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Generation and Cyclization of Unsaturated Carbamoyl Radicals Derived from *S*-4-Pentynyl Carbamothioates under Tin-Free Conditions

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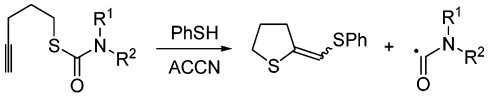

R^1= Bn, Ts; R^2= 2-(3-)alkenyl, 2-vinylphenyl

The radical reaction of benzenethiol with *S*-4-pentynyl carbamothioates provides a valuable protocol for the tin-free generation of carbamoyl radicals, which arise from intramolecular substitution at sulfur by the initial sulfanylvinyl radicals. This procedure can be usefully employed to achieve *N*-benzylcarbamoyl radical 5-exo and 4-exo cyclizations leading, respectively, to pyrrolidinones and azetidinones, although, for the latter, it seems of lesser utility. Novel evidence is presented that *N*-tosyl-substituted carbamoyl radicals display a peculiar tendency to yield the corresponding isocyanate by β-elimination of the tosyl radical.

Introduction

The use of radical reactions in modern synthetic chemistry is now well-established.[1] Organotin compounds, in particular, have found widespread application in many types of radical processes. However, tin-based radical chemistry suffers from many drawbacks, namely toxicity, hazardous handling, and difficult removal of tin residues from the final reaction mixtures. Therefore, a major area of current research is the development of processes that seek to either alleviate the problems associated with tin residues or remove the need for tin completely.[2]

In a previous work, we have devised a novel method for the generation of acyl radicals under reducing tin-free conditions by using readily available 4-pentynylthiol esters in combination with benzenethiol.[2h] Indeed, the radical addition of PhSH to the terminal triple bond of these thiol esters results in intermediate sulfanylvinyl radicals that are highly capable of performing intramolecular substitution at sulfur to yield a cyclized 2-alkylidenetetrahydrothiophene with concomitant release of acyl radicals. Acyl radicals had been previously generated by a similar substitution process of aryl radicals at the sulfur atom of thiol esters.[3] Our protocol has been successfully applied to the synthesis of cyclic ketones through cyclization of the acyl radicals onto suitably placed alkenyl substituents.[2h] In a subsequent study, our procedure became a new synthetic method for the reduction of carboxylic acids to aromatic and aliphatic aldehydes under radical conditions.[4] During this study, we happened to observe that the *S*-4-pentynyl derivative of *N*-methyl-*N*-phenylcarbamothioic acid reacted nicely with benzenethiol to yield *N*-methylformanilide in fairly high yield. This

(1) For a comprehensive review on synthetic radical chemistry, see: *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vols. 1 and 2.

(2) For recent papers on this subject, see: (a) Baguley, P. A.; Walton, J. C. *Angew. Chem., Int. Ed.* **1998**, *37*, 3072. (b) Gagosz, F.; Moutrille, C.; Zard, S. Z. *Org. Lett.* **2002**, *4*, 2707. (c) Kim, S.; Lim, C. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 3265. (d) Gagosz, F.; Zard, S. Z. *Org. Lett.* **2002**, *4*, 4345. (e) Kim, S.; Song, H.-J. *Synlett* **2002**, *12*, 2110. (f) Studer, A.; Amrein, S. *Synthesis* **2002**, 835. (g) Ouvry, G.; Zard, S. Z. *Chem. Commun.* **2003**, *6*, 778. (h) Benati, L.; Calestani, G.; Leardini, R.; Minozzi, M.; Nanni, D.; Spagnolo, P.; Strazzari, S. *Org. Lett.* **2003**, *5*, 1313. (i) Boivin, J.; Jrad, R.; Juge, S.; Nguyen, V. T. *Org. Lett.* **2003**, *5*, 1645. (j) Schaffner, A.-P.; Renaud, P. *Angew. Chem., Int. Ed.* **2003**, *42*, 2658. (k) Osornio, Y. M.; Cruz-Almanza, R.; Jimenez-Montano, V.; Miranda, L. D. *Chem. Commun.* **2003**, 2316. (l) Studer, A.; Amrein, S.; Schleth, F.; Schulte, T.; Walton, J. C. *J. Am. Chem. Soc.* **2003**, *125*, 5726. (m) Studer, A. *Chem. Soc. Rev.* **2004**, *33*, 267. (n) Benati, L.; Leardini, R.; Minozzi, M.; Nanni, D.; Scialpi, R.; Spagnolo, P.; Strazzari, S.; Zanardi, G. *Angew. Chem., Int. Ed.* **2004**, *43*, 3598. (o) Molawi, K.; Schulte, T.; Siegenthaler, K. O.; Wetter, C.; Studer, A. *Chem. Eur. J.* **2005**, *11*, 2335.

(3) (a) Crich, D.; Yao, Q. *J. Org. Chem.* **1996**, *61*, 3566. (b) Crich, D.; Hao, X. *J. Org. Chem.* **1997**, *62*, 5982.

(4) Benati, L.; Leardini, R.; Minozzi, M.; Nanni, D.; Scialpi, R.; Spagnolo, P.; Zanardi, G. *Synlett* **2004**, *6*, 987.

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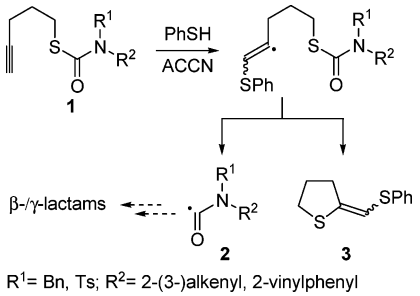
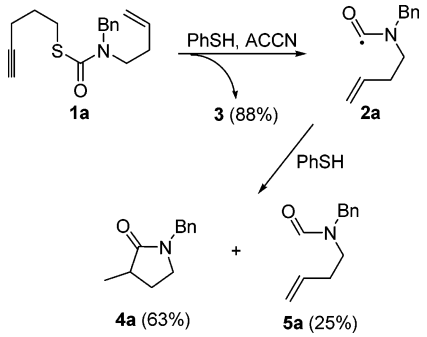
SCHEME 1



finding revealed that *S*-4-pentynyl carbamothioates might be promising precursors of aminoacyl (carbamoyl) radicals. On this basis, we were prompted to prepare a variety of novel unsaturated *N*-benzyl- and *N*-tosyl-substituted carbamothioates **1** with the aim of producing the corresponding carbamoyl radicals **2** (and the accompanying tetrahydrothiophene **3**) upon radical reaction with benzenethiol (Scheme 1). A proper choice of unsaturated substrates was made to ascertain whether, in the presence of the electrophilic thiol H-donor, those nucleophilic radical species might successfully undergo intramolecular cyclization onto the internal alkene to give four- and/or five-membered ring lactam products.[5]

Several free-radical mediated syntheses of lactams have been previously reported. Among these, we can mention the organotin hydride promoted cyclizations of unsaturated α-haloamides, which have been applied in particular to the synthesis of PS-5 and thienamycin;[6] the 4-exo cyclizations of carbamoylcobalt salophens[7a,b] and the Mn(III)/Ce(IV)-promoted cyclizations of enamides, both yielding *β*-lactams;[7c] and the TMS_3SiH- or Bu_3-SnH-mediated 5-exo cyclizations of selenocarbamates, affording moderate yields of *γ*-lactams.[8] The early radical synthesis of lactams either suffered from poor yields or often employed toxic organotin reagents. However, *β*- and/or *γ*-lactams have been very recently produced in appealing yields under tin-free conditions via ring closures of unsaturated *N*-benzylcarbamoyl radicals derived from both thermal fragmentation of 1-carbamoyl-1-methylcyclohexa-2,5-dienes in the presence of radical initiators[9] and photochemical homolysis of oxime oxalate amides.[10] Moreover, efficient production of dithiocarbamoyl derivatives of *β*-, *γ*-, and *δ*-lactams has been very recently achieved through group transfer cyclization of *N*-benzylcarbamoyl radicals arising from *N*,*N*-diethyldithiocarbamate precursors upon heating in the presence of dilauroyl peroxide or alternative irradiation.[11]

SCHEME 2



Results and Discussion

The requisite pentynyl carbamothioates **1** were usually prepared in moderate to good yields by reacting the appropriate carbamoyl chlorides with 4-pentyne-1-thiol in the presence of DMAP by an adaptation of the procedure previously employed for the preparation of our pentynyl carbothioates.[2h,4] Their radical reactions were normally performed by adding a toluene solution of PhSH (1.1 mmol) over ca. 4 h to a refluxing toluene solution of the appropriate substrate (1 mmol) and ACCN (1,1′-azo-bis-cyclohexane-1-carbonitrile) initiator (0.3 mmol) under a nitrogen atmosphere. The resulting mixture was further refluxed until virtual disappearance of the starting material (3−6 h) and then separated by column chromatography.

We first examined the generation of carbamoyl radicals that could lead to pyrrolidinones through 5-exo cyclization onto suitable alkenylic moieties. The reaction of *N*-benzyl-*N*-3-butenylcarbamothioate **1a** smoothly afforded the expected 2-methylidenetrahydrothiophene **3** as a mixture of (*E*)- and (*Z*)-isomers, and the associated carbamoyl radical **2a**, which provided a fairly good yield of the desired pyrrolidinone **4a**. However, compound **4a** was accompanied by a significant amount of the butenylformamide **5a**, arising from hydrogen abstraction of radical **2a** from the thiol (Scheme 2).

Comparable efficiency was observed for the production of carbamoyl radicals **2b**−**d** from the corresponding *N*-benzyl-*N*-(2-alkenylphenyl)carbamothioates **1b**−**d**. Radicals **2b**-**d**, however, unlike their congener **1a**, did not undergo reduction by benzenethiol but exhibited exclusive ring closure onto the internal alkene. Indeed, carbamoyl radical **2b** only furnished the cyclized indolinone **6b** in good yield, whereas the congener **2c**, besides affording a comparable amount of the corresponding indolinone **6c**, also gave minor amounts of the six-membered ring quinolinone **7**. In the latter case, the additional formation of the formal 6-endo cyclization product **7** was presumably caused by the intermediate occurrence of a highly stabilized, tertiary benzylic radical.[12] Moreover, carbamoyl radical **2d** afforded the sole indolinone **6d** in a slightly enhanced yield, its 5-exo cyclization being probably encouraged by the presence of the adjacent electron-deficient alkene (Scheme 3).

(5) *N*-Substituted carbamoyl radicals are known to exist as mixtures of the respective *E*- and *Z*-conformers; see: Sutcliffe, R.; Ingold, K. U. *J. Am. Chem. Soc.* **1981**, *103*, 7686. The predominance of rotamers unfavorable to ring formation in secondary carbamoyl radicals is a possible reason for the known reluctance of these radicals to undergo cyclization onto alkenes; see refs 8 and 9a.

(6) (a) Ishibashi, H.; Kameoka, C.; Iriyama, H.; Kodama, K.; Sato, T.; Ikeda, M. *J. Org. Chem.* **1995**, *60*, 1276. (b) Ishibashi, H.; Kameoka, C.; Kodama, K.; Sato, T.; Ikeda, M. *Tetrahedron* **1996**, *52*, 489.

(7) (a) Gill, G. B.; Pattenden, G.; Reynolds, S. J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 369. (b) Pattenden, G.; Reynolds, S. J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 379. (c) D'Annibale, A.; Nanni, D.; Trogolo, C.; Umani, F. *Org. Lett.* **2000**, *2*, 401 and refs cited therein.

(8) Rigby, J. H.; Danca, D. M.; Horner, H. *Tetrahedron Lett.* **1998**, *39*, 8413.

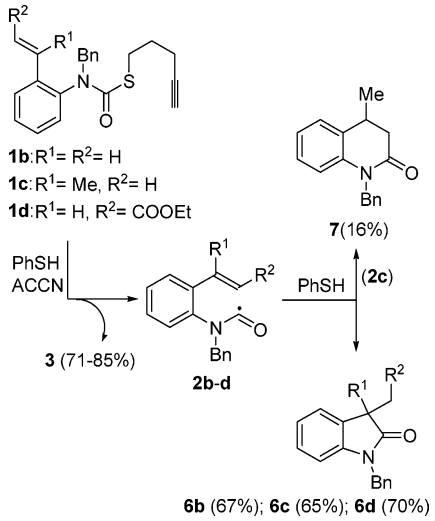
(9) (a) Bella, A. F.; Jackson, L. V.; Walton, J. C. *Org. Biomol. Chem.* **2004**, *2*, 421. (b) Bella, A. F.; Slawin, A. M. Z.; Walton, J. C. *J. Org. Chem.* **2004**, *69*, 5926. (c) Bella, A. F.; Jackson, L. V.; Walton, J. C. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1839. (d) Jackson, L. V.; Walton, J. C. *Chem. Commun.* **2000**, 2327.

(10) (a) Scanlan, E. M.; Slawin, A. M. Z.; Walton, J. C. *Org. Biomol. Chem.* **2004**, *2*, 716. (b) Scanlan, E. M.; Walton, J. C. *Chem. Commun.* **2002**, 2086.

(11) Grainger, R. S.; Innocenti, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 3443.

(12) In principle, a formally 6-endo-cyclized benzylic radical might result from ring expansion of the initial 5-exo ring-closed *β*-oxoindolinylmethyl radical via 3-exo cyclization onto the adjacent carbonyl group and subsequent *β*-scission of the ensuing alkoxyl radical; see: Chatgilialoglu, C.; Crich, D.; Komatsu, M.; Ryu, J. *Chem. Rev.* **1999**, *99*, 1991 and ref 9a.

SCHEME 3

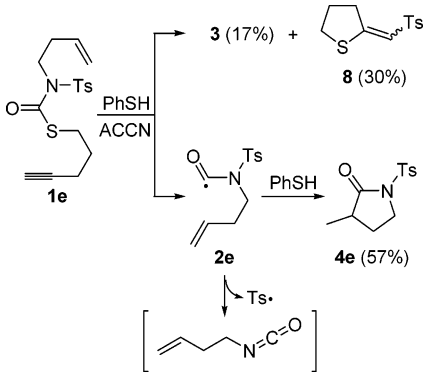


The above findings therefore revealed that the thiol-mediated radical reaction of the *N*-benzylated carbamothioates **1a**−**d** can serve as a reliable means to generate carbamoyl radicals **2a**−**d**. Interestingly, the produced radicals **2a**−**d** were usually found to be highly prone to form cyclized lactams; their concomitant reduction to formamide, which in principle might have been a rather crucial side reaction under our reducing conditions, proved to be a serious limitation only to cyclization of radical **2a**.

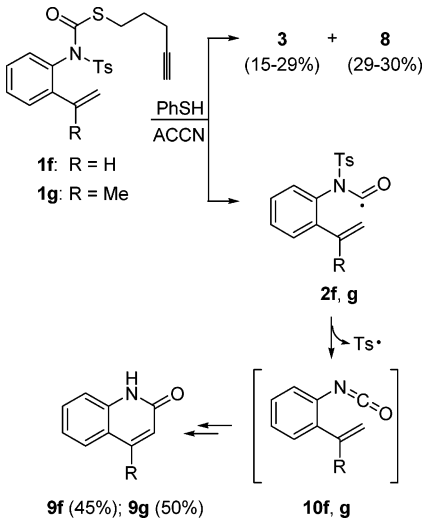
We next examined the corresponding reactions of compounds **1e**−**g**, i.e., the *N*-tosyl analogues of carbamothioates **1a**−**c**. We originally expected that replacement of the benzyl with the electron-withdrawing tosyl substituent might conceivably depress the nucleophilic properties of carbamoyl radicals. Consequently, the *N*-tosyl carbamoyl radicals **2e**−**g** should have been more reluctant to undergo reduction by the electrophilic benzenethiol and hence even more prone to cyclize onto an electron-rich alkene than the *N*-benzyl counterparts **2a**−**c**. Nevertheless, our results with compounds **1e**−**g** unexpectedly revealed that carbamoyl radicals **2e**−**g** exhibit a peculiar tendency to undergo β-scission to afford tosyl radical and an alkenyl/alkenylaryl isocyanate, which, however, in every case escaped detection. To our knowledge, such a type of radical process is unprecedented in carbamoyl radical chemistry.[13]

Every reaction of carbamothioates **1e**−**g** furnished the tosylated tetrahydrothiophene **8**[14] in preference to the usual sulfenylated analogue **3**, which under these circumstances was formed only to a limited extent (Schemes 4 and 5). Compound **8** could plausibly arise from addition of the released tosyl radical to the activated PhS-substituted ethylene carbon of the initially formed tetrahydrothiophene **3** followed by β-elimination of benzenesulfanyl radical from the ensuing carbon-centered radical.[15,16] However, it is more likely that, similar to congener

SCHEME 4



SCHEME 5



3, compound **8** could additionally occur by direct addition of tosyl radical to the alkynylic bond of the starting substrates **1e**−**g**.[17]

The usual reaction of compound **1e**, besides the two tetrahydrothiophenes **3** and **8**, gave the tosylated pyrrolidinone **4e** (57%) as the only identifiable product of carbamoyl radical **2e**. Despite the lack of any evidence at all for possible hydrogen abstraction of radical **2e** from the thiol, observed instead with the *N*-benzyl counterpart **2a**, the outcoming yield of pyrrolidinone **4e** was lower than that of the analogous compound **4a** obtained from **2a** (Schemes 2 and 4). This observation is consistent with the concomitant disappearance of carbamoyl radical **2e** by the supposed likely elimination of tosyl radical.

In sharp contrast with the *N*-benzyl analogues **2b**,**c**, the tosylated radicals **2f**,**g**, generated from carbamothioates **1f**,**g**, furnished no indolinone products, but gave instead useful yields of the corresponding quinolinones **9f**,**g** only (Scheme 5).[18] Quinolinones **9f**,**g** were probably due to the key intervention of the intermediate ìsocyanates **10f**,**g**, which under these circumstances would readily arise from their presumed progenitors **2f**,**g**. Indeed, 2-vinylphenyl isocyanates **10f**,**g** are known

(13) No evidence for any β-elimination of tosyl radical was gained in previous cyclization reactions of *N*-tosylcarbamoyl radicals derived from corresponding selenocarbamates, see ref 8.

(14) Similar to the analogue **3** (ref 2h), the tosylated tetrahydrothiophene **8** occurred as a mixture of (*E*)- and (*Z*)-isomer in unestablished ratio.

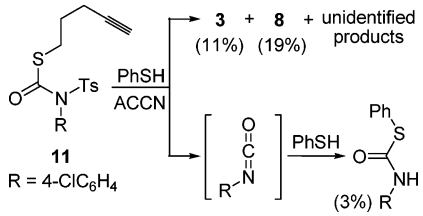
(15) The β-elimination of benzenesulfanyl radical from carbon-centered radicals is faster than that of tosyl radical, see: Timokhin, V. I.; Gastaldi, S.; Bertrand, M. P.; Chatgilialoglu, C. *J. Org. Chem.* **2003**, *68*, 3532.

(16) A control experiment established that tetrahydrothiophene **3** can be converted to the tosylated analogue **8** upon radical reaction with TsSPh/AIBN in refluxing benzene.

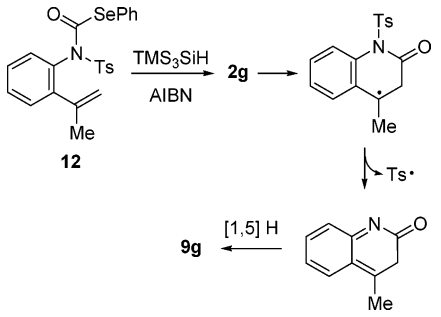
(17) A control experiment interestingly showed that the radical chain reaction of *S*-4-pentynyl benzenecarbothioate with TsSPh/AIBN in refluxing benzene cleanly afforded compound **8** as well as *S*-phenyl benzenecarbothioate.

(18) For unclear reasons, the carbamoyl radical **2g** could also undergo significant decarbonylation leading to reduced *N*-(2-isopropenylphenyl)-4-methylbenzenesulfonamide (25%).

SCHEME 6



SCHEME 7

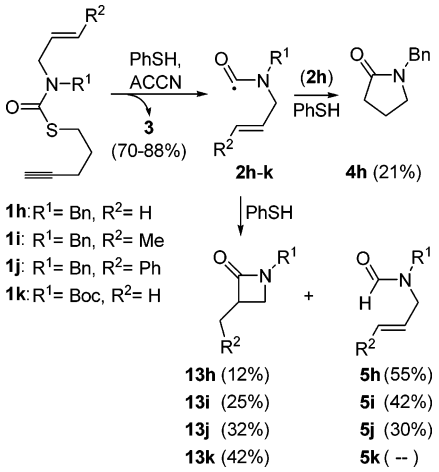


to smoothly afford quinolinones **9f**,**g** through thermal electrocyclization followed by 1,5-H sigmatropic shift (Scheme 5).[19] In an attempt to gain direct proof of isocyanate occurrence in our reactions involving *N*-tosyl carbamoyl radicals, we also investigated the behavior of *S*-4-pentynyl *N*-tosyl-*N*-(4-chlorophenyl)carbamothioate **11** under our usual conditions (Scheme 6). Unfortunately, compound **11** led to a complex reaction mixture that failed to reveal the presence of possible 4-chlorophenyl isocyanate. However, in addition to modest amounts of the expected tetrahydrothiophenes **3** and **8**, column chromatography separated small amounts (3%) of *S*-phenyl *N*-(4-chlorophenyl)carbamothioate which was the formal product of benzenethiol addition to 4-chlorophenyl isocyanate (Scheme 6).

It is worth noting that the above quinolinone **9g** had already been reported to occur upon cyclization of the same radical **2g**, at that time generated by reacting carbamoyl phenyl selenide **12** with TMS_3SiH/AIBN. Lacking any conclusive evidence, the authors were led to explain the occurrence of **9g** in terms of primary radical 6-endo ring closure followed by extrusion of tosyl radical from the cyclized benzylic radical (Scheme 7).[8] Our present chemical evidence strongly suggests that this original mechanistic explanation should be essentially rejected.

As we proved that *N*-benzylcarbamothioates provide a valuable radical entry to pyrrolidinone compounds,[20] we were finally prompted to attempt extension of our tin-free protocol to the construction of four-membered ring azetidinones. We were aware that our reductive protocol might have been less rewarding for azetidinones in view of the known fact that radical 4-exo ring closures, including those of carbamoyl radicals, are significantly slower than the 5-exo analogues.[21] In fact, the successful outcome of very recent carbamoyl radical cyclizations

SCHEME 8



leading to β-lactams was largely based on the use of nonreductive reaction conditions.[9−11]

Our first attempt to obtain azetidinone **13h** from *N*-benzyl-*N*-allylcarbamothioate **1h** was largely frustrating. The usual reaction of **1h** resulted in extensive production of formamide **5h** (55%), whereas azetidinone **13h** occurred only to a very poor extent (12%) and was even accompanied by a larger amount of pyrrolidinone **4h** (Scheme 8). Evidently, the ensuing carbamoyl radical **2h** was highly reluctant to undergo 4-exo cyclization onto the terminal alkene and thus preferred to exhibit major hydrogen abstraction from the thiol as well as alternative 5-endo cyclization.[22]

More rewarding results were, however, obtained from the reactions of *N*-benzyl-*N*-2-butenyl-, **1i**, and *N*-benzyl-*N*-(3-phenyl-2-propenyl)carbamothioate **1j**. In such cases, the azetidinones **13i**,**j** were obtained in noticeably enhanced yields (25−32%) as the sole cyclized products, although still associated with important amounts of the concomitant formamides **5i**,**j** (Scheme 8). Apparently, the resultant carbamoyl radicals **2i**,**j** exhibited more efficient 4-exo cyclization owing to the enhanced stabilization provided by the methyl and, especially, the phenyl substituent to the ring-closed β-oxoazetidinylmethyl radical. An even more promising result was obtained from our final reaction with the *N*-Boc-substituted *N*-allylcarbamothioate **1k**. In contrast with the *N*-benzyl analogue **1h**, compound **1k** furnished a useful yield (42%) of azetidinone **13k**, and no traces of any accompanying pyrrolidinone or reduced formamide **5k** were observed (Scheme 8).[23] This finding interestingly discovered that the presence of the electron-withdrawing Boc substituent on the carbamoyl nitrogen might play a beneficial role in carbamoyl radical cyclizations onto alkenes.

Conclusions

In this work, we have devised a new, valuable tin-free protocol for the generation of carbamoyl radicals using accessible *S*-4-pentynyl carbamothioate precursors. The present procedure can be usefully employed to attain cyclizations of *N*-benzylcarbamoyl radicals leading to pyrrolidinones, but it seems of minor utility for those leading to azetidinones. To obtain better results with the latter, a crucial role might be played

(19) Luo, L.; Bartberger, M. D.; Dolbier, W. R., Jr. *J. Am. Chem. Soc.* **1997**, *119*, 12366.

(20) Comparable yields of pyrrolydinones and indolinones have been reported in previous cyclizations of *N*-benzylcarbamoyl radicals derived from 1-benzylcarbamoyl-1-methylcyclohexa-2,5-dienes; see ref 9a,b. However, a better yield of pyrrolidinone **4a** was achieved when the carbamoyl radical **2a** was generated by UV photolysis of the corresponding oxime oxalate amide; see ref 10a.

(21) DiLabio, G. A.; Scanlan, E. M.; Walton, J. C. *Org. Lett.* **2005**, *7*, 155.

(22) In principle, pyrrolidinone **4h** might also arise from ring enlargement of the initial 4-exo ring-closed β-oxoazetidinylmethyl radical, see ref 12.

(23) Only minor amounts of a mixture of unidentified products were obtained.

by *N*-Boc substituent. In this work, we have additionally shown that *N*-tosylated carbamoyl radicals have a peculiar tendency to form the corresponding isocyanate by β-elimination of tosyl radical. The peculiar behavior of *N*-tosyl-*N*-(2-vinylphenyl)-carbamoyl radicals might be exploited for the construction of quinolinone ring systems.

Experimental Section

Physical and analytical data for the new pentynyl carbamothioates **1a**−**k** and **11** are as follows:[24]

***S*-(4-Pentynyl) *N*-benzyl-*N*-(3-butenyl)carbamothioate (1a):** oil; IR ($CHCl_3$) ν_{max} (cm^{-1}) 3298 (≡CH), 1648 (CO); ^1H NMR (300 MHz, $CDCl_3$) δ 1.83−1.93 (2 H, m), 1.97 (1 H, t, J = 2.7 Hz), 2.24−2.36 (4 H, m), 3.05 (2 H, t, J = 7.2 Hz), 3.26−3.47 (2 H, br s), 4.52−4.67 (2 H, m), 4.98−5.10 (2 H, m), 5.66−5.80 (1 H, m), 7.20−7.38 (5 H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.4 (CH_2), 28.8 (CH_2), 29.3 (CH_2), 32.2 (CH_2), 46.6 (CH_2), 50.1 (CH_2), 51.4 (CH_2), 69.0, 83.2 (C), 116.9 (CH_2), 117.2 (CH_2), 127.1, 127.4, 127.7, 128.5, 134.3 (C), 134.8 (C), 168.0 (CO); MS (ESI) 310 $(M + Na)^+$. Anal. Calcd for $C_{17}H_{21}NOS$: C, 71.04; H, 7.36; N, 4.87. Found: C, 71.07; H, 7.34; N, 4.86.

***S*-(4-Pentynyl) *N*-benzyl-*N*-(2-vinylphenyl)carbamothioate (1b):** oil; IR (neat) ν_{max} (cm^{-1}) 3297 (≡CH), 1654 (CO); ^1H NMR (300 MHz, $CDCl_3$) δ 1.75−1.86 (2 H, m), 1.93 (1 H, t, J = 2.7 Hz), 2.24 (2 H, dt, J = 2.7, 6.9 Hz), 2.95 (2 H, m), 4.24 (1 H, d, J = 14.2 Hz), 5.31 (1 H, dd, J = 1.1, 11.1 Hz), 5.36 (1 H, d, J = 14.2 Hz), 5.75 (1 H, dd, J = 1.1, 17.4 Hz), 6.63 (1 H, dd, J = 11.1, 17.4 Hz), 6.81 (1 H, dd, J = 1.2, 7.9 Hz), 7.17 (3 H, m), 7.25 (3 H, m), 7.35 (1 H, m), 7.62 (1 H, dd, J = 1.2, 7.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.4 (CH_2), 28.8 (CH_2), 29.9 (CH_2), 53.8 (CH_2), 68.8, 83.3 (C), 116.8 (CH_2), 126.2, 126.4, 127.6, 128.4, 129.3, 131.1, 131.5, 136.5 (C), 136.6 (C), 137. 2 (C), 169.1 (CO); MS (ESI) 359 $(M + Na)^+$. Anal. Calcd for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18. Found: C, 75.22; H, 6.30; N, 4.20.

***S*-(4-Pentynyl) *N*-benzyl-*N*-(2-isopropenylphenyl)carbamothioate (1c):** oil; IR ($CHCl_3$) ν_{max} (cm^{-1}) 3307 (≡CH), 1649 (CO); ^1H NMR (300 MHz, $CDCl_3$) δ 1.74−1.85 (2 H, m), 1.91 (1 H, t, J = 2.7 Hz), 2.12 (3 H, s), 2.23 (2 H, dt, J = 2.7, 7.1 Hz), 2.83−3.06 (2 H, m), 3.96 (1 H, d, J = 14.4 Hz), 5.16−5.24 (2 H, m), 5.55 (1 H, d, J = 14.4 Hz), 6.81 (1 H, d, J = 7.9 Hz), 7.06−7.20 (3 H, m), 7.21−7.28 (3 H, m), 7.30−7.32 (2 H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.5 (CH_2), 23.2, 28.9 (CH_2), 29.9 (CH_2), 53.0 (CH_2), 68.8, 83.3 (C), 116.8 (CH_2), 127.3, 127.4, 128.3, 128.9, 128.9, 129.8, 131.9, 136.4 (C), 136.8 (C), 142.3 (C), 142.9 (C), 169.1 (CO). Anal. Calcd for $C_{22}H_{23}NOS$: C, 75.61; H, 6.63; N, 4.01. Found: C, 75.58; H, 6.62; N, 4.02.

Ethyl (*E*)-3-(2-{benzyl[(4-pentynylsulfanyl)carbonyl]amino}-phenyl)-2-propenoate (1d): oil; IR (neat) ν_{max} (cm^{-1}) 3297 (≡CH), 1729 (CO), 1713 (CO); ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (3 H, t, J = 7.1 Hz), 1.74−1.86 (2 H, m), 1.92 (1 H, t, J = 2.8 Hz), 2.23 (2 H, dt, J = 2.8, 7.1 Hz), 2.87−3.05 (2 H, m), 4.24 (2 H, q, J = 7.1 Hz), 4.54 (1 H, d, J = 14.5 Hz), 5.14 (1 H, d, J = 14.5 Hz), 6.31 (1 H, d, J = 15.8 Hz), 6.94 (1 H, dd, J = 1.6, 7.9 Hz), 7.13−7.18 (2 H, m), 7.22−7.26 (3 H, m), 7.31 (1 H, dt, J = 1.6, 7.7 Hz), 7.39 (1 H, dt, J = 1.1, 7.7 Hz), 7.47 (1 H, d, J = 15.8 Hz), 7.63 (1 H, dd, J = 1.6, 7.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 16.8 (CH_2), 28.5 (CH_2), 29.4 (CH_2), 53.8 (CH_2), 59.8 (CH_2), 68.5, 82.5 (C), 120.3, 126.8, 127.3, 127.9, 128.9, 130.2, 130.9 (C), 133.8 (C), 135.7 (C), 138.4, 165.5 (CO), 168.4 (CO). Anal. Calcd for $C_{24}H_{25}NO_3S$: C, 70.73; H, 6.18; N, 3.44. Found: C, 70.76; H, 6.19; N, 3.45.

***S*-(4-Pentynyl) *N*-3-butenyl-*N*-[(4-methylphenyl)sulfonyl]carbamothioate (1e):** solid; mp 40−41 °C; IR ($CHCl_3$) ν_{max} (cm^{-1}) 3290 (≡CH), 1678 (CO); ^1H NMR (300 MHz, $CDCl_3$) δ 1.73−1.83 (2 H, m), 1.95 (1 H, t, J = 2.8), 2.24 (2 H, dt, J = 6.6, 2.8 Hz), 2.44 (3 H, s), 2.50−2.60 (2 H, m), 2.96 (2 H, t, J = 6.6 Hz), 3.87−3.94 (2 H, m), 5.09−5.21 (2 H, m), 5.76−5.87 (1 H, m), 7.32 (2 H, d, J = 8.4 Hz), 7.87 (2 H, d, J = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.4 (CH_2), 21.7, 27.9 (CH_2), 29.6 (CH_2), 34.4 (CH_2), 46.7 (CH_2), 69.3, 82.7 (C), 117.9 (CH_2), 128.4, 129.4, 133.6, 136.2 (C), 145.1 (C), 168.4 (CO); MS (ESI) 374 $(M + Na)^+$. Anal. Calcd for $C_{17}H_{21}NO_3S_2$: C, 58.09; H, 6.02; N, 3.99. Found: C, 58.01; H, 6.03; N, 4.01.

***S*-(4-Pentynyl) *N*-(2-vinylphenyl)-*N*-[(4-methylphenyl)sulfonyl]carbamothioate (1f):** oil; IR ($CHCl_3$) ν_{max} (cm^{-1}) 3293 (≡CH), 1682 (CO); ^1H NMR (300 MHz, $CDCl_3$) δ 1.66−1.76 (2 H, m), 1.89 (1 H, t, J = 2.6 Hz), 2.15 (2 H, dt, J = 2.6, 7.0 Hz), 2.46 (3 H, s), 2.75−2.92 (2 H, m), 5.41 (1 H, dd, J = 0.9, 11.0 Hz), 5.90 (1 H, dd, J = 0.9, 17.4 Hz), 6.79 (1 H, dd, J = 11.0, 17.4 Hz), 7.20 (1 H, d, J = 8.1 Hz), 7.21−7.43 (3 H, m), 7.50 (1 H, t, J = 7.2 Hz), 7.72 (1 H, d, J = 7.7 Hz), 7.96 (2 H, d, J = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.3 (CH_2), 21.7 (CH_3), 27.8 (CH_2), 30.1 (CH_2), 69.1, 82.7 (C), 117.9 (CH_2), 126.2, 128.7, 129.0, 129.3, 131.0, 131.2, 131.4, 132.0 (C), 135.7 (C), 138.9 (C), 145.3 (C), 169.1 (CO); MS (ESI) 422 $(M + Na)^+$. Anal. Calcd for $C_{21}H_{21}NO_3S_2$: C, 63.13; H, 5.30; N, 3.51. Found: C, 63.10; H, 5.31; N, 3.50.

***S*-(4-Pentynyl) *N*-(2-isopropenylphenyl)-*N*-[(4-methylphenyl)-sulfonyl]carbamothioate (1g):** solid; mp 78−79 °C; IR ($CHCl_3$) ν_{max} (cm^{-1}) 3308 (≡CH), 1676 (CO); ^1H NMR (300 MHz, $CDCl_3$) δ 1.66−1.78 (2 H, m), 1.90 (1 H, t, J = 2.8 Hz), 2.13−2.20 (2 H, m), 2.18 (3 H, s), 2.58 (3 H, s), 2.74−2.96 (2 H, m), 5.24−5.28 (1 H, m), 5.29−5.32 (1 H, m), 7.16 (1 H, dd, J = 1.2, 7.7 Hz), 7.30−7.66 (5 H, m), 7.96(2 H, d, J = 8.5 Hz); 7.13−7. ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.5 (CH_2), 21.8, 24.0, 28.1 (CH_2), 30.3 (CH_2), 69.3, 82.9 (C), 117.1 (C), 117.8 (CH_2), 120.6, 124.4, 127.3, 128.0, 129.3, 129.6, 130.1, 130.9, 131.3, 136.2 (C), 141.7 (C), 145.1 (C), 145.9 (C), 169.5 (CO); MS (ESI) 436 $(M + Na)^+$. Anal. Calcd for $C_{22}H_{23}NO_3S_2$: C, 63.89; H, 5.61; N, 3.39. Found: C, 63.95; H, 5.62; N, 3.40.

***S*-(4-Pentynyl) *N*-allyl-*N*-benzylcarbamothioate (1h):** oil; IR ($CHCl_3$) ν_{max} (cm^{-1}) 3305 (≡CH), 1694 (CO); ^1H NMR (300 MHz, $CDCl_3$) δ 1.83−1.93 (2 H, m), 1.97 (1 H, t, J = 2.7 Hz), 2.32 (2 H, dt, J = 2.6, 7.0 Hz), 3.07 (2 H, t, J = 7.0 Hz), 3.91(2 H, br s), 4.57 (2 H, s), 5.08−5.26 (2 H, m), 5.75 (1 H, ddt, J = 5.7, 10.2, 17.1 Hz), 7.21−7.38 (5 H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.4 (CH_2), 28.8 (CH_2), 29.3 (CH_2), 33.2 (CH_2), 49.0 (CH_2), 69.8, 83.2 (C), 117.8 (CH_2), 127.4, 127.9, 128.5, 132.1, 168.1 (CO) (the quaternary aromatic carbon was hidden); MS (ESI) 296 $(M + Na)^+$. Anal. Calcd for $C_{16}H_{19}NOS$: C, 70.29; H, 7.00; N, 5.12. Found: C, 70.31; H, 6.99; N, 5.13.

***S*-(4-Pentynyl) *N*-benzyl-*N*-2-butenylcarbamothioate (1i):** oily mixture of the cis/trans isomers; IR ($CHCl_3$) ν_{max} (cm^{-1}) 3297 (≡CH), 1651 (CO); ^1H NMR (300 MHz, $CDCl_3$) *d* 1.70 (3 H, br d, J = 5.8 Hz), 1.84−1.94 (2 H, m), 1.98 (1 H, t, J = 2.5 Hz), 2.32 (2 H, dt, J = 2.5, 6.9 Hz), 3.06 (2 H, t, J = 6.9 Hz), 3.76−3.93 (2 H, m), 4.56 (2 H, br s), 5.34−5.44 (1 H, m), 5.56 (1 H, br s), 7.21−7.38 (5 H, m); ^{13}C NMR (75 MHz, $CDCl_3$) *d* 17.2 (CH_2), 17.3, 28.7 (CH_2), 29.0 (CH_2), 36.9 (CH_2), 47.8 (CH_2), 48.7 (CH_2), 68.8, 82.9 (C), 124.6, 127.1, 127.7, 128.0, 128.2, 129.3, 135.9 (C), 136.7 (C), 167.5 (CO); MS (ESI) 310 $(M + Na)^+$. Anal. Calcd for $C_{17}H_{21}NOS$: C, 71.04; H, 7.36; N, 4.87. Found: C, 71.07; H, 7.35; N, 4.88.

***S*-(4-Pentynyl) *N*-benzyl-*N*-[(*E*)-3-phenyl-2-propenyl]carbamothioate (1j):** oil; IR ($CHCl_3$) ν_{max} (cm^{-1}) 3295 (≡CH), 1648 (CO); ^1H NMR (300 MHz, $CDCl_3$) *d* 1.86−1.96 (2 H, m), 1.98 (1 H, t, J = 2.5 Hz), 2.32 (2 H, dt, J = 2.5, 7.1 Hz), 3.10 (2 H, t, J = 7.1 Hz), 4.08 (2 H, br s), 4.62 (2 H, br s), 6.10 (1 H, dt, J = 6.3, 16.4 Hz), 6.44 (1 H, br d, J = 16.4 Hz), 7.22−7.38 (10 H, m); ^{13}C NMR (75 MHz, $CDCl_3$) *d* 17.5 (CH_2), 28.9 (CH_2), 29.4 (CH_2), 48.3 (CH_2), 65.9 (CH_2), 69.0, 83.2 (C), 123.6, 126.4, 127.3 (C), 127.5, 127.8, 128.5, 128.6, 133.2, 136.2 (C), 168.2 (CO); MS (ESI)

(24) Owing to slow rotation around the carbonyl carbon−nitrogen bond, carbamothioate carbons near to nitrogen usually showed broad or split signals in the ^{13}C NMR spectra.

372 $(M + Na)^+$. Anal. Calcd for $C_{22}H_{23}NOS$: C, 75.61; H, 6.63; N, 4.01. Found: C, 75.58; H, 6.64; N, 4.00.

5-({[Allyl(*tert*-butoxycarbonyl)amino]carbonyl}sulfanyl)-1-pentyne (1k): oil; IR ($CHCl_3$) ν_{max} (cm^{-1}) 3294 (≡CH), 1656 (CO); ^1H NMR (300 MHz, $CDCl_3$) *d* 1.53 (9 H, s), 1.80−1.92 (2 H, m), 1.97 (1 H, t, $J = 2.5$ Hz), 2.32 (2 H, dt, $J = 2.5$, 6.8 Hz), 2.96 (2 H, t, $J = 7.4$ Hz), 4.34 (2 H, dt, $J = 1.5$, 5.6 Hz), 5.07−5.21(2 H, m), 5.80 (1 H, ddt, $J = 5.6$, 5.8, 10.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) *d* 17.6 (CH_2), 27.8 (CH_2), 27.9, 29.6 (CH_2), 47.5 (CH_2), 68.9, 83.1 (C), 83.8 (C), 116.7, 132.7 (CH_2), 152.6 (CO), 170.6 (CO); MS (ESI) 306 $(M + Na)^+$. Anal. Calcd for $C_{14}H_{21}NO_3S$: C, 59.34; H, 7.47; N, 4.94. Found: C, 59.36; H, 7.46; N, 4.95.

***S*-4-Pentynyl *N*-(4-chlorophenyl)-*N*-[(4-methylphenyl)sulfonyl]carbamothioate (11):** solid; mp 112−113 °C; IR ($CHCl_3$) ν_{max} (cm^{-1}) 3308 (≡CH), 1681(CO); ^1H NMR (300 MHz, $CDCl_3$) δ 1.81−1.91 (2 H, m), 1.91 (1 H, t, $J = 2.8$ Hz), 2.17 (2 H, dt, $J = 2.8$, 7.4 Hz), 2.47 (3 H, s), 2.86 (2 H, t, $J = 7.4$ Hz), 7.25 (2 H, d, $J = 8.2$ Hz), 7.37 (2 H, d, $J = 8.6$ Hz), 7.45 (2 H, d, $J = 8.6$ Hz), 7.91 (2 H, d, $J = 8.2$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.6 (CH_2), 21.7, 28.0 (CH_2), 30.5 (CH_2), 69.5, 82.7 (C), 129.0, 129.6, 129.8, 132.5, 133.0 (C), 135.7 (C), 137.0 (C), 145.4 (C), 169.1 (CO); MS (ESI) 430 $(M + Na)^+$. Anal. Calcd for $C_{19}H_{18}ClNO_3S_2$: C, 55.94; H, 4.45; N, 3.43. Found: C, 55.90; H, 4.46; N, 3.42.

Physical and analytical data for the new products (*E*)- and (*Z*)-**8** and **13k** were as follows:

Dihydro-(*E*)-2(3*H*)-thiophenylidenemethyl 4-methylphenyl sulfone [(*E*)-8]:[25] solid; mp 94−95 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 2.18 (2 H, m), 2.43 (3 H, s), 3.06 (2 H, t, $J = 6.6$ Hz), 3.15 (2 H, dt, $J_d = 1.9$ Hz, $J_t = 6.6$ Hz), 6.26 (1 H, t, $J = 1.9$ Hz), 7.30 (2 H, d, $J = 8.3$ Hz), 7.76 (2 H, d, $J = 8.3$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.3, 30.4 (CH_2), 34.7 (CH_2), 35.2 (CH_2), 115.8, 127.6, 130.4, 140.5 (C), 144.4 (C), 167.4 (C); HRMS (*m*/*z*, M^+) calcd for $C_{12}H_{14}S_2O_2$ 254.04353, found 254.04374. Anal. Calcd for $C_{12}H_{14}O_2S_2$: C, 56.66; H, 5.55. Found: C, 56.80; H, 5.56.

Dihydro-(*Z*)-2(3*H*)-thiophenylidenemethyl 4-methylphenyl sulfone [(*Z*)-8]:[25] solid; mp 199−200 °C;^1H NMR (300 MHz, $CDCl_3$) δ 2.07 (2 H, m), 2.43 (3 H, s), 2.75 (2 H, dt, $J_d = 1.4$ Hz, $J_t = 7.0$ Hz), 3.11 (2 H, t, $J = 6.4$ Hz), 6.25 (1 H, t, $J = 1.4$ Hz), 7.31 (2 H, d, $J = 8.2$ Hz), 7.84 (2 H, d, $J = 8.2$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.3, 28.8 (CH_2), 36.3 (CH_2), 40.8 (CH_2), 115.8, 127.8, 130.3, 140.0 (C), 144.5 (C), 165.3 (C); HRMS (*m*/*z*, M^+) calcd for $C_{12}H_{14}S_2O_2$ 254.04353, found 254.04352. Anal. Calcd for $C_{12}H_{14}O_2S_2$: C, 56.66; H, 5.55. Found: C, 56.82; H, 5.58.

***tert*-Butyl 3-methyl-2-oxo-1-azetanecarboxylate (13k):** oil; IR ($CHCl_3$) ν_{max} (cm^{-1}) 1804 (CO), 1718 (CO); ^1H NMR (300 MHz, $CDCl_3$) δ 1.35 (3 H, d, $J = 7.1$ Hz), 1.53 (9 H, s), 3.18−3.29 (2 H, m), 3.68−3.74 (1 H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.5, 28.0, 43.9, 45.7 (CH_2), 83.4 (C), 148.2 (CO), 168.5 (CO); MS (ESI) 208 $(M + Na)^+$. Anal. Calcd for $C_9H_{15}NO_3$: C, 58.36; H, 8.17; N, 7.57. Found: C, 58.31; H, 8.18; N, 7.60.

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Supporting Information Available: General remarks; general synthesis of pentynyl carbamothioates **1a**−**k** and **11**; general procedure for the reactions of carbamothioates **1a**−**k** and **11** with benzenethiol and table of the results. This material is available free of charge via the Internet at http://pubs.acs.org.

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(25) Configurational assignment to (*E*)-**8a** and (*Z*)-**8a** was based on the expectation that the ^4J of the vinylic proton with the allylic-like ring protons should be larger for the (*E*)- than for the (*Z*)-isomer; see ref 2h.