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Specific intramolecular aromatic C–H insertion of diazosulfonamides

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ABSTRACT

The chemoselectivity in the intramolecular C–H insertion of various diazosulfonamides has been experimentally studied. The results reveal that the aliphatic 1,4-, 1,5-, or 1,6-C(sp^3)–H insertions of diazosulfonamides are not accessible, while the aromatic 1,5-C(sp^2)–H insertion can be realized specifically by adjusting the diazo-adjacent group. In addition, the general chemoselectivities in the intramolecular C–H insertions of diazosulfonyl compounds are summarized. Generally, diazosulfones undergo both aromatic 1,5-C(sp^2)–H and aliphatic 1,5- and 1,6-C(sp^3)–H insertions, while diazosulfonates undergo aliphatic 1,5- and 1,6-C(sp^3)–H insertions. However, diazosulfonamides only undergo aromatic 1,5-C(sp^2)–H insertion.

1. Introduction

The transition metal-catalyzed intramolecular aromatic (sp^2) and aliphatic (sp^3) C–H insertions of diazo compounds have provided one of important and efficient synthetic methods of carbocycles and heterocycles through the new C–C bond formation.[1] Generally, the chemoselectivity in the intramolecular C–H insertion of diazocarbonyl compounds (Fig. 1, **1**), including diazoketones (**1**, X = CR^1R^2), diazoesters (**1**, X = O), and diazoamides (**1**, X = NR^1), has been well clarified,[1] and it has been widely used to construct complex and useful structures, for example, natural products.[2] Contrastingly, diazosulfonyl compounds (Fig. 1, **2**), of which the intramolecular C–H insertion would lead to thiacycles, have not received much attention to date. Only a limited number of reports on diazosulfones (**2**, X = CR^1R^2) and diazosulfonates (**2**, X = O) have been accessible.[3–7] In 1986, Durst and co-workers realized the aromatic 1,5-C(sp^2)–H insertion of (diaryl)methyl diazosulfones.[3] Pioneering work from Novikov's,[4a] Du Bois's,[5] and Maguire's[6a] groups revealed that diazosulfones and diazosulfonates were susceptible to the aliphatic 1,6-C(sp^3)–H insertion to deliver the corresponding six-membered cyclosulfones and δ-sultones under rhodium- and copper-catalyzed conditions. Although it was stated by Du Bois that diazosulfones and diazosulfonates had a strong proclivity for the aliphatic 1,6-C(sp^3)–H insertion, the aliphatic 1,5-C(sp^3)–H insertion was also observed in several cases.[4b,6b,7] Novikov's group discovered that the chemoselectivity between aliphatic 1,5- and 1,6-C(sp^3)–H insertions could be tuned by the Thorpe-Ingold effect and catalyst ligand effect.[4b] Maguire's[6b] and Zhang's[7] groups realized the specificity of the aliphatic 1,5-C(sp^3)–H insertion of diazosulfones via copper and cobalt catalyses, respectively. The specificity was mainly caused by the pendant aryl,[6b,7] alkenyl,[7] and allenyl[7] groups that activated their adjacent C–H bonds.

Recently, we put forward the concept of *diazosulfonamides* (**2**, X = NR′),[8] and realized the rhodium- and copper-catalyzed specifically intramolecular aromatic 1,5-C(sp^2)–H insertion of *N,N*-diaryl diazosulfonamides to prepare *N*-aryl benzo-γ-sultams.[8] However, when *N*-aryl-*N*-alkyl or *N,N*-dialkyl diazosulfonamides are employed, the C(sp^3)–H insertion—potentially including 1,4-, 1,5-, and even 1,6-insertion—of the *N*-alkyl group of diazosulfonamides also represents one of the concerned issues in this field (Scheme 1). Thus, the chemoselectivity will become complex, and it is of significant use to find out which reaction pathway predominates. We have experimentally studied the general chemoselectivities between different types of the intramolecular C–H insertions of diazosulfonamides, and found that diazosulfonamides favored to undergo aromatic 1,5-C(sp^2)–H insertion only (Scheme 1). We hope the current study on the chemoselectivity could offer

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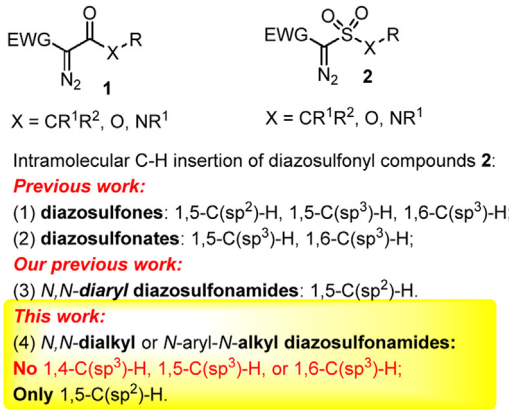


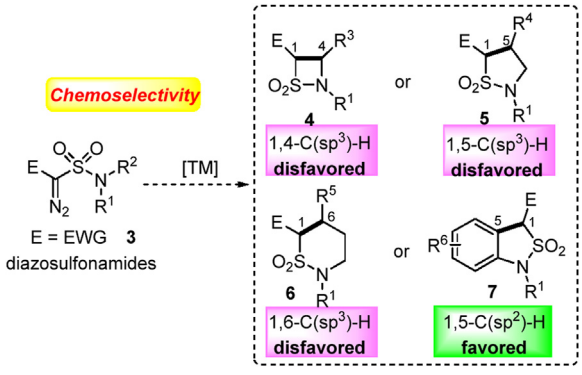
Fig. 1. Intramolecular insertions of diazocarbonyl compounds (**1**) and diazosulfonyl compounds (**2**).

some guidance to the synthetic community concerning diazosulfonyl chemistry.

2. Results and discussion

2.1. Aliphatic sp^3 C–H insertions

To observe the aliphatic C–H insertion selectivity (Scheme 1), we designed and synthesized a number of *N*-alkyl diazosulfonamides **3a-m** (Fig. 2), and subjected them to various transition-metal catalytic conditions. On the basis of previously results,[1h] the aliphatic C–H insertion follows a concerted electrophilic mechanism via a three-membered transition state. *N,N*-Dibenzylsulfonamide **3a** and *N*-aryl diazosulfonamides **3b-e** were completely consumed and gave complex brown mixtures, from which no aliphatic 1,4-C(sp^3)–H insertion product β-sultams were observed, even though different copper and rhodium catalysts in various solvents at different temperatures were attempted.[9] Next, we tested the aliphatic 1,5- and 1,6-C–H insertions, of which the products would be γ-sultams and δ-sultams, respectively. Significantly different from the results of diazosulfones and diazosulfonates, under the tested conditions, diazosulfonamides **3f-i** were completely converted into complex brown mixtures, without any 1,4-, 1,5-, or 1,6-C(sp^3)–H insertion products observed. In the aliphatic C–H insertions of diazocarbonyl compounds, the rigid structure such as a cyclic component would render unexpected regioselectivity.[10] However, the reactions of similarly structured diazosulfonamides **3j-m** with aliphatic rings gave no identified products but complex brown mixtures.



Scheme 1. Aliphatic 1,4-, 1,5-, 1,6-C(sp^3)–H and aromatic 1,5-C(sp^2)–H insertions of diazosulfonamides.

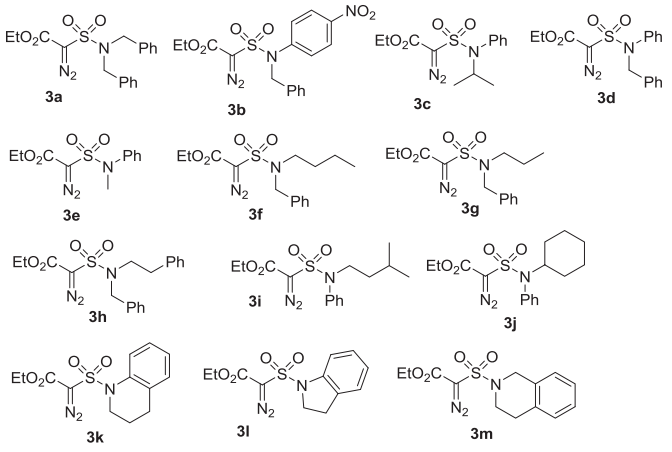
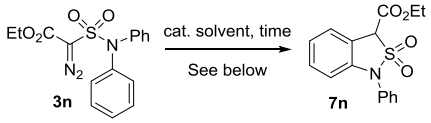


Fig. 2. Designed diazosulfonamides for the C(sp^3)–H insertion investigations.

It is well established that the metalocarbenes prefer to insert into the benzylic or tertiary C–H bonds[1h]; however, this empirical rule apparently does not apply to the reactions of diazosulfonamides. The results of the reactions of diazosulfonamides **3a-m** preliminarily revealed that the intramolecular aliphatic 1,4-, 1,5-, or 1,6-C(sp^3)–H inserton of diazosulfonamides is not preferred.

2.2. The aromatic sp^2 C–H insertion

With the failure to achieve the aliphatic 1,4-, 1,5-, and 1,6-C(sp^3)–H insertions, we moved on to study the aromatic C(sp^2)–H insertion of diazosulfonamides. According to previous publications,[1] the aromatic C–H insertion follows a stepwise mechanism, including electrophilic addition of carbenoid to aryl rings and subsequent elimination of metal catalyst. Actually, the failed reactions of **3c-e,i-l** in Fig. 2 led us to believe that *N*-alkyl groups of diazosulfonamides would exert a disastrous influence on the aromatic C–H insertion. Thus, the *N,N*-diaryl diazosulfonamides were designed. In our previous work,[8] *N,N*-diphenyl diazosulfonamide **3n** underwent the aromatic 1,5-C(sp^2)–H insertion smoothly, delivering benzo-γ-sultam **7n** in 28%–99% yields under different conditions (Scheme 2, entries 1–8). A series of copper and rhodium catalysts was efficient to catalyze the aromatic C–H insertion, with $Rh_2(oct)_4$ the most efficient. Different symmetric *N,N*-diaryl diazosulfonamides **3n-u** underwent the aromatic C–H insertion to form the corresponding benzo-γ-sultams **7n-u** in 65%–99% yields (Scheme 3). The aromatic C–H insertion was not affected by the electron-donating-groups such as methoxy and methyl groups on aryl rings (**7o,p**), the halo-atoms such as fluoro-, chloro-, or bromo-atoms (**7q,r,s**), or the different substituted positions on the aryl



Entry 1:	1 mol% $Rh_2(OAc)_4$,	DCE, rfx, 11 h,	28%;
Entry 2:	1 mol% $Rh_2(oct)_4$,	DCE, rfx, 0.5 h,	99%;
Entry 3:	1 mol% $Cu(acac)_2$,	DCE, rfx, 13 h,	91%;
Entry 4:	1 mol% $Cu(OAc)_2{\cdot}H_2O$,	DCE, rfx, 3 h,	71%;
Entry 5:	1 mol% $Cu(OTf)_2$,	DCE, rfx, 1 h,	79%;
Entry 6:	1 mol% $(CuOTf)_2C_6H_6$,	DCE, rfx, 2 h,	50%;
Entry 7:	1 mol% $Rh_2(oct)_4$,	DCM, rfx, 0.5 h,	99%;
Entry 8:	**0.25 mol% $Rh_2(oct)_4$,**	**DCE, rfx, 0.5 h,**	**99%;**

Scheme 2. Our previous reported aromatic 1,5-C(sp^2)–H insertion of 1-diazo-2-ethoxy-*N,N*-diphenyl-2-oxoethanesulfonamide (**3n**) under different conditions.