform); $\nu_{max}^{CCl_4}$ 3100 (OH), 1700 (C=O), 1660 (C=C), 1375 and 1365 ($CMe_2$), 1270 (C-O-C), 1150, 1060, and 850 $cm^{-1}$ (dioxolane ring); $\lambda_{max}^{MeOH}$ 221 nm ($\varepsilon$, 11500). $^1$H-N.m.r. data ($CDCl_3$): $\delta$ 10.58 (s, 1 H, COOH), 6.81 (dq, 1 H, $J_{3,Me}$ 1.5, $J_{3,4}$ 7.5 Hz, H-3), 4.85 (dt, 1 H, $J_{4,5}$ 6.0, $J_{4,5'}$ 7.5 Hz, H-4), 4.41 (dd, 1 H, $J_{5,5'}$ 7.5 Hz, H-5), 3.59 (t, 1 H, H-5'), 1.85 (d, 3 H, Me-2), and 1.43 (s, 6 H, $CMe_2$). The sample retained for elemental analysis decomposed during storage.

*Reaction of* **10** *with methyl-lithium.* — To a cooled and stirred solution of methyl-lithium (11 mmol) in anhydrous ether (15 mL) was added, dropwise, a solution of **10**

(2 g, 10.8 mmol) in the same solvent (10 mL). The mixture was stirred and heated under reflux for 6 h, cooled, and diluted with ether and water until two layers were obtained. The ethereal layer was separated, washed with water, and concentrated, to give a mobile oil (0.8 g), t.l.c. (ether–hexane, 3:2) of which revealed two components ($R_F$ 0.61 and 0.28) that were separated by column chromatography. The compound of higher mobility was *trans*-1,3,4-trideoxy-5,6-*O*-isopropylidene-3-*C*-methyl-D-*glycero*-hex-3-enulose (**6**; 550 mg, 28%), $[\alpha]_D$ +28° (*c* 1.25, chloroform) {lit.[2] $[\alpha]_D$ +36° (chloroform)}, having spectroscopic data in accord with those in the literature[2]. The second component was syrupy *trans*-1,3,4-trideoxy-5,6-*O*-isopropylidene-2,3-di-*C*-methyl-D-*glycero*-hex-3-enitol (**11**; 200 mg, 9.3%), $[\alpha]_D$ +16° (*c* 0.8, chloroform); $\nu_{max}^{film}$ 3465 (OH), 1375 ($CMe_2$), 1155, 1050, and 845 $cm^{-1}$ (dioxolane ring). $^1$H-N.m.r. data ($CDCl_3$): $\delta$ 5.56 (dq, 1 H, $J_{4,Me}$ 1.5, $J_{4,5}$ 8.25 Hz, H-4), 4.78 (dt, 1 H, $J_{5,6}$ 6, $J_{5,6'}$ 8.25 Hz, H-5), 4.04 (dd, 1 H, $J_{6,6'}$ 8.25 Hz, H-6), 3.46 (t, 1 H, H-6'), 2.29 (bs, 1 H, HO-2), 1.71 (d, 3 H, Me-3), 1.38 and 1.30 (2 s, 12 H, intensity ratio 1:1, H-6,6,6, Me-5, and $CMe_2$). Mass spectrum: *m/z* 201 ($M^+$ + 1), 185 ($M^+$ − Me), 142 ($M^+$ − $Me_2CO$), 127 ($M^+$ − Me − $Me_2CO$), 125 ($M^+$ − Me − AcOH), 117, 101 ($C_5H_9O_2^+$), 99 ($M^+$ − $C_5H_9O_2$), 59 ($Me_2COH^+$), and 43 ($Ac^+$, base peak).

## REFERENCES

1 I. Izquierdo Cubero, *Carbohydr. Res.*, 114 (1983) 311–316.
2 F. J. Lopez Aparicio, I. Izquierdo Cubero, and M. D. Portal Olea, *Carbohydr. Res.*, 103 (1982) 158–164.
3 M. D. Portal Olea, Ph. D. Thesis, University of Granada, Granada, Spain, 1983.
4 O. Isler, H. Gutmann, M. Montavon, R. Rüegg, G. Ryser, and P. Zeller, *Helv. Chim. Acta*, 40 (1957) 1242–1249.
5 H. O. House and G. H. Rasmunsson, *J. Am. Chem. Soc.*, 26 (1961) 4278–4281.