Lithium Perchlorate/Diethyl Ether (LPDE)

Compiled by Chidambaram Gunanathan

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Introduction

Lithium perchlorate in diethyl ether has become a widely used medium in organic synthesis in recent years for effecting various organic transformations. The special property inherent to LPDE medium is that it offers a convenient procedure to carry out reactions under essentially neutral reaction and workup conditions. It promotes organic reactions such as aldol condensation, cycloaddition, and sigmatropic rearrangements. Among the many organic reactions mediated by LPDE, one-pot three component aminoalkylation of aldehydes, Mannich reaction, Biginelli reaction are worth to notice. The three component condensation reaction of aldehydes and amines with various nucleophiles also takes place in this medium and leads to the facile synthesis of α-aminonitriles, α-aminophosphonates, α-cyanohydroxylamines, N-trimethylsilyloxy-α-aminophosphonates, and α-hydrazinophosphonates. It is expected that more applications will be found with this remarkable reagent and investigations in this medium will be rewarding.

Preparation of LPDE: Commercially available lithium perchlorate was dried under vacuum (10⁻¹ Torr) at 160 °C for 48 h. Lithium perchlorate is stable up to or above its mp of 247 °C. Anhydrous LiClO₄ and diethyl ether were cooled separately in an ice bath under a nitrogen atmosphere, and then the ice cold ether was added very slowly to LiClO₄ via syringe. The dissolution was highly exothermic. The clear solution can be stored in a desiccator and used as required.

Abstracts

(A) Aldehydes and ketones were protected as acyclic and cyclic dithioacetals by LPDE at ambient temperature in high yield. The difference in their reactivity was successfully employed in the chemoselective dithioacetalization of aldehydes and acetals in the presence of ketones and their acetals.

(B) Grieco et al. reported the [4+2] cycloaddition reactions facilitated by LPDE. Diels–Alder adducts that are inaccessible via conventional means can be achieved by this remarkable medium.

\[ \text{CHO} + \text{SH} \rightarrow \text{S-S} + \text{O} \]

80%

\[ \text{HS} + \text{CO}_{2}\text{Me} \rightarrow \text{O} \]

80%

\[ \text{endo : exo} = 2.9 : 1 \]
(C) The allyl vinyl ethers contrary to expectation, did not undergo [3,3] sigmatropic rearrangement in LPDE but yielded aldehydes via [1,3] sigmatropic rearrangement.\(^\text{12}\)

(D) An expeditious synthesis of bis(indolyl)methanes has been achieved recently.\(^\text{13}\) LPDE catalyzed the electrophilic substitution reaction of indoles with aldehydes and ketones to give the corresponding bis(indolyl)methanes.

(E) In this medium epoxides can effectively be converted to carboxyl compounds with high chemo- and regioselectivity.\(^\text{14}\)

(F) The allylation of quinone is an important reaction for the preparation of biologically active isoprenoid quinones. Ipaktschi et al. reported the allylation of quinones with allyltrimethylsilane.\(^\text{15}\)

(G) Recently the ring opening at the bridgehead of oxabicyclo[3.2.1]octenes employing silyl ketene acetals has been achieved in LPDE. This methodology gives rise to the highly functionalized cycloheptadienes. The operational simplicity of the bridgehead ring opening reactions leads to the construction of C(19)–C(27) fragment of Rifamycin S.\(^\text{16}\)

References

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