Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters
Tetrahedron Letters 45 (2004) 401–405

Mild and efficient synthesis of carbazates and dithiocarbazates via a three-component coupling using Cs_2CO_3 and TBAI

Daniel L. Fox, John T. Ruxer, John M. Oliver, Kasey L. Alford and Ralph Nicholas Salvatore*

Department of Chemistry, Western Kentucky University, 1 Big Red Way, Bowling Green, KY 42101-3576, USA

Received 30 September 2003; revised 21 October 2003; accepted 23 October 2003

Abstract—Efficient methods for the synthesis of carbazates and dithiocarbazates have been developed. In the presence of cesium carbonate (Cs_2CO_3) and tetrabutylammonium iodide (TBAI) a hydrazine, CO_2 or CS_2, and an alkyl halide underwent a three-component coupling at room temperature. Various unprotected hydrazines and alkyl halides were examined and the results demonstrated this methodology was highly chemoselective. Applications toward the synthesis of azadepsipeptides and other pseudopeptides are described.

Substituted hydrazines continue to attract considerable attention due to their widespread use in organic synthesis, industrial, and biological/medicinal applications.[1] In particular, carbazates and dithiocarbazates hold unique applications serving as protecting groups,[2] synthetic precursors,[3] and donor ligands in complexation reactions with transition metals.[4] Likewise, the carbazate moiety has enjoyed success in the synthesis of azadepsipeptides,[5] a novel class of peptidomimetics, which have been recognized as promising targets for novel pharmaceuticals in the treatment of various diseases. In a similar fashion, the dithiocarbonyl moiety may also serve as a novel linker in peptidomimetic synthesis.[6] Traditional synthetic methods for the preparation of carbazates and dithiocarbazates are limited by the need for the use of specialized or toxic reagents such as phosgene[7] in the presence of *N*-protecting groups on the hydrazine (e.g., Boc).[8] As an attractive alternative, carbon dioxide was recently employed as a phosgene equivalent in the synthesis of azadepsipeptides. However, this protocol lacks generality since the procedure was limited to the use of *N*-Boc-alkylhydrazines with primary alkyl halides.[7] Therefore, phosgene and its equivalents still remain the common reagents of choice.

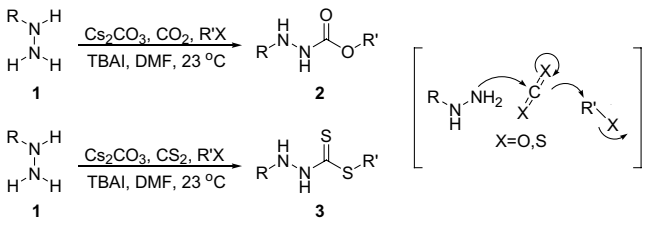
In connection with our ongoing interest toward the synthesis of azadepsipeptides and other pseudopeptide analogues containing backbone modifications, we set out to investigate the development of more efficient and safer protocols better suited for peptidomimetic synthesis. Herein, we report a three-component coupling reaction for the synthesis of carbazates and dithiocarbazates in the absence of nitrogen protecting groups with various alkyl halides.

In the presence of cesium carbonate (Cs_2CO_3), tetrabutylammonium iodide (TBAI), and *N*,*N*-dimethylformamide (DMF), as the solvent of choice, various unprotected hydrazines **1** smoothly coupled with either carbon dioxide or carbon disulfide at ambient temperature to produce the resultant carbazate or dithiocarbazate anion, respectively.[9] Subsequent addition of an alkyl halide produced the corresponding carbazate **2** or dithiocarbazate **3** exclusively in moderate to high yield (Scheme 1).

The reaction conditions have shown to be highly chemoselective facilitating the three-component coupling at the least sterically hindered nitrogen atom on the hydrazine. Moreover, employing these conditions, direct *N*-alkylation products and competing overalkylations at the more nucleophilic secondary nitrogen were

Keywords: hydrazine; carbazates; dithiocarbazates; azadepsipeptide; cesium carbonate.
* Corresponding author. Tel.: +1-270-745-3271; fax: +1-270-745-5361; e-mail: ralph.salvatore@wku.edu

0040-4039/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2003.10.144



Scheme 1.

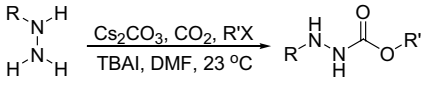
suppressed.[10] Therefore, we believe this methodology strongly compliments the Cs_2CO_3-promoted carbamation of primary amines previously reported.[10]

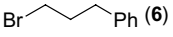
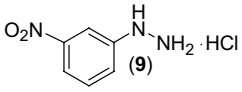
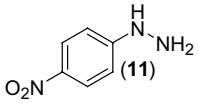
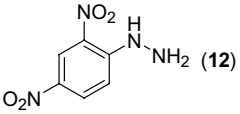
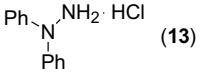
Initially, structurally diverse hydrazines were probed to test the feasibility of carbazate formation employing the given conditions. We were pleased to find that various hydrazines underwent facile *N*-alkylation to afford carbazates **2** in moderate to high yield. In this conversion, the CO_2 moiety was easily incorporated into the hydrazine by rapidly bubbling carbon dioxide gas through the reaction mixture to afford the carbazic acid intermediate, followed by addition of the alkyl halide. Conversely, if the reaction mixture was not initially saturated with the environmentally benign gas prior to halide addition, as in the case with the use of dry ice as the CO_2 source, low yields of **2** typically resulted and direct *N*-alkylation products arise.

Several examples illustrating the simplicity and practicality of this methodology are summarized in Table 1. As a preliminary study of feasibility, phenylhydrazine hydrochloride (**4**) underwent reaction with carbon dioxide, which subsequently united with benzyl bromide (**5**) as the halide of choice, to give the desired benzyl carbazate in 79% isolated yield (Table 1, entry 1). Similarly, **4** underwent insertion to CO_2 followed by reaction with an unreactive bromide, 1-bromo-3-phenylpropane (**6**) to give the desired product in good yield after the same time period (entry 2). Likewise, benzylhydrazine dihydrochloride (**7**), a reactive hydrazine was joined with **6** via a CO_2 bridge to afford the target carbazate **2** in excellent yield (entry 3). Having thus established that the aforementioned protocol was highly useful with unhindered hydrazines, we next set out to explore the synthetic utility of these conditions by examining a sterically bulky hydrazine. We were pleased to find that *tert*-butylhydrazine hydrochloride (**8**) reacted smoothly with **6** in the presence of carbon dioxide to produce the corresponding carbazate **2** in an excellent yield (entry 4).[11]

In a continuing study, we next turned our attention to the synthesis of carbazates using aromatic hydrazines that contain an electron-withdrawing substituent. Using the conditions described above, *m*-nitrophenylhydrazine hydrochloride (**9**) underwent a three-component coupling reaction with PMBCl (**10**) to produce the carbazate product, albeit, in lower yield (entry 5). On the other

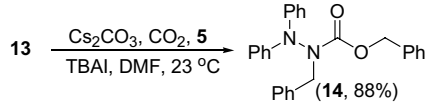
Table 1. Carbazate formation using hydrazines, halides, and CO_2 in the presence of Cs_2CO_3 and TBAI



Entry	Hydrazine ($RNHNH_2$)	Halide (R′X)	Time (h)	Yield (%)
1	$PhNHNH_2 \cdot HCl$ (**4**)	BnBr (**5**)	46	79
2	**4**	 (**6**)	46	73
3	$BnNHNH_2 \cdot 2HCl$ (**7**)	**6**	60	88
4	$^tBuNHNH_2 \cdot HCl$ (**8**)	**6**	72	89
5	 (**9**)	PMBCl (**10**)	60	43
6	 (**11**)	**5**	72	67
7	 (**12**)	**5**	128	45
8	 (**13**)	**5**	28	58

hand, *p*-nitrophenylhydrazine (**11**) reacted with BnBr (**5**), generating the desired product in 67% yield after 72 h (entry 6). As expected, 2,4-dinitrophenylhydrazine (**12**) was sluggish resulting in the desired carbazate accompanied along with unreacted starting material **12**, which was recovered (entry 7). Finally, an *N*,*N*-disubstituted hydrazine, 1,1-diphenylhydrazine hydrochloride (**13**) also underwent facile consolidation with **5** to afford the desired product in modest yield after 28 h (entry 8). It is important to note that side products stemming from overalkylations and direct *N*-alkylation with the alkyl halide were mitigated using this procedure.

Owing to the above-mentioned protocols, we also uncovered a facile three-component, one-pot synthesis of *N*-alkyl carbazates (Scheme 2). Employing the conditions mentioned above, 1,1-diphenylhydrazine·HCl (**13**) underwent a three-way coupling with benzyl bromide (**5**) and CO_2. Upon conversion of the starting hydrazine **13** to carbazate **2** (monitored via TLC), an additional 3 equiv of Cs_2CO_3 was added and stirred for an additional hour at room temperature. Subsequent addition of excess **5** (3 equiv) resulted indirect *N*-alkylation for the exclusive formation *N*-alkyl carbazate (**14**) in 88% isolated yield. It is important to highlight, that isolation of intermediate **2** proved unnecessary offering shortened synthetic sequences. Currently, a one-pot carbazate followed by *N*-alkylation procedure using a different alkyl halide is under investigation and these results will be reported in due course.

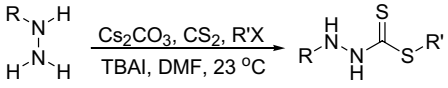


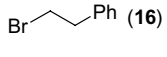
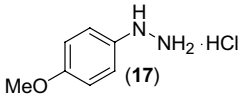
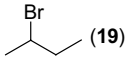
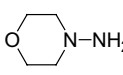
Scheme 2.

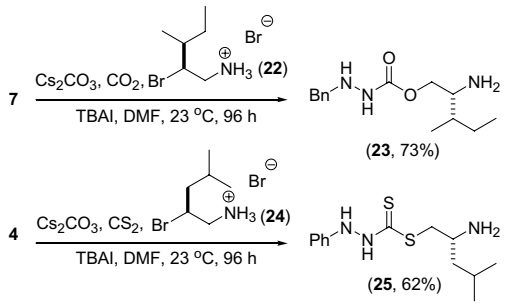
Having established an effective procedure for the synthesis of carbazates, we next decided to extend our efforts toward the synthesis of dithiocarbazates using carbon disulfide. As shown in Table 2, numerous bare hydrazines were screened with various halides to test the potential of this protocol to the full extent. For instance, methylhydrazine (**15**), a very reactive hydrazine, underwent a three-component coupling with CS_2, and (2-bromoethyl)benzene (**16**) in short reaction time to afford **3** in a good yield (entry 1). Likewise, *p*-methoxyphenylhydrazine hydrochloride (**17**), also underwent consolidation with 1-bromobutane (**18**) to form the dithiocarbazate adduct in an excellent yield (entry 2).[12] Similarly, benzylhydrazine dihydrochloride (**7**) reacted with a secondary bromide, 2-bromobutane (**19**), to afford the coupled product in high yield (entry 3). Next, hydrazines containing either a sterically hindered or electron-withdrawing substituent were examined to provide a more complete picture of the synthetic utility of the reaction conditions. *tert*-Butylhydrazine (**8**) united with CS_2, which in turn coupled with 1-bromo-3-phenylpropane (**6**) offering **3** in an optimum 58% yield (entry 4). Also, 2,4-dinitrophenylhydrazine (**12**) reacted slowly with MeI (**20**) to afford dithiocarbazate **3** in high yield (entry 5). In addition, heterocyclic hydrazines also proved successful using the developed techniques. For example, *N*-aminomorpholine (**21**), united with carbon disulfide to form the dithiocarbazate anion after 1 h, and then with **5** to offer **3** in acceptable yield. Finally, 1,1-diphenylhydrazine (**13**) underwent a reaction with **20** to produce the corresponding methyl dithiocarbazate in an outstanding 92% yield (entry 7).

Keeping the synthesis of azadepsipeptides and other peptidomimetics in mind, we next launched our efforts toward the synthesis of short dimeric analogues, which contain the carbazate or dithiocarbazate moiety as the skeletal backbone. After two unreactive amino bromides

Table 2. Dithiocarbazate formation using hydrazines, halides, and CS_2 in the presence of Cs_2CO_3 and TBAI



Entry	Hydrazine ($RNHNH_2$)	Halide (R′X)	Time (h)	Yield (%)
1	$MeNHNH_2$ (**15**)	 (**16**)	18	76
2	 (**17**)	*n*-BuBr (**18**)	34	94
3	**7**	 (**19**)	120	90
4	**8**	**6**	96	58
5	**12**	MeI (**20**)	144	74
6	 (**21**)	**5**	38	63
7	**13**	**20**	12	92



Scheme 3.

22 and **24** were prepared as hydrobromide salts using a previously reported bromination technique,[13] they were subjected to the standard conditions. As depicted in Scheme 3, benzylhydrazine (**7**) reacted with isoleucine bromide (**22**) via a CO_2 bridge in high yield. Likewise, phenylhydrazine (**7**) also underwent a similar three-component coupling with carbon disulfide and leucine bromide (**24**) to afford the target compound **25** in a 62% yield. In both cases, the secondary bromide rearranged to the primary form via the corresponding aziridinium salt during the alkylations.[13] Using our developed protocol, racemizations were not detected during any alkylations of these chiral substrates and complications stemming from side reactions including secondary alkylations were not observed to a noticeable extent.[14] Moreover, the use of protecting groups proved unnecessary. Carbazate **23** and dithiocarbazate **25** in turn can be used as interesting scaffoldings in order to fashion higher order peptidomimetic compounds, which may prove very interesting in further studies in organic and medicinal chemistry.

In conclusion, a mild and efficient three-way coupling was performed to combine a hydrazine with carbon dioxide or carbon disulfide and halides using cesium carbonate and tetrabutylammonium iodide at room temperature offering a more direct synthesis of carbazates and dithiocarbazates. Various bare hydrazines containing sterically hindered, electron-donating or withdrawing substituents were all compatible while reactive, unreactive, and secondary halides were examined to demonstrate substrate versatility. In addition, chiral substrates encompassing amino acid derivatives were resistant to racemization offering numerous applications in the efficient synthesis of azadepsipeptides and peptidomimetic synthesis. Moreover, these improved reaction conditions are safe and more convenient when compared to conventional synthetic methods averting common side reactions such as direct *N*-alkylation and overalkylations offering a general synthetic protocol.

Acknowledgements

Financial support from the National Science Foundation—Kentucky EPSCoR (596166) is gratefully acknowledged, as is support from Western Kentucky University. Also, we wish to thank Chemetall for their generous supply of cesium bases.

References and Notes

1. (a) Hydrazine and its Derivatives. 4th ed.; *Kirk–Othmer Encyclopedia of Chemical Technology*; Wiley: New York, 1995; Vol. 13; (b) Schmidt, E. W. *Hydrazine and its Derivatives Preparation, Properties, Applications*. 2nd ed.; Wiley-Interscience: New York, 2001; (c) Ragnarsson, U. *Chem. Soc. Rev.* **2001**, *30*, 205–213; (d) Atkinson, R. S. In *Comprehensive Organic Synthesis*; Barton, D., Ollis, W. D., Eds.; Pergamon: London, 1979; Vol. 2, p 219; (e) *Chemistry of Hydrazo-, Azo- and Azoxy Groups*; Patai, S., Ed.; Wiley: New York, 1975; Chapter 4.
2. (a) Sakakibara, S.; Honda, I.; Naruse, M.; Kanaoka, M. *Experientia* **1969**, *25*, 576; (b) Makarova, E. A.; Kosheleva, G. N. *Metody Polucheniya Khim. Reakt. I Preparatov* **1967**, *17*, 26–28; (c) Sakakisbara, S.; Honda, I.; Takada, K.; Miyoshi, M.; Ohnishi, T.; Okumura, K. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 809; (d) Ito, M.; Morino, D. *Experientia* **1968**, *24*, 101; (e) Honda, I.; Shimonishi, Y.; Sakakibara, S. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2415; (f) Quibell, M.; Turnell, W. G.; Johnson, T. *J. Chem. Soc., Perkin Trans. 1* **1993**, *22*, 2843; (g) Sofuku, S.; Mizumura, M.; Hagitani, A. *Nippon Kagaku Zasshi* **1968**, *89*, 721; (h) Gray, C. J.; Quibell, M.; Baggett, N.; Hammerle, T. *Int. J. Pept. Protein Res.* **1992**, *40*, 351.
3. (a) Connolly, T. J.; Crittall, A. J.; Ebrahim, A. S.; Ji, G. *Org. Process Res. Dev.* **2000**, *4*, 526; (b) Henriksen, L.; Jensen, O. R. *Acta Chem. Scand.* **1968**, *22*, 3042; (c) Dovlatyan, V. V.; Avetissyan, F. V.; Papoyan, T. Z.; Gevorgyan, R. A.; Kinoyan, F. S. *Khim. Zh. Aremenii* **2001**, *54*, 85; (d) Nesynov, E. P.; Pel'kis, P. S. *Zh. Prganicheskoi Khimii* **1968**, *4*, 837; (e) Delaby, R.; Brustlein, F.; Warolin, C.; Chabrier, P. *Bull. Soc. Chim. Fr.* **1961**, 2056; (f) Eloy, F.; Moussebois, C. *Bull. Soc. Chim. Belges* **1959**, *68*, 423; (g) Eloy, F.; Moussebois, C. *Bull. Soc. Chim. Belges* **1959**, *68*, 409; (h) Hauser, M. *J. Org. Chem.* **1966**, *31*, 968; (i) Hanefeld, W.; Schlitzer, M. *Arch Pharm.* **1994**, *327*, 413; (j) Lalezari, I. *J. Heterocycl. Chem.* **1985**, *22*, 741; (k) Gordon, M. S.; Krause, J. G.; Linneman-Mohr, M. A.; Parchue, R. R. *Synthesis* **1980**, *3*, 244; (l) Zinner, G.; Krause, T.; Doerschner, K. *Arch Pharm.* **1977**, *310*, 642; (m) Clive, D. L. J.; Denyer, C. V. *J. Chem. Soc., Chem. Commun.* **1971**, *18*, 1112.
4. (a) Dutta, S. K.; Samanta, S.; Ghosh, D.; Butcher, R. J.; Chaudhury, M. *Inorg. Chem.* **2002**, *41*, 5555; (b) Bellerby, J. M.; Edwards, D. A.; Thompsett, D. *Inorg. Chim. Acta* **1986**, *117*, L31; (c) dos Santo-Filho, F.; Kaiser, P.; Roland, C.; Momesso, M. A. *J. Brazilian Chem. Soc.* **1994**, *5*, 97; (d) Huan, D.; Zhiming, G.; Zhijian, H. *Wuji Huaxue Xuebao* **1989**, *5*, 73; (e) Karra, R.; Singh, Y. P.; Rai, A. K. *Phosphorus, Sulfur, Silicon Relat. Elem.* **2000**, *166*, 125; (f) Chauhan, A. K. S.; Misra, M. *J. Indian Chem. Soc.* **1993**, *70*, 148.
5. (a) Marchand-Brynaert, J. *Farmaco* **1995**, *50*, 455; (b) Dorn, C. P.; Zimmermann, M.; Yang, S. S.; Yurewicz, E. C.; Ashe, B. M.; Frankshun, R.; Jones, H. *J. Med. Chem.* **1977**, *20*, 1464; (c) Dorn, C. P.; Yang, S. S. U.S. Patent P2658254.7, 1975; (d) Shemyakin, M. M.; Ovchinnikov, Yu. A.; Kiryushkin, A. A.; Ivanov, V. T. *Tetrahedron Lett.* **1963**, 885.
6. Nagle, A. S.; Salvatore, R. N.; Cross, R. M.; Kapxhiu, E. A.; Sahab, S.; Yoon, C. H.; Jung, K. W. *Tetrahedron Lett.* **2003**, *44*, 5695.
7. Dyker, H.; Scherkenbeck, J.; Gondol, D.; Goehrt, A.; Harder, A. *J. Org. Chem.* **2001**, *66*, 3760.
8. (a) Dutta, A. S.; Morley, J. S. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1712; (b) Nara, S.; Sakamoto, T.; Miyazawa, E.; Kikugawa, Y. *Synth. Commun.* **2003**, *33*, 87, and refer-

ences cited therein; (c) Biel, J. H.; Drukker, A. E.; Mitchell, T. F.; Sprengeler, E. P.; Nuhfer, P. A.; Conway, A. C.; Horita, A. *J. Am. Chem. Soc.* **1959**, *81*, 2805.

9. TBAI was found to be a crucial additive in averting direct *N*-alkylations and overalkylations. TBAI helps to minimize or prohibit overalkylation of the produced carbazate (or dithiocarbazate anion) presumably by enhancing the rate of CO_2 (or CS_2) incorporation and/or stabilizing the incipient anion through the conjugation with the tetrabutylammonium cation. In the absence of TBAI, poor product yields resulted along with side products stemming from direct *N*-alkylation. For similar results using TBAI in faciliating carbamate and carbonate formation, see: Salvatore, R. N.; Chu, F.; Nagle, A. S.; Kapxhiou, E. A.; Cross, R. M.; Jung, K. W. *Tetrahedron* **2002**, *58*, 3329; Also, tetrabutylammonium bromide (TBAB) and various other onium salts have been utilized in supercritical carbon dioxide for the selective formation of urethanes. See: Yoshida, M.; Hara, N.; Okuyama, S. *Chem. Commun.* **2000**, 151.
10. For other chemoselective *N*-alkylations using cesium bases, see: (a) Salvatore, R. N.; Shin, S. I.; Nagle, A. S.; Jung, K. W. *J. Org. Chem.* **2001**, *66*, 1035; (b) Salvatore, R. N.; Flanders, V. L.; Ha, D.; Jung, K. W. *Org. Lett.* **2000**, *2*, 2797; (c) Butcher, K. J. *Synlett* **1994**, 825; (d) McGhee, W.; Riley, D.; Christ, K.; Pan, Y.; Parnas, B. *J. Org. Chem.* **1995**, *60*, 2820; (e) Salvatore, R. N.; Nagle, A. S.; Jung, K. W. *J. Org. Chem.* **2002**, *67*, 674; (f) Salvatore, R. N.; Schmidt, S. E.; Shin, S. I.; Nagle, A. S.; Worrell, J. H.; Jung, K. W. *Tetrahedron Lett.* **2000**, *41*, 9705; (g) Salvatore, R. N.; Ledger, J. A.; Jung, K. W. *Tetrahedron Lett.* **2001**, *42*, 6023; (h) Salvatore, R. N.; Nagle, A. S.; Schmidt, S. E.; Jung, K. W. *Org. Lett.* **1999**, *1*, 1893.
11. Representative experimental procedure for carbazate **2** preparation: To *tert*-butylhydrazine hydrochloride (**8**) (200 mg, 1.61 mmol) in anhydrous *N*,*N*-dimethylformamide (8 mL) were added cesium carbonate (2.1 g, 6.44 mmol, 4 equiv) and tetrabutylammonium iodide (2.1 g, 4.83 mmol, 3 equiv). The reaction mixture was stirred for 2 h at room temperature. Carbon dioxide gas (flow rate $\approx$ 25–30 mL/min) was rapidly bubbled into the reaction mixture for 1 h and then 1-bromo-3-phenylpropane (**6**) (962 mg, 4.83 mmol, 3 equiv) was added into the suspension. The reaction proceeded at ambient temperature with CO_2 gas bubbling for 72 h, during which point **8** was consumed. The reaction mixture was then poured into water (30 mL) and extracted with EtOAc (3 × 30 mL). The organic layer was washed with water (2 × 30 mL), brine (30 mL), and dried over anhydrous sodium sulfate. Evaporation of the solvent followed by flash column chromatography (hexanes–EtOAc, 9:1 v/v) afforded carbazate **2** (360 mg, 89%) as an oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.08 (s, 9H), 1.89 (m, 2H), 2.55 (t, 2H, $J = 7.5$ Hz), 4.10 (t, 2H, $J = 6.5$ Hz), 5.3 (br s, NH), 7.10–7.45 (m, 5H), 8.05 (s, NH). ^{13}C NMR (70 MHz, $CDCl_3$) δ 25.8, 30.5, 31.0, 51.0, 64.0, 125.8, 128.3, 128.6, 138.8, 157.0. MS (EI) m/z 250.17 (M^+). Anal. Calcd for $C_{14}H_{22}N_2O_2$: C, 67.17; H, 8.86; N, 11.19. Found: C, 67.12; H, 8.82; N, 11.21.
12. Representative experimental procedure for dithiocarbazate **3** preparation: To a solution of *p*-methoxyphenylhydrazine hydrochloride (**17**) (200 mg, 1.14 mmol) in anhydrous DMF (6 mL) was added cesium carbonate (1.48 g, 4.56 mmol, 4 equiv) and tetrabutylammonium iodide (1.26 g, 3.42 mmol, 3 equiv) with vigorous stirring for 1 h at ambient temperature under a nitrogen atmosphere. The solution was cooled to 0 °C and carbon disulfide (0.072 mL, 1.2 mmol, 1.1 equiv) was added and stirred for 1 h. After this time period, 1-bromobutane (**18**) (0.13 mL, 1.2 mmol, 1.1 equiv) was added and stirred for 34 h with gentle warming to room temperature. The resultant yellow reaction supension was then poured into water (30 mL) and extracted with EtOAc (3 × 30 mL). The organic layer was washed with water (2 × 30 mL), brine (30 mL), and dried over anhydrous sodium sulfate. The solution was filtered, concentrated in vacuo, and purified via flash column chromatography (hexanes–EtOAc, 9:1 v/v) to afford dithiocarbazate **3** as a yellow oil (280 mg, 94%). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85 (t, 3H, $J = 7.3$ Hz), 1.33 (m, 2H), 1.85 (m, 2H), 2.0 (s, NH), 2.95 (t, 2H, $J = 6.3$ Hz), 3.73 (s, 3H), 4.05 (m, NH), 6.75–7.60 (m, 4H). ^{13}C NMR (70 MHz, $CDCl_3$) δ 13.4, 21.7, 32.2, 33.7, 55.5, 112.0, 114.6, 134.5, 152.4. 203.0. MS (EI) m/z 270.42 (M^+). Anal. Calcd for $C_{12}H_{18}N_2OS_2$: C, 53.30; H, 6.71; N, 10.36. Found: C, 53.26; H, 6.65; N, 10.33.
13. Nagle, A. S.; Salvatore, R. N.; Chong, B. D.; Jung, K. W. *Tetrahedron Lett.* **2000**, *41*, 3011.
14. H NMR, ^{13}C NMR, and 2D NMR analysis indicate the product as a single diastereomer.