# New Easy Approach to the Synthesis of 2,5-Disubstituted and 2,4,5-Trisubstituted 1,3-Oxazoles. The Reaction of 1-(Methylthio)acetone with Nitriles

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# New Easy Approach to the Synthesis of 2,5-Disubstituted and 2,4,5-Trisubstituted 1,3-Oxazoles. The Reaction of 1-(Methylthio)acetone with Nitriles

Antonio Herrera,[†] Roberto Martínez-Alvarez,*[,†] Pedro Ramiro,[†] Dolores Molero,[‡] and John Almy[§]

*Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Complutense, E-28040 Madrid, Spain, CAI de RMN, Facultad de Ciencias Químicas, Universidad Complutense, E-28040 Madrid, Spain, and Department of Chemistry, California State University, Stanislaus, Turlock, California 95382*

*rma@quim.ucm.es*

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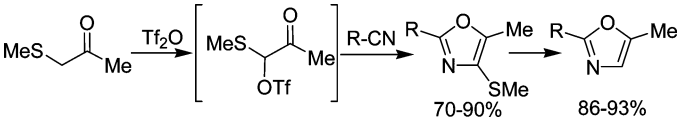
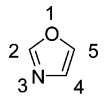



The reaction of 1-(methylthio)acetone with different nitriles in the presence of triflic anhydride led to the one-pot formation of 2-substituted 5-methyl-4-methylthio-1,3-oxazoles in good yield. 1,2- and 1,4-Bisozaxolyl-substituted benzenes were obtained when the reaction was carried out using aromatic dinitriles. The methylthio group at the C4 position of the oxazole ring was easily removed with Raney nickel to form 2-substituted 5-methyl-1,3-oxazoles in good yields. 4-Methylsulfonyl derivatives were prepared by the oxidation of the MeS group with *m*-CPBA. The proposed mechanism for the formation of oxazoles involves an unstable 1-(methylthio)-2-oxopropyl triflate, which was detected from the low-temperature NMR spectra.

## Introduction

1,3-Oxazole (Chart 1), also known simply as oxazole, is not found in nature in the free state, but the ring is usually encountered as a 2,4-disubstituted oxazole within the structures of complex natural products. A large number of oxazole-containing natural products have been isolated from marine invertebrates and microorganisms, many of which exhibit potent biological activities.[1−3] The synthesis of natural products with the common biogenic 2,4-disubstituted oxazole moiety has attracted the attention of several chemists.[4−6] The 2,4-disubstituted oxazoles are formally biosynthesized from acylserine precursors by enzyme-catalyzed cyclodehydration-oxidation.[7] Synthetic procedures for the preparation of the target oxazoles are based on biomimetic variations of the latter sequence. To date, there is no general synthesis of oxazoles that is satisfactory for the preparation of all substituted analogues.[8] The most general and widely used method is still the procedure developed by Cornforth and Cornforth[9] and improved by Yokohama et al.[10] Common methods for the preparation of 2,5- and 2,4,5-substituted oxazoles include dehydration of α-acylaminocarbo-

**CHART 1. The 1,3-Oxazole Ring and Its Numbering System**




* To whom correspondence should be addressed. Phone: +34913944325. Fax: +34913944103.
[†] Departamento de Química Orgánica, Universidad Complutense.
[‡] CAI de RMN, Universidad Complutense.
[§] California State University.

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nyl compounds,[11] catalytic decomposition of α-diazocarbonyl compounds in nitriles,[12] photolysis and pyrolysis of *N*-acylisoozalones,[13] improved and modified Robison−Gabriel reactions,[14] and various rhodium-,[15] ruthenium-,[16] and gold-catalyzed[17] reactions.

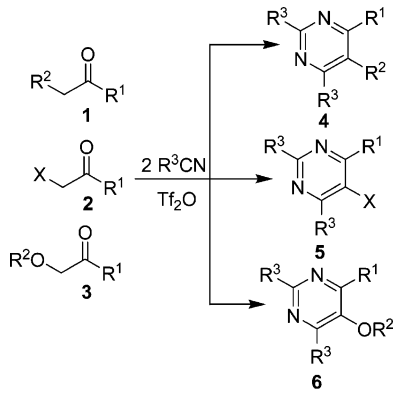
The synthetic procedures for the conversion of ketones to oxazoles reported to date involve multistep reactions[8,18] that suffer one or more drawbacks including reactive starting materials, long reaction times, low yields, and harsh reaction conditions. In contrast, the direct conversion of ketones to substituted oxazoles has received little attention. The reaction of aromatic ketones with thallium(III) acetate[19] or iodobenzene diacetate[20] in the presence of TfOH with nitriles affords 2-alkyl-5-aryl disubstituted oxazoles. Aromatic ketones and benzonitrile react in the presence of mercury(II) tosylate under microwave irradiation to form 4-aryl-2-phenyloxazoles.[21] The treatment of aromatic ketones with [hydroxy-(2,4-dinitrobenzenesulfonyloxy)iodo]benzene and amides under solvent-free conditions and microwave irradiation gives multisubstituted oxazoles.[22] Either strong acidic conditions or hypervalent iodine(III) sulfonates that are not directly available are the principal drawbacks of these procedures. Moreover, a limited class of ketones and nitriles must be used, and the mechanism remains unclear. Therefore, a development of a more convenient and efficient method is needed for the direct preparation of substituted oxazoles from ketones together with an explanation of their formation.

We report here a novel and direct synthesis of oxazoles. The reaction of 1-(methylthio)acetone with various nitriles in the presence of triflic anhydride under mild conditions affords a variety of 2-substituted 5-methyl-4-methylthio-1,3-oxazoles. The MeS group at the C4 position can be easily removed by reductive displacement to form substituted oxazoles with the C4 position free. The methylthio group can also be transformed by oxidation to yield the corresponding 4-methylsulfonyl derivatives. The use of aromatic dinitriles and control of the reaction stoichiometry permits the preparation of mono- and bisoxazolyl derivatives. In addition, we propose a reaction mechanism on the basis of the reactive intermediates observed from low-temperature NMR experiments.

## Results and Discussion

The reaction of ketones **1** with nitriles in the presence of triflic anhydride affords substituted pyrimidines **4**.[23] Substituted ketones such as α-haloketones **2** undergo the same process giving substituted 5-halopyrimidines **5**.[24] Similarly, α-alkoxyketones **3** form the corresponding substituted 5-alkoxypyrimidines **6**[25] (Scheme 1).

**SCHEME 1. Reaction of α-Substituted Ketones with Nitriles**




**SCHEME 2. Reaction of 1-(Methylthio)acetone 7 with Nitriles**

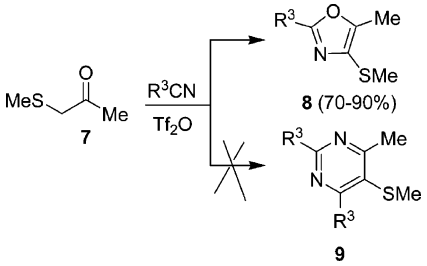



**TABLE 1. Preparation of 2,4,5-Trisubstituted 1,3-Oxazoles 8**

| nitrile $R^3CN$ | compound | yield[a] (%) |
|---|---|---|
| $R^3$ = Me | **8a** | 88 |
| $R^3$= Et | **8b** | 80 |
| $R^3$ = MeS | **8c** | 70 |
| $R^3$ = $C_6H_5$ | **8d** | 92 |
| $R^3$ = 4-$MeC_6H_4$ | **8e** | 89 |
| $R^3$ = 4-$ClC_6H_4$ | **8f** | 90 |
| $R^3$ = 4-$MeOC_6H_4$ | **8g** | 86 |
| $R^3$ = 4-$MeC_6H_4CH_2$ | **8h** | 76 |
| $R^3$ = 4-$ClC_6H_4CH_2$ | **8i** | 75 |
| $R^3$ = 4-$NO_2C_6H_4CH_2$ | **8j** | 72 |

[a] Yield of isolated product.

We have extended this synthetic study by examining the reaction of 1-(methylthio)acetone **7** with nitriles in the presence of $Tf_2O$. In contrast to the previous results, trisubstituted 1,3-oxazoles **8** were formed in good yields, while the expected 5-methylthiopyrimidines **9** were not detected (Scheme 2).

The reaction was carried out under mild conditions (0 °C, 36 h) with a variety of nitriles (Table 1). Higher temperatures considerably reduce the yields. The structure of the nitrile seems to have no influence on the observed yields. The structural elucidation was accomplished by means of one-dimensional

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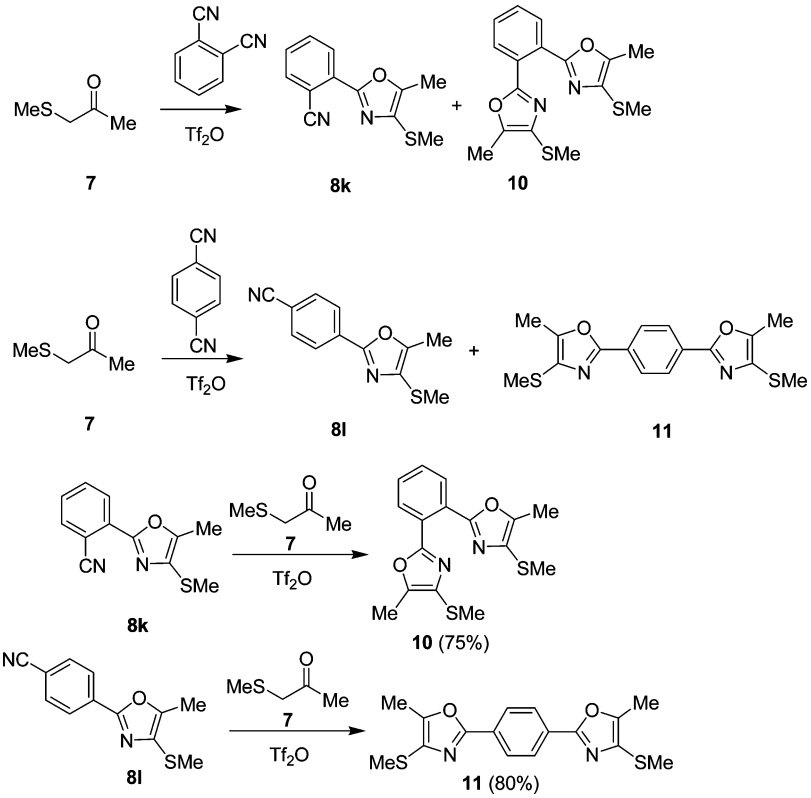
**SCHEME 3. Reaction of Methylthioacetone 7 with Dinitriles to Form Mono- and Bisoxazolyl Derivatives**




(1D) and two-dimensional (2D) NMR spectra. These spectra revealed that only one molecule of nitrile is involved in the reaction. The same spectra also showed the formation of three new $sp^2$ carbon atoms that resonate around 160, 130, and 150 ppm; these signals are almost invariant with respect to sustitution.[8] These signals were assigned to C2, C4, and C5 positions, respectively, on the oxazole ring. In addition, electron impact mass spectra show the characteristic fission of the C2−C3 and C5−O bonds to form the corresponding $R^3CO^+$ ion, which is frequently the base peak of the spectra.[26]

We also investigated the reaction of aromatic dinitriles with methylthioacetone **7** and obtained mono- and bisoxazolyl benzene derivatives. Thus, **7** reacts with phthalonitrile in the presence of triflic anhydride to form two new 1,3-oxazoles **8k** and **10**. Similarly, terephthalonitrile gave the new compounds **8l** and **11** (Scheme 3).

Monooxazolyl derivatives **8k** and **8l** are the predominant products if stoichiometric amounts of starting materials are reacted at low temperature. The formation of **10** and **11** was not enhanced by using higher amounts of the starting ketone and a higher temperature (Table 2). Instead, bisoxazolyl derivatives **8k** and **8l** were isolated and then treated again with **7** in the presence of triflic anhydride to afford **10** and **11** in good yields (Scheme 3).

The versatility of the MeS group was used to advantage by its ability to undergo reductive displacement to form oxazoles without substitution at C4. Subsequent deprotonation at this position followed by electrophilic addition can give the corresponding 4-substituted derivatives.[27] Reductive desulfuration of oxazoles **8** was achieved with Raney nickel in ethanol at room temperature.[28] Illustrative examples are collected in Table 3. Raney nickel was prepared prior to use, because this commercially available reagent was unable to perform the reaction.

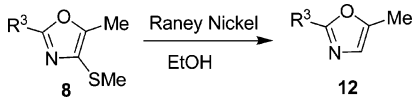
The hydrogen atom at the C4 position of the oxazole ring in compounds **12** was easily observed from the $^1H$ NMR spectra as it appears as a quartet with a $^3J = 1.1$ Hz. Signals for methyl groups at C5 which are singlets for compounds **8** become doublets for compounds **12**.

**TABLE 2. Temperature and Stoichiometry Dependence of the Product Ratios in the Reaction of Methylthioacetone 7 and Dinitriles**

| dinitrile | ratio ketone/dinitrile | temp (°C) | product and yield[a] (%) |
|---|---|---|---|
| phthalonitrile | 1/1 | 0 | **8k** (52) + **10** (12) |
| phthalonitrile | 2/1 | 0 | **8k** (41) + **10** (18) |
| phthalonitrile | 2/1 | 40 | **8k** (7) + **10** (48) |
| terephthalonitrile | 1/1 | 0 | **8l** (46) + **11** (22) |
| terephthalonitrile | 2/1 | 0 | **8l** (36) + **11** (5) |
| terephthalonitrile | 2/1 | 40 | **8l** (25) + **11** (23) |

[a] Yield of isolated product.

**TABLE 3. Reductive Desulfuration of 8 to 2-substituted 5-Methyl-1,3-oxazoles 12**




8 12

| starting material | product | yield[a] (%) |
|---|---|---|
| **8d** | **12d** | 86 |
| **8g** | **12g** | 93 |

[a] Yield of isolated product.

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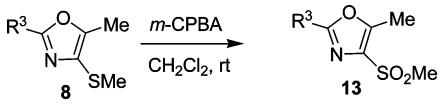
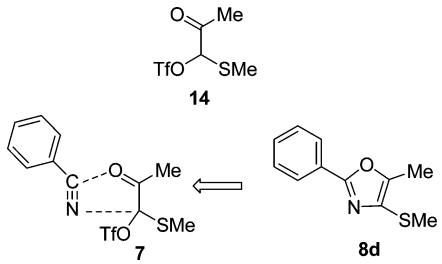
**TABLE 4. Oxidation of Oxazoles 8 To Form 4-Methylsulfonyloxazoles 13**




| starting material | product | yield[a] (%) |
|---|---|---|
| **8c** | **13c** | 91 |
| **8d** | **13d** | 93 |
| **8f** | **13f** | 97 |
| **8j** | **13j** | 97 |

[a] Yield of isolated product.

**SCHEME 4**




Nucleophilic displacement of the MeS group normally requires very harsh conditions, but these can be avoided if the MeS is oxidized to the methylsulfonyl, a more reactive leaving group. Thus, oxidation of the methylthio group of oxazoles **8** with *m*-CPBA leads to the formation of 4-methylsulfonyl derivatives, **13**. Table 4 gives some illustrative examples.

Studies of nucleophilic substitutions in substituted oxazole rings show that the C2 position is more reactive than the C4 position, with C5 being the least reactive position.[29] We carried out the reaction of sulfones **13** with ammonia and with sodium methoxide. In both cases, no reaction products were found, although attempts were carried out with ammonia under atmospheric pressure for 2 days and with sodium methoxide in methanol under reflux for 2 days.

In regard to the mechanism of the formation of the oxazoles, two findings, the participation of only one nitrile molecule and the C−O bond formation (between the carbon of the cyano group and the carbonyl oxygen, Scheme 4), are incompatible with a reaction path involving the intermediate trifliloxycarbenium ion that explained prior results.[23] The structure of **8** suggests a nucleophilic attack of the nitrogen atom of the nitrile to the methylene group of thioketone **7**. For this, the $CH_2$ group (α to the carbonyl group) needs to be activated by a powerful leaving group triflate, as in the intermediate **14**.

To support this hypothesis, we studied the role of $Tf_2O$, finding that catalytic amounts of triflic anhydride did not produce a significant reaction of the starting materials. The same results were obtained using a catalytic amount of triflic acid. This indicated that $Tf_2O$ plays an important role in the rate-determining step, probably forming a reactive intermediate. To identify the possible reaction intermediates and to propose a mechanism, we have investigated the reaction at low temperature (5 °C) by means of NMR spectroscopy. $^1H$ and $^{13}C$ NMR spectra (500 and 125 MHz) of the methylthioacetone **7** are collected in Figure 1. The addition of an equimolar amount of

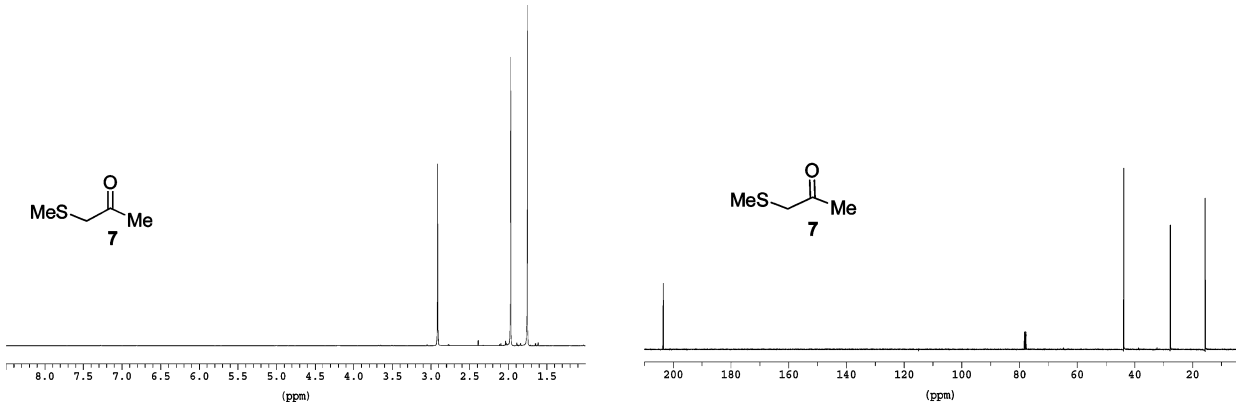



**FIGURE 1.** $^1H$ (500 MHz) and $^{13}C$ NMR spectra (125 MHz) of methylthioacetone **7** at 5 °C.

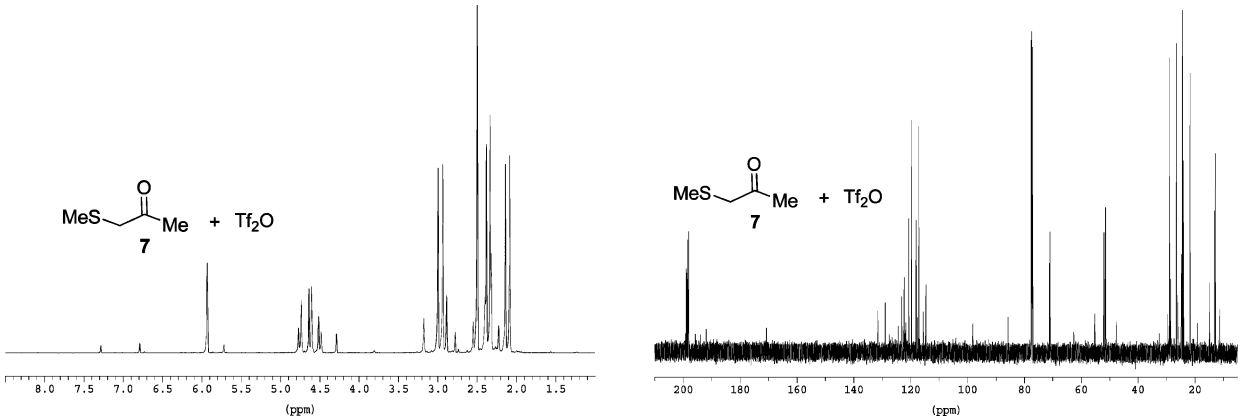
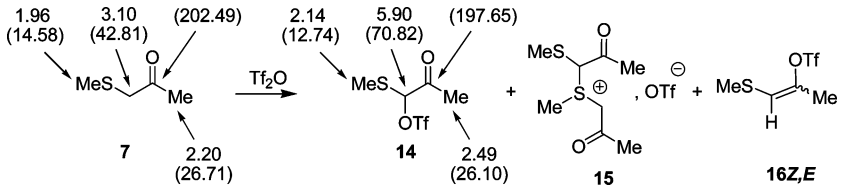
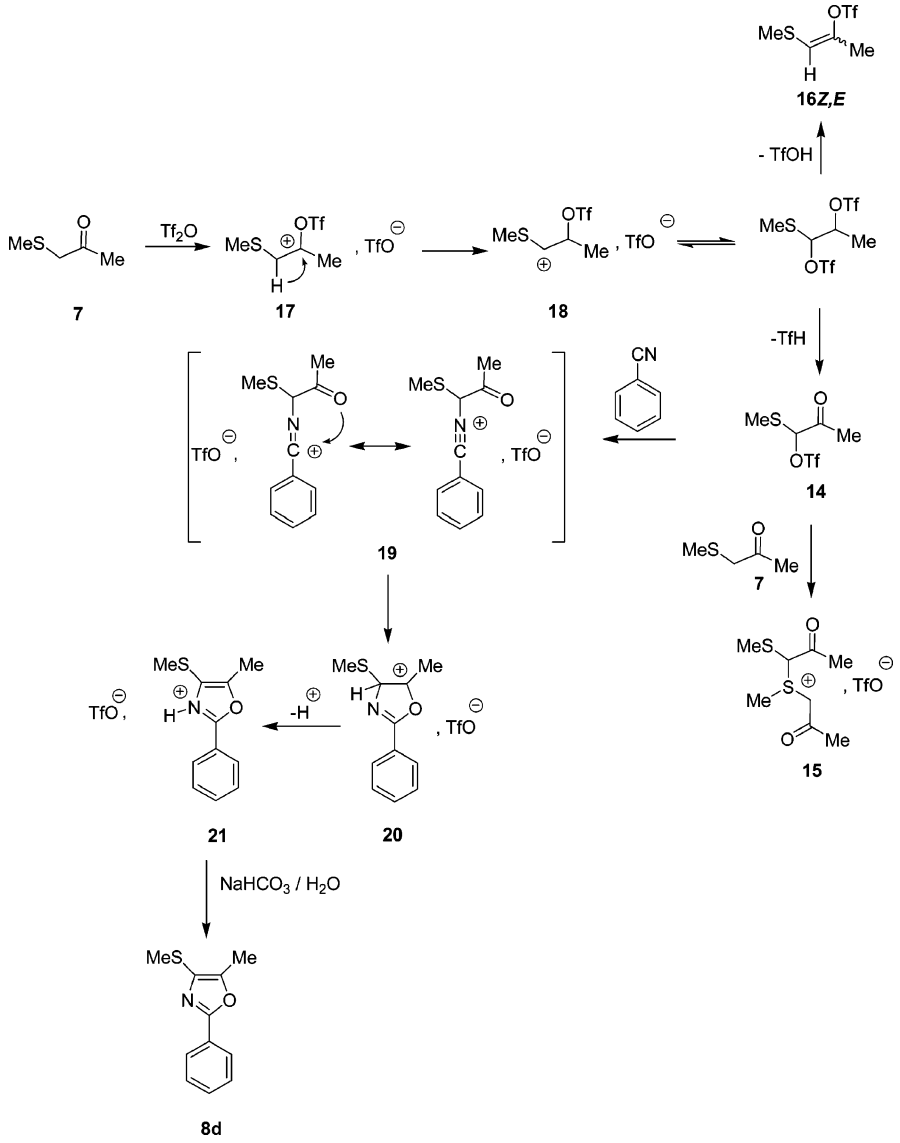



**FIGURE 2.** $^1H$ (500 MHz) and $^{13}C$ NMR spectra (125 MHz) of the reaction mixture after 1 h at 5 °C.

**SCHEME 5. Proposed Intermediates and Their Observed $^{1}H$ Chemical Shifts ($^{13}C$ Data Are Enclosed in Brackets) in ppm**




**SCHEME 6. Proposed Mechanism for the Formation of Oxazole 8d from Methylthioacetone 7 and Benzonitrile in the Presence of $Tf_2O$**




$Tf_2O$ produces a significant increase in the number of signals as a result of the formation of several intermediates. The reaction mixture was allowed to stand at this temperature for 1 h (Figure 2). A detailed study of the 1D and 2D spectra (Supporting Information) permits the identification of some reaction intermediates. Among these was the main species detected, 1-(methylthio)-2-oxopropyl triflate **14** (Schemes 4 and 5). Other observed intermediates include compound **15**, which can be considered as the dimer of the starting ketone **7** and vinyl triflate **16**, albeit in low concentrations. The integration of the NMR signals has permitted a determination of the intermediate ratio as **14** (40%), **15** (40%), **16*Z*** (10%), and **16*E*** (10%). Observed chemical shifts (Supporting Information) were in agreement with the corresponding calculated values.[30] The reaction mixture slowly decomposes, and the spectra revealed that any of the above-reported intermediates cannot be detected from the mixture after 15 h at 5 °C (Supporting Information).

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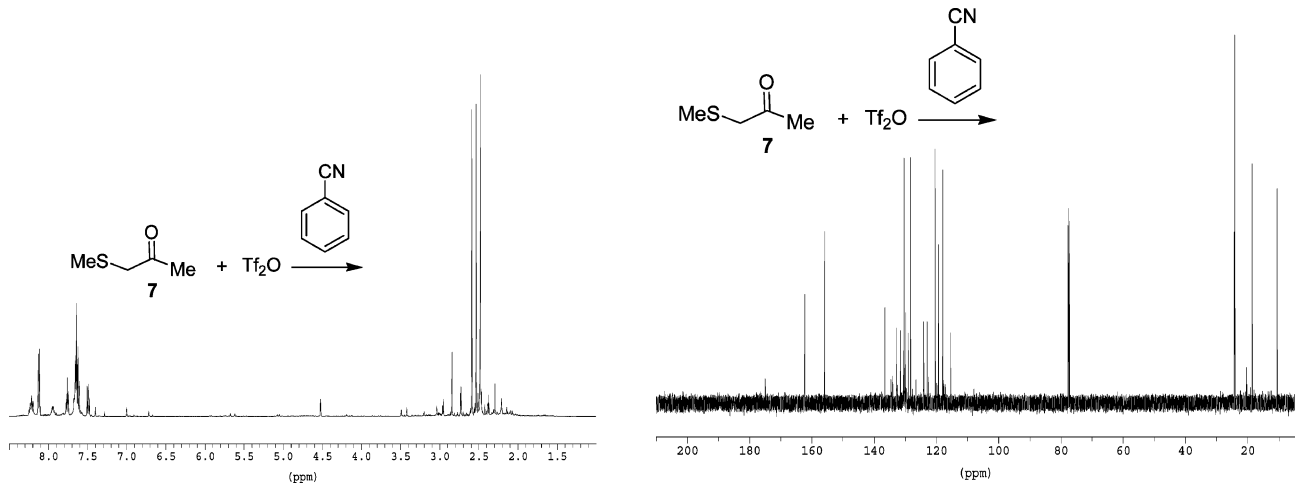


**FIGURE 3.** NMR spectra of the reaction mixture at 5 °C and 15 h after the benzonitrile addition.

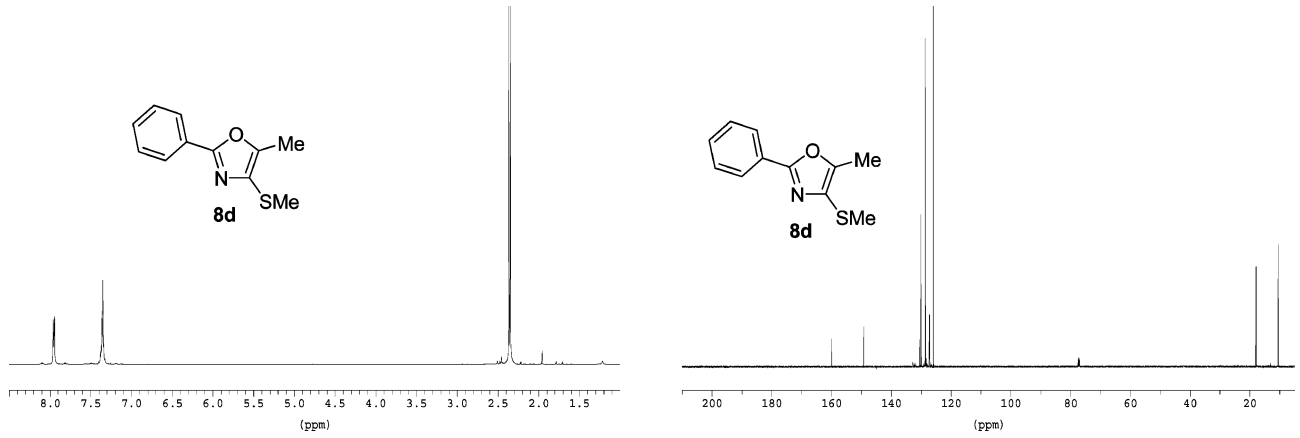


**FIGURE 4.** $^{1}H$ and $^{13}C$ NMR spectra of compound **8d**.

An addition of an equimolar amount of benzonitrile after 1 h to the reaction mixture produced the slow disappearance of the signals from intermediate **14** and the emergence of new ones that were attributed to the protonated oxazole **20** (Scheme 6). Figure 3 shows the spectra of the reaction mixture after 15 h. Finally, after a 24 h reaction time, the conversion was almost complete. Figure 4 shows the spectra of the final product **8d**, obtained after basic hydrolysis of the reaction mixture.

From the results of the NMR experiments, we propose a mechanism on the basis of the observed intermediates **14** and **15** (Scheme 6). The first step is the formation of a trifliloxycarbenium ion **17** that, after a hydride shift, leads to cation **18**, which is stabilized directly by the methylthio group. Subsequent elimination of trifluoromethanesulfinic acid forms the α-ketotriflate **14**. The nucleophilic displacement of the triflate by the nitrogen of the cyano group of nitrile afforded the intermediate **19**. A further cyclization process forms **20**, which leads to a more stable substituted oxazol-3-ium triflate, **21**. Finally, the basic hydrolysis leads to the corresponding oxazole **8d**. The formation of **14** from **7** seems to be the rate-determining step of the reaction. To confirm this, we carried out the competitive reaction of **7** and $Tf_2O$ with two different nitriles in equal amounts (Supporting Information). The ratio products (nearly 1/1) clearly indicated that the reaction pathway is determined by the formation of the intermediate ketotriflate **14**.

To explain the side products **15** and **16**, we propose that **16** is the product of elimination of TfOH from the intermediate **18**, but it is well-known that a vinyl triflate like **16** cannot react with benzonitrile at low temperature.[31] The formation of the dimer species **15** can be explained from **14** as a result of a nucleophilic displacement of the triflate by methylthioketone **7**. Hence, due to the formation of dimer **15**, yields of the obtained oxazoles decreased when equimolar amounts of ketone and nitrile were used. Higher amounts of ketone **7** improved notably the yields of oxazoles **8**.

Unstable intermediates such as **14** have been postulated to explain the reaction mechanism of oxazole formation from aryl ketones and thallium(III) acetate or iodobenzene diacetate with TfOH.[19,20] Neither chemical nor spectroscopic proof was offered to support this hypothesis. The above-reported results represent the first spectroscopic observation of an intermediate α-ketotriflate. Attempts to trap **14** by the addition to the reaction mixture of nucleophiles other than nitriles were unsuccessful. To isolate **14**, we carried out the reaction of **7** with $Tf_2O$ under

(31) (a) García, A.; Herrera, A.; Martínez-Alvarez, R.; Teso, E.; García, A.; Osío, J.; Pargada, L. *Tetrahedron Lett.* **1987**, *38*, 1929−1932. (b) García, A.; Herrera, A.; Martínez-Alvarez, R.; Teso, E.; García, A.; Osío, J.; Pargada, L.; Unanue, R.; Hanack, M.; Subramanian, L. R. *J. Heterocycl. Chem.* **1988**, *25*, 1237−1241. (c) Hanack, M.; Subramanian, L. R. *Houben-Weyl, Carbokationen, Carbokationen-Radikale*, Band E19c; Georg Thieme: Stuttgart, 1990; p 98.

classical conditions to obtain triflates from ketones.[32] The instability of **14** did not allow its isolation.

In summary, we reported a new and simple procedure to prepare 2,4,5-trisubstituted 1,3-oxazoles. The easy desulfuration with Raney nickel of the methylthio group at the C4 position allows the synthesis of 2,5-disubstituted 1,3-oxazoles. The oxidation of the methylthio group with *m*-CPBA permits the preparation of 4-methylsulfonyl derivatives. A NMR study of the reaction at low temperature revealed species that were incorporated in a proposed mechanism for the reaction.

## Experimental Section

**General Procedure for the Synthesis of 2-Substituted 5-Methyl-4-(methylthio)-1,3-oxazoles, 8.** To a solution of 1-(methylthio)-acetone **7** (2.00 g, 19.2 mmol) in dry $CH_2Cl_2$ (25 mL) was added triflic anhydride (5.34 g, 19.2 mmol) in $CH_2Cl_2$ (20 mL) dropwise at 0 °C. The mixture was stirred for 1 h at this temperature, and then a solution of the corresponding nitrile (9.6 mmol) in $CH_2Cl_2$ (20 mL) was added. The mixture was stirred and allowed to stand at 0 °C for 3 days. The progress of the reaction was monitored by TLC. The reaction mixture was hydrolyzed by the careful addition of saturated $NaHCO_3$. The organic layer was separated, washed with brine, and dried over $MgSO_4$. The solvent was evaporated in vacuo, and the residue was purified by distillation or recrystallization after column chromatography (eluent, EtOAc/hexanes = 5/95).

**2-Phenyl-5-methyl-4-(methylthio)-1,3-oxazole (8d):** yellow oil; yield 92%; bp 125 °C/0.4 Torr (kugelrohr); IR (film) $\nu$ 2924, 1591, 1487, 1109, 714 $cm^{-1}$; $^1H$ NMR $\delta$ 2.35 (s, 3H, $CH_3$), 2.37 (s, 3H, $CH_3S$), 7.35 (m, 3H, Ar−H), 7.95 (m, 2H, Ar−H); $^{13}C$ NMR $\delta$ 10.3 ($CH_3$−C5), 17.7 ($CH_3S$), 125.8, 127.0, 128.41, 128.9 (aromatic), 130.4 (C5), 148.9 (C4), 159.7 (C2); MS (EI) *m*/*z* (% B) 205 ($M^{+\bullet}$, 43), 172 (M − SH, 38), 105 ($C_6H_5CO^+$, 100), 77 ($C_6H_5^+$, 54); Anal. Calcd for $C_{11}H_{11}NOS$: C, 64.36; H, 5.40; N, 6.82; S, 15.62. Found: C, 64.13; H, 5.22; N, 6.69; S, 15.49.

Bisoxazolyl derivatives **10** and **11** were prepared using the general procedure from methylthioacetone **7** and nitriles **8k** and **8l**.

**5-Methyl-2-{4-[5-methyl-4-(methylthio)-1,3-oxazol-2-yl]phenyl}-4-(methylthio)-1,3-oxazole (11):** pale yellow solid (from EtOH); yield 80%, mp 142−143 °C; this compound presents in solution an intense greenish fluorescence; IR (KBr) $\nu$ 1589, 1418, 1063, 719 $cm^{-1}$; $^1H$ NMR $\delta$ 2.47 (s, 6H, $2CH_3$), 2.48 (s, 6H, $2CH_3S$), 8.17 (s, 4H, Ar−H); $^{13}C$ NMR $\delta$ 10.6 ($CH_3$−C5), 18.0 ($CH_3S$), 126.5, 128.37 (aromatic), 131.0 (C5), 149.8 (C4), 159.4 (C2); MS (EI) *m*/*z* (% B) 332 ($M^{+\bullet}$, 100), 317 (M − $CH_3$, 5), 299 (M − SH, 50), 232 ([$C_5H_6NOS$]$C_6H_5CO^+$, 14); Anal. Calcd. for $C_{16}H_{16}N_2O_2S_2$: C, 57.81; H, 4.85; N, 8.43; S, 19.29. Found: C, 57.70; H, 4.69; N, 8.32; S, 19.14.

**General Procedure for the Synthesis of 2-Substituted 5-Methyl-1,3-oxazoles, 12.** Compound **8** (3 mmol) was dissolved in EtOH and added to a suspension of recently prepared Raney nickel[32] in 20 mL EtOH. The reaction mixture was refluxed for 48 h and then filtered through Celite, which was washed with EtOH (100 mL). The solvent was removed in vacuo, and the residue was purified by distillation or recrystallization after column chromatography (eluent, EtOAc/hexanes = 5/95).

**5-Methyl-2-(4-methoxyphenyl)-1,3-oxazole (12g):** white needles (from MeOH); yield 93%; mp 60−61 °C; IR (KBr) $\nu$ 1616, 1501, 1254, 1173, 837 $cm^{-1}$; $^1H$ NMR ($CD_3OD$) $\delta$ 2.39 (d, $J$ = 1.1 Hz, 3H, $CH_3$), 3.85 (s, 3H, $CH_3O$), 6.85 (q, $J$ = 1.1 Hz, 1H, H4), 7.02 (m, 2H, Ar−H), 7.88 (m, 2H, Ar−H); $^{13}C$ NMR ($CD_3OD$) $\delta$ 10.77 ($CH_3$−C5), 55.9 ($CH_3O$), 121.0, 124.1 (aromatic), 128.6 (C5), 150.3 (C4), 162.3 (C2), 162.9 (aromatic); MS (EI) *m*/*z* (% B) 189 ($M^{+\bullet}$, 100), 174 (M − $CH_3$, 16), 146 (M − $CH_3CO$, 44); Anal. Calcd. for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.72; H, 5.73; N, 7.33.

**General Procedure for the Synthesis of 2-Substituted 5-Methyl-4-(methylsulfonyl)-1,3-oxazoles, 13.** To a solution of the corresponding oxazole **8** (3 mmol) in 25 mL dry $CH_2Cl_2$ was added dropwise a solution of *m*-CPBA (7 mmol, 12 mmol for **8c**) in 25 mL of dry $CH_2Cl_2$. The reaction mixture was stirred at room temperature for 12 h. The reaction was hydrolyzed by the addition of 20 mL of 5% sodium thiosulfate. The organic layer was washed with saturated $NaHCO_3$ and brine and dried over $MgSO_4$. The solvent was removed in vacuo, and the residue was purified by distillation or recrystallization after column chromatography (eluent, EtOAc/hexanes = 5/95).

**2-Phenyl-5-methyl-4-(methylsulfonyl)-1,3-oxazole (13d):** white crystals (from MeOH); yield 93%; mp 130−131 °C; IR (KBr) $\nu$ 1595, 1313, 1153, 785, 714 $cm^{-1}$; $^1H$ NMR $\delta$ 2.71 (s, 3H, $CH_3$), 3.22 (s, 3H, $CH_3SO_2$), 7.48 (m, 3H, Ar−H), 8.03 (m, 2H, Ar−H); $^{13}C$ NMR $\delta$ 11.4 ($CH_3$−C5), 42.7 ($CH_3SO_2$), 125.8, 126.6, 128.8, 131.2 (aromatic), 135.7 (C5), 153.0 (C4), 160.2 (C2); MS (EI) *m*/*z* (% B) 237 ($M^{+\bullet}$, 19), 105 ($C_6H_5CO^+$, 100), 77 ($C_6H_5^+$, 39); Anal. Calcd. for $C_{11}H_{11}NO_3S$: C, 55.68; H, 4.67; N, 5.90; S, 13.51. Found: C, 55.55; H, 4.56; N, 5.80; S, 13.43.

**Low-Temperature NMR Spectra.** To a solution of 0.0104 g (0.10 mmol) of **7** in 0.8 mL of $CDCl_3$ at 5 °C contained in a NMR tube was added 0.0282 g (0.10 mmol) of $Tf_2O$. The tube was sealed with a septum, introduced in the spectrometer, and spun. The spectra were recorded at 30 min intervals. After the appropriate time, benzonitrile (0.0103 g, 0.10 mmol) was added, and the spectra were recorded at the same time intervals.

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**Supporting Information Available:** General experimental methods and characterization data of compounds **8a**−**c**, **8e**−**l**, **10**, **12d**, **13c**, **13f**, and **13j**; $^1H$, $^{13}C$, and DEPT (135) NMR spectra of compounds **8a**−**l**, **10**, **11**, **12d**, **12g**, **13c**, **13d**, **13f**, and **13j**; 2D NMR (HMQC and HMBC) spectra of compound **8d**; fluorescence spectra of **11**; $^1H$, $^{13}C$, and 2D NMR spectra of the reaction mixture at low temperature (5 °C); and $^1H$ and $^{13}C$ chemical shifts of intermediates **14**, **15**, and **16**. This material is available free of charge via the Internet at http://pubs.acs.org.

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