α - Keto - γ - p - tolylmercapto - γ - phenylbutyric Acid.—
Two grams of benzalpyruvic acid was heated with one
mole of p-tolylmercaptan for ten minutes (steam-bath).
The product was dissolved in 10 cc. of benzene, and a
considerable amount of petroleum ether (Skellysolve F)
added. An oil precipitated at once, which, when properly
seeded, crystallized nicely. When not seeded, some days
of standing was at times necessary. A good yield was
obtained of a product which, after three similar crystalliza-
tions, melted at 97–98°.

Anal. (Parr bomb) Calcd. for $C_{17}H_{16}O_3S$: S, 10.67.
Found: S, 10.69, 10.75.

α-Oximino-γ-p-tolylmercapto-γ-phenylbutyric Acid.—
One gram of the keto acid and 0.3 g. each of hydroxyl-
amine hydrochloride and sodium acetate were heated in
10 cc. of alcohol for an hour. After several recrystalliza-
tions from somewhat diluted alcohol, the oxime melted at
160°.

Anal. (Parr bomb) Calcd. for $C_{17}H_{17}O_3NS$: S, 10.15.
Found: S, 10.11, 10.32.

α-Oximino-γ-benzylmercapto-γ-phenylbutyric Acid.—
Benzalpyruvic acid and benzylmercaptan were condensed
as described above. As the product failed to crystallize,
it was converted directly to the oxime. This was obtained
by precipitation from benzene with petroleum ether as a
solid the crystalline character of which was rather doubt-
ful. It melted at 95–97°.

Anal. (Parr bomb) Calcd. for $C_{17}H_{17}O_3NS$: S, 10.15.
Found: S, 10.33, 10.40.

Methyl β-Phenyl-β-p-tolylmercaptopropionate.—Equi-
molecular quantities of methyl cinnamate and p-tolyl-
mercaptan were heated (steam-bath) for periods up to
five hours. Little reaction had, apparently, taken place
in any case. With the addition of 0.1 cc. of piperidine,
the reaction was very incomplete in half an hour, but
after two hours, a good yield of the addition product was
obtained, m. p. 59–60°.

Anal. (Parr bomb) Calcd. for $C_{17}H_{18}O_2S$: S, 11.19.
Found: S, 11.16, 11.31.

Ethyl α-Benzoylamino-β-phenyl-β-benzylmercaptopro-
pionate.—Four grams of ethyl α-benzoylaminocinnamate,
1 mole of benzylmercaptan, and 0.1 cc. of piperidine in
10 cc. of absolute alcohol gave after five hours of refluxing
followed by crystallization from diluted alcohol, 3.5 g. of
the above ester of m. p. 119–120°.

Anal. (Parr bomb) Calcd. for $C_{25}H_{25}O_3NS$: S, 7.64.
Found: S, 7.82, 7.81.

Summary

1. The addition of benzyl- and p-tolylmer-
captans to α,β-unsaturated ketones takes place
very readily at 100° without catalysts.

2. Similar additions to α,β-unsaturated esters
occur rather less readily, and in the presence of
piperidine.

3. The relation of these facts to the natural syn-
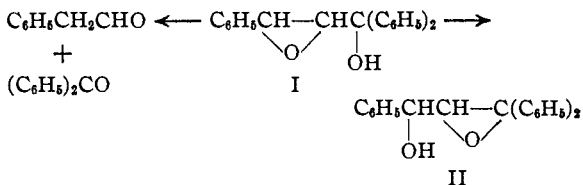thesis of methionine will be discussed elsewhere.

The Properties of Certain Beta Oxanols

BY E. P. KOHLER AND C. L. BICKEL

An earlier paper from this Laboratory[1] con-
tains a description of the peculiar properties of a
β-oxanol which under certain conditions is cleaved
and under others that are not very different is re-
arranged to an isomer.

$C_6H_5CH_2CHO$ ⟵— C_6H_5CH—$CHC(C_6H_5)_2$ —⟶

   +   \O/   OH

$(C_6H_5)_2CO$ I

             C_6H_5CHCH—$C(C_6H_5)_2$

               OH   \O/

                II

As a result of further study it is possible now to
define more sharply the conditions under which
these transformations occur and to exclude some of
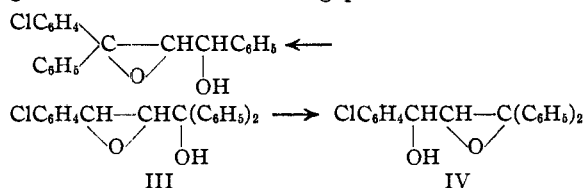the mechanisms that were suggested.

The cleavage is dependent on the replacement
of the hydrogen of the hydroxyl group with a
metal. By treating the oxanol at low temperatures

(1) Kohler, Richtmyer and Hester, THIS JOURNAL, 53, 205 (1931).

with Grignard reagents, lithium organic com-
pounds, or sodium in liquid ammonia it is pos-
sible to convert it into metallic derivatives from
which it is regenerated by acids. At higher tem-
peratures all these metallic derivatives decompose
into benzophenone and the corresponding metallic
derivatives of the aldehyde. This cleavage is
quite general for β-oxanols; by similar treatment
the isomeric oxanol II is cleaved into benzaldehyde
and a metallic derivative of diphenyl acetaldehyde.

In contrast with cleavage the rearrangement
from one oxanol to another can be effected
catalytically. It is induced by methyl alcoholic
solutions of small quantities of alkaline hydrox-
ides, alkaline carbonates, barium oxide, magne-
sium methylate and tetramethylammonium hy-
droxide, but not by acetates, ammonia, pyridine
and piperidine. In the cases which have been
investigated it is not reversible.

This "β-oxanol rearrangement" resembles the "allylic rearrangement" in that the result is an isomer which is different in structure but not in type. In the case in which the rearrangement was first observed the product might be due either to an interchange of hydrogen and phenyl or to a transposition of the hydroxyl group and the oxide ring. Although the former mechanism seemed *a priori* improbable we nevertheless decided to examine it. To this end we prepared a new oxanol which differed from the old only in having an *o*-chlorophenyl group in place of the phenyl group in the β-position. Depending on the mode of rearrangement this chloro compound would give either of the following products.

$$ClC_6H_4 \diagdown C \diagup CHCHC_6H_5 \leftarrow$$
$$C_6H_5 \diagup \diagdown O \diagup \underset{OH}{|}$$

$$ClC_6H_4CH\underset{\diagdown O \diagup}{\text{—}}CHC(C_6H_5)_2 \longrightarrow ClC_6H_4CHCH\underset{OH}{\text{—}}C(C_6H_5)_2$$
$$\underset{OH}{|} \qquad\qquad \underset{OH}{|} \diagup O \diagdown$$
$$\text{III} \qquad\qquad\qquad \text{IV}$$

The substance was rearranged with great ease and when the isomer was oxidized the products were chlorobenzoic acid and benzophenone; the rearrangement therefore does not involve any shifting of the hydrocarbon residues.

One way in which a transposition of the hydroxyl group and the oxide ring might be brought about would be by addition of water to the oxide ring, forming a trihydroxy compound which subsequently lost water in a different manner. This mechanism, likewise, is *a priori* improbable because it involves the closure of an ethylene oxide ring from a glycol in the presence of a base. We were unable to prepare the intermediate trihydroxy compound but an examination of the corresponding mono methyl ether, $C_6H_5CH(OCH_3)$-$CH(OH)C(OH)(C_6H_5)_2$, showed that glycols of this type cannot be converted into ethylene oxides with bases. This mechanism, therefore, is also definitely excluded.

The new facts do not provide an adequate basis for establishing the mechanism by which these oxanols are cleaved or rearranged but they accurately define the conditions under which these transformations occur. Both the fission and the rearrangement proceed in the direction leading to compounds which are more acidic. Fission occurs only under conditions under which oxanols are converted into metallic derivatives and its extent depends upon the degree of conversion. Rearrangement occurs in solutions of hydroxyl

or methoxyl ions. The action of bases is catalytic and an increase in their concentration merely speeds up the reaction.

Experimental Part

β-Hydroxy-β-(*o*-chlorophenyl) Propiophenone, *o*-$ClC_6H_4CH(OH)CH_2COC_6H_5$, and *o*-Chlorobenzalacetophenone, *o*-$ClC_6H_4CH=CHCOC_6H_5$.—When *o*-chlorobenzaldehyde was condensed with acetophenone by the procedure that is generally employed for preparing benzalacetophenone the result was not the unsaturated ketone but the primary aldol condensation product. Thus a mixture of 6.2 g. of the aldehyde and 5.3 g. of the ketone, when shaken under the tap with a solution of 2 g. of sodium hydroxide in 20 cc. of water and 12 cc. of ethyl alcohol, soon deposited a pale yellow crystalline solid. The solid was washed with water and iced alcohol until free from base, then recrystallized from ether and petroleum ether. It separated in colorless needles and melted at 80°. The yield was 95%.

Anal. Calcd. for $C_{15}H_{13}O_2Cl$: C, 69.1; H, 5.0. Found: C, 68.6; H, 5.1.

The hydroxyl compound reverts to its components both when shaken with aqueous methyl alcohol and when heated by itself, and it is not dehydrated to the unsaturated ketone when it is heated with glacial acetic acid. The unsaturated ketone, however, was readily obtained by condensing the aldehyde with the ketone in dilute methyl alcoholic sodium methylate. It has been adequately described by Pfeiffer.[2]

o-Chlorobenzalacetophenone Oxide, $ClC_6H_4\overset{O}{\overset{\diagup\diagdown}{CH-CH}}COC_6H_5$.—A solution of sodium peroxide was prepared by gradually stirring 55 g. of the powder into 300 cc. of ice and water in a flask surrounded with a freezing mixture. To this solution was added 97 cc. of concd. hydrochloric acid at such a rate that the temperature could be maintained below 5°. The resulting feebly alkaline solution was diluted with 100 cc. of water and 35 cc. of alcohol, then filtered through glass wool into a solution of 80 g. of the unsaturated ketone in 1300 cc. of alcohol that was stirred vigorously and kept at 35°. The oxide formed with great rapidity. After ten minutes the mixture was cooled to 0° in a freezing mixture and filtered. The solid was washed, first with ice-cold 60% alcohol then thoroughly with water to remove all trace of alkali. The yield was 84%. The oxido ketone crystallizes from ether–petroleum ether in large plates and it melts at 73–74°.

Anal. Calcd. for $C_{15}H_{11}O_2Cl$: C, 69.6; H, 4.3. Found: C, 69.2; H, 4.4.

α,α-Diphenyl-β-oxido-γ-(*o*-chlorophenyl) Propanol, III.—To a solution of phenylmagnesium bromide, which had been prepared from 2.82 g. of magnesium and cooled to −15°, was added in the course of twenty minutes 15 g. of powdered *o*-chlorobenzalacetophenone oxide. A pink color developed in the solution and a pasty magnesium derivative accumulated on the walls of the vessel. After the mixture had been stirred for an hour, the ethereal solution was decanted into iced acid and the product was isolated in the usual manner. The pasty magnesium

(2) Pfeiffer, *J. prakt. Chem.*, [2] 119, 119 (1928).

compound on the walls of the vessel, treated in the same manner, yielded 2 g. of unchanged oxido ketone.

The oxanol is moderately soluble in methyl alcohol and in ether, very sparingly soluble in petroleum ether. It separates from ether–petroleum ether in stout plates and it melts at 107–108°. The yield was 13.5 g.

Anal. Calcd. for $C_{21}H_{17}O_2Cl$: C, 74.9; H, 5.1. Found: C, 74.6; H, 5.2.

Cleavage with Ethylmagnesium Bromide.—When the oxanol was added to an ethereal solution of ethylmagnesium bromide it developed a pale pink color which gradually faded. The mixture was left to itself for twenty-four hours then decomposed with iced acid in the usual manner. The resulting oil failed to crystallize but when it was distilled with steam the distillate yielded a solid which melted at 94° and which was identified as diphenyl ethyl carbinol by comparison with a known sample. There was no evidence of rearrangement.

Cleavage with Lithium Phenyl.—To a solution of lithium phenyl which contained 0.9 g. of lithium in 250 cc. ether and which was cooled to −18° was added 10 g. of solid oxanol. The oxanol dissolved rapidly and a lithium compound separated in fine white needles. By decomposing the lithium compound with iced acid 9.85 g. of oxanol was recovered. A similar solution when boiled for thirty minutes before decomposition yielded triphenylcarbinol, the polymeric aldehyde and 1.5 g. of unaltered oxanol. Apparently the lithium compound is less rapidly cleaved than the magnesium halide derivative.

Cleavage with Sodium.—A solution obtained by adding 2 g. of the oxanol very slowly to a solution of 0.7 g. of sodium in liquid ammonia was allowed to evaporate spontaneously. It left a resin which was extracted with ether. The ethereal solution, on distillation with steam, yielded benzophenone and left the usual resinous aldehyde.

Rearrangement with Bases: α-Chlorophenyl-β-oxido-γ,γ-diphenyl Propanol, IV.—The general procedure employed with the various bases is illustrated by the following experiment with potassium hydroxide. To a solution of 0.2 g. of potassium hydroxide in 75 cc. of methyl alcohol was added 5 g. of the sparingly soluble oxanol. The mixture was allowed to stand for fifteen hours during which time the solid gradually dissolved, then poured into ice water. The product crystallized from ether–petroleum

ether in small cubes melting at 114–115°. The yield was 98% of crude and 95% of pure oxanol. At the boiling point of the solvent the transformation is much faster but the yield is less.

Anal. Calcd. for $C_{21}H_{17}O_2Cl$: C, 74.9; H, 5.1. Found: C, 74.5; H, 5.2.

Oxidation.—In order to prove that the rearrangement does not involve a shift of a hydrocarbon residue, the oxanol was oxidized with chromic acid in the usual manner. Only two products were formed—*o*-chlorobenzoic acid melting at 139° and benzophenone which was identified by converting it into the oxime melting at 140°.

Autoxidation.—Like the corresponding chlorine-free compound, the oxanol is rapidly oxidized in the air of the laboratory. A freshly prepared sample softened and developed the odor of chlorobenzaldehyde after a few hours of exposure while a sample kept over potassium hydroxide remained unchanged after a month. The peroxide resulting from the autoxidation was described in an earlier paper.[3]

α-Hydroxy-β-methoxy-β-phenyl Propiophenone and α, α,γ - Triphenyl - α,β - dihydroxy - γ - methoxy Propane, $C_6H_5CH(OCH_3)CH(OH)COC_6H_5$ and $C_6H_5CH(OCH_3)$-$CH(OH)C(OH)C_6H_5)_2$.—The hydroxy ketone, which had been used as an intermediate but not isolated in earlier work,[4] was obtained as a solid. It crystallized from ether–petroleum ether in long plates melting at 47–48°.

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 75.0; H, 6.3. Found: C, 74.9; H, 6.4.

When the solid ketone was treated with phenylmagnesium bromide it yielded the same dihydroxy ether that had been obtained previously from the oil. The ether was quite indifferent to cold and hot methyl alcoholic potassium hydroxide.

Summary

This paper defines the conditions under which β-oxanols are cleaved by bases and those in which they are rearranged to isomeric β-oxanols.

(3) Kohler and Nygaard, THIS JOURNAL, **55**, 310 (1933).
(4) Ref. 1, p. 215.