Highly Selective Synthetic Transformations Catalyzed by Lithium Perchlorate in Organic Media

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Highly concentrated solutions of lithium perchlorate in various organic solvents have been used as media for many synthetic transformations at room temperature which are otherwise difficult to carry out under ordinary conditions. The rates of several organic reactions are faster in these media compared than in pure solvents. More importantly high chemo-, regio- and stereoselectivities have been observed. The mild Lewis acidity of the lithium ion in donor solvents such as diethyl ether is responsible for these selectivities. Fine tuning of the Lewis acidity of the lithium ion, depending upon the solvent basicity and polarity, has been possible for selective activation of organic substrates in these media. The activation of carbonyl- and other oxygen-containing organic compounds in 5 M lithium perchlorate in diethyl ether (LPDE) and in nitromethane (LPNM) is presented.

1. Introduction

Organic reactions involving polar transition states and ionic intermediates are profoundly influenced by the polarity of the medium.[1] The influence of solvent polarity on the rate of reactions was recognized as early as 1862 by Berthelot and Pean de Saint Gilles[2] in connection with their studies on the esterification of acetic acid with ethanol. The addition of salts to an organic medium changes not only the polarity but also the Lewis acid/base properties of that medium. These added salts not only alter the rate of the organic reactions but also change the course of certain reactions proceeding through ion pair intermediates.[3] Winstein recognized that the dissolution of lithium perchlorate in diethyl ether increases the polarity of the medium dramatically, a solution of lithium perchlorate in ether is more polar than acetic acid.[4] He demonstrated that the ionization of *p*-methoxyneophyl *p*-toluenesulfonate in 0.1 M

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MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

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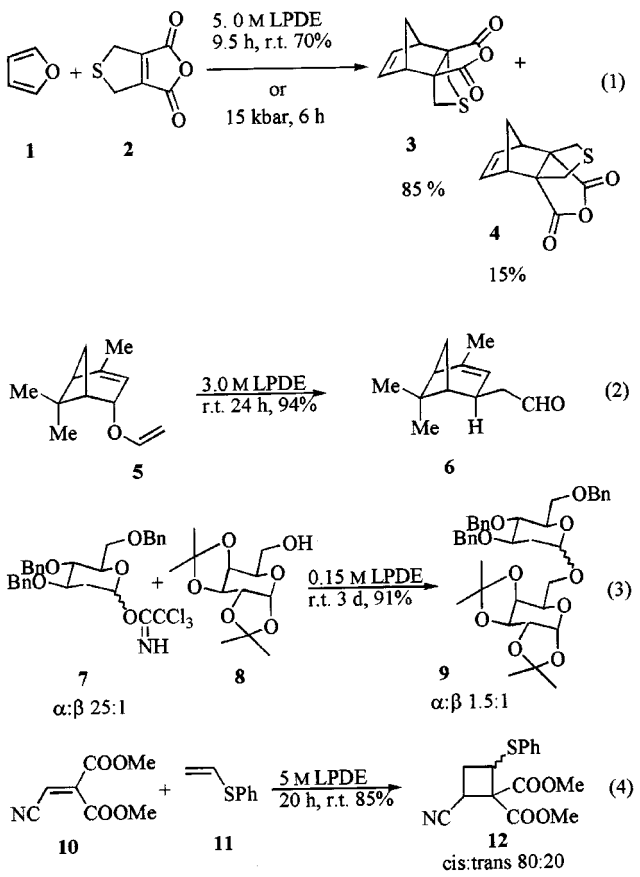
lithium perchlorate/diethyl ether (LPDE) is increased by a factor of 10^5.[4] Pocker observed that the rate of ionization of trityl chloride is increased by a factor of 10^9 in a 5.0 M LPDE medium compared to diethyl ether alone.[5] Although the pioneering work of Winstein and others[6] on the salt effects on solvolysis reactions is of mostly mechanistic interest it was later put to use in organic synthesis. Sauer[7] was the first one to recognize the advantage of using a solution of 4 M lithium perchlorate in diethyl ether for carrying out the Diels–Alder reaction between cyclopentadiene and methyl methacrylate wherein he observed an increased *endo* selectivity compared to that in ether. Subsequently, the seminal contributions from Grieco and co-workers[8] on the use of highly concentrated solutions of lithium perchlorate in diethyl ether for synthetic transformations led to the recognition of the LPDE medium for various organic transformations which are otherwise very difficult to perform under ordinary conditions. Selected examples of organic transformations carried out in an LPDE medium are given in Scheme 1.



Scheme 1. Selected synthetic transformations in LPDE

The first example in Scheme 1 involves a Diels–Alder reaction between furan **1** and a derivative of maleic anhydride **2**.[9] Due to its aromaticity the [4+2] cycloaddition of furan is difficult. However, in a 5 M LPDE medium the Diels–Alder reaction between **1** and **2** proceeds smoothly leading to a diastereomeric mixture of products **3** and **4** (reaction 1). It must be emphasized that this reaction otherwise proceeds only at 15 kbar pressure.[10] In the second example, the allyl vinyl ether **5** undergoes an unusual 1,3-shift rather than the well-known 3,3-shift (Claisen rearrangement) in an LPDE medium to give **6** (reaction 2).[11] Although this reaction has been shown to be nonconcerted, involving a cleavage-recombination mechanism,[11] it serves as a good method for promoting 1,3-shifts which are rather difficult to carry out under normal thermal and Lewis acid catalyzed conditions due to the predominance of the 3,3-shift.

Waldmann and co-workers[12] have used lithium perchlorate in various organic solvents to activate glycosyl donors in the absence of any other harsh and strong Lewis acids and heavy metal salts, and have reported a number of glycosylation reactions under essentially neutral conditions; the example in reaction 3 illustrates the synthesis of a disaccharide using this method.[13] Finally, Hall and co-workers[14] have reported the [2+2] cycloaddition reaction of electronically biased olefin systems to yield cyclobutane derivatives which are otherwise difficult to prepare under normal thermal conditions. Reaction of **10** and **11** in LPDE leads to the formation of **12** via a [2+2] cycloaddition process (reaction 4), whereas the same substrates in acetonitrile yield a pyran derivative by a hetero Diels–Alder reaction. Apart from the above examples there are many other synthetic transformations catalyzed by lithium perchlorate in organic solvents reported in the literature.[15]

2. Nature of the Lithium Perchlorate/Diethyl Ether Medium

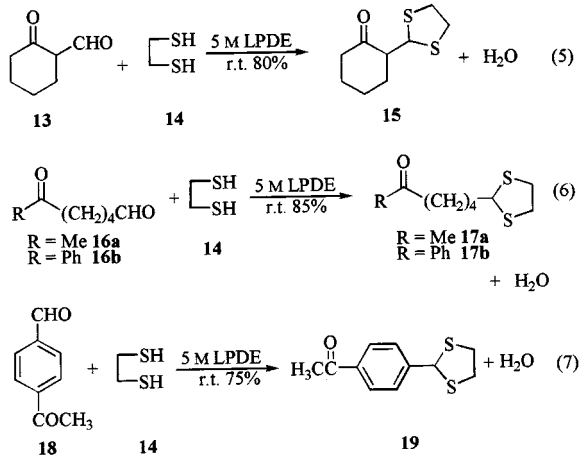
Anhydrous lithium perchlorate is highly soluble in dry ether (highly exothermic!!) and gives a maximum concentration of 6.5 M. (**Caution**: *Although solid lithium perchlorate is stable up to its melting point, solutions in organic solvents should be prepared and handled with the utmost care).* The 5 M solution is highly viscous. Based on the NMR spectroscopic studies, according to Pocker and co-workers, lithium perchlorate forms a 1:2 etherate ($LiClO_4{\cdot}2Et_2O$) below 4.25 M concentration and a mixture of 2:1 and 1:1 etherates above 4.25 M.[16] According to Kabalka and co-workers, based on spectroscopic and chemical evidence, the increased rates of reaction of certain Diels–Alder reactions and high selectivities are due to the mild Lewis acidity of the lithium ion in ether.[17] According to these authors, the strong and intrinsic Lewis acidity of lithium ion is moderated in diethyl ether due to its complexation with the solvent and the counter ion. Forman and Dailey,[18] and Righetti and co-workers,[19] have also shown that the rate enhancement of Diels–Alder reactions is due to Lewis acid catalysis by the lithium ion. Apart from the Lewis acidity of the lithium ion, the increased polarity of the medium also plays a role in the rate enhancement. The polarity of a 1.5 M LPDE medium on the E_T scale is 53 which is close to the value of acetic acid, and much higher than that of pure diethyl ether (E_T = 34.5).[7]

3. Activation of Carbonyl- and other Oxygen-Containing Substrates in an LPDE Medium

Our objective in using lithium perchlorate in organic solvents is to activate carbonyl- and other oxygen-containing functional groups for selective synthetic transformations. The lithium ion is a hard Lewis acid and its Lewis acidity is quite high in the gas phase.[20] However, in organic solvents such as diethyl ether, the Lewis acidity of the lithium ion is moderated due to solvation. The lithium ion coordinates to the lone pair of electrons on the oxygen of the carbonyl- or other oxygen-containing functional groups in organic substrates and thereby activates them to undergo selective transformation due to its mild Lewis acidity. This hypothesis has been realized in the following synthetic transformations.

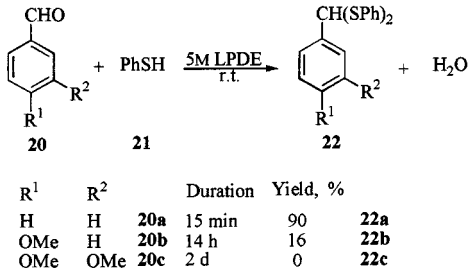
3.1 Chemoselective Dithioacetalization of Aldehydes and Acetals

The protection of the carbonyl functional group as an acetal or thioacetal is an important and useful synthetic transformation.[21] Dithioacetals often serve not only as protecting groups but also as acyl anion equivalents.[22] Though a number of methods are available for the protection of the carbonyl functional group as a dithioacetal using protic and Lewis acid catalysts,[23] methods for the chemoselective thioacetalization of the aldehydes in the presence of ketones under "essentially neutral reaction conditions" are very rare.[24] Highly chemoselective protection of the aldehydes is achieved in an LPDE medium.[25] Reactions 5−7 in Scheme 2 illustrate the utility of the LPDE medium for chemoselective thioacetalization.



Scheme 2. Chemoselective dithioacetalization of aldehydes in 5 M LPDE

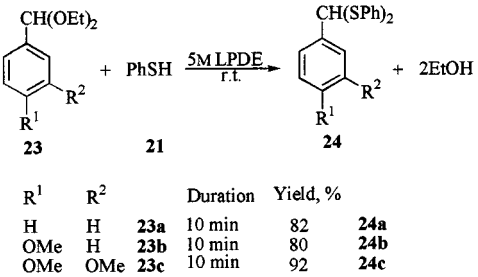
The keto aldehydes **13**, **16** and **18** react with dithiol **14** in LPDE at ambient and neutral conditions to give the dithioacetals **15**, **17** and **19**, respectively, in which only the aldehyde functional group is protected, in a clean manner. Chemoselectivity is achieved even among the substituted benzaldehydes in that only benzaldehyde and the ones with electron-withdrawing substituents readily undergo thioacetalization (Scheme 3). *p*-Methoxy- and 3,4-dimethoxybenzaldehyde, owing to the reduced electrophilic character of their carbonyl functional groups, either react very slowly or do not undergo this reaction in LPDE.



R^1	R^2		Duration	Yield, %	
H	H	**20a**	15 min	90	**22a**
OMe	H	**20b**	14 h	16	**22b**
OMe	OMe	**20c**	2 d	0	**22c**

Scheme 3. Substituent effect on the dithioacetalization of benzaldehyde in 5 M LPDE

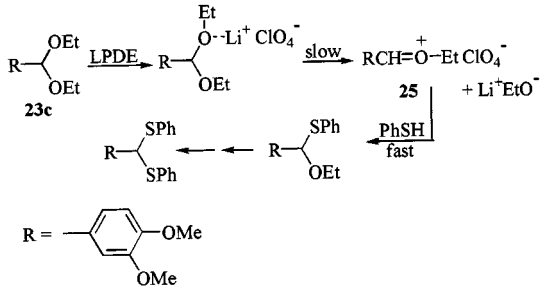
This kind of substrate selectivity is seldom achieved using conventional Lewis acid catalysts such as BF_3, $AlCl_3$ etc. In sharp contrast to the inertness of methoxy-substituted benzaldehydes towards dithioacetalization in LPDE, substitution of the corresponding acetals proceeds readily and the acetals are converted into their dithioacetals in good yields at room temperature under neutral conditions (Scheme 4).



R^1	R^2		Duration	Yield, %	
H	H	**23a**	10 min	82	**24a**
OMe	H	**23b**	10 min	80	**24b**
OMe	OMe	**23c**	10 min	92	**24c**

Scheme 4. Substituent effect on the dithioacetalization of benzaldehyde acetal in 5 M LPDE

In the case of the acetals from 4-methoxy- and 3,4-dimethoxybenzaldehyde, chemical and spectroscopic evidence suggests the formation of oxocarbenium ion intermediates in LPDE;[25] the substitution of these acetals proceeds by an S_N1 type mechanism as shown in Scheme 5.

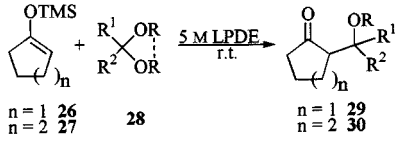


Scheme 5. Mechanism of dithioacetalization of acetals in 5 M LPDE

As in the case of the dithioacetalization of carbonyl compounds, high chemoselectivity is also observed in the dithioacetalization of acetals from aldehydes and ketones in that the former are selectively converted into the corresponding dithioacetal much more efficiently than the latter.

3.2. Substitution of Acetals in LPDE with Carbon Nucleophiles

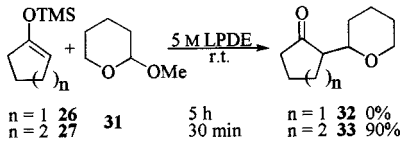
The nucleophilic substitution of acetals by silyl enol ethers to give aldol ethers is a useful C−C bond forming reaction and is generally carried out under strong Lewis acidic conditions.[26] Although very high diastereoselectivities have been reported the reactions are seldom chemoselective. For examples, the acetals from aldehydes and ketones react with equal facility to give the corresponding aldol ethers. Since a high chemoselectivity is observed with acetals and ketals with sulfur nucleophiles in 5 M LPDE, we investigated the use of carbon nucleophiles, namely silyl enol ethers, for the substitution of acetals and ketals.[27] 1-Trimethylsilyloxycyclohexene **(27)** reacted with various acyclic acetals to yield the corresponding aldol ethers **30** in high yields in 5 M LPDE at room temperature, whereas under identical conditions, cyclic ketals failed to react, resulting in a very high chemoselectivity of the substrates for the acetal substitution reaction (Scheme 6).[27]



Enol ether	R^1	R^2	R	Acetal	Duration	Yield,%	Product
27	Ph	H	Et	**28a**	10 min	81	**30a**
27	*p*-Anisyl	H	Et	**28b**	10 min	70	**30b**
27	$CH_3(CH_2)_2$	H	Me	**28c**	30 min	85	**30c**
27	Ph	Me	CH_2	**28d**	24 h	0	**30d**
27	$PhCH_2$	$PhCH_2$	CH_2	**28e**	24 h	0	**30e**
26	Ph	H	Et	**28a**	24 h	0	**29a**
26	*p*-Anisyl	H	Et	**28b**	24 h	0	**29b**
26	$CH_3(CH_2)_2$	H	Me	**28c**	1 h	90	**29c**

Scheme 6. Chemoselective substitution of acetals in 5 M LPDE

Surprisingly, 1-trimethylsilyloxycyclopentene **(26)** reacted much more slowly than 1-trimethylsilyloxycyclohexene **(27)** under otherwise identical conditions. The difference in the reactivity between these two enol ethers is exemplified in their reaction with 2-methoxytetrahydropyran **(31)** (Scheme 7).

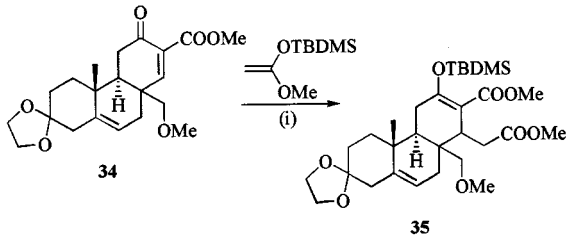


Scheme 7. Chemoselective substitution of acetal with silyl enol ether in 5 M LPDE

While the silyl enol ether **27** reacted with **31** to give the corresponding aldol ether in 90% yield within 30 min, the silyl enol ether **26** failed to react under these conditions even after 5 h. These results are in sharp contrast to the aldol-type condensation promoted by conventional Lewis acids in which such fine tuning of the reactivity for chemoselectivity could not be observed. It must be emphasized that the attempted aldol condensation of silyl enol ethers with aldehydes and ketones failed in 5 M LPDE.[28]

3.3 Michael Addition Reaction in LPDE

Grieco has reported the Michael addition of ketene silyl acetals to activated but highly hindered α,β-unsaturated carbonyl compounds which otherwise undergo Michael addition only under high pressure conditions (Scheme 8).[29]

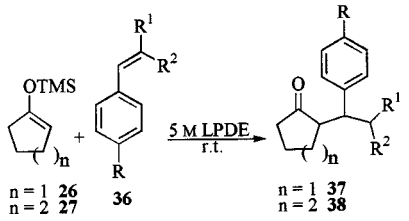


Scheme 8. Michael addition of ketene silyl acetal to hindered α,β-unsaturated ketone: (i) Reagents and reaction conditions (a) 1.0 M LP-DME, 37 °C, 24 h, 93%; (b) 1.0 M LPDE, 36 °C, 1 h, 70%; (c) 1:1 $TiCl_4$ $Ti(OiPr)_4$, <10%

In our studies on the Michael addition of silyl enol ethers to α,β-unsaturated carbonyl compounds we observed that the less reactive silyl enol ethers failed to undergo any Michael addition reaction (Scheme 9).[28,30] It is well-known in the literature that these reactions could be easily promoted using stronger Lewis acids such as $TiCl_4$, trimethylsilyl triflate etc.[31] Therefore, we concluded that the mild Lewis acidity of the lithium ion in LPDE is not strong enough to promote such reactions. However, the Michael addition of silyl enol ethers with the more reactive Michael acceptors such as β-nitro- and β-cyanostyrenes proceeded smoothly in 5 M LPDE leading to the formation of the corresponding Michael adducts in good yields.[30] A series of *para* substituted β-nitro- and β,β-dicyanostyrenes yielded the corresponding Michael adducts as a mixture of diastereoisomers in good yields (Scheme 9).

Experimental evidence strongly suggests a novel silyl transfer mechanism for the Michael addition in 5 M LPDE in that the first equivalent of the silyl enol ether acts as a silylating agent for the silylation and activation of the Michael acceptor and the second equivalent of the silyl enol ether acts as the Michael donor.[30] Complexation of the lithium cation to the lone pair of electrons on the oxygen of the silyl enol ether activates it and makes it a good silylating agent. The mild Lewis acidity of the lithium ion is responsible for the chemoselective complexation in that it complexes with the most basic of the substrates among the silyl enol ether and the nitro- and cyanostyrenes. This mechanism is different from the usually accepted mechanism for the Lewis acid mediated Michael reaction in which the Michael acceptor is activated by the coordination of the Lewis acid followed by the addition of the Michael donor.

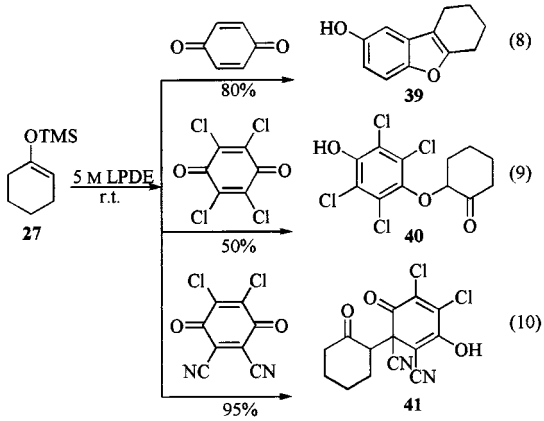
Quinones are excellent Michael acceptors and, due to their low reduction potential, they also undergo electron transfer mediated reactions with nucleophiles.[32] Alkylation of quinones with ketene silyl acetals and allylation with allylsilanes have been reported in 5 M LPDE.[33] Mixing silyl



R	R^1	R^2	Yield, %
H	NO_2	H	85
Cl	NO_2	H	85
Me	NO_2	H	79
OMe	NO_2	H	75
H	CN	CN	85
NO_2	CN	CN	84
H	CHO	H	0
Me	CHO	H	0
OMe	CHO	H	0
H	COMe	H	0

Scheme 9. Chemoselective Michael addition of silyl enol ethers

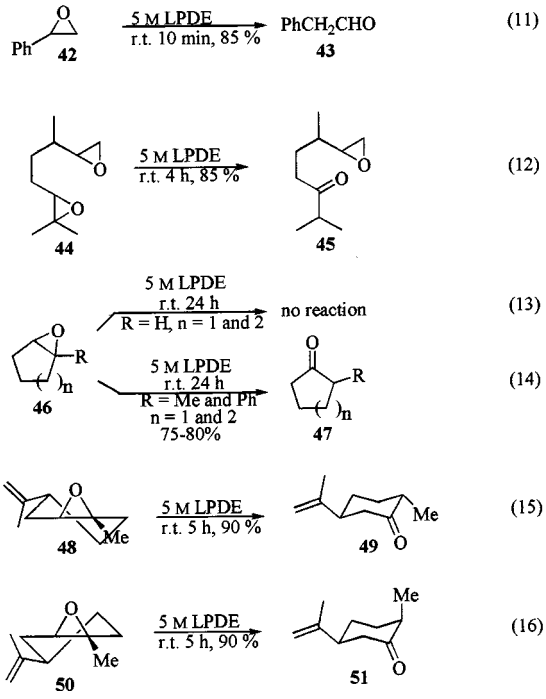
enol ethers with various quinones in 5 M LPDE resulted in the development of the vivid colours characteristic of charge-transfer complexes, which slowly faded with the progress of the reaction. The reaction of benzoquinone, chloranil or DDQ with silyl enol ethers in 5 M LPDE yielded both *C*-alkylated (reaction 10) and *O*-alkylated (reaction 9) products depending upon the quinone (Scheme 10).[30] The LPDE medium should favour the formation of the radical ion-pair intermediates arising from an initial electron transfer from the silyl enol ethers to the quinones; formation of the various products has been explained on the basis of the radical ion-pair coupling reactions either at the oxygen or at the carbon yielding the *O*-alkylated or *C*-alkylated products.[30]



Scheme 10. Reactions of silyl enol ether 27 with various substituted benzoquinones in 5 M LPDE

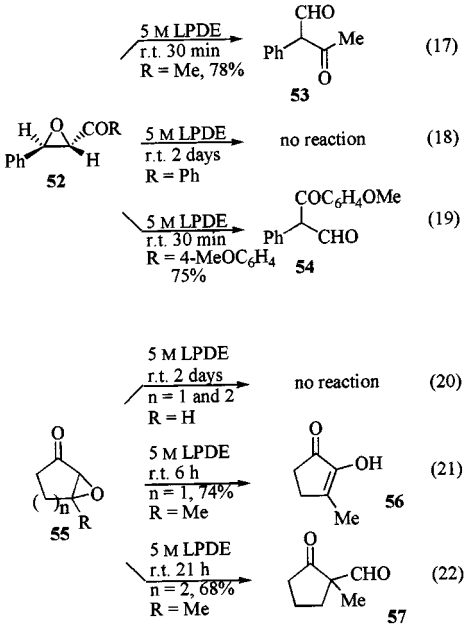
3.4 Rearrangement of Epoxides to Carbonyl Compounds in LPDE

The conversion of an epoxide to a carbonyl compound is a synthetically very useful reaction.[34] However the lack of chemo-, regio-, and stereoselectivity in the epoxide ring opening/rearrangement steps can lead to the formation of multiple products and can limit the use of this reaction in synthetic sequences.[34] Although the most commonly used reagent for this reaction is BF_3 it does not offer any chemoselectivity and often leads to the formation of a mixture of products unless the epoxide is structurally biased for regiospecificity in the ring opening step.[34] Hence it is desirable to have a mild reagent that is capable of effecting this transformation under neutral conditions. The rearrangement of epoxides in 5 M LPDE showed high chemo- and regioselectivity often resulting in a single product which is easily isolated under neutral reaction and workup conditions.[35] The examples in Scheme 11 illustrate the high chemo- and regioselectivity observed in LPDE. Only those oxiranes with either a benzylic (reaction 11) or a tertiary centre (reactions 12 and 14) undergo rearrangement in LPDE. The epoxides of terminal olefins are much less reactive than internal olefin epoxides, thus enabling chemoselectivity (reaction 12).



Scheme 11. Rearrangement of epoxides to carbonyl compounds in 5 M LPDE

In the case of limonene epoxide the rearrangement was stereospecific in that the *cis* epoxide **50** rearranged to give the *cis*-dihydrocarvone **51** (reaction 16), whereas the *trans* epoxide **48** gave only *trans*-dihydrocarvone **49** (reaction 15). In a similar manner, the epoxides from α,β-unsaturated carbonyl compounds rearranged with high chemo- and regioselectivities leading to the formation of 1,3-dicarbonyl com-

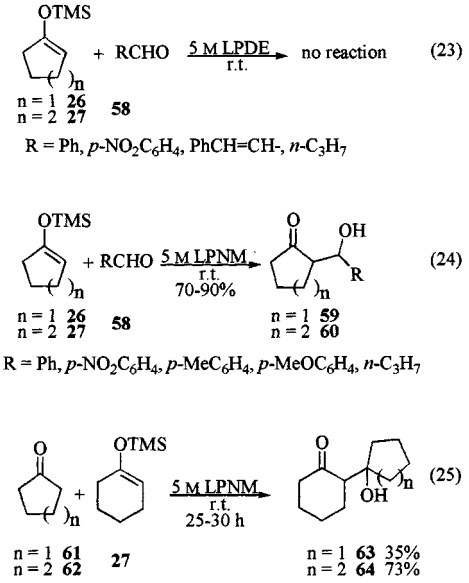


Scheme 12. Rearrangement of α,β-epoxy ketones in LPDE

pounds in 5 M LPDE (Scheme 12, reactions 17−22).[36] The epoxide ring opening/rearrangement reaction in LPDE could proceed by the coordination of the lithium ion to the epoxide oxygen, resulting in the weakening of the epoxide C−O bond, followed by the regioselective ring opening of the epoxide to give the most stable carbenium ion.[36] This explains why only benzylic and tertiary epoxides undergo rearrangement, because only then can a stable tertiary or benzylic carbenium ion be formed. The mild Lewis acidity of the lithium ion ensures high chemoselectivity.

4. A Comparison of Lithium Perchlorate in Diethyl Ether and Nitromethane

Although lithium perchlorate has been used in several organic solvents for effecting synthetic transformations, the most commonly used solvent is diethyl ether. The Lewis acidity of the lithium ion is a major factor, although probably not the only factor that governs the reactivity of organic substrates in lithium perchlorate/organic solvent media. The Lewis acidity of the lithium ion in organic solvents depends on the basicity and coordinating ability of the solvent. Diethyl ether is a coordinating solvent (n-donor) and the coordination of the lithium ion to the lone pair of oxygen in ether moderates the Lewis acidity of the lithium ion.[17,20] Although the moderated Lewis acidity of the lithium ion is useful in effecting very selective synthetic transformations, some reactions fail to proceed in LPDE due to the weak Lewis acidity of the lithium ion. For example, the aldol and Michael reactions of silyl enol ethers with aldehydes and ketones failed to proceed in 5 M LPDE medium (Scheme 13, reaction 23).[28,30] In order to overcome these limitations we explored the possibility of using nitromethane as a solvent in combination with lithium perchlorate. Ayerbe and Cossio have reported lithium perchlorate in nitromethane to be a more effective medium than LPDE for certain Diels−Alder reactions.[37] In comparison to diethyl ether, nitromethane is a poor cation-coordinating solvent as reflected by its donor number (19.2 vs. 2.7 for diethyl ether and nitromethane, respectively).[1] Due to its higher dielectric constant and dipole moment, nitromethane is a more polar solvent than diethyl ether.[1] Due to these factors the Lewis acidity of the lithium ion in nitromethane is expected to be higher than that in diethyl ether. The formation of polar and ionic intermediates would also be facilitated in nitromethane. In order to verify these hypotheses we examined the aldol and Michael reaction of silyl enol ethers in 5 M lithium perchlorate/nitromethane (LPNM).

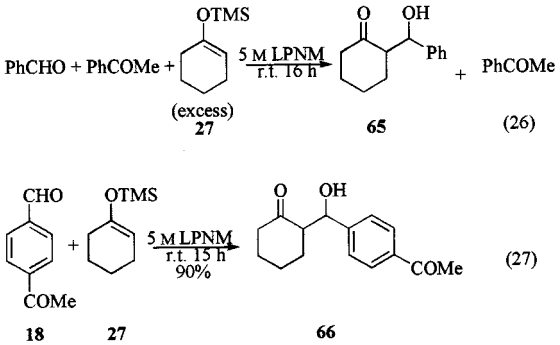


Scheme 13. Aldol condensation of silyl enol ethers in 5 M LPNM

4.1 The Aldol and Michael Reactions of Silyl enol Ethers in LPNM

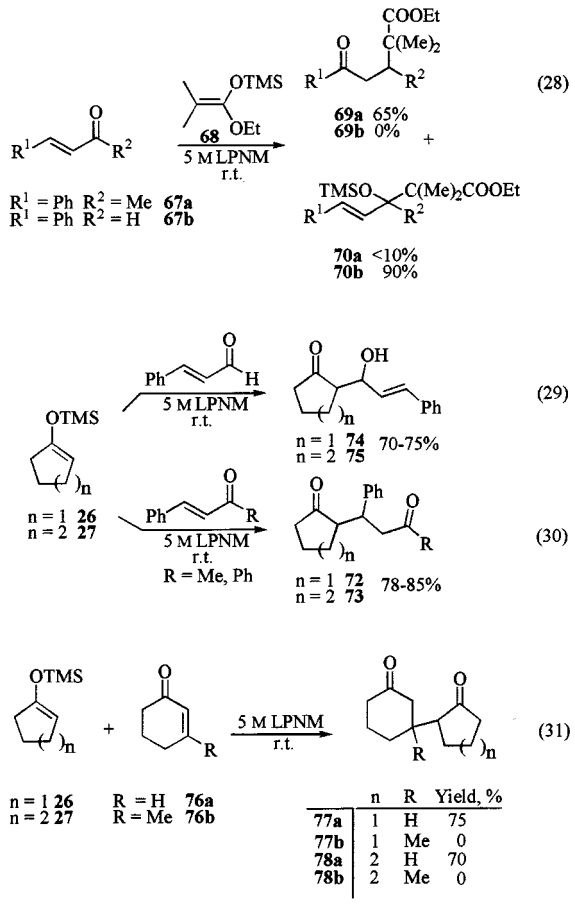
The aldol condensation of silyl enol ethers **26** and **27** with aliphatic and aromatic aldehydes, and also with cyclic ketones, proceeded smoothly, although the aldehydes reacted much faster than the cyclic ketones to give the corresponding aldol product in good yields as a mixture of diastereoisomers. (Scheme 13, reactions 24 and 25).[38]

The chemoselectivity is illustrated in the examples shown in reactions 26 and 27 (Scheme 14) wherein an aldehyde and a ketone are clearly differentiated.



Scheme 14. Chemoselectivity in aldol condensation in 5 M LPNM

A high regioselectivity (1,2 vs. 1,4-addition) is observed in the addition of silyl enol ethers to α,β-unsaturated aldehydes and ketones in LPNM.[39] The aldehydes selectively undergo 1,2-addition (reactions 28 and 29), whereas the ketones undergo 1,4-addition (reactions 28 and 30) very selectively (Scheme 15). In the case of cyclic ketones the sterically hindered β-substituted ketone did not react (reaction 31).

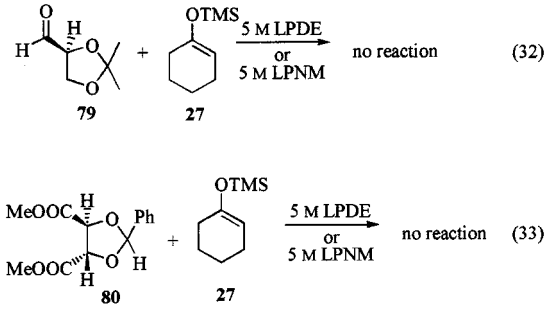


Scheme 15. Selective 1,2- and 1,4-addition of silyl enol ethers in LPNM

From a comparison of the aldol and Michael reactions of carbonyl compounds with silyl enol ethers in LPDE and LPNM it is evident that the Lewis acidity of the lithium ion in nitromethane is greater than that in ether for the reasons stated above. Infrared spectroscopy provides direct evidence not only for the activation of carbonyl compounds by lithium ion in these media but it also gives information on the relative Lewis acidity of the lithium ion. For example, the C=O stretching frequency of benzaldehyde is 1708 cm^{-1} in ether compared to 1699 cm^{-1} in 5 M LPDE, and that for isobutyraldehyde is 1734 cm^{-1} in ether compared to 1718 cm^{-1} in 5 M LPDE.[25,39] Such a decrease in the carbonyl stretching frequency is consistent with the lithium ion coordination to the carbonyl oxygen. A similar conclusion has also been reported by other workers abased on IR and NMR spectroscopic studies.[20,40] Similarly, the carbonyl stretching frequency of benzaldehyde is shifted from 1724 cm^{-1} in nitromethane to 1712 cm^{-1} in 5 M LPNM.[39] The carbonyl stretching frequency shifts are lower in the case of LPDE than for LPNM. The extent of the shift in the presence or absence of lithium perchlorate is a qualitative reflection of the Lewis acidity of the lithium ion, which depends on the basicity of the medium: the lower the solvent basicity the higher is the Lewis acidity of the lithium ion in that solvent. Therefore, the higher reactivity of carbonyl compounds with silyl enol ethers towards aldol- and Michael-type reactions in LPNM compared to LPDE is due to the increased Lewis acidity of the lithium ion in nitromethane in comparison with diethyl ether.

5. Future Prospects

There is an enormous scope in utilizing the alkali and alkaline earth metal salts that are soluble in organic solvents as Lewis acids to carry out synthetic transformations. The attempted reaction of silyl enol ether **27** with D-gylceraldehyde acetal (**79**) (aldol condensation) or the dimethyl tartrate acetal of benzaldehyde (**80**) (acetal substitution) failed in both LPDE and LPNM media (Scheme 16, reactions 32 and 33)[41] leaving room for further improvement of the lithium-perchlorate-based medium for synthetic transformations.



Scheme 16. Attempted aldol and acetal substitution in LPDE and LPNM

The ability to tune the Lewis acidity of metal ions based on the solvent polarity and basicity and the counter ion basicity is important in achieving selectivity in Lewis acid catalyzed reactions. With respect to the modulation of the Lewis acidity of the lithium ion and related alkali and alkaline earth metal ions, solvent basicity and the counterion play a major role. There is also potential for the variation of the counter anion to enhance the Lewis acidity of the metal ion. For example, lithium triflate is a good candidate in this respect because the Lewis acidity of lithium ion in a given solvent is expected to be higher than that of lithium perchlorate.[42] Diastereoselective and enantioselective transformations need to be explored using these Lewis acids. It should be possible to accomplish high diastereo- and enantioselectivites by suitably adjusting the reactivity of substrates which are in turn controlled by tuning the Lewis acidity of the metal ion.

6. Conclusions

Anhydrous lithium perchlorate is highly soluble in several organic solvents such as diethyl ether, nitromethane, acetonitrile and ethyl acetate. The lithium ion in these solvents acts as a Lewis acid and the Lewis acidity is dependent on the solvent basicity. Highly concentrated solutions of lithium perchlorate in the above solvents promote several synthetic transformations which are otherwise difficult to perform under normal conditions. Apart from the acceleration of the rate of the reaction, high chemo-, regio-, and stereoselectivities have been observed, as demonstrated by the many examples cited in the text. The reactions are generally carried out under very mild conditions, often at room temperature and under essentially neutral reaction and workup conditions, which makes lithium perchlorate/organic solvent systems highly desirable and useful to synthetic organic chemists.

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