

SYNLETT Spotlight 106

Oxalic Acid: A Very Useful Brønsted Acid in Organic Synthesis

Compiled by Kovuru Gopalaiah



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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Introduction

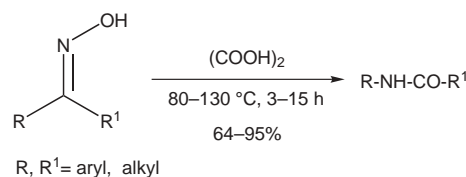
The title compound oxalic acid is available in anhydrous and dihydrate forms and exhibits several features which have made it particularly attractive as a reagent in organic synthesis. Oxalic acid is a mild Brønsted acid, which finds application in the Beckmann reaction,¹ protection and deprotection of carbonyl compounds,^{2–4} and various selective cleavage and hydrolytic reactions. It is frequently used as a mild acidic quench for a variety of reactions including oxidations.⁵ Oxalic acid has also been used as an

acidic agent in a number of condensation processes such as condensation of allylic alcohols with aromatic rings,⁶ carbonyl compounds and hydrazines,⁷ aromatic amines and aldehydes,⁸ and it has been utilized as a bifunctional condensation partner in the synthesis of heterocyclic systems.⁹

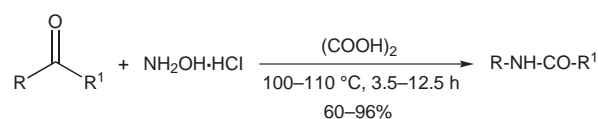
Oxalic acid is the simplest of the dicarboxylic acids and is widely used in inorganic chemistry as a precipitant and chelating agent (oxalate as a bidentate ligand has been of great interest in coordination chemistry).¹⁰

Abstracts

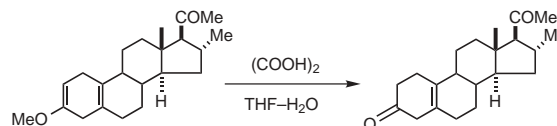
(A) Oxalic acid is an efficient reagent for the Beckmann reaction – a variety of ketoximes are converted into the corresponding secondary amides by classical anti-periplanar migration upon heating to ca. 100 °C, and aldoximes afford the corresponding nitriles. The procedure offers high yield of the desired products, gaseous by-products (CO + CO₂) and the absence of reaction solvent.¹



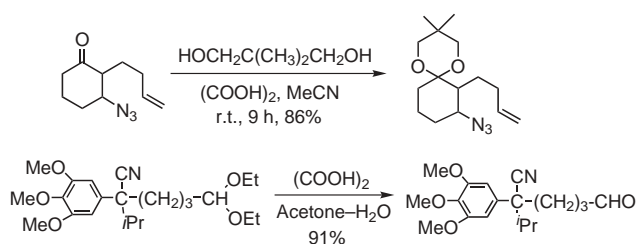
(B) Anhydrous oxalic acid is an excellent mediator for one-pot transformation of ketones to amides in the presence of hydroxylamine hydrochloride. The method is effective for various aromatic and aliphatic ketones, and provides excellent yield of the products.¹



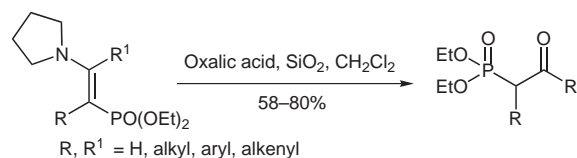
(C) In the presence of aqueous oxalic acid, enol ethers undergo expeditious hydrolysis to the corresponding ketones without concomitant migration of the double bond.¹¹ In contrast, use of a mineral acid typically gives the conjugated ketone. This method offers considerable advantage in terms of regioselectivity of the product.



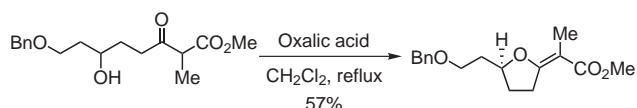
(D) Oxalic acid has been used for both the preparation and the cleavage of acetal and ketal functionalities. Ketones and aldehydes react with ethylene glycol or ethanol in the presence of anhydrous oxalic acid to provide the corresponding ketals and acetals. Cleavage of ketals and acetals to regenerate the carbonyl group has been accomplished with the use of aqueous oxalic acid. Acid-sensitive functionality is well tolerated under these conditions.^{2–4}



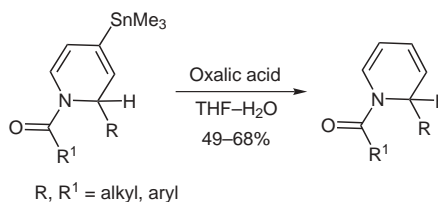
(E) Oxalic acid on SiO₂ facilitates mild acidic hydrolysis of diethyl β-dialkylamino vinylphosphonates (vinyllogous phosphoramides) to β-keto phosphonates. β-Keto phosphonates are excellent reagents for homologation of aldehydes and ketones to α,β-unsaturated aldehydes and ketones via the Wadsworth–Emmons–Horner reaction.¹²



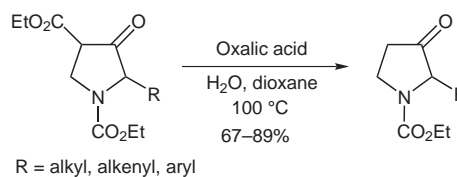
(F) Alcohols have been efficiently converted into alkenes either by heating with anhydrous oxalic acid or refluxing in aqueous oxalic acid.¹³ Appropriately inclined hydroxyl ketones have been cyclodehydrated to give cyclic ethers.¹⁴



(G) Oxalic acid has been used to perform selective protodesilylation and protodesilylation of dihydropyridine compounds.¹⁵



(H) Oxalic acid is an efficient reagent for the selective removal of the ester functionality of β-keto esters to the corresponding ketone by conventional acid hydrolysis and decarboxylation in aqueous media.¹⁶



References

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