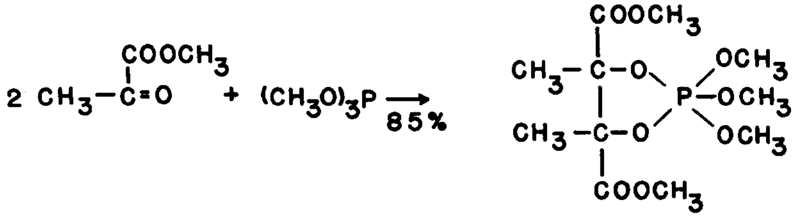
Tetrahedron Letters No. 5, pp. 323-328, 1963. Pergamon Press Ltd.
Printed in Great Britain.

A NEW CARBON-CARBON CONDENSATION VIA CYCLIC OXYPHOSPHORANES. TARTARIC ACIDS FROM α-KETOESTERS

By Fausto Ramirez[1], N. B. Desai and N. Ramanathan.
Department of Chemistry, State University of New York
Stony Brook, N. Y.

(Received 26 November 1962)

Two moles of methyl pyruvate (I) react with one mole of trimethyl phosphite (II) to give a liquid mixture of the two possible diastereomeric forms of a cyclic saturated oxyphosphorane (IIIA and IIIB).



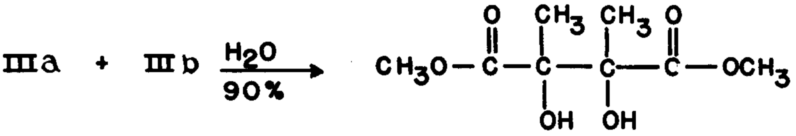
I II IIIa, IIIb

---

[1] Alfred P. Sloan Fellow 1961-1963. Work supported by the Cancer Institute of the National Institute of Health (CY-4769); the Petroleum Research Fund Administered by the American Chemical Society (286-A) and the National Science Foundation (19509).

The oxyphosphorane structure is based on the following observations: (1) The analytical data conforms to the formula $C_{11}H_{21}O_9P$.

(2) Hydrolysis gives a liquid mixture of the two diastereomeric dimethyl C,C-dimethyl tartrates (IVA and IVB).



$$\mathrm{IIIa} + \mathrm{IIIb} \xrightarrow[90\%]{H_2O} CH_3O-\overset{\overset{\displaystyle O}{\|}}{C}-\underset{\underset{\displaystyle OH}{|}}{\overset{\overset{\displaystyle CH_3}{|}}{C}}-\underset{\underset{\displaystyle OH}{|}}{\overset{\overset{\displaystyle CH_3}{|}}{C}}-\overset{\overset{\displaystyle O}{\|}}{C}-OCH_3$$

IVa, IVb

(3) The P^{31} n.m.r. spectrum of the 2:1 pyruvate adduct, III, has a peak at +50±2 ppm. to high field of the external phosphoric acid reference. This type of shift has been found in other oxyphosphorane structures[2,3]. (4) The I.R. spectrum of III shows the very strong band at 9.26μ which appears to be due to the $POCH_3$ in oxyphosphoranes[2,3]; in addition, there is an ester carbonyl at 5.70μ with a shoulder at 5.75μ.

(5) The proton n.m.r. spectrum, given in entry (1) of Table I, shows the eight peaks to be expected from a mixture of diastereomers IIIA and IIIB. The major isomer IIIA is thought to be the DL-form because its C-methyl protons give signals at higher field than those of the minor isomer IIIB; the latter is then the meso- form. This assignment assumes that the carbo-

---

[2] (a) F. Ramirez, N. Ramanathan and N. B. Desai, J. Am. Chem. Soc. 84, 1317 (1962); (b) F. Ramirez and N. Ramanathan, J. Org. Chem. 26, 3041 (1961).

[3] F. Ramirez and N. B. Desai, J. Am. Chem. Soc. 82, 2652 (1960).

methoxy group shields the protons of the cis-methyl group[4]. The assumption is consistent with our observations[2a] on the 2:1 biacetyl-trimethyl phosphite adducts, VA and VB; the corresponding proton n.m.r. data is given in entry (2) of Table I.

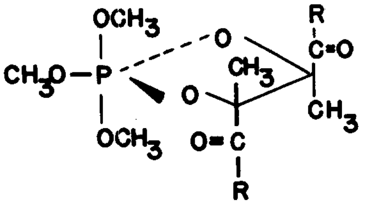
In the biacetyl-case, the major isomer VA was obtained in pure crystalline form[2a] and was shown to have the meso-configuration[5] by independent means. The minor isomer VB, with the DL-configuration and a cis-methyl-acetyl arrangement, had in fact the methyl signals at higher field (8.83τ vs 8.69τ). The 3-dimensional oxyphosphorane drawings are based on a hypothetical trigonal bipyramidal structure.

Entry (3) of Table I lists the signals for the protons of the 1:1 biacetyl-trimethyl phosphite adduct[3] (VI). This adduct was shown[2a] to be an intermediate in the formation of the 2:1 adducts, VA and VB. We assume, therefore that the methyl pyruvate-trimethyl phosphite reaction involves also an intermediate 1:1-adduct which is quite reactive toward a second molecule of α-ketoester. This adduct could be, predominantly or exclusively an open dipolar form, VII, with little or no oxyphosphorane character. In this respect, methyl pyruvate resembles acenaphthenequinone in its behavior toward trimethyl phosphite: from this α-diketone, only a 2:1 adduct could be isolated.[2b]

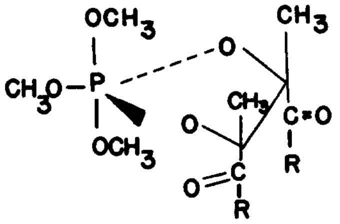
---

[4] F. A. Bovey and G. V. D. Tiers, J. Polym. Science 44, 173 (1960).

[5] To be published.



DL { IIIa, R = OCH_3
Vb, R = CH_3



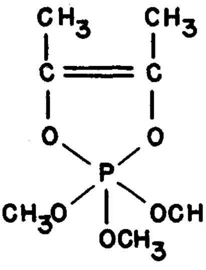
MESO { IIIb ; R = OCH_3
Va ; R = CH_3

Table I

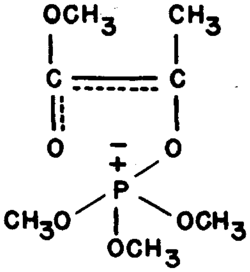
Proton n.m.r. spectra of saturated and unsaturated cyclic oxyphosphoranes; 10% CCl_4-solutions vs internal TMS[a] at 60 MC, in tau-units. A=Major isomer; B=Minor isomer

	Oxyphosphorane	$CH_3OP<$ J=13 cps[b]	CH_3O-CO or CH_3-CO	CH_3-C-
1	IIIA[c] IIIB	6.30; 6.51 6.34; 6.54	6.32 6.24	8.69 8.56
2	VA[d] VB	6.40; 6.62 6.30; 6.50	7.85 7.75	8.69 8.83
3	VI[e]	6.40; 6.62	—	8.23
4	IVA[f] IVB	— —	6.24 6.30	8.60 8.63

[a] Similar results with cyclohexane. [b] For trimethyl phosphate: 6.20 and 6.40τ, J=13 cps; the splitting is due to the P^{31} nucleus. [c] 2:1 Pyruvate adduct [d] 2:1 Biacetyl adduct. [e] 1:1 Biacetyl adduct. [f] Dimethyl C,C-dimethyl tartrate.



VI



VII

The structure of the dimethyl C,C-dimethyltartrates, IVa and IVb, follows from: (1) the analytical data which corresponded to the formula $C_8H_{14}O_6$; (2) the presence of O-H band at 2.86μ, of C=O at 5.76μ and of O-H deformation and C-O stretching at 8.00μ and 8.55, 8.66μ (CCl_4); (3) the presence of four peaks in the proton n.m.r. spectrum, as shown in entry (4) of Table I. These peaks are in the positions to be expected from the mixture of diastereomers. The -OH proton was hiden under the 6.30τ signal; therefore, the hydrolysis of the oxyphosphoranes was repeated in an excess of D_2O. The mixture of deuterated tartrates had a weak infrared OH-band at 2.85μ and a stronger OD-band at 3.84μ (*ca* 1:3). The H'-n.m.r. spectrum had four peaks with the expected relative intensities.

Methyl pyruvate (51.0 g.), was slowly added (2.5 hr.) *to* trimethyl phosphite (62.0 g.) with stirring and external cooling (-5° to 0°). The mixture was kept 1 hr. at 0° and 8 hrs. at 20°. The excess phosphite was removed in *vacuo* and the viscous, colorless, *2:1 adduct*[6], III, was collected at 105°-110° (0.1 mm.):

---

[6] The elemental analysis and the M.w. were in agreement with the formula.

68 g., 82%; $N_D^{25°}$ 1.4470. If the temperature of the reaction is not closely controlled, the product shows an extraneous weak I.R.-band at 5.56μ.

The 2:1 adduct, III, (56.76 g.) was added to water (40 ml.) and the strongly acidic solution was treated with one equivalent of 2N NaOH. The solution was kept at reflux temperature for 7 hrs., titration of an aliquot consumed one additional equivalent of alkali [$CH_3OP(O)(OH)_2$]. The main solution was saturated with NaCl and extracted with chloroform. Removal of solvent left a viscous oil (33 g.) which was distilled. The yield of diastereomeric dimethyl C,C-dimethyl-tartrates[6], IVA + IVB, was 31 g., 87%; b.p. 80°-85° (0.1 mm.); $n_D^{25°}$ 1.4475.

Acknowledgement. We are grateful to Prof. E. Eliel of the University of Notre Dame for the H^1n.m.r. Spectra and to Dr. J. Lancaster of the American Cyanamid Co. for the P^{31}n.m.r. Spectrum.