Ketenes. XI. Preparation of β-Lactone Dimer by Dimerization of Dimethylketene in the Presence of Derivatives of Trivalent Phosphorus

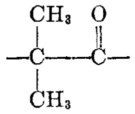
EDWARD U. ELAM

Research Laboratories, Tennessee Eastman Company, Division of Eastman Kodak Company, Kingsport, Tennessee

Received August 12, 1966

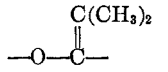
It was pointed out recently that triethylamine or its hydrochloride is effective for catalyzing the dimerization of aldoketenes to their β-lactone dimers.[1] These compounds are not effective catalysts for preparing β-lactone dimers of ketoketenes, however, and tetramethyl-1,3-cyclobutanedione (1) is obtained when isobutyryl chloride is dehydrohalogenated in the presence of triethylamine.[2] Strong Lewis acids such as aluminum chloride have been found to catalyze the dimerization of dimethylketene to its β-lactone dimer, 3-hydroxy-2,2,4-trimethyl-3-pentenoic acid β-lactone (2),[3] while sodium methoxide catalyzes this type of dimerization of diphenylketene.[4]

In the presence of strong bases such as sodium methoxide, dimethylketene polymerizes to a poly(enol ester). Evidence has been presented which indicates that this polymerization does not involve the β-lactone dimer as an intermediate.[3] Staudinger and co-workers reported that dimethylketene is polymerized in the presence of triethylamine.[5] Later he suggested that this polymer contained random arrangements of units 3 and 4.[6] The effect of bases on dimethylketene, therefore, appears to depend upon the nature of the base: strong ionic bases such as sodium methoxide give poly(enol ester), and the Lewis base, triethylamine, gives a polymer containing random ketone and ketene acetal units.



$-C(CH_3)_2-C(=O)-$

3



$-O-C(=C(CH_3)_2)-$

4

Trivalent phosphorus compounds are Lewis bases. Their nucleophilicity varies widely, depending upon the nature of the substituents on the phosphorus atom. Some of these compounds, particularly trialkyl phosphites and dialkylphenyl phosphonites, are very effective catalysts for promoting the formation of the β-lactone dimer from dimethylketene.[7] For example, when dimethylketene was added gradually to triethyl phosphite, a strongly exothermic reaction occurred which was still vigorous when the concentration of triethyl phosphite in the reaction mixture had fallen below 2%. The reaction product was analyzed by glpc and found to contain approximately 94% of 2 and only 3% of 1, together with several minor impurities. It is quite possible that the small amount of 1 was formed by spontaneous dimerization of the ketene in the inlet lines or on the condensing surfaces of the reactor before it came into contact with the reaction mixture.

The nature and degree of catalytic activity of other compounds of trivalent phosphorus depends upon the substituents attached to the phosphorus atom. At one extreme, the relatively strong Lewis base, tributyl phosphine, gave only a tough, horny polymer whose physical appearance and infrared spectrum were the same as those of the polymer obtained by allowing dimethylketene to polymerize in the presence of a trace of triethylamine. Triphenyl phosphite, at the opposite end of the basicity scale, was almost totally ineffective for catalyzing formation of 2. Compound 1 was virtually the sole product of the reaction. In the presence of phosphorus compounds whose strengths as Lewis bases varied between these extremes, polymer and β-lactone and dione dimers were formed to varying degrees. Although no effort was made in most cases to make quantitative measurements, the data in Table I indicate qualitatively how the nature of the catalyst affects the relative amounts of each product formed. A plausible mechanism for this dimerization, which is analogous to that proposed by Anet for the methoxide-catalyzed dimerization of diphenylketene is shown in Scheme I.

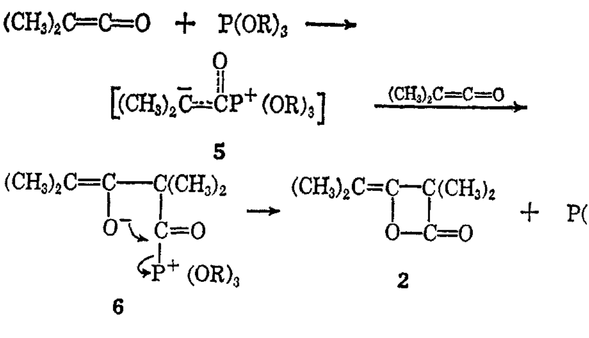
TABLE I

CATALYSTS, $R^1R^2R^3P$, FOR DIMERIZING DIMETHYLKETENE

Catalyst			
R_1	R^2	R^3	Results
C_2H_5O	C_2H_5O	C_2H_5O[a]	93% 2, 4% 1, 3% unidentified, no polymer
$C_{10}H_{21}O$	$C_{10}H_{21}O$	C_6H_5O[a]	Mostly 1, some 2[b]
$C_{10}H_{21}O$	C_6H_5O	C_6H_5O[a]	Mostly 1, some 2[b]
C_6H_5O	C_6H_5O	C_6H_5O[a]	1, with trace of 2[b]
$CH_3(CH_2)_3S$	$CH_3(CH_2)_3S$	$CH_3(CH_2)_3S$[c]	1, with trace of 2[b]
$CH_3(CH_2)_3O$	$CH_3(CH_2)_3O$	C_6H_5[d]	89% 2, 11% 1
C_6H_5	C_6H_5	C_6H_5[e]	Mostly polymer, some 2[f]
$CH_3(CH_2)_3$	$CH_3(CH_2)_3$	$CH_3(CH_2)_3$[g]	Polymer

[a] Hooker Chemical Corp. [b] The crude product from these experiments was almost completely solid. Compound 2 was detected by slurrying the product with benzene and analyzing the extract by glpc. [c] A. Lippert and E. E. Reid, *J. Am. Chem. Soc.*, **60**, 2370 (1938). [d] Victor Chemical Division, Stauffer Chemical Co. [e] M and T Chemicals, Inc. [f] The product from this reaction consisted of tough, horny polymer and a small amount of viscous liquid in which 2 was detected by glpc. [g] Aldrich Chemical Co.

SCHEME I



---

[1] D. G. Farnum, J. R. Johnson, R. E. Hess, T. B. Marshall, and B. Webster, *J. Am. Chem. Soc.*, **87**, 5191 (1965).

[2] W. E. Hanford and J. C. Sauer, *Org. Reactions*, **3**, 126 (1946).

[3] R. H. Hasek, R. D. Clark, E. U. Elam, and J. C. Martin, *J. Org. Chem.*, **27**, 60 (1962).

[4] R. Anet, *Chem. Ind.* (London), 1313 (1961).

[5] H. Staudinger, R. Felix, P. Meyer, H. Harder, and D. Strinemann, *Helv. Chim. Acta*, **8**, 322 (1925).

[6] H. Staudinger, "Die Hochmolekularem Organische Verbindungen," Julius Springer, Berlin, 1932, p 146.

[7] E. U. Elam (to Eastman Kodak Co.), U. S. Patent 3,234,241 (1966).

If this mechanism is correct, the effectiveness of a nucleophile as a catalyst for the formation of the β-lactone dimer (2) depends upon its ability to coordinate with the carbonyl carbon of the ketene to give zwitterions **5** and **6**. Triphenyl phosphite is apparently too weak a nucleophile to form zwitterions of this type. At the other extreme, it appears that the phosphines (and tertiary amines) coordinate so strongly that ring closure to the β-lactone does not occur and **6** reacts instead with more dimethylketene, ultimately giving polymer.

Experimental Section

With the exceptions noted, the experiments listed in Table I were carried out according to the general procedure described below. The phosphorus compounds obtained from commercial sources were used without purification. Dimethylketene was generated by the pyrolysis of isobutyric anhydride[8] and was passed as the gas into the reaction vessel, where it was condensed and allowed to fall into the solution.

Five grams of triethyl phosphite was placed in a 1-l., three-necked flask which was fitted with a Dry Ice cooled reflux condenser, thermometer, inlet for dimethylketene, and magnetic stirrer. Stirring was started and dimethylketene was passed in. A strongly exothermic reaction occurred and the temperature rose spontaneously to between 90 and 100° and remained there until the dimethylketene stream was shut off. A total of approximately 300 g of product had collected. Gas chromatographic analysis of the crude product indicated that it contained 93% of 3-hydroxy-2,2,4-trimethyl-3-pentenoic acid β-lactone (2) and 4% of tetramethyl-1,3-cyclobutanedione (1). Distillation gave 235 ml of pure 2, bp 78.5–79° (25 mm), n^{20}_{D} 1.4380, the infrared spectrum and glpc retention time of which were identical with those of authentic material.

When this experiment was repeated with tributylphosphine as the catalyst, only a tough, horny, transparent polymer was obtained. The infrared spectrum of this polymer (KBr pellet) contained strong bands at 5.75, 5.85, 8.45, and 9.25 μ. This spectrum was identical with the spectrum of a polymer prepared as described by Staudinger.[5]

---

[8] R. H. Hasek and E. U. Elam (to Eastman Kodak Co.), U. S. Patent 3,201,474 (1964).

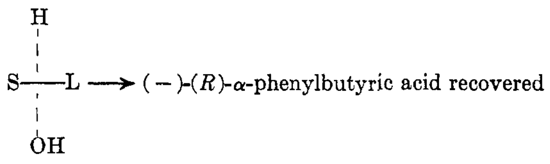
Determination of the Absolute Configuration of Hydroxylated Sesquiterpene Lactones by Horeau's Method of Asymmetric Esterification[1]

Werner Herz[2] and Henri B. Kagan[3]

Department of Chemistry, Florida State University, Tallahassee, Florida 32306, and Laboratoire de Chimie Organique des Hormones, Collège de France, Paris 5e, France

Received August 26, 1966

Horeau's method[4,5] for the determination of the absolute configuration of alcohols has been successfully applied to natural products such as terpenes,[4,5] caryophyllene derivatives,[6] steroids,[7] and the grayanotoxins.[8] Since esterification of an asymmetric alcohol, LCHOHS, where L is a bigger substituent than S in a steric sense,[9] by an excess of racemic α-phenylbutyric acid anhydride results in preferential combination with one of the antipodes of the acid, the excess of the acid which is recovered is optically active. Horeau[4,5,7] has empirically correlated in a great number of examples the sign of the recovered acid with the absolute configuration of the starting alcohol as follows.



$$\mathrm{S}\overset{\mathrm{H}}{\underset{\mathrm{OH}}{—}}\mathrm{L} \longrightarrow (-)\text{-}(R)\text{-}\alpha\text{-phenylbutyric acid recovered}$$

In order to test the applicability of the method in the sesquiterpene lactone series,[11] we applied it first to several hydroxylated sesquiterpene lactones previously studied by W. H., where the absolute configuration of the hydroxyl group had been established unequivocally by chemical or physical means. Chart I lists these compounds (**1**, **2**, and **3**) which are of the type RCH$_2$-CH(OH)CR$_1$R$_2$R$_3$[13–20] as well as three others of the same type (**4**, **5**, and **6**) where the configuration of the hydroxyl group was somewhat uncertain or completely unknown. The results of Horeau's method given in Chart I are in agreement with the previously known absolute configurations (**1**, **2**, and **3**) and, in the case of compound **4**, a derivative of pulchellin, in agreement with the configuration deduced[23] by the application of the Hudson–Klyne rule. For **5**[24] and **6**[24] we indicate

---

[1] Work at Florida State University supported in part by grants from the National Science Foundation (GP-1962) and the U. S. Public Health Service (GM-05814).

[2] Florida State University.

[3] Collège de France.

[4] A. Horeau, *Tetrahedron Letters*, 506 (1961).

[5] A. Horeau, *ibid.*, 965 (1962).

[6] A. Horeau and J. K. Sutherland, *J. Chem. Soc.*, C247 (1966).

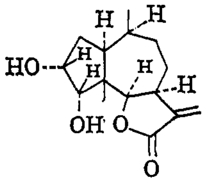
[7] A. Horeau and H. B. Kagan, *Tetrahedron*, **20**, 2431 (1964).

[8] H. Kakijawa, T. Kozima, M. Yanai, and K. Nakanishi, *ibid.*, **21**, 3091 (1965).

[9] S is CH$_2$R and L is a more heavily substituted carbon atom such as CHR$_1$R$_2$. For a discussion of this classification, see ref 10.

[10] A. Marquet and A. Horeau, *Bull. Soc. Chim. France*, in press.

[11] H. B. K. has previously employed the method to determine the absolute configuration of the *cis*-glycol system of ambrosiol (i).[12]



i

[12] T. J. Mabry, W. Renold, H. E. Miller, and H. B. Kagan, *J. Org. Chem.*, **31**, 681 (1966).

[13] The equatorial orientation of the hydroxyl group of asperilin (**1**) was deduced[14] from the sodium borohydride reduction of dehydrotetrahydroasperilin which regenerated tetrahydroasperilin. The absolute configuration follows from correlation with alantolactone.

[14] W. Herz and N. Viswanathan, *J. Org. Chem.*, **29**, 1022 (1964).

[15] The relative and absolute configuration of **2** follows from its correlation[16] with helenalin,[17] the relative and absolute configuration of which has been established by X-ray analysis of a bromo derivative,[18] ORD data,[19] and correlation with isotenulin.[19]

[16] A. Romo de Vivar, L. Rodriguez-Hahn, J. Romo, M. V. Lakshmikantham, R. N. Mirrington, J. Kagan, and W. Herz, *Tetrahedron*, in press.

[17] W. Herz, A. Romo de Vivar, J. Romo, and N. Viswanathan, *J. Am. Chem. Soc.*, **85**, 19 (1963).

[18] M. T. Emerson, C. N. Caughlan, and W. Herz, *Tetrahedron Letters*, 621 (1961).

[19] W. Herz, A. Romo de Vivar, J. Romo, and N. Viswanathan, *Tetrahedron*, **19**, 1359 (1963).

[20] The relative and absolute configuration of **3** follows from its correlation with isotenulin,[21] the relative and absolute configuration of which have been established by X-ray analysis[22] and ORD data.[19]

[21] W. Herz, W. A. Rohde, K. Rabindran, P. Jayaraman, and N. Viswanathan, *J. Am. Chem. Soc.*, **84**, 3857 (1962).

[22] D. Rogers and Mazhar-ul-Haque, *Proc. Chem. Soc.*, 92 (1963). See also W. Herz, Y. Kishida, and M. V. Lakshmikantham, *Tetrahedron*, **20**, 1986 (1964).

[23] W. Herz, K. Ueda, and S. Inayama, *ibid.*, **19**, 483 (1963).

[24] W. Herz, Y. Kishida, and M. V. Lakshmikantham, *ibid.*, **20**, 979 (1964).