Exploring the reactivity of 1,5-disubstituted sulfonyl-triazoles: Thermolysis and Rh(II)-catalyzed synthesis of α-sulfonyl nitriles

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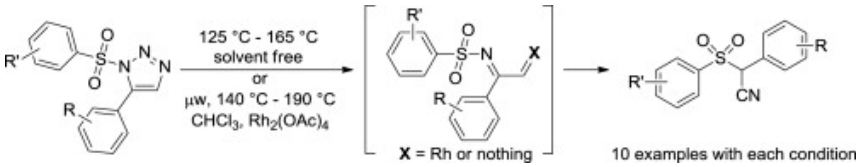
Abstract:

The reactivity of a series of 1,5-disubstituted sulfonyl-triazoles was explored using either thermolytic or metal-catalyzed conditions. Both the thermolysis and the Rh(II)-catalyzed reactions led to the synthesis of α-sulfonyl-nitriles, which presumably occurred through a carbene or carbenoid mechanism. The reactivity of the carbenes and carbenoids resulting from the loss of dinitrogen from the 1,5-disubstituted sulfonyl-triazoles were different from those of the previously explored 1,4-disubstituted sulfonyl-triazoles. It was observed by NMR that the Rh(II)-catalyst coordinates strongly but reversibly with the 1,5-disubstituted sulfonyl-triazoles. Other catalysts, including both Brønsted and Lewis acids, were found to catalyze this transformation, although less efficiently compared to neat thermolysis or Rh(II)-catalyzed conditions. These data illustrate both the unique nature of 1,5-disubstituted sulfonyl-triazoles and potential future avenues for their utilization.



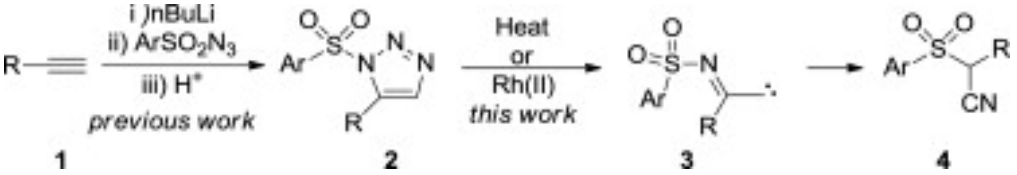
Keywords: Triazoles | Thermolysis | Rhodium | Nitriles | Carbenes | organic chemistry

Article:

1. Introduction

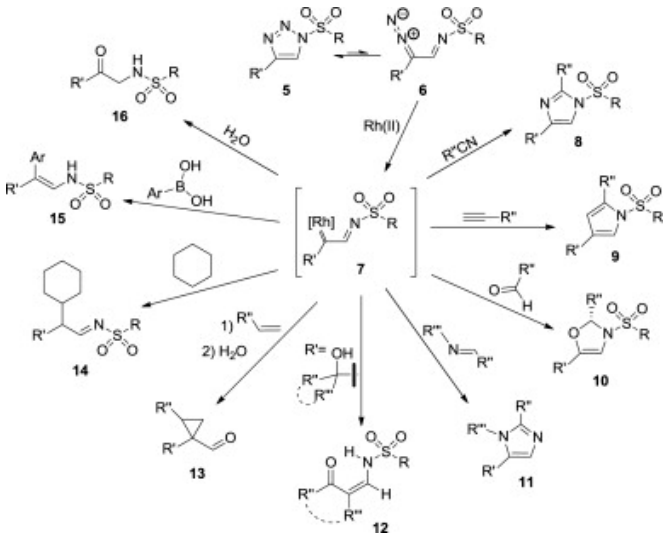
The use of 1,2,3-triazoles, and heterocycles in general, as building blocks in medicinal chemistry has led to a broad variety of synthetic methods to obtain them.1 For example, triazoles have been used to link together components, often using a copper(I) catalyst in a so-called 'Click Reaction', and they are often utilized as a bioisostere of esters and amides.2 The methods to synthesize 1,4-

disubstituted triazoles are numerous, but only recently our group reported a method to selectively and efficiently form 1,5-disubstituted sulfonyl-triazoles3 during our quest to form cyanocarbenes from alkynes and azides.4 Other researchers had previously disclosed similar reactions to form these triazoles,5 however, since our report was the first extensive study to form 1,2,3-triazoles with this type of substitution, we had the opportunity to explore the reactivity of this unique class of triazoles. Herein, we report the reactivity of these compounds under both thermolytic and metal-catalyzed conditions and contrast the reactivity with that of the previously reported 1,4-disubstituted sulfonyl-triazoles (Scheme 1).



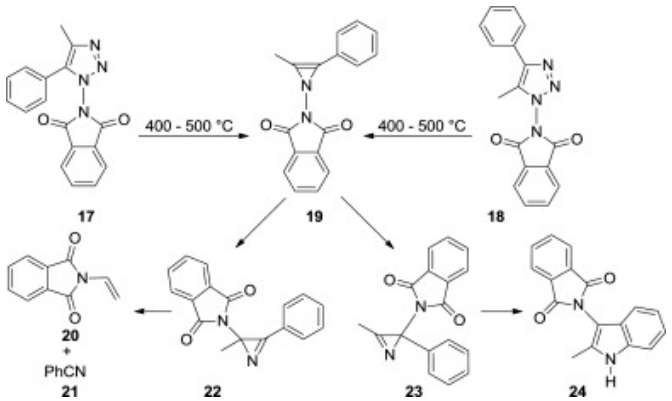
Scheme 1. Synthesis of 1,5-disubstituted sulfonyl-triazoles.

Although methods to form 1,4-disubstituted triazoles have been reported for quite some time, it was only relatively recent that efficient methods to make 1,4-disubstituted sulfonyl-triazoles was reported.6 A primary reason for this is that these sulfonyl-triazoles (5) are often in equilibrium with the opened form, an α-diazosulfonylimine (6; Scheme 2).7 Because of this, many groups have exploited this equilibrium by the addition of Rh(II) catalysts to form a carbenoid species (7) that can be reacted in a diverse set of reactions. These reactions have been extensively studied by the groups of Fokin, Gevorgyan, and Murakami.8 As is illustrated in Scheme 2, the rhodium carbenoid (7) can be reacted with nitriles, alkynes, aldehydes, imines, alcohols, alkenes, alkanes, boronic acids, or water to form sulfonyl-substituted imidazoles,8a pyrroles,8d dihydrooxazoles,8e imidazoles,8e β-sulfonamido enones,8g and 8h cyclopropyl carboxaldehydes,8b alkylated sulfonylaldimines,8c arylated sulfonylenamines,8i and α-sulfonamido ketones,8h respectively. Based on this wealth of interesting reactivities for 1,4-disubstituted sulfonyl-triazoles, we decided that it would be interesting to examine the reactivity of 1,5-disubstiuted sulfonyl-triazoles. Importantly, we wanted to determine if their reactivity would mimic or even match that of 1,4-disubstituted sulfonyl-triazoles or if they would establish their own unique reactivity.



Scheme 2. Reactions of 1,4-disubstituted sulfonyl-triazoles.8

During our characterization of 1,5-disubstituted sulfonyl-triazoles, two interesting observations were made. First, the ring-open form of the triazole was not observed, which is in contrast to the 1,4-sulfonyl-triazoles (5 in equilibrium with 6; Scheme 2).8 Second, while obtaining the melting points of some products, extrusion of N2 was occurring prior to or simultaneous with melting. For mechanistic reactions, it should be noted that there are reports of vacuum pyrolysis9 at 400–500 °C of trisubstituted triazoles (17 and 18, Scheme 3). In this report, they determine that both triazoles yielded the same products (20–24), and in the equivalent proportions, so they proposed the formation of an identical azirine (19) for both triazoles. The authors hypothesize that the reaction is occurring by a diradical mechanism. The pyrolysis with the sulfonyl-triazoles described herein occurs at temperatures well below 400–500 °C so it is likely that a different mechanism could be occurring.



Scheme 3. Vacuum pyrolysis of trisubstituted triazoles.9

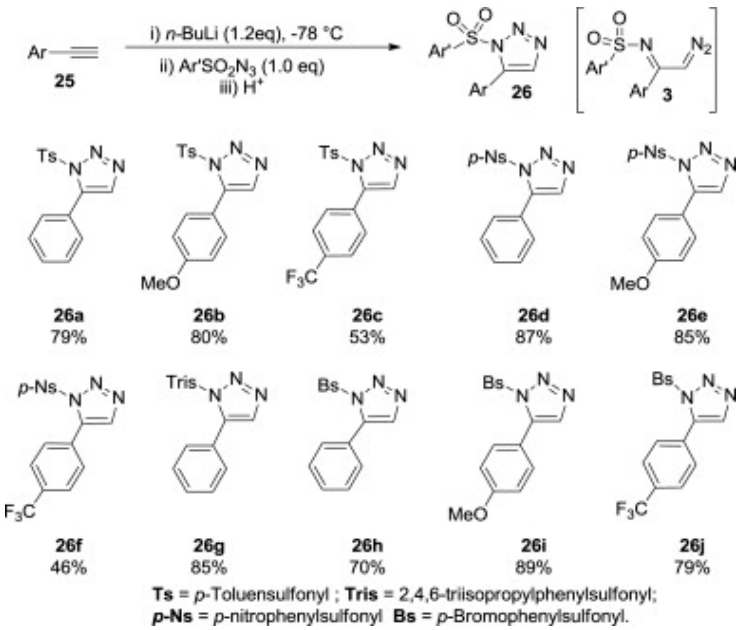
In theory, the sulfonyl-triazoles examined in the present study (2, Scheme 1) could lose dinitrogen, form an azirine similar to azirine 19, and then react similar to the prior work of

Scheme 2. To explore the reactivity of a series of 1,5-disubstituted sulfonyl-triazoles, it was decided to examine both Rh(II) catalyzed reactions and thermolytic conditions in the absence of a transition metal catalyst. It was hypothesized that the 1,5-isomers (2) will provide access to unique reactivity since extrusion of N2 yields a primary carbene or carbenoid species (3) instead of the secondary benzylic species found by Fokin and others (7).8

2. Results and discussion

2.1. Synthesis of 1,5-disubstituted sulfonyl-triazoles

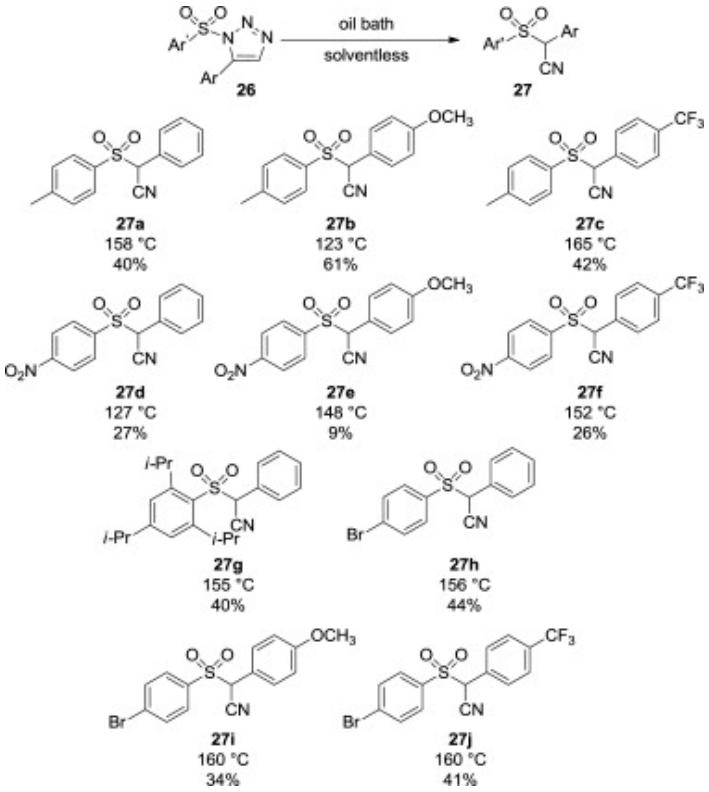
Following the general procedure previously reported, 10 triazoles (five new and five previously reported) were synthesized (Scheme 4).3 Isomerization of the 1,5-isomer to the 1,4-isomer is observed after a short period of time, so the compounds were prepared no more than 1 or 2 days in advance. The compounds synthesized used four different sulfonyl groups and either electron-rich or electron-poor aryl alkynes. Aliphatic alkynes were also used successfully for the synthesis of 1,5-disubstituted sulfonyl-triazoles,3 but they were not successful in the subsequent reactions described in this manuscript. Trisubstituted triazoles were also synthesized by trapping the initially formed triazole anion with an electrophile, however, these triazoles also did not undergo the reactions reported herein. It should be noted that even though the Dimroth rearrangement of triazoles with electron-withdrawing groups like p-toluenesulfonyl, at the N1 position has been reported,7 we were not able to observe any of the ring-open structure. This result is in agreement with the observations for related compounds.10



Scheme 4. Synthesis of 1,5-disubstituted sulfonyl-triazoles with isolated yields.

2.2. Thermolysis

The first substrate that we chose to analyze was triazole 26b because it was found to decompose prior to melting in our prior report.3 When this compound was heated in an oil bath at 123 °C, the solid immediately and simultaneously melted while extruding gas. The mixture turned from light yellow to orange and then brown within 5 min at which point no more gas was observed bubbling out the sample. The thick oil was dissolved in CDCl3, and the 1H NMR had a new signal at 5.06 ppm and the aromatic proton of the triazole had disappeared. Analysis by HRMS indicated a loss of dinitrogen and the structure was identified to be α-nitrile sulfone 27b as the major product (Scheme 5). Although this was not an anticipated product, it is a known compound and the 1H NMR was found to be identical.11



Scheme 5. Thermolysis of 1,5-disubstituted sulfonyl-triazoles with temperatures and isolated yields.

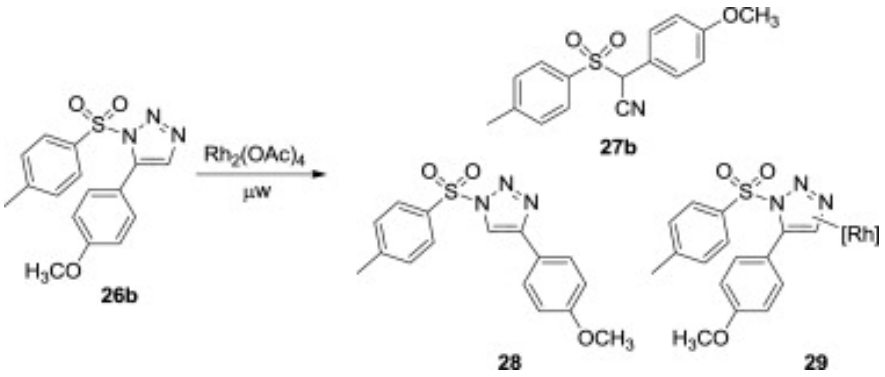
For the thermolysis of the triazoles, first the melting points or decomposition temperatures were determined, and then a temperature ~2–5 °C (decomp.) or ~20–50 °C (mp) higher was used. This is because we observed that, in general, a very short reaction time was required with the temperature high enough to undergo the N2 extrusion. If the temperature was not high enough, isomerization of the 1,5-isomer to the 1,4-isomer was observed as the major product. Interestingly, the 1,4-isomer was not as reactive with these conditions for at least one substrate. For the series with the p-nitrophenylsulfonyl group in the 1-position (27d–f), the reactions were

very fast (around 1 min), and the yields were low with formation of insoluble material. The crude 1H NMRs of the thermolysis illustrated the α-nitrile sulfone as the main product, however, the bulk of the mass balance was insoluble, black solids.

2.3. Rh(II)-catalyzed reactions

Taking into consideration the reports on the reactivity of the 1,4-triazoles with Rh(II), we decided to follow a recently reported procedure described by Fokin8a where they use 0.5 mol % of a Rh(II) catalyst and 3 equiv of a nitrile in chloroform under microwave conditions for 15 min. The only alteration that we made was using between 8 and 10 mol % of catalyst (Table 1). We observed the same α-sulfonyl nitriles as previously discussed when heated without a catalyst (entry 1), so we decided to increase the amount of acetonitrile and used it as the solvent (entry 2). The product was again the sulfonyl-nitrile, which was also formed using only chloroform as a solvent (entry 3). To establish if the catalyst has any effect in this outcome, the triazole was dissolved in chloroform and heated in the microwave to 140 °C for 15 min in the absence of catalyst (entry 4). This time only starting material was recovered.

Table 1. Qualitative Rh(II)-catalyzed optimization



Entry	Rh2(OAc)4 mol %	Solvent/reagent	Temp/time	Producta
1	10 mol %	CHCl3/CH3CN (3 equiv)	140 °C/15 min	27b
2	10 mol %	CH3CN	140 °C/15 min	27b
3	8 mol %	CHCl3	140 °C/15 min	27b
4	0 mol %	CHCl3	140 °C/15 min	26b
5	8 mol %	CHCl3	100 °C/60 min	27b
6	10 mol %	CHCl3/CH3CN (3 equiv)	100 °C/15 min	27b, 28, 29
7	10 mol %	CHCl3/CH3CN (3 equiv)	80 °C/15 min	29b

8 1, 3, 5, 10, 25, 50, 100 mol % CHCl3 50 °C/15 min 29

9 0.5, 8, 10 mol % CHCl3 rt/3 h 29

a Main product based on crude 1H NMR.

b Trace amounts of 27 and 28 were observed.

The temperature of the reaction was lowered to 100 °C and, not surprisingly, a longer reaction time was required to fully convert the triazole to sulfonyl nitrile 27b (entry 5). When the reaction at either 100 °C or 80 °C was stopped before the reaction was complete (entries 6 and 7), a mixture of the 1,4-isomer, the sulfonyl nitrile, and another product that later we identified as the Rh complex of the 1,5-isomer (29) were observed.

Interestingly, when the catalyst loading was varied from 1 to 100 mol % at 50 °C (Table 1, entry 8 and Fig. 1) and 0.5, 8 and 10 mol % at room temperature for 3 h (entry 9), a Rh complex was observed (29). As is illustrated in Fig. 1, the vinylic proton on position 4 in the triazole is shifted to low field as the amount of catalyst was increased. Also, the other signals shift and the two doublets that are overlapped at 7.26–7.33 ppm get resolved to two doublets at 7.38 ppm and 7.27 ppm. With all of these reactions where the triazole is complexed with the catalyst, starting material (26b) is recovered when purified by silica gel chromatography.

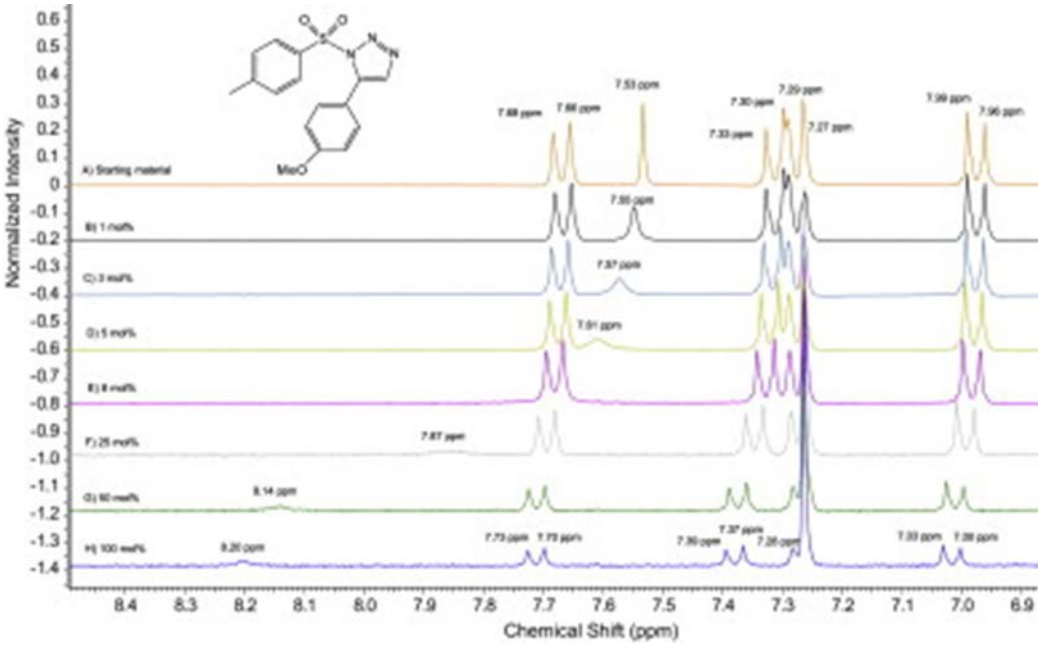
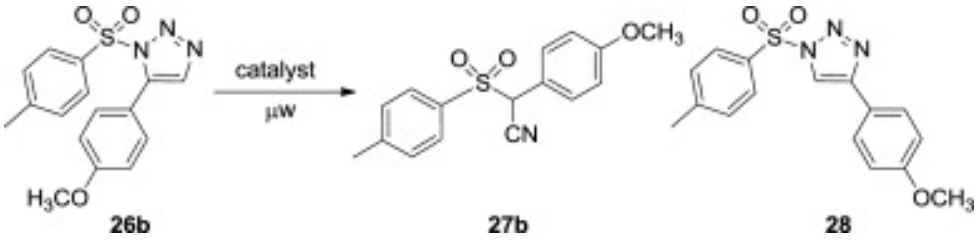


Fig. 1 Observation of catalyst coordination with catalyst loadings from 0 mol % (top) to 100 mol % (bottom) as determined by 1 H NMR.

Since formation of the sulfonyl-nitrile from the triazoles occurred under both thermal conditions in the absence of solvent and with the addition of a Rh(II)-catalyst, we decided to try other additives including HCl·Et2O, AgSbF6, TFA, and CuI. The vials were heated in the microwave initially for 15 min at 50 °C and then subjected to further heating after an aliquot was removed for analysis. HCl·Et2O at 50 °C/15 min and 140 °C/15 min (Table 2, entries 1 and 2) and CuI at 50 °C/15 min (entry 8) had no reaction by 1H NMR. Crude 1H NMR of the reaction with AgSbF6 at 50 °C/15 min (entry 4), TFA at 50 °C/15 min (entry 6), and CuI at 140 °C/15 min (entry 9) showed a mixture of 1,5- and 1,4-sulfonyl triazole isomers 26b and 28. The reactions with HCl·Et2O at 140 °C/45 min (entry 3), AgSbF6 at 115 °C/4 h (entry 5), TFA at 140 °C/15 min (entry 7) and CuI at 140 °C/1 h (entry 10) led to the formation of α-nitrile sulfone 27b as the major product in the crude 1H NMR. It is important to mention that, compared to the reactions where we use the Rh(II) catalyst, all of the reactions with additives that produced the sulfonyl nitrile had crude NMR's with major amounts of impurities.



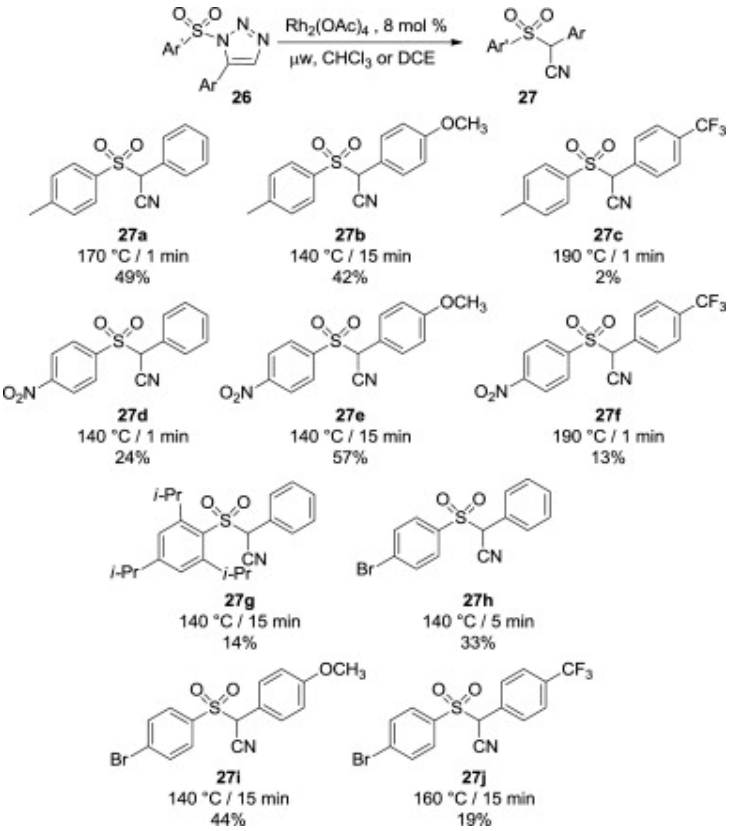
26b 27b 28

Entry	Catalyst	Temp/time	Producta
1	HCl·Et2O, 10 mol %	50 °C/15 min	26b
2	HCl·Et2O, 10 mol %	140 °C/15 min	26b
3	HCl·Et2O, 10 mol %	140 °C/45 min	27bb
4	AgSbF6, 13 mol %	50 °C/15 min	26b, 28
5	AgSbF6, 13 mol %	115 °C/4 h	27bb
6	TFA, 10 mol %	50 °C/15 min	26b, 28
7	TFA, 10 mol %	140 °C/15 min	27bb
8	CuI, 10 mol %	50 °C/15 min	26b
9	CuI, 10 mol %	140 °C/15 min	26b, 28b
10	CuI, 10 mol %	140 °C/1 h	27bb

a Main product based on crude 1H NMR.

b Reaction was inefficient and had many other side products.

Since the reactions were more efficient with the Rh2(OAc)4 as the catalyst compared to other catalysts, the entire series of 1,5-disubstituted sulfonyl-triazoles were studied with these conditions (Scheme 6). In some cases (27a, c, and i) the reactions to form the sulfonyl nitriles were more efficient using a Rh(II)-catalyst, but in other cases (27b, c, f, h, and j) heating without solvent was actually more efficient. The yields for these metal-catalyzed transformation varied widely, from 2% to 57%, and do not appear to follow any general trend using either sterics or electronics of either of the aryl-groups.

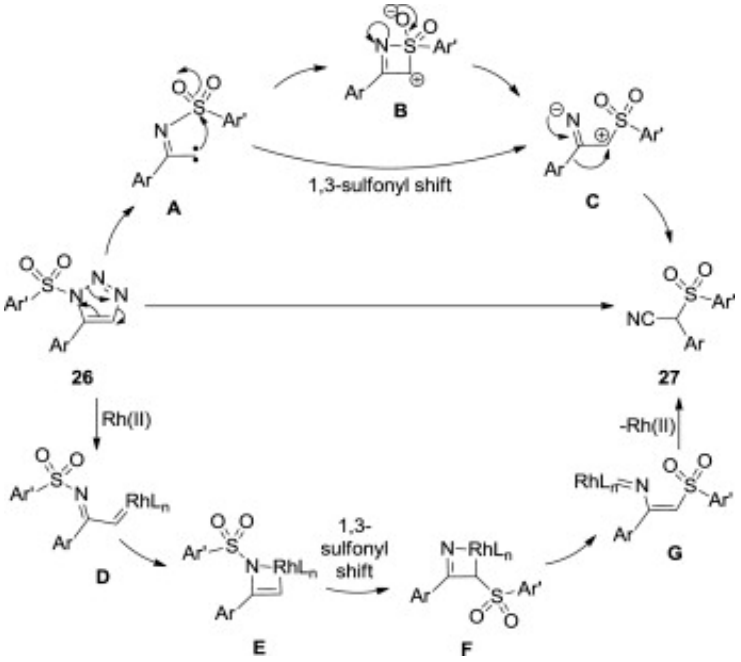


Scheme 6. Rh(II)-catalyzed formation of sulfonyl-nitriles with conditions and isolated yields.

2.4. Discussion

An important observation from this study is that the 1,5-disubstituted sulfonyl-triazoles have different reactivity compared to the 1,4-disubstituted sulfonyl-triazoles. Both triazoles react to extrude dinitrogen, however, the subsequent reactions and rearrangements are remarkably different. This could be due to both steric and electronic factors since the carbene or carbenoid in this case is primary and not benzylic. It should also be noted that when the triazoles were either trisubstituted or substituted with an alkyl-chain at carbon 5 instead of an aryl-group, the reactions described herein do not proceed. Instead the triazoles slowly decompose to a complex mixture of unidentified products.

In Scheme 7, we propose a reaction mechanism that leads to the products that we observe, both for the metal-catalyzed route and the metal-free system. In either reaction, N2 is initially released and a carbene (A) or carbenoid species (D) is formed. In the metal-free system, the next step involves a 1,3-sulfonyl shift, either by the intermediacy of a cyclic system (B) or directly by a sigmatropic rearrangement. Zwitterion C is then set up for a shifting of the aryl group to form the nitrile. The metal catalyzed pathway is similar since the sulfonyl group is transferred from the nitrogen to the carbon, a carbenoid is converted to a nitrenoid (which is similar to a resonance form of zwitterion C), and the aryl-group is then migrated to allow for formation of a nitrile. Attempts were made to trap the carbenes using allyl benzene, but in all cases sulfonyl-nitriles were observed and products resulting from cyclopropanation or C–H insertion were not observed. This is likely due to the more rapid intramolecular reactions.



Scheme 7. Proposed mechanism.

Of mechanistic significance with this reaction, the products are dissimilar to those of 1,4-disubstituted sulfonyl-triazoles even though it is likely that a sulfonylimine with a carbene or carbenoid species adjacent is formed in both cases. A rationalization of this difference is that the sulfonyl group can be near the carbene or carbenoid species in this case, whereas the prior systems (7) would strongly prefer to have the sulfonyl group away from the carbene or carbenoid for steric reasons.

3. Conclusion

A group of 1,5-disubstituted sulfonyl-triazoles were synthesized and all of them reacted under thermolytic and Rh(II)-catalyzed conditions to provide α-sulfonyl nitrile products. These products are different from the products of similar reactions with the more commonly explored 1,4-disubstituted sulfonyl-triazoles. Under Rh(II)-catalyzed conditions a coordination to the catalyst was observed and the reaction also took place with the addition of other catalysts. The interesting reactivities of 1,5-disubstituted sulfonyl-triazoles and sulfonyl-nitriles are currently being explored in our group.

4. Experimental

4.1. General information

The anhydrous reactions were performed in oven-dried glassware under nitrogen atmosphere. Unless noted, all solvents and reagents were obtained from commercial sources and used without further purification. Anhydrous solvents were dried following standard procedure, reaction progress was monitored by TLC (Silica gel 60 F254) using glass plates visualized with UV light and potassium permanganate stain.12 Chromatographic purification was performed using silica gel (60 Å, 32–63 μm) or Biotage® SP1™. The microwave reactions were performed on a Biotage® Initiator Microwave Synthesizer. NMR spectra were recorded in $CDCl_3$ using a Bruker AVANCE DRX 300 spectrometer (300 MHz for 1H), JEOL ECA spectrometer (500 MHz for 1H and 125 MHz for 13C), or Agilent Technologies Spectrometer (700 MHz for 1H and 176 MHz for 13C). Chemical shifts reported in δ parts per million using tetramethylsilane as reference for the 1H NMR and the residual solvent peak for 13C (77 ppm). The abbreviations used to describe peak splitting patterns are: s=singlet, d=doublet, t=triplet, sept=septet, m=multiplet. Coupling constants, J, are reported in hertz (Hz). IR spectra were obtained with Perkin Elmer FTIR Spectrometer One and Spectrometer 65 with ATR sampling accessories. Frequencies are in cm^{-1}. High Resolution Mass Spectra were acquired at the Triad Mass Spectrometry Laboratory at the University of North Carolina at Greensboro on a ThermoFisher Scientific LTQ Orbitrap XL MS system using APCI or ESI in positive or negative mode or at the David H. Murdock Research Institute on a Waters Qtof MS system using ESI in negative mode.

4.2. Synthesis of 1,5-disubstituted sulfonyl-triazoles

All the triazoles were synthesized following the method previously reported3 by our research group and the characterization of triazoles 26a–d and 26g were reported in Ref. 3. Spectroscopy data for 26e–f and 26h–j are reported below.

4.2.1. 1-(4-Nitrobenzenesulfonyl)-5-(4-methoxyphenyl)-1,2,3-triazole (26e)

Yellow solid (404 mg, 85%); 1H NMR (500 MHz) δ 8.33 (d, J=9.2 Hz, 2H), 8.00 (d, J=9.2 Hz, 2H), 7.57 (s, 1H), 7.33 (d, J=8.6 Hz, 2H), 7.00 (d, J=8.6 Hz, 2H), 3.93 (s, 3H). 13C NMR (125 MHz) 161.6, 151.6, 142.2, 140.3, 134.4, 131.7 (2C), 130.2 (2C), 124.8 (2C), 116.6, 114.2 (2C), 55.7. IR 3068, 2970, 1608, 1531, 1493, 1404, 1395, 1347, 1308, 1288, 1251, 1190, 1178, 1169, 1084, 1026, 954, 854, 742, 676, 619, 605, 575, 548 cm−1. HRMS [M+H]+ C15H13N4O5S calculated: 361.06012; found: 361.05936.

4.2.2. 1-(4-Nitrobenzenesulfonyl)-5-(4-trifluoromethylphenyl)-1,2,3-triazole (26f)

Yellow solid (241 mg, 46%); 1H NMR (500 MHz) δ 8.39 (d, J=9.2 Hz, 2H), 8.10 (d, J=9.2 Hz, 2H), 7.79 (d, J=8.6 Hz, 2H), 7.68 (s, 1H), 7.58 (d, J=8.6 Hz, 2H). 13C NMR (125 MHz) 151.8, 141.9, 138.8, 134.8, 132.9 (q, J=33.4 Hz, 1C), 130.7 (2C), 130.5 (2C), 128.7, 125.7 (q, J=3.6 Hz, 2C), 125.0 (2C), 123.7 (q, J=271.0 Hz, 1C). IR 3105, 1531, 1407, 1344, 1329, 1195, 1169, 1158, 1117, 1103, 1069, 959, 846, 747, 738, 676, 628, 614, 567 cm−1. HRMS [M+H]+ C15H10N4O4SF3 calculated: 399.03749; found: 399.03665.

4.2.3. 1-(4-Bromobenzenesulfonyl)-5-phenyl-1,2,3-triazole (26h)

Yellow solid (292 mg, 70%); 1H NMR (500 MHz) δ 7.64–7.62 (m, 4H), 7.60 (s, 1H), 7.56–7.53 (m, 1H), 7.49–7.46 (m, 2H), 7.37 (d, J=7.5 Hz, 2H). 13C NMR (125 MHz) 139.9, 135.6, 134.5, 133.1 (2C), 131.5, 130.6, 130.3 (2C), 130.2 (2C), 128.6 (2C), 125.2. IR 3079, 3058, 1570, 1481, 1393, 1241, 1195, 1167, 1069, 976, 957, 820, 744, 688, 604, 573 cm−1. HRMS [M+H]+ C14H11N3O2S79Br calculated: 363.97554; found: 363.97488; C14H11N3O2S81Br calculated: 365.97349; found: 365.97284.

4.2.4. 1-(4-Bromobenzenesulfonyl)-5-(4-methoxyphenyl)-1,2,3-triazole (26i)

White solid (180 mg, 89%); 1H NMR (500 MHz) δ 7.65–7.61 (m, 4H), 7.55 (s, 1H), 7.31 (d, J=9.0 Hz, 2H), 6.99 (d, J=9.0 Hz, 2H), 3.89 (s, 3H). 13C NMR (125 MHz) 161.4, 139.9, 135.7, 134.4, 133.0 (2C), 131.7 (2C), 131.4, 130.2 (2C), 117.0, 114.0 (2C), 55.6. IR 3144, 3086, 2970, 2906, 1613, 1569, 1489, 1469, 1393, 1255, 1195, 1170, 1026, 977, 955, 854, 829, 817, 745, 619, 601, 571 cm−1. HRMS [M+H]+ C15H13N3O3S79Br calculated: 393.98610; found: 393.98553; C15H13N3O3S81Br calculated: 395.98405; found: 395.98321.

4.2.5. 1-(4-Bromobenzenesulfonyl)-5-(4-trifluoromethylphenyl)-1,2,3-triazole (26j)

White solid (65 mg, 79%); 1H NMR (700 MHz) δ 7.76 (d, J=8.0 Hz, 2H), 7.72–7.67 (m, 4H), 7.66 (s, 1H), 7.56 (d, J=8.0 Hz, 2H). 13C NMR (176 MHz) 138.4, 135.5, 134.7, 133.3 (2C), 132.6 (q, J=33.4 Hz, 1C), 131.9, 130.7 (2C), 130.3 (2C), 129.1, 125.5 (q, J=4.1 Hz, 2C), 124.0 (q, J=271.0 Hz, 1C). IR 1610, 1574, 1534, 1397, 1324, 1237, 1191, 1169, 1123, 1065, 1001, 826, 744, 608, 575 cm−1. HRMS [M+H]+C15H10N3O23SF79Br calculated: 431.96237; found: 431.96298; C15H10N3O23SF81Br calculated: 433.96032; found: 433.96048.

4.3. General method for the thermolysis of 1,5-triazole

Neat triazole (0.12–0.36 mmol) in a vial is put in an oil bath and heated until gas evolution occurs. It is more efficient if this temperature is ∼10 °C higher than the initial point that melting occurs. There is a color change, from yellow to dark brown or black when the reaction ended and no more gas is evolved. If the melting point is known, the pyrolysis is performed at least 20–40 °C higher than the melting point temperature. In all the experiments, the best results were obtained when the reaction lasted between 3 and 6 min. If the time is longer and the temperature is not high enough, a major product is the respective 1,4-triazole. For all the triazoles synthesized from 4-nitro-benzene-sulfonyl azide, the yields were very low with insoluble material and yellow-orange gas evolved. The solvent was evaporated and the product was isolated using column chromatography.

4.4. General method for Rh(II) catalyzed microwave reactions of 1,5-triazole

The triazole (0.041–0.41 mmol) was dissolved in chloroform (0.03 M) and 9 mol % of Rh2(OAc)4 was added, heated in the microwave at 140 °C for 1 or 15 min or 190 °C for 1 or 15 min. The solvent was evaporated and the product was isolated using column chromatography.

4.5. Characterization of α-sulfonyl nitriles

The characterization of compounds 27a and b were reported in Ref. 11. Spectroscopy data for 27c–j are reported below.

4.5.1. (4-Trifluoromethylphenyl)-(4-methylbenzenesulfonyl)-acetonitrile (27c)

White solid (thermolysis: 165 °C, 40 mg, 42%; Rh cat: 190 °C/1 min, 3.1 mg, 2.3%); 1H NMR (500 MHz) δ 7.68–7.62 (m, 4H), 7.46 (d, J=8.0 Hz, 2H), 7.36 (d, J=8.0 Hz, 2H), 5.17 (s, 1H), 2.49 (s, 3H). 13C NMR (125 MHz) 147.5, 132.8 (q, J=33.4 Hz, 1C), 131.3, 130.5 (2C), 130.3 (4C), 129.6, 126.2 (q, J=3.6 Hz, 2C), 123.7 (q, J=271.1 Hz, 1C), 113.2, 62.8, 22.1. IR 292, 1594,

1323, 1164, 1149, 1116, 1068, 1018, 849, 810, 720, 678, 644, 577 cm−1. HRMS [M+H]+ C16H13NO2SF3 calculated: 340.06191; found: 340.06164.

4.5.2. Phenyl-(4-nitrobenzenesulfonyl)-acetonitrile (27d)

Yellow solid (thermolysis: 127 °C, 16.4 mg, 27%; Rh cat: 140 °C/1 min, 18 mg, 24%); 1H NMR (500 MHz) δ 8.36 (d, J=8.6 Hz, 2H), 7.91 (d, J=8.6 Hz, 2H), 7.52–7.49 (m, 1H), 7.43–7.40 (m, 2H), 7.31 (d, J=8.1 Hz, 2H), 5.23 (s, 1H). 13C NMR (125 MHz) 151.8, 139.7, 131.9 (2C), 131.2, 129.9 (2C), 129.6 (2C), 124.6, 124.4 (2C), 113.0, 63.4. IR 3104, 2928, 1606, 1533, 1456, 1348, 1313, 1158, 1081, 856, 794, 749, 737, 695, 681, 592, 580 cm−1. HRMS [M−H]− C14H9N2O4S calculated: 301.0283; found: 301.0297.

4.5.3. (4-Methoxyphenyl)-(4-nitrobenzenesulfonyl)-acetonitrile (27e)

Yellow solid (thermolysis: 148 °C, 10 mg, 9%; Rh cat: 140 °C/15 min, 20 mg, 57%); 1H NMR (500 MHz) δ 8.37 (d, J=9.2 Hz, 2H), 7.92 (d, J=9.2 Hz, 2H), 7.21 (d, J=8.6 Hz, 2H), 6.91 (d, J=8.6 Hz, 2H), 5.17 (s, 1H), 3.84 (s, 3H). 13C NMR (125 MHz) 161.9, 151.7, 139.8, 131.9 (2C), 131.3 (2C), 124.4 (2C), 116.0, 115.0 (2C), 113.2, 62.9, 55.7. IR 2954, 2928, 1711, 1598, 1457, 1425, 1361, 1317, 1260, 1221, 1194, 1155, 774, 694, 667, 582 cm−1. HRMS [M−H]− C15H11N2O5S calculated: 331.0389; found: 331.0395.

4.5.4. (4-Trifluoromethylphenyl)-(4-nitrobenzenesulfonyl)-acetonitrile (27f)

Yellow solid (thermolysis: 152 °C, 16.4 mg, 26%; Rh cat: 190 °C/1 min, 4.3 mg, 13%); 1H NMR (500 MHz) δ 8.43 (d, J=8.6 Hz, 2H), 8.02 (d, J=8.6 Hz, 2H), 7.73 (d, J=8.0 Hz, 2H), 7.53 (d, J=8.0 Hz, 2H), 5.26 (s, 1H). 13C NMR (176 MHz) 152.1, 139.7, 133.5 (q, J=33.4 Hz, 1C), 131.9 (2C), 130.6 (2C), 128.3, 126.7 (q, J=3.52 Hz, 2C), 124.8 (2C), 123.5 (q, J=272.8 Hz, 1C), 112.6, 62.8. IR 3110, 2936, 1531, 1348, 1322, 1151, 1126, 1067, 848, 747, 734, 678, 668, 610, 563 cm−1. HRMS [M−H]− C15H10N2O4SF3 calculated: 369.01624; found: 369.01439.

4.5.5. Phenyl-(2,4,6-triisopropylbenzenesulfonyl)-acetonitrile (27g)

White solid (thermolysis: 155 °C, 38 mg, 40%; Rh cat: 140 °C/15 min, 2.3 mg, 14%); 1H NMR (500 MHz) δ 7.49–7.43 (m, 5H), 7.22 (s, 2H), 5.14 (s, 1H), 3.92 (sept, J=6.9 Hz, 2H), 2.93 (sept, J=6.9 Hz, 1H), 1.28 (d, J=6.9 Hz, 6H), 1.27 (d, J=6.9 Hz, 6H), 1.20 (d, J=6.9 Hz, 6H). 13C NMR (125 MHz) 156.7, 153.0, 141.0, 130.7, 130.4 (2C), 129.4 (2C), 125.4, 124.8 (2C), 113.6, 100.1, 63.8, 34.5, 30.6 (4C), 25.4, 25.2, 23.7 (2C). IR 3138, 2956, 2928, 2868, 1597, 1457, 1430, 1386,

1361, 1193, 1159, 973, 950, 774, 694, 666, 579, 553 cm−1. HRMS [M+H]+ C23H30NO2S calculated: 384.19918; found: 384.19930.

4.5.6. Phenyl-(4-bromobenzenesulfonyl)-acetonitrile (27h)

Yellow solid (thermolysis: 156 °C, 42 mg, 44%; Rh cat: 140 °C/5 min, 30 mg, 33%); 1H NMR (500 MHz) δ 7.67 (d, J=8.6 Hz, 2H), 7.55 (d, J=8.6 Hz, 2H), 7.50–7.46 (m, 1H), 7.42–7.38 (m, 2H), 7.29 (d, J=7.5 Hz, 2H), 5.15 (s, 1H). 13C NMR (125 MHz) 133.2, 132.8 (2C), 131.7 (2C), 131.4, 130.9, 129.9 (2C), 129.4 (2C), 125.2, 113.4, 63.3. IR 3086, 3065, 2921, 2852, 1572, 1455, 1389, 1333, 1162, 1147, 1080, 1067, 1009, 824, 783, 741, 694, 645, 587, 559 cm−1. HRMS [M−H]− C14H9NO2S79Br calculated: 333.953735; found: 333.95358; C14H9NO2S81Br calculated: 335.951689; found: 335.95175.

4.5.7. (4-Methoxyphenyl)-(4-bromobenzenesulfonyl)-acetonitrile (27i)

Yellow solid (thermolysis: 160 °C, 33 mg, 34%; Rh cat: 140 °C/15 min, 68 mg, 44%); 1H NMR (500 MHz) δ 7.68 (d, J=8.6 Hz, 2H), 7.57 (d, J=9.2 Hz, 2H), 7.20 (d, J=8.6 Hz, 2H), 6.90 (d, J=9.2 Hz, 2H), 5.09 (s, 1H), 3.84 (s, 3H). 13C NMR (125 MHz) 161.6, 133.3, 132.8 (2C), 131.7 (2C), 131.3 (2C), 131.2, 116.7, 114.8 (2C), 113.6, 62.7, 55.7. IR 3089, 2929, 2840, 1730, 1608, 1571, 1510, 1468, 1389, 1335, 1307, 1253, 1177, 1153, 1081, 1067, 1029, 1009, 825, 776, 739, 616, 574 cm−1. HRMS [M−H]− C15H11NO3S79Br calculated: 363.9643; found: 363.9659; C15H11NO3S81Br calculated: 365.9628; found: 365.9643.

4.5.8. (4-Trifluoromethylphenyl)-(4-bromobenzenesulfonyl)-acetonitrile (27j)

Yellow solid (thermolysis: 160 °C, 41 mg, 41%; Rh cat: 160 °C/15 min, 9 mg, 19%); 1H NMR (500 MHz) δ 7.73 (d, J=8.6 Hz, 2H), 7.70 (d, J=8.6 Hz, 2H), 7.62 (d, J=8.6 Hz, 2H), 7.49 (d, J=8.6 Hz, 2H), 5.18 (s, 1H). 13C NMR (125 MHz) 133.0 (q, J=32.4 Hz, 1C), 133.1 (2C), 131.9, 131.7 (2C), 130.5 (2C), 129.0, 126.4 (q, J=3.6 Hz, 2C), 124.8, 123.6 (q, J=270.0 Hz, 1C), 113.0, 62.7. IR 3092, 2930, 1572, 1391, 1322, 1161, 1129, 1068, 1019, 1010, 851, 824, 741, 606 cm−1. HRMS [M+H]+ C15H10NO2S79BrF3 calculated: 403.95677; found: 403.95630; C15H10NO2S81BrF3 calculated: 405.95473; found: 405.95423.

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References and notes

1

For a set of reviews in this area, see the themed issue: Chem. Soc. Rev., 39 (2010), pp. 1221–1408

2

(a) G.A. Patani, E.J. LaVoie. Chem. Rev., 96 (1996), pp. 3147–3176

(b) K. Odlo, J. Fournier-Dit-Chabert, S. Ducki, O.A.B.S.M. Gani, I. Sylte, T.V. Hansen. Bioorg. Med. Chem., 18 (2010), pp. 6874–6885

(c) K. Odlo, J. Hentzen, J.F. dit Chabert, S. Ducki, O.A.B.S.M. Gani, I. Sylte, M. Skrede, V.A. Fløre nes, T.V. Hansen. Bioorg. Med. Chem., 16 (2008), pp. 4829–4838

3

M.E. Meza-Aviña, M.K. Patel, C.B. Lee, T.J. Dietz, M.P. Croatt. Org. Lett., 13 (2011), pp. 2984–2987

4

(a) I.F.D. Hyatt, M.P. Croatt. Angew. Chem., Int. Ed., 51 (2012), pp. 7511–7514

(b) I.F.D. Hyatt, M.E. Meza-Aviña, M.P. Croatt. Synlett (2012), pp. 2869–2874

5

(a) J.H. Boyer, C.H. Mack, N. Goebel, L.R. Morgan. J. Org. Chem., 23 (1958), pp. 1051–1053

(b) E. Robson, J.M. Tedder, B. Webster. J. Chem. Soc. (1963), pp. 1863–1865

(c) R. Helwig, M. Hanack. Chem. Ber., 118 (1985), pp. 1008–1021

(d) R. Huisgen, R. Knorr, L. Möbius, G. Szeimies. Chem. Ber., 98 (1965), pp. 4014–4021

6

(a) E.J. Yoo, M. Ahlquist, S.H. Kim, I. Bae, V.V. Fokin, K.B. Sharpless, S. Chang. Angew. Chem., Int. Ed., 46 (2007), pp. 1730–1733

(b) F. Wang, H. Fu, Y. Jiang, Y. Zhao. Adv. Synth. Catal., 350 (2008), pp. 1830–1834

7

R.E. Harmon, F. Stanley, S.K. Gupta, J. Johnson. J. Org. Chem., 35 (1970), pp. 3444–3448

8

(a) T. Horneff, S. Chuprakov, N. Chernyak, V. Gevorgyan, V.V. Fokin. J. Am. Chem. Soc., 130 (2008), pp. 14972–14974

(b) S. Chuprakov, S.W. Kwok, L. Zhang, L. Lercher, V.V. Fokin. J. Am. Chem. Soc., 131 (2009), pp. 18034–18035

(c) S. Chuprakov, J.A. Malik, M. Zibinsky, V.V. Fokin. J. Am. Chem. Soc., 133 (2011), pp. 10352–10355

(d) B. Chattopadhyay, V. Gevorgyan. Org. Lett., 13 (2011), pp. 3746–3749

(e) M. Zibinsky, V.V. Fokin. Angew. Chem., Int. Ed., 52 (2013), pp. 1507–1510

(f) A.V. Gulevich, V. Gevorgyan. Angew. Chem., Int. Ed., 52 (2013), pp. 1371–1373

(g) N. Selander, B.T. Worrell, V.V. Fokin. Angew. Chem., Int. Ed., 51 (2012), pp. 13054–13057

(h) T. Miura, Y. Funakoshi, M. Morimoto, T. Biyajima, M. Murakami. J. Am. Chem. Soc., 134 (2012), pp. 17440–17443

(i) N. Selander, B.T. Worrell, S. Chuprakov, S. Velaparthi, V.V. Fokin. J. Am. Chem. Soc., 134 (2012), pp. 14670–14673

9

(a) T.L. Gilchrist, G.E. Gymer, C.W. Rees. J. Chem. Soc. D, Chem. Commun. (1971), pp. 1519–1520

(b) T.L. Gilchrist, G.E. Gymer, C.W. Rees. J. Chem. Soc., Perkin Trans. 1 (1973), pp. 555–561

10

I. Bae, H. Han, S. Chang. J. Am. Chem. Soc., 127 (2005), pp. 2038–2039

11

(a) H. Zhao, E.R. Biehl. Synth. Commun., 25 (1995), pp. 4063–4069

(b) M.B. Cid, J. López-Cantarero, S. Duce, J.L.G. Ruano. J. Org. Chem., 74 (2008), pp. 431–434

M.C. Pirrung. The Synthetic Organic Chemist's Companion, John Wiley & Sons, Hoboken, NJ (2007), pp. 171–172