and v.p.c. results were corroborated by examining mixtures of known composition of the pure halo aromatics involved.

Chemicals.—Practical N-bromosuccinimide (Arapahoe) or purified NBS (Matheson Coleman and Bell) gave equivalent yields of product as did practical or purified N-chlorosuccinimide (Matheson Coleman and Bell) after allowance for inert content. Of the substances used as standards in the v.p.c. or infrared analyses, o-bromochlorobenzene was synthesized by the standard procedure[10]; all other chemicals were White Label Eastman or reagent grade Matheson Coleman and Bell products whose purity was established by v.p.c. and/or infrared examination.

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[10] J. L. Hartwell, "Organic Syntheses," Coll. Vol. III, E. C. Horning, Ed., John Wiley and Sons, Inc., New York, N. Y., 1955, p. 185.

Reaction of Benzil with Cyanide Ion in Dimethyl Sulfoxide

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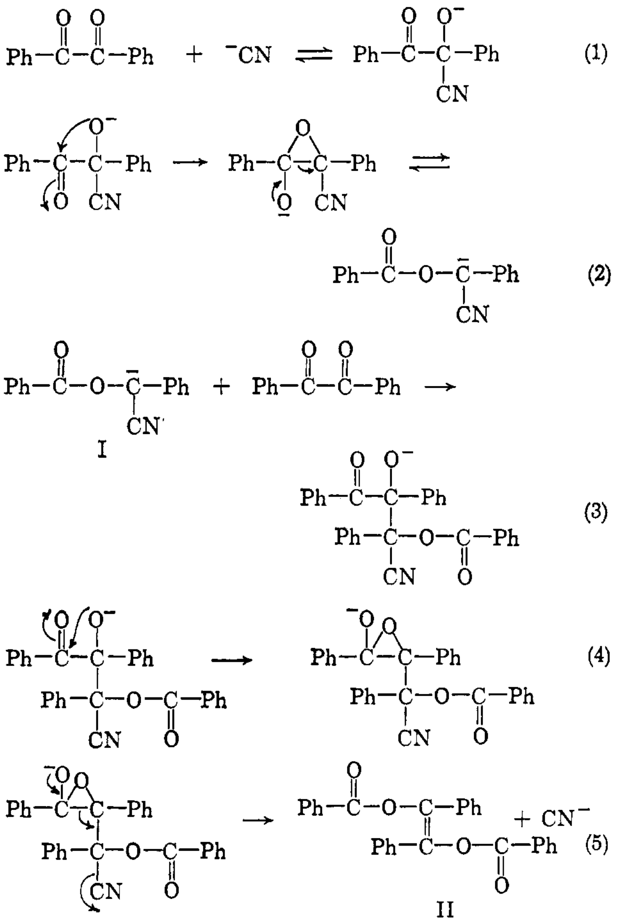
A number of reports concerning the cleavage of benzil by cyanide ion has appeared in the literature. Jourdan[2] and more recently Kwart and Baevsky[3] reported that cleavage products in alcoholic solution are benzaldehyde and the corresponding benzoic ester.

$$(PhCO)_2 + ROH \xrightarrow{^-CN} PhCHO + PhCO_2R$$

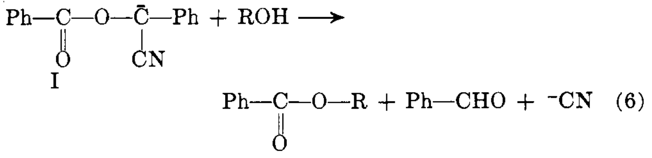
Dilthey and Scheidt[4] observed that the benzilic acid rearrangement is inhibited by cyanide ion and that cleavage products, benzoic acid and benzaldehyde, are obtained. Dakin and Harington[5] found that benzil is converted to benzamide and benzaldehyde by alcoholic ammonium cyanide. Other aromatic α-diketones were observed to exhibit similar behavior. Weiss[6] has shown that a mixture of benzoin and benzil can be separated by taking advantage of the facile cleavage of benzil by cyanide ion in aqueous ethanol at room temperature. Benzoin is also cleaved by cyanide ion, but under more vigorous conditions[7]; the reaction is carried out in refluxing aqueous ethanol and for a longer period of time than that required for benzil cleavage.

Although cleavage of benzil by cyanide ion in protic solvents has been extensively studied, to our knowledge an investigation of the reaction in an aprotic solvent has not been made. With this thought in mind benzil was treated with sodium cyanide in dimethyl sulfoxide and *trans*-α,α′-stilbenediol dibenzoate (II) was obtained as the cleavage product. Thus, it is seen that a change from protic to aprotic solvent causes a change in the type of product obtained. The reaction is quite rapid at room temperature, being complete in less than 1 min.

The following mechanism is suggested to account for the formation of the observed product.



Reaction steps 1 and 2 in alcoholic solution have been established by the work of Kwart and Baevsky.[3] These investigators proposed that step 2 is followed by neutralization of anion I with subsequent cleavage to benzoic ester and benzaldehyde as shown in eq. 6.



$$\underset{\text{I}}{Ph{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}O{-}\underset{CN}{\overset{-}{C}}{-}Ph} + ROH \longrightarrow Ph{-}\underset{O}{\underset{\|}{C}}{-}O{-}R + Ph{-}CHO + {}^-CN \quad (6)$$

It is seen that in an aprotic solvent reaction step 6 is not likely to occur. In dimethyl sulfoxide a proton is not readily available and, since this solvent has a tendency to greatly enhance nucleophilic activity,[8] anion I would be expected to attack the available electrophile which is another molecule of benzil. Actually steps 4 and 5 are quite similar to step 2 with the exception that cleavage is accompanied by the loss of cyanide ion and formation of the stable compound II. In addition to accounting for the observed product in a logical manner, the suggested mechanism tends to further support the mechanism proposed by Kwart and Baevsky[3] for the cleavage reaction in alcoholic solution.

Reports concerning α,α′-stilbenediol dibenzoate usually refer to the isomer melting at 159°, "isobenzil",

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[1] Taken in part from the M.S. Thesis of J. L. F.

[2] F. Jourdan, *Ber.*, **16**, 659 (1883).

[3] H. Kwart and M. Baevsky, *J. Am. Chem. Soc.*, **80**, 580 (1958).

[4] W. Dilthey and P. Scheidt, *J. prakt. Chem.*, **142**, 125 (1935).

[5] H. D. Dakin and C. R. Harington, *J. Biol. Chem.*, **55**, 487 (1923).

[6] M. Weiss and M. Appel, *J. Am. Chem. Soc.*, **70**, 3666 (1948).

[7] J. S. Buck and W. S. Ide, *ibid.*, **53**, 2784 (1931).

[8] A. J. Parker, *Quart. Rev.* (London), **16**, 163 (1962).

with no reference to whether the compound has a *cis* or *trans* configuration.[9] Staudinger and Binkert[10] reported the preparation of stilbenediol dibenzoate, m.p. 159°, along with a small quantity of a material melting at 185–187° from the reaction of benzoyl chloride with the potassium salt of stilbenediol. The material melting at the higher temperature was said to be "probably the α-compound". More recently Ried and Keil[11] referred to the higher melting compound as *trans*-stilbenediol dibenzoate. The compound was formed in low yield (1%) from the reaction of the benzoin–piperidine Mannich base with benzoyl chloride in pyridine. Blake, Coates, and Tate[12] reported the compound melting at 159° as *cis*-stilbenediol dibenzoate.

We have found that both isomers of α,α'-stilbenediol dibenzoate are conveniently prepared by first reducing benzil with potassium metal in refluxing benzene followed by the addition of benzoyl chloride to the reaction mixture. Presumably the potassium salt of stilbenediol is formed prior to the addition of benzoyl chloride.[10] Separation of the two isomers is easily accomplished by taking advantage of the fact that the *cis* isomer is considerably more soluble than the *trans* isomer in benzene.

Experimental[13]

Starting Materials.—Sodium cyanide was commercial material of the highest available purity and was dried for several hours at 100° under vacuum prior to use. Benzil, m.p. 94–95°, was obtained commercially and was used without further purification. Dimethyl sulfoxide[14] was dried with Molecular Sieves and in some cases distilled from calcium hydride (1 mm.).[15] Other materials were of reagent grade and were used as obtained.

Benzil and Sodium Cyanide in Dimethyl Sulfoxide.—Sodium cyanide, 0.49 g. (0.01 mole), was heated with stirring in 80 ml. of dimethyl sulfoxide to 70° under a nitrogen atmosphere. After most of the solute had dissolved, the solution was allowed to cool slowly to room temperature at which time 2.10 g. (0.01 mole) of benzil was added in one portion. The solution instantly became dark brown in color and after a reaction time of 1 min. was poured into cold water. The resulting aqueous suspension was acidified and extracted with ether. The ether solution was washed with water, extracted with sodium bicarbonate solution, washed again with water, dried, and evaporated. The residue, on trituration with ethanol, afforded 1.65 g. (78% yield) of *trans*-α,α'-stilbenediol dibenzoate (II), m.p. 189° (from benzene), lit.[11] m.p. 188.5–189°. On admixture with an authentic sample no depression in melting point was observed.

Anal. Calcd. for $C_{28}H_{20}O_4$: C, 79.89; H, 4.79. Found: C, 79.55; H, 5.15.

The sodium bicarbonate layer was acidified and extracted with ether from which was obtained 0.10 g. of benzoic acid, m.p. 121–122° (from water).

Preparation of *cis*- and *trans*-α,α'-Stilbenediol Dibenzoate.—Potassium metal, 0.78 g. (0.02 g.-atom), was placed in a flask containing 50 ml. of anhydrous benzene. The flask was heated while being stirred in an atmosphere of nitrogen, to the boiling point of the solvent. Benzil, 2.10 g. (0.01 mole), in 25 ml. of benzene was added slowly. When addition was complete the brown solution was stirred for 30 min. followed by the addition of 2.3 ml. (0.02 mole) of benzoyl chloride in 15 ml. of benzene. After stirring for an additional 15 min. the hot reaction mixture was filtered and the inorganic residue was extracted twice with hot benzene. The combined filtrates, after being concentrated to 20 ml. and allowed to cool, afforded 1.53 g. (36% yield) of *trans*-α,α'-stilbenediol dibenzoate (II), m.p. 189° (from benzene), lit.[11] m.p. 188.5–189°.

The filtrate remaining after isolation of the *trans* isomer was evaporated and the residue was triturated with aqueous acetone yielding 1.60 g. (38% yield) of *cis*-α,α'-stilbenediol dibenzoate, m.p. 158–159° (from 95% ethanol), lit.[10] m.p. 159°.

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(9) M. S. Kharasch, W. Nudenburg, and S. Archer, *J. Am. Chem. Soc.*, **65**, 495 (1943); M. Gomberg and W. E. Bachmann, *ibid.*, **49**, 2584 (1927); G. Scheuing and A. Heusle, *Ann.*, **440**, 72 (1924); H. Klinger and L. Schmitz, *Ber.*, **24**, 1277 (1891), and references cited therein.

(10) H. Staudinger and A. Binkert, *Helv. Chim. Acta*, **5**, 703 (1922).

(11) W. Ried and G. Keil, *Ann.*, **616**, 96 (1958).

(12) D. Blake, G. E. Coates, and J. M. Tate, *J. Chem. Soc.*, 618 (1961).

(13) Melting points are uncorrected. Elemental analysis was carried out by Swarzkopff Microanalytical Laboratories, Woodside 77, N. Y.

(14) We gratefully acknowledge a free sample of dimethyl sulfoxide from Crown Zellerbach Corp., Camas, Wash.

(15) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **84**, 866 (1962).

A New Microbiological Steroid Reaction

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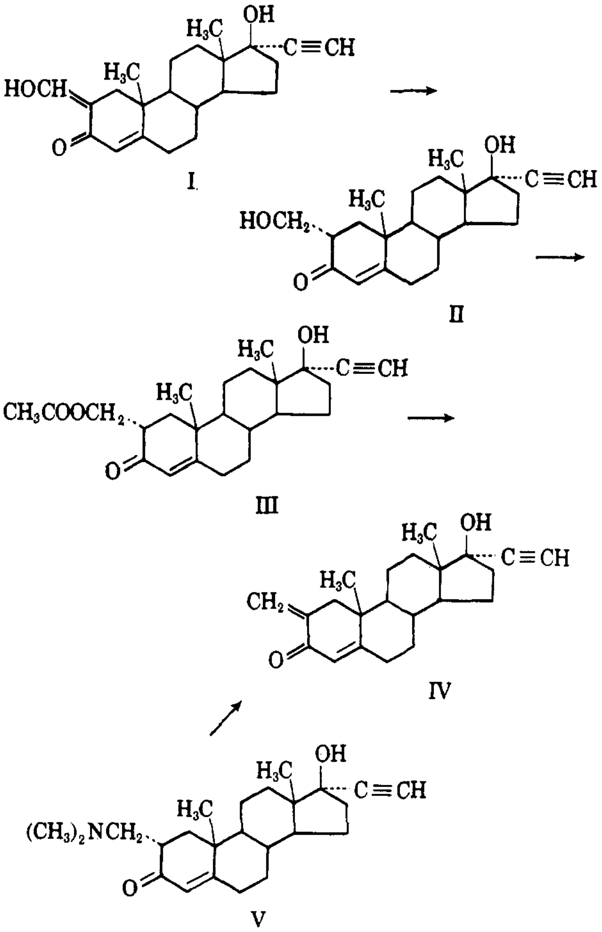
During an investigation[1] of the action of various microorganisms on 2-hydroxymethylene-3-keto steroids,[2] it was observed that when these substrates were submitted to the enzymatic action of *Rhizopus stolonifer* (also known as *Rhizopus nigricans*) an unusual reduction of the β-hydroxy-α,β-unsaturated ketone to a β-hydroxy ketone occurred in preference to the more characteristic reactions of this microorganism (*i.e.*, hydroxylation). This Note reports the microbial reduction of 17α-ethinyl-17-hydroxy-2-hydroxymethyleneandrost-4-en-3-one (I) and the pertinent chemical evidence in support of the assignment of structure II.



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(1) M. Riano, *et al.*, to be published.

(2) The preparation of these compounds is reported by A. J. Manson, F. W. Stonner, H. C. Neumann, R. G. Christiansen, R. L. Clarke, J. H. Ackerman, D. F. Page, J. W. Dean, D. K. Phillips, G. O. Potts, A. Arnold, A. L. Beyler, and R. O. Clinton, *J. Med. Chem.*, **6**, 1 (1963), and references cited therein.