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THE CONVERSION OF ALCOHOLS TO ALDEHYDES AND KETONES: A SUPERIOR METHOD

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The oxidative powers of lead tetraacetate are proving to be quite interesting and several papers recently published have indicated the versatility of this reagent in organic synthesis (1, 2, 3, 4). This communication relates an extremely mild, yet high yield method of obtaining carbonyl compounds from the corresponding alcohols.

Reagents (5) most often used to oxidize alcohols are; chromium ion in sulfuric acid or pyridine (6), manganese dioxide (7, 8), dimethyl sulfoxide (9), or aluminum isopropoxide in acetone (10). The Sarrett Reagent (6) is possibly the mildest of the above-mentioned reagents in that no heat is required for oxidation to occur. Often there is difficulty in preparing the chromium oxide-pyridine reagent, however, as the combination evolves much heat on mixing. Manganese dioxide has been shown to be a good oxidant for certain aliphatic and aromatic alcohols.

Harrison (8) has recently shown that given enough oxidant and solvent of sufficient purity, saturated primary and secondary alcohols are oxidized in good yield to the corresponding aldehyde or ketone. However, the oxidation does not seem to stop at this point if excess oxidant is present (11). A less versatile oxidant is dimethyl sulfoxide - specific for arylcarbinols. For these alcohols the reaction gives high yields of aldehydes. An undesirable feature is the high reflux temperature apparently required for oxidation. Finally, the Oppenauer Oxidation is well known as a general oxidation procedure. The presence of the strong base catalyst is again undesirable in that isomerization and/or condensation can occur with more active molecules.

Lead tetraacetate is a good oxidant for alcohols in solvents such as benzene, hexane (4, 12) or chloroform (13) at reflux temperatures. In these solvents, primary and secondary alcohols not containing a δ-methyl, - methylene, or -methyne group (α is adjacent to the hydroxyl oxygen) usually are oxidized to the corresponding ketone or aldehyde in good yield. Minor byproducts are the acetate esters and unreacted (or regenerated) alcohol. All other alcohols yield a more complex product mixture in that tetrahydrofuran and tetrahydropyran derivatives are formed in addition to (and sometimes predominate) the above-mentioned products (13, 14, 15, 16).

In an attempt to incorporate a base for neutralization into the reaction solvent (calcium carbonate was used with the other solvents), we carried out a series of alcohol oxidations in pyridine (17). Table I lists the alcohols and their corresponding products. It is important that all oxidations were carried out at room temperature for periods of 10-20 hours. The reaction medium acts as an indicator as it turns from deep red to pale yellow when all of the oxidant has been reduced. Oxidation always stopped at the aldehyde or ketone stage and the product mixture could be left for several days prior to workup without destroying the desired product. In all cases the only by-products were acetate ester (∼ 5%) and unreacted alcohol (5-20%). These could easily be separated from the desired product by distillation, recrystallization or elution over alumina.

A typical procedure is as follows: The alcohol, 0.02 mole, was dissolved in pyridine (100 ml.) and stirred at room temperature. To this was added, in powder form (18), the same amount of lead tetraacetate. The mixture immediately turned deep red and became homogeneous within 30 minutes. After stirring for several hours, the color lightened and became pale yellow. At this point all of the lead tetraacetate had been reduced to the

TABLE I[a]

REACTANT	PRODUCT	YIELD (%)
Butanol	Butyraldehyde	70
n-Amyl Alcohol	Valeraldehyde	70
Benzyl Alcohol	Benzaldehyde	85
Allyl Alcohol	Acrolein	35[b]
Cinammyl Alcohol	Cinammaldehyde	91
p-Nitro-benzyl Alcohol	p-Nitro-benzaldehyde	80
Furfuryl Alcohol	Furfural	70
Tetrahydropyran-2-methanol	2-Formyltetrahydropyran	80
2-Chloroethanol	Chloroacetaldehyde	40[b]
Benzhydrol	Benzophenone	80
Isophorol	Isophorone	85
2-Propylcyclohexanol	2-Propylcyclohexanone	73
Isoborneol	Camphor	43[c]
Benzoin	Benzil	90[d]
2,5-Hexandiol	2,5-Hexandione	89

a) Liquid product composition was determined by GLPC methods as well as by infrared comparison with authentic samples. Solid products were isolated in the pure form and compared with authentic samples by infrared and mixture melting point.

b) Considerable polymerization took place upon distillation.

c) Some lost by sublimation during the work-up.

d) Compare the oxidation in acetic acid: K. Ichikawa and Y. Takeuchi, Nippon Kagaku Zasshi, **79**, 1060 (1958); cf. CA, **54**, 24506 (1960).

diacetate, which precipitated on cooling, and the reaction was complete. Workup procedures depended on the physical properties of the desired product. For butanal, the product mixture was carefully distilled to yield the product directly. For a solid product, e.g. benzil, the solvent was removed under reduced pressure and the solid residue taken up in ether and washed with water. After drying, the ether layer yielded the product.

Recrystallization yielded material comparable with an authentic sample (IR, UV and mixture melting point). Neither the use of more than a 1:1 mole ratio of oxidant to alcohol, nor elevated reaction temperature seemed to increase the final yield of carbonyl product. Studies of product concentration as a function of time have shown that oxidation takes place at a very slow rate and that, until the color change occurs, oxidation is continuous. The sequence of addition can be reversed with very little loss of oxidant power. We have studied the complex of pyridine with lead tetraacetate spectrophotometrically and have not as yet elucidated a structure. The reaction seems to take place by complex formation of the oxidant with pyridine followed by alcohol oxidation. The solvent, pyridine, can be diluted to 25% with benzene and the reaction proceeds as above. With the more volatile products, however, isolation becomes more difficult.

The novelty and usefulness of this oxidation procedure is that the conditions are extremely mild. There is no heat evolved when lead tetraacetate is dissolved in pyridine and the yields of desired product are good for all types of primary and secondary alcohols, allylic as well as saturated (19). We are currently investigating the kinetics, scope and relationship of these reactions to other lead tetraacetate oxidations (20).

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