Ethanolysis of 2-Substituted-4-arylidene-5-oxazolones. Effect of Trifluoromethyl Substitution on the Arylidene Ring

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The ultraviolet absorption spectra of azlactones are usually measured in 95% ethanol, chloroform, ether, or acetic acid as solvents. A hypsochromic shift of the principal maximum of unsaturated azlactones has been observed[1] when dilute ethanolic solutions were allowed to stand at room temperature for several days. This shift is due to the noncatalyzed solvolysis of the oxazolone to form the open chain ester and this change offers a convenient means for following the course of the reaction spectrophotometrically.

Thus, 2-phenyl-4-benzylidene-5-oxazolone (Ia), λ_{max}^{EtOH} 360 mμ[2] was gradually converted into ethyl α-benzamidocinnamate (IIa), λ_{max}^{EtOH} 282 mμ. After three to four days, about 50% conversion had occurred and the reaction was complete within twenty-one days.[1] We have confirmed these results and have further observed that 2-methyl-4-benzylidene-5-oxazolone (Ib), λ_{max} 328 mμ, was much more readily solvolyzed to IIb, λ_{max} 281 mμ, with conversion almost complete after twenty-eight hours. This increased rate of alcoholysis of 2-methyl analogs has been observed previously with another oxazolone[1] and is consistent with the facile hydrolysis of Ib with boiling water-acetone to give the α-acetamido acid.[3] Ia is stable under the latter conditions.

In the course of our studies on trifluoromethyl-substituted aromatic amino acids, we have prepared and similarly examined several analogs of Ia and Ib (see Table I), possessing trifluoromethyl groups in the *ortho* and *meta* positions of the arylidene ring. The preparation of these compounds will be discussed in a forthcoming paper.[4]

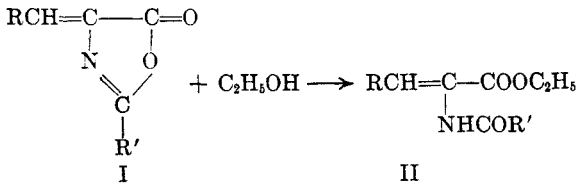
Ic (λ_{max} 359 mμ) was largely converted to the open-chain, α,β-unsaturated ester after twenty-four hours and had reacted completely within seventy-two hours, while the *meta* trifluoromethyl compound, Id (λ_{max} 358 mμ), and the 2-methyl counterparts, Ie (λ_{max} 324 mμ) and If (λ_{max} 322 mμ), showed no evidence of unchanged oxazolone after twenty four hours.

These results reflect the enhancement of solvolysis due to the electronic influence of the trifluoromethyl group in labilizing the oxazolone ring. The site of attack is the lactone carbonyl moiety and it is difficult, as the results are not quantitative, to evaluate, particularly in the case of the *o*-trifluoromethyl compound, the relative importance of the *inductive* and *field* effects in the total electrical effect. Such an evaluation has been made by Roberts[5] for *o*-substituted phenylpropiolic acids and esters.

It is also of interest to note that the spectra of the 2-phenyl-4-trifluoromethylbenzylidene-5-oxazolones (Ic and Id) did not reveal any sign of *trans*-acylation during their preparation by the Erlenmeyer-Plöchl reaction, in contrast to the observations of Bennett and Niemann in the preparation of the 4-(*p*-fluorobenzylidene) analog.[6]

Concentrations of solutions were about 5 μg oxazolone/cc. Measurements were made with a Beckman DK-2 spectrophotometer.

TABLE I



I II

Compound	Substituents R	R'
a	C_6H_5	C_6H_5
b	C_6H_5	CH_3
c	*o*-$C_6H_4CF_3$	C_6H_5
d	*m*-$C_6H_4CF_3$	C_6H_5
e	*o*-$C_6H_4CF_3$	CH_3
f	*m*-$C_6H_4CF_3$	CH_3

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(1) E. L. Bennett and E. Hoerger, *J. Am. Chem. Soc.*, **74**, 5975 (1952).

(2) D. A. Bassi, V. Deulofeu, and F. A. F. Ortega, *J. Am. Chem. Soc.*, **75**, 171 (1953).

(3) *Org. Syntheses*, **Coll. Vol. II**, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 1.

(4) R. Filler and H. Novar, in press.

(5) J. D. Roberts and R. A. Carboni, *J. Am. Chem. Soc.*, **77**, 5554 (1955).

(6) E. L. Bennett and C. Niemann, *J. Am. Chem. Soc.*, **72**, 1803 (1950).

The Synthesis of a Novel Ester of Phosphorus and of Arsenic

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Stetter and Steinacker[2] report the synthesis of 1-phospha-2,8,9-trioxa-adamantane (II) and the corresponding 1-oxide and 1-sulfide. Using a modification of their synthetic method, we have pre-

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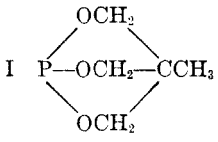
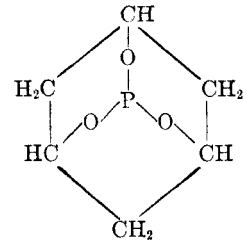
(2) H. Stetter and K. Steinacker, *Ber.*, **85**, 451 (1952).

pared the heretofore unknown 1-methyl-4-phospha-3,5,8-trioxabicyclo[2.2.2]octane (I) in which the phosphorus-oxygen bond angles are even more restricted and the organic group less bulky.



I



II

Compounds I and II function as excellent donors. This is the consequence of the minimal steric hindrance, increased availability of the phosphorus lone-pair electrons, and the high symmetry of the ligands. By contrast, the trialkoxyphosphorus compounds of comparable molecular weight are relatively poor donors.[3] It has been found[4] that I and II form stable complexes with various metal ions and addition compounds with Group III Lewis acids. The arsenic analogues of I and II are also presently being investigated in this respect.

Despite the opportunity for polymer formation in the preparation, it is possible to obtain I in 40% yield. The preparation is effected by allowing phosphorus trichloride to react with 2-hydroxymethyl-2-methyl-1,3-propanediol at high dilution in tetrahydrofuran in the presence of a base (pyridine). Because of its volatility, I is separated from the reaction products by sublimation *in vacuo*. Contrary to expectation, I is very stable to air oxidation over a period of months, although it is quite hygroscopic. On the other hand, II is quite unstable in air.[2]

The slightly soluble 1-methyl-4-phospha-3,5,8-trioxabicyclo[2.2.2]octane - 4 - sulfide is obtained in nearly quantitative yield when sulfur is allowed to react with I at 140° in a sealed tube. The solid product remains after any unreacted starting materials have been extracted with carbon disulfide.

The previously unknown -4-arsa- analogue of I is obtained in 38% yield by using arsenic trichloride instead of phosphorus trichloride in the preparation of the bicyclic arsenic compound. The volatile product is separated from the polymeric reaction mixture by sublimation *in vacuo*. The colorless crystalline sublimate is quite unstable to moisture and hydrolyzes readily.

Attempts to synthesize the 4-oxide and the 4-sulfide of the -4-arsa- compound have thus far been unsuccessful.

The infrared spectra of these compounds are commensurate with the assigned structures. The P=O stretching frequency appears as a strong band at 1325 cm^{-1}. It is interesting to note that this frequency lies somewhat above the range generally assigned to this band.[5] The P=S stretching frequency occurs as a band of medium intensity at 800 $cm.^{-1}$ which lies within the range generally assigned to such compounds.[6]

(3) A. Arbuzov and V. Zoroastrova, *Doklady Akad. Nauk S.S.S.R.*, **84**, 503 (1952).

(4) To be published elsewhere.

EXPERIMENTAL[7,8]

1-Methyl-4-phospha-3,5,8-trioxabicyclo[2.2.2]octane. Tetrahydrofuran was distilled after refluxing over lithium aluminum hydride for 3 hr.; the portion boiling from 65–66° was taken. Pyridine was distilled after refluxing over barium oxide for 3 days; the portion boiling at 115° was taken. Two solutions were prepared: (1) a solution of 8.8 ml. (0.1 mole) freshly distilled phosphorus trichloride diluted to 75 ml. with tetrahydrofuran and (2) a solution of 12 g. (0.1 mole) 2-hydroxymethyl-2-methyl-1,3-propanediol in 24.2 ml. (0.3 mole) pyridine. The latter solution was also diluted to 75 ml. with tetrahydrofuran. These two solutions were simultaneously added dropwise over a period of 45 min. to 100 ml. of vigorously stirred tetrahydrofuran under dry nitrogen. The white reaction mixture was then stirred for 30 min., after which the pyridinium hydrochloride was allowed to settle. The clear supernatant liquid was filtered and the residue washed with two 30-ml. portions of tetrahydrofuran. Tetrahydrofuran was then distilled from the solution *in vacuo* until the residue became a white syrupy mass. The product was sublimed at 1 mm. pressure and room temperature on to a water-cooled finger until sublimation ceased. The temperature was then gradually raised by means of an oil bath to 80° and held constant within 2° of this temperature until no more product sublimed. To effect purification, the crude product was sublimed three times at 50° and 1 mm. pressure, yield, 5.9 g. (40%), m.p. of the colorless prismatic crystals 97–98°.

Instead of further sublimation, the product may be recrystallized from hot *n*-heptane.

Anal. Calcd.: C, 40.60; H, 6.08. Found: C, 40.55; H, 6.07. Mol. wt. Calcd.: 148. Found: 157.

1-Methyl-4-phospha-3,5,8-trioxabicyclo[2.2.2]octane-4-oxide. To a solution of 1.48 g. (0.01 mole) 1-methyl-4-phospha-3,5,8-trioxabicyclo[2.2.2]octane in 5 ml. absolute ethanol was added dropwise 1.13 ml. (0.01 mole) of 100 volume hydrogen peroxide. The crystals formed on cooling the solution were filtered, washed with 4 ml. cold absolute ethanol, dried, and sublimed three times at 155° and 1 mm. pressure, yield, 1.5 g. (92%), m.p. of the colorless acicular crystals 249–250°.

Anal. Calcd.: C, 36.60; H, 5.48. Found: C, 36.90; H, 5.48.

Mol. wt. Calcd.: 164. Found: 171.

The residue may also be recrystallized from absolute ethanol instead of subliming to effect purification.

1-Methyl-4-phospha-3,5,8-trioxabicyclo[2.2.2]octane-4-sulfide. A glass tube containing a mixture of 1.48 g. (0.01 mole) of I and 0.32 g. (0.01 mole) sulfur was evacuated, sealed, and heated to 140° in an oil bath for 5 min. After the vigorous reaction subsided, the tube was allowed to cool and the contents ground to a fine powder. The yellow powder was allowed to stand under 30 ml. of carbon disulfide for 24 hr. in order to dissolve any unchanged starting materials. The

(5) L. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley & Sons, Inc., New York, Ed. 2, 1958, p. 312.

(6) L. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley & Sons, Inc., New York, Ed. 2, 1958, p. 321.

(7) Melting points are uncorrected.

(8) Molecular weights were obtained by cryoscopic determination in nitrobenzene.

white powder was further extracted with three 20-ml. portions of carbon disulfide, dried and sublimed three times at 140° and 1 mm. pressure, yield, 1.6 g. (89%), m.p. of the colorless acicular crystals 224–225°.

Anal. Calcd.: C, 33.40; H, 5.00. Found: C, 33.56; H, 5.18.

Mol. wt. Calcd.: 180. Found: 174.

1-Methyl-4-arsa-3,5,8-trioxabicyclo[2.2.2]octane. The preparation of this compound involved arsenic trichloride and was analogous to that of the -4-phospha- compound. The first sublimation of the crude syrup, however, was carried out at room temperature. The solid sublimate, contaminated with a small amount of oily material, was dissolved in ether, in which the oily substance was insoluble. The ether solution was decanted and evaporated to dryness. The residual white solid was sublimed three times at room temperature and 1 mm. pressure, yield, 38%, m.p. of the colorless prismatic crystals 41–42°.

Anal. Calcd.: C, 31.25; H, 4.68. Found: C, 31.15; H, 4.68.

Mol. wt. Calcd.: 192. Found: 185.

Infrared Spectra. Spectra were taken in chloroform and carbon disulfide solutions as well as in nujol mulls on a Perkin-Elmer Model 21 Spectrophotometer.

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Phosphonic Acid and Esters. II. Formation of Telomers in Olefin/Phosphorous Acid Reactions

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In Part I it was shown that alkylphosphonic acids (I) could be formed by the addition of phosphorous acid to olefins in the presence of peroxides or ultraviolet irradiation (steps 1–2).[1] The low

$$RCH{=}CH_2 + \underset{II}{\cdot P(O)(OH)_2} \longrightarrow \underset{III}{RCHCH_2P(O)(OH)_2} \quad (1)$$

$$III + HP(O)(OH)_2 \longrightarrow \underset{I}{RCH_2CH_2P(O)(OH)_2} + II \quad (2)$$

yields of products obtained were attributed to the occurrence of polymerization, inhibition by allylic abstraction and telomerization (steps 3–4). Specific evidence for the occurrence of telomerization was provided by the isolation of a telomeric 2:1 adduct,

$$III + RCH{=}CH_2 \longrightarrow \underset{IV}{RCHCH_2CHRCH_2P(O)(OH)_2} \quad (3)$$

$$IV + HP(O)(OH)_2 \longrightarrow \underset{V}{RCH_2CH_2CHRCH_2P(O)(OH)_2} + II \quad (4)$$

2-hexyldecylphosphonic acid (VI; V, R = *n*-hexyl), as well as the primary reaction product (*n*-octylphosphonic acid) from the reaction of 1-octene and phosphorous acid. Similar telomers have been shown to arise in the peroxide initiated addition of dialkyl phosphonates to olefins.[2] In order to determine the extent of telomer formation, the previous investigation[1] has now been extended to a study of the reactions of 1-hexene, 1-decene, and cyclohexene.

1-Hexene was treated with phosphorous acid in the presence of dibenzoyl peroxide at reflux temperature; fractionation of the products led to the isolation of *n*-hexylphosphonic acid (23%) and the 2:1 adduct, 2-butyloctylphosphonic acid (VII; V, R = *n*-butyl). Reaction with 1-decene gave *n*-decylphosphonic acid (18%) and 2-octyldodecylphosphonic acid (VIII: V, R = *n*-octyl). A reinvestigation of the cyclohexene/phosphorous acid reaction led to the isolation of 2-cyclohexylcyclohexylphosphonic acid (IX) and the primary reaction product, cyclohexylphosphonic acid. Thus, telomerization appears to be generally characteristic of the olefin/phosphorous acid reactions and additional evidence for the low transfer constant of phosphorous acid is provided.

The structures proposed for the telomeric acids (V) are those which would arise from telomerization of conventional (head to tail) orientation, i.e., attack of the radical (III) at the terminal olefinic carbon.[3] The identity of the acids (V) was confirmed by comparison with samples prepared by an independent route: peroxide initiated addition of diethyl phosphonate to the appropriate olefin and acidic hydrolysis of the resulting diethyl alkylphosphonate. The requisite olefins, including

$$RCH_2CH_2CR{=}CH_2 + HP(O)(OC_2H_5)_2 \longrightarrow V$$

the previously unreported 2-hexyl-1-decene, were conveniently prepared from the corresponding ketones by means of the Wittig reaction. In each case the acid prepared independently was identical with the 2:1 adduct isolated from the olefin/phosphorous acid reactions.

The independent route employed above is, however, capable of yielding two produts: V by attack of the phosphonate radical at the terminal olefinic carbon and the isomeric 2-methyl alkylphosphonic acid $RCH_2CH_2CR(CH_3)P(O)(OH)_2$ by attack at carbon two. On the basis of the known chemistry and orientation of this and similar free radical addition reactions, terminal attack is most probable.[2,4,5] A conclusive demonstration was

(1) C. E. Griffin and H. J. Wells, *J. Org. Chem.*, **24**, 2049 (1959).

(2) A. R. Stiles, W. E. Vaughan, and F. F. Rust, *J. Am. Chem. Soc.*, **80**, 714 (1958).

(3) Alternatively, the attack of III at carbon two of the olefin would yield a primary radical (less stable than the secondary radical IV) and, ultimately, the isomeric acid $RCH(CH_3)CHRCH_2P(O)(OH)_2$.

(4) P. C. Crofts, *Quarterly Revs.*, **12**, 363 (1958).

(5) C. Walling, *Free Radicals in Solution*, John Wiley and Sons, Inc., New York, 1957, pp. 239–89.