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Oxidative α-sulfonyloxylation of aryl ketones with sulfonic acids by lead tetraacetate

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A new method portraying the utility of lead tetraacetate as an oxidizing agent in the synthesis of α-sulfonyloxyketones from aryl ketones and sulfonic acids has been described. This methodology offers a new alternative for the synthesis of a series of α-sulfonyloxyketones with broad substrate scope, easy availability of reactants as well as the use of simple oxidant.

Keywords: Oxidation, α-Sulfonyloxyketones, Aryl ketones, Sulfonic acids, Lead tetraacetate

α-Sulfonyloxyketones have been widely explored in organic syntheses[1,2] because of the presence of the versatile sulfonyloxy moiety which can function as a protecting group or leaving group depending on the nature of the reaction. Prominent among these are their uses as precursors in Favorskii ring contraction reactions[1a,1e], in photochemical reactivity studies[1b], in the synthesis of optically active 1,2-diol monosulfonates and terminal epoxides[1d], synthesis of furo[3,2-*c*]coumarins[1f] and in the formation of polysubstituted cyclopropanes[1g]. α-Sulfonyloxyketones are also important organic intermediates for azidation of ketones[2] and in the synthesis of various heteroaromatics compounds such as thiazoles, selenazoles, imidazoles, coumarins, oxazoles, benzofurans, pyrazoles and triazoles[3a-g].

Various synthetic approaches have been reported for the synthesis of α-sulfonyloxyketones[4-7]. Mostly, these reported methods undergo oxidative transformation of ketones[4], alcohols[4b,4e,5a-b] and alkynes[6] into the corresponding α-sulfonyloxyketones in the presence of hypervalent iodine reagents as tosylating agents. While only scanty methods have been found for the preparation of α-sulfonyloxyketones from acid chlorides, enolizable ketones and alkynes using *p*-toluenesulfonic acid, thallium(III) *p*-tolylsulphonate (TTS) and ammonium persulfate, $\{(NH_4)_2S_2O_8\}$ as the tosylating agents.

In regard to this, our literature survey revealed that using lead tetraacetate (LTA) would have been one of the first oxidant to have been considered for the above conversion as no such report is available so far. We thus report a new method using lead tetraacetate (LTA) as oxidant in a variety of oxidative transformations of ketones to α-sulfonyloxyketones using sulfonic acids as the tosylating agent.

Experimental Section

Lead tetraacetate have been prepared using literature procedures[9]. All commercially available reagent grade chemicals were purchased from Sigma Aldrich, Alfa Aesar, Spectrochem and TCI Chemicals and used as received without further purification unless otherwise stated. All solvents were directly used without drying. Thin layer chromatography (TLC) was performed on aluminium sheets pre-coated with silica gel 60F254 (0.2 mm thicknesses) in which the spots were visualized with UV light (λ = 254 nm). For purification, column chromatography was carried out over silica gel 100-200 mesh. Melting points were recorded by the open capillary tube method and are uncorrected. IR spectra were recorded on a Perkin-Elmer Spectrum 400 FTIR instrument, and the frequencies are expressed in cm^{-1}. ^1H and ^{13}C NMR were recorded in $CDCl_3$ on a Bruker Avance III 400 spectrometer with TMS as internal standard (400 MHz for ^1H NMR, 100 MHz for ^{13}C NMR) at room temperature, the chemical shifts (δ) are expressed in ppm and *J* values are given in Hertz (Hz). The following abbreviations are used to indicate the multiplicity: singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). All first order splitting

patterns were assigned based on the appearance of the multiplet. Splitting patterns that could not be easily interpreted were designated as multiplet (m). Mass analyses and HRMS were obtained on a Finnigan-LCQDECA mass spectrometer and a Bruker Daltonics Bio-TOF-Q mass spectrometer by the ESI method, respectively.

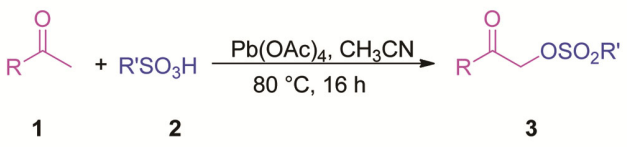
General procedure for the oxidation of aryl ketones and sulfonic acids by lead tetraacetate for the synthesis of α-sulfonyloxy aryl ketones, 3a-q

A mixture of aryl ketones (**1**) (1.0 mmol) and sulfonic acids (**2**) (1.0 mmol) were added to a magnetically stirred suspension of LTA (2.0 mmol) in 5 mL of acetonitrile. The reaction was first stirred in an oil bath at 80°C for 16 h. The completion of the reaction was monitored by thin layer chromatography (TLC). The mixture was diluted with ethyl acetate (3×10 mL). The combined filtrate was transferred to a separating funnel, neutralized with aqueous $NaHCO_3$ (2×10 mL) and washed with brine (2×10 mL). The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude products were purified by silica column chromatography using ethyl acetate-hexane as an eluent to obtain the corresponding products **3a-q**. The spectroscopic analytical data of the synthesized compounds are given in the Supporting Information.

Results and Discussion

Based on the successful utility of LTA on our earlier work, *i.e*. the Favorskii type rearrangements of aryl ketones[8a] and α,β-unsaturated ketones[8b], we herein wish to report a direct method for the α-sulfonyloxylation of aryl ketones with sulfonic acids using LTA as the oxidant (Scheme 1).

To obtain the optimized reaction condition for the synthesis of α-sulfonyloxyketones, we have chosen acetophenone (**1a**) (1.0 mmol) and *p*-toluenesulfonic acid monohydrate (**2a**) (1.0 mmol) as the model substrates (Table 1). Initially, a mixture of acetophenone (**1a**) (1.0 mmol) and *p*-toluenesulfonic acid (**2a**) (1.0 mmol) was stirred with LTA (1.0 mmol) in 5 mL of hexane at RT for



Scheme 1 — Synthesis of α-sulfonyloxyketones

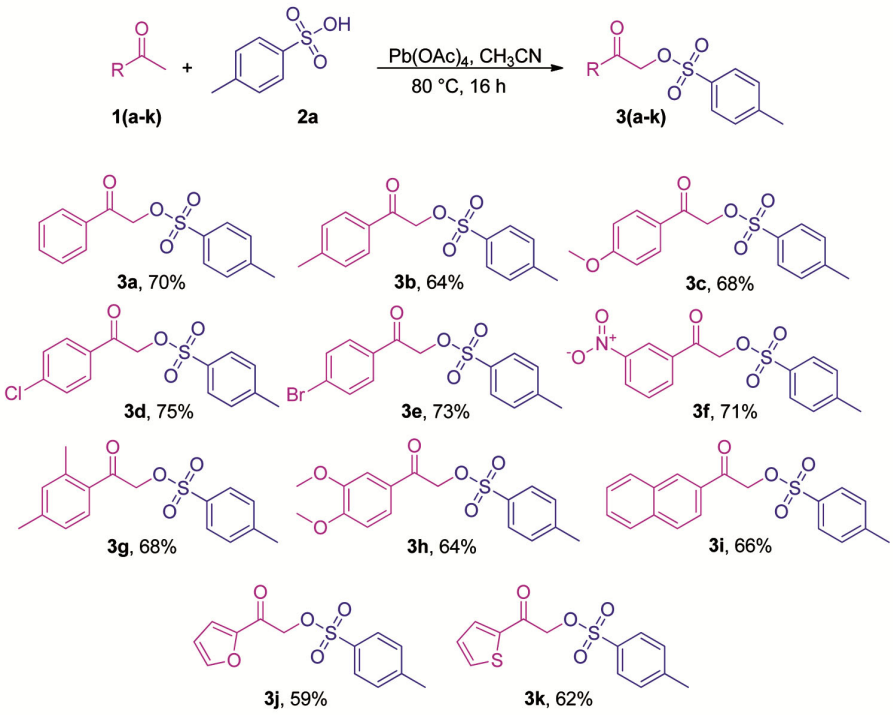
36 hours, the desired product 2-oxo-2-phenylethyl 4-methylbenzenesulfonate (**3a**) was obtained in 20% yield (Table 1, entry 1). The reaction mixture was then allowed to stir in an oil bath at 40°C and the yield of product **3a** increases to 37% in 24 hours (Table 1, entry 2). The reaction temperature was further raised (Table 1, entry 3 and 4) and improvement in the yield product of product **3a** (50%) was observed at 80°C (Table 1, entry 4). We then examined the solvent effect (Table 1, entry 4-9) in this reaction; it was found that the best result was achieved when CH_3CN was used as a solvent (**3a**, 65%, Table 1, entry 9). The effect of the amount of LTA was also investigated (Table 1, entry 10-11). When **1a** and **2a** was stirred with 1.5 equiv of LTA in CH_3CN for 24 hours product **3a** moderately increases to 68% (Table 1, entry 10). When the amount of LTA was increased to 2.0 equiv, the yield of product **3a** obtained was 70% in 16 hours (Table 1, entry 11). Further increased of the reaction temperature did not increase the yield of product **3a** (Table 1, entry 12-13). It may be noted that when the reaction mixture was performed in the absence of LTA no desired product was detected (Table 1, entry 14). From these findings, it was found that from Table 1, entry 11 gave the optimum yield of the product **3a** (70%).

Under the optimized reaction conditions, the scope of the reaction was explored by varying the substrates of aryl ketones (**1**) and sulfonic acids (**2**) as presented in Scheme 2 and Scheme 3.

Table 1 — Optimization of Reaction Conditions[a]

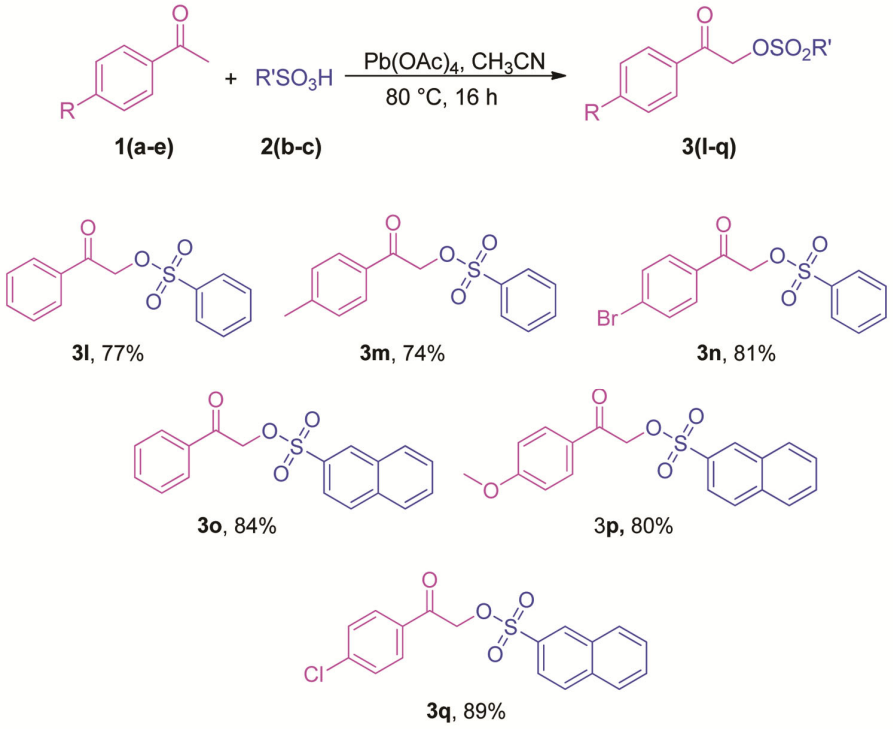
Entry	Solvent	LTA (equiv)	Temperature °C	Time (h)	Yield (%)
1	Hexane	1.0	RT	36	20
2	Hexane	1.0	40	24	37
3	Hexane	1.0	60	24	45
4	Hexane	1.0	80	24	50
5	Toluene	1.0	80	24	52
6	Benzene	1.0	80	24	57
7	DCM	1.0	80	24	55
8	EtOH	1.0	80	24	20
9	CH_3CN	1.0	80	24	65
10	CH_3CN	1.5	80	24	68
11	CH_3CN	2.0	80	16	70
12	CH_3CN	2.0	100	16	70
13	CH_3CN	2.0	100	24	72
14	CH_3CN	–	80	16	0

[a]Reaction conditions: ketone **18** (1 mmol), sulfonic acid **25** (1 mmol), solvent (5 mL)



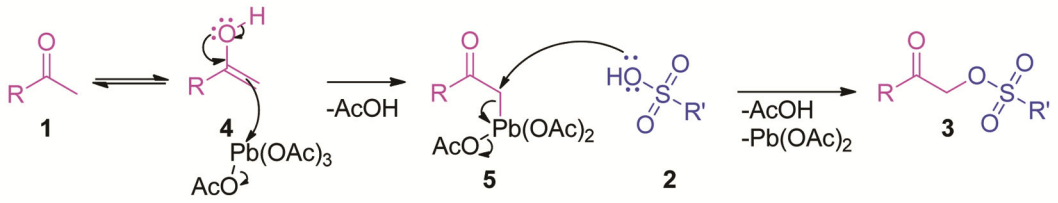
Reaction conditions: **18** (1 mmol), **25** (1 mmol), LTA (2 mmol), CH_3CN (5 mL), 80°C, 16 h.

Scheme 2 — Substrate scope of derivatives of aryl ketones with *p*-toluenesulfonic acid



Reaction conditions: **18** (1 mmol), **25** (1 mmol), LTA (2 mmol), CH_3CN (5 mL), 80°C, 16 h.

Scheme 3 — Substrate scope of derivatives of aryl ketones and sulfonic acids



Scheme 4 — Plausible mechanism for the formation of α-sulfonyloxyketones

The reaction of a variety of substituted aryl ketones (**1**) and *p*-toluenesulfonic acid (**2a**) with LTA in acetonitrile was investigated first. Various substituted acetophenone with electron-donating or withdrawing groups such as **1b** (*p*-Me), **1c** (*p*-OMe), **1d** (*p*-Cl), **1e** (*p*-Br) and **1f** (*m*-NO_2) were carried out and irrespective of the nature of the substituents on the ring, all the reactions proceeded smoothly to give the corresponding α-tosyloxyketones in good yields (Scheme 2, **3b**, 64%; **3c**, 68%; **3d**, 75%; **3e**, 73%; **3f**, 71%). Di-substituted acetophenones such as 2,4-dimethyl acetophenones (**1g**) and 2,3-dimethoxy acetophenones (**1h**) also reacted readily and the corresponding products **3g** and **3h** were afforded in 68% and 64% yields. The protocol was also extended to bulkier substrates of aromatic ketone which is the 2-acetylnaphthalene (**1i**) and the respective α-tosyloxy product **3i** was obtained in 66% yield. However, the reaction with heteroaryl ketones like 2-acetylfuran (**1j**) and 2-acetylthiophene (**1k**) with *p*-toluenesulfonic acid (**2a**) produced the corresponding products in moderate yields (Scheme 2, **3j**, 59% and **3k**, 62%).

We then extended the generality of the method to other sulfonic acid derivatives such as phenylsulfonic acid (**2b**) and naphthalene sulfonic acid (**2c**) under the same reaction condition. Reactions of phenylsulfonic acid (**2b**) and naphthalene sulfonic acid (**2c**) with aryl methyl ketones bearing no substituent (*p*–H), electron-donating substituents (*p*–Me, *p*–OMe) and halogenated electron-withdrawing substituents (*p*–Br, *p*–Cl) proceeded smoothly to give the corresponding products in excellent yields (Scheme 3, **3l**, 77%; **3m**, 74%; **3n**, 81%; **3o**, 84%; **3p**, 80%; **3q**, 89%).

A plausible mechanism for the reaction is proposed as shown in Scheme 4. The first step includes the enolization of aryl ketones (**1**) to **4** followed by the nucleophilic attack of **4** on LTA resulting in the formation of intermediate **5**. Finally, sulfonic acids (**2**) attack the α-position of the intermediate **5** producing the corresponding α-sulfonyloxyketone (**3**) with the release of $Pb(OAc)_2$ where Pb (IV) gets reduced to Pb (II) with the elimination of AcOH.

Conclusion

In conclusion, we have developed a new method for the synthesis of α-sulfonyloxyketones starting from aryl ketones and sulfonic acid in the presence of LTA in moderate to excellent yields. We believe that the present method provides a useful alternative for the synthesis of α-sulfonyloxy ketones which are important precursors in organic synthesis.

Supplementary Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

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