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Communication

Synthesis of Sulfonyldiazomethanes and Acetyldiazomethanes via an Alumina-Mediated Decarboxylation Strategy

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Diazo compounds are widely adopted in organic synthesis due to their carbine characteristics. One of the most interesting diazo compounds is diazolsulfonyl. Here, in the current study, we found that diazolsufonyl compounds could be prepared with moderate to excellent yield through decarboxylation of diazosulfonyl acetates by neutral alumina. We hope that this mild and simple method might inspire wider application of these useful compounds.

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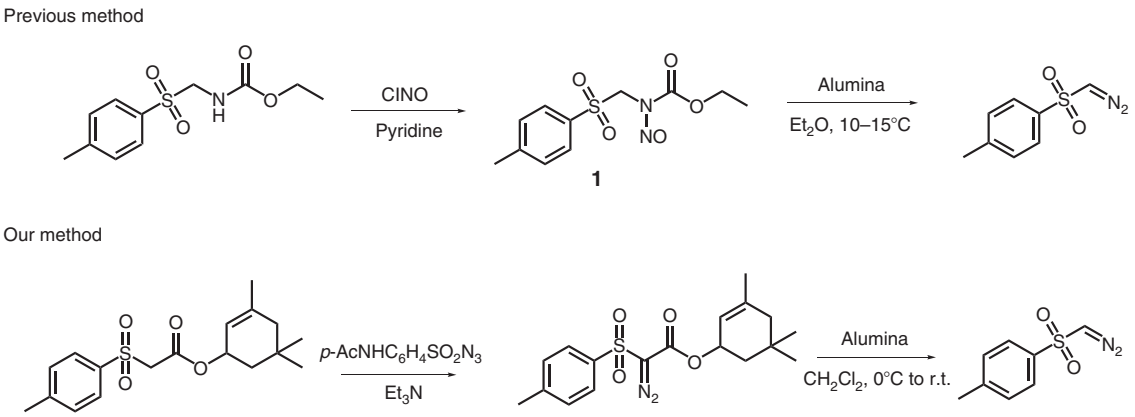
Diazo compounds are very useful in organic synthesis.[1] Due to their carbene characteristics, these types of compounds have been studied extensively for their applications including cyclopropanation,[2] C–H insertion reaction,[3] and Wolff rearrangement.[4] α-Diazocarbonyls are well-known species regarding their synthesis and reactivity,[5] whereas α-diazosulfonyl compounds have been less explored in spite of the expected reactivity resemblance with that of α-diazocarbonyls.[6] Due to their metabolic stability and generally favourable physical properties of the sulfonyl groups,[7] α-diazosulfonyl compounds could potentially provide straightforward access to structurally unique small libraries for medicinal chemistry. Here, we describe a simple procedure for the preparation of diazosulfones through a novel neutral alumina-mediated decarboxylation of diazosulfonyl acetates. Interesting substrate dependence is discussed, which led to our proposed mechanism.

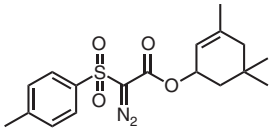
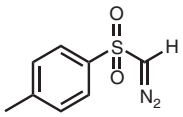
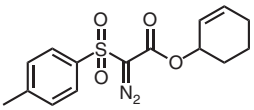
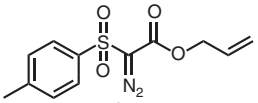
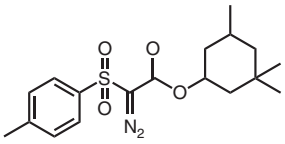
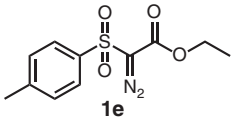
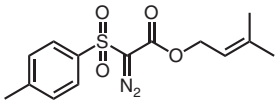
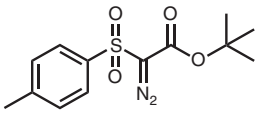
Currently, the most widely used methods to synthesize diazosulfonyl compounds are via the alumina-promoted decarboxylation of nitroso compound **1** (Scheme 1)[8] and the deacetylation of acetyl compounds.[9] Notably, the former process required the use of highly toxic nitrosyl chloride gas.

While attempting to synthesize tosyldiazomethane using the deacetylation protocol, we discovered that the formation of the desired product was much more facile when we replaced the acetyl group with a 3,5,5-trimethylcyclohex-2-enol-derived



Scheme 1. Methods employed to synthesize sulfonyldiazomethane. ClNO = nitrosyl chloride; r.t. = room temperature.

Table 1. Decarboxylation of various ester analogues

Entry	Substrates	Product[A]
1	 **1a**	 **2a** (98 %)
2	 **1b**	No reaction
3	 **1c**	No reaction
4	 **1d**	No reaction
5	 **1e**	No reaction
6	 **1f**	**2a** (70 %)
7	 **1g**	**2a** (61 %)

[A]The numbers in parentheses represent the yields.

ester. During initial substrate screening, we were surprised to find that decarboxylation seemed to occur exclusively for this particular ester. Simpler ethyl, benzyl, or saturated analogues did not afford any desired tosyldiazomethane product under otherwise identical conditions (Table 1).

These seemingly peculiar results inspired us to propose a carbocation decarboxylation pathway (Scheme 2). In the case of 3,5,5-trimethylcyclohex-2-enyl ester, decarboxylation occurs through the formation of thermodynamically stable tertiary allylic carbocation. Either the esters lack the double bond or substitution does not proceed due to the resulting higher energetic cationic species. To verify this hypothesis, we examined *t*-Bu and 3-methylbut-2-enyl esters. To our delight, decarboxylation occurred smoothly for both substrates in the presence of neutral alumina. Spectroscopically pure product was obtained by simple filtration and concentration. No flash column is required for most substrates. It is noted that certain tosyldiazomethanes decomposed slightly on Al_2O_3, as evidenced by the pink colour on the alumina surface. The yield and purity were nevertheless not affected. Silica gel can also promote this reaction, although yields were lower. Decarboxylation under basic conditions (KOH, LiOH, or pyrrolidine) also led to tosyldiazomethane formation, however, with a lower efficiency.

This method is general for various benzene-sulfonyldiazomethanes-bearing substituents, regardless of electronic properties. Interestingly, it can also be extended to simple alkyl sulfonyldiazomethane synthesis. Those compounds were obtained at slightly lower yields, partially due to product instability in the presence of alumina (Table 2).

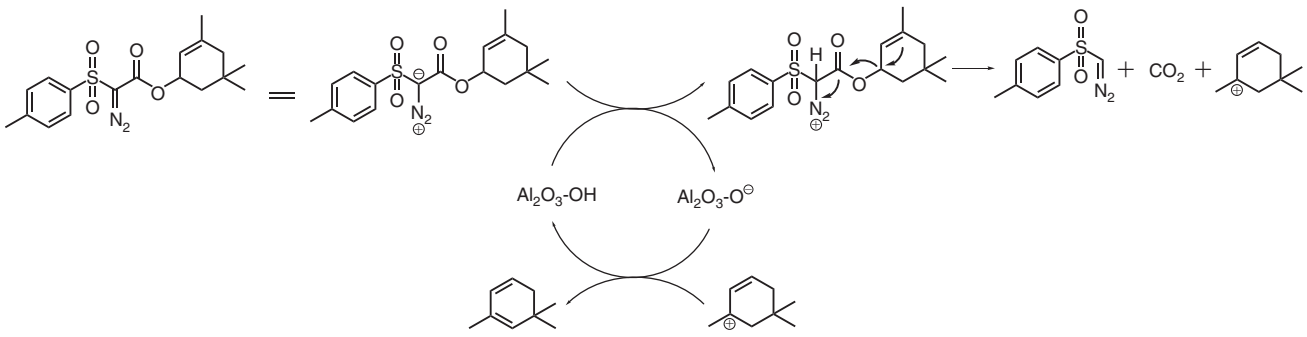
This method can be also used for decarboxylation of acetyldiazomethanes, and the yield was modest (Scheme 3).

In summary, we have developed a simple method for the synthesis of α-diazosulfonyl compounds. The products were obtained in high yield and purity through neutral alumina-mediated decarboxylation. The formation of a stable allylic carbocation was proposed to be the driving force for the facile decarboxylation, supported by experimental data. Further studies and applications of these useful diazo analogues will be reported in due course.

Experimental

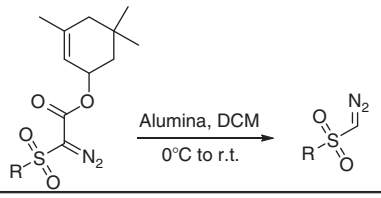
General Procedure for Decarboxylation by Neutral Al_2O_3

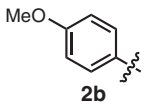
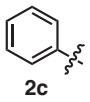
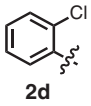
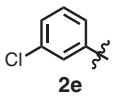
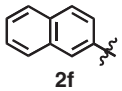
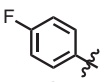
To the white solid of 5 g Al_2O_3 in a Schlenk tube was added anhydrous dichloromethane (DCM; 15 mL) under the protection of nitrogen, and the suspension was stirred at 0°C. The Schlenk

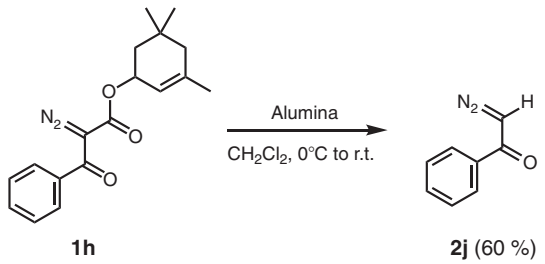


Scheme 2. Proposed mechanism for decarboxylation.

Table 2. Synthesis of sulfonyldiazomethanes



Entry	R	Yield [%]
1	 **2b**	73
2	 **2c**	99
3	 **2d**	98
4	 **2e**	77
5	 **2f**	96
6	 **2g**	90
7	 **2h**	70
8	 **2i**	64



Scheme 3. Decarboxylation of acetyldiazomethanes.

tube was covered with aluminium foil for protection from light. Then, diazo acetate was introduced into the tube at 0°C and reacted at room temperature. The reaction was monitored by thin layer chromatography until diazo acetate was consumed. The reaction mixture was filtrated and washed with DCM to ensure that the product was thoroughly washed out. The yellow filtrate was concentrated by rotary evaporation at room temperature to obtain a yellow oil or solid. The raw product was purified by chromatography column (ethyl acetate/petroleum ether). The product was stored well at −20°C in the dark.

Supplementary Material

Additional experimental details and spectroscopic data are available on the journal's website.

Acknowledgement

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