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Efficient Carboazidation of Alkenes Using a Radical Desulfonylative Azide Transfer Process

Karin Weidner, André Giroult, Philippe Panchaud, and Philippe Renaud*

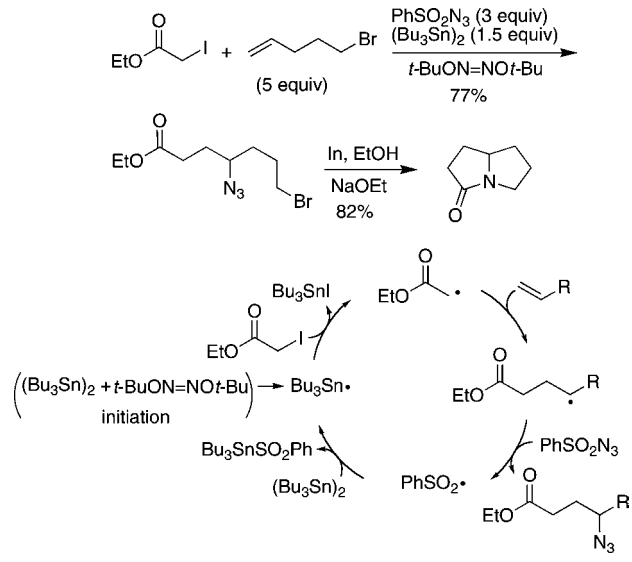
Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, 3012 Bern, Switzerland

Received July 30, 2010; E-mail: philippe.renaud@ioc.unibe.ch

Abstract: The radical-mediated carboazidation of terminal alkenes using electrophilic alkanesulfonyl azides is reported. A single reagent delivers the necessary electrophilic alkyl radical as well as the azido group, and good yields are obtained by using a moderate excess of the carboazidating reagent (1.5−2 equiv). Interestingly, in addition to the starting sulfonyl azide, this method requires only the use of a radical initiator, di-*tert*-butyldiazene. In terms of atom economy, this azide transfer reaction is close to ideal, as SO_2 (1 equiv) is the only side product. The synthetic potential of this process has been demonstrated by a formal synthesis of the alkaloid lepadiformine C.

As part of our ongoing research program directed toward the synthesis of various biologically active alkaloids, we recently developed a method for the radical carboazidation reaction of alkenes.[1] This method proved to be very efficient for the synthesis of several classes of alkaloids, such as pyrrolidine, pyrrolizidine, and indolizidine derivatives.[2] The potential of this method was illustrated by the synthesis of the natural products lepadiformine A,[3] hyacinthacine A1,[4] and indolizidine 167B.[5] From a technical point of view, the carboazidation of an alkene requires the use of a radical precursor (typically an α-iodo or α-xanthate ester), an arenesulfonyl azide as a source of azide, hexabutylditin as a chain-transfer agent, and di-*tert*-butyl hyponitrite as an initiator. A 3-fold excess of the sulfonyl azide is required, and the ditin derivative is used in stoichiometric amounts. The toxicity and the difficulties encountered in removing traces of tin byproduct is a recurring problem in such reactions. Moreover, the best results are obtained when the alkene is used in excess (Scheme 1).

Scheme 1. Carboazidation for a Straightforward Synthesis of Bicyclic Lactams[1a,2]



More recently, a tin-free version involving the use of an excess of triethylborane instead of hexabutylditin was described.[6] Under these conditions, an excess of the azidating reagent was still necessary. Ideally, the most efficient way to run a carboazidation process would be the simple azide transfer reaction depicted in Scheme 2. However, this direct approach cannot be achieved since the second step of this process (eq 2.2 in Scheme 2) does not take place because of the low reactivity of alkyl azides as radical traps. Furthermore, the similar reactivities between the starting azide and the carboazidation product.[7]

A few years ago, Zard developed a tin-free radical allylation procedure based on α-scission of alkylsulfonyl radicals.[8] In this process, a single reagent (an allylsulfone) acts as a source of an alkyl radical as well as a radical trap. Kim developed a closely related chemistry for carbon−carbon bond-forming reactions[9] and in collaboration with Ryu applied this strategy

(1) (a) Renaud, P.; Ollivier, C.; Panchaud, P. *Angew. Chem., Int. Ed.* **2002**, *41*, 3460. (b) Panchaud, P.; Chabaud, L.; Landais, Y.; Ollivier, C.; Renaud, P.; Zigmantas, S. *Chem.—Eur. J.* **2004**, *10*, 3606.
(2) Panchaud, P.; Ollivier, C.; Renaud, P.; Zigmantas, S. *J. Org. Chem.* **2004**, *69*, 2755.
(3) Schär, P.; Renaud, P. *Org. Lett.* **2006**, *8*, 1569.
(4) Chabaud, L.; Landais, Y.; Renaud, P. *Org. Lett.* **2005**, *7*, 2587.
(5) Kapat, A.; Nyfeler, E.; Giuffredi, G. T.; Renaud, P. *J. Am. Chem. Soc.* **2009**, *131*, 17746.
(6) (a) Panchaud, P.; Renaud, P. *J. Org. Chem.* **2004**, *69*, 3205. (b) Panchaud, P.; Renaud, P. *Chimia* **2004**, *57*, 232.
(7) Jimeno, C.; Renaud, P. In *Organic Azides: Syntheses and Applications*; Gansäuer, A., Banert, K., Eds.; Wiley-VCH: Weinheim, Germany, 2009; pp 239.
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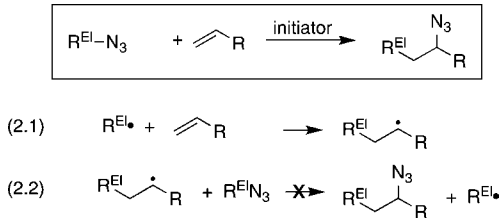
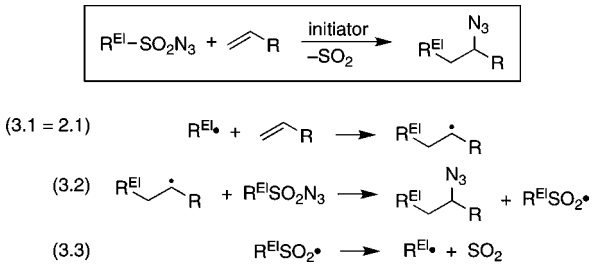
(9) (a) Kim, S. G.; Lim, C. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 3265. (b) Kim, S. *Bull. Chem. Soc. Jpn.* **2007**, *80*, 809.

Scheme 2. The Azide Transfer Process: An Ideal but Unrealistic Carboazidation Reaction



Scheme 3. Proposed Strategy for the Carboazidation of Alkenes Using a Single Reagent (R^{El} Is an Alkyl Residue Bearing at Least One Electron-Withdrawing Group)



for multicomponent reactions involving a carbonylation process.[10] On the basis of a related principle, we decided to explore whether a single reagent could deliver an alkyl radical possessing electrophilic character and also act as the azidating agent for C−N bond formation (Scheme 3). We report here a new class of reagents that allows an atom-economical carboazidation reaction to be run under tin-free conditions. A single reagent and a radical initiator are sufficient to perform carboazidation reactions in high yields. From a mechanistic point of view, the reaction involves first the addition of an electrophilic carbon-centered radical ($R^{El}\cdot$) to the double bond of a terminal alkene (eq 3.1 in Scheme 3). The resulting radical reacts with the sulfonyl azide to provide the product and a sulfonyl radical (eq 3.2 in Scheme 3). After extrusion of SO_2 (eq 3.3 in Scheme 3), the initial carbon-centered radical $R^{El}\cdot$ propagates the chain process. This reaction corresponds to a desulfonylative azide transfer reaction. The problematic step (eq 2.2 in Scheme 2,) is replaced by two potentially rapid and efficient steps (eqs 3.2 and 3.3).

Carboazidation with Ethyl 2-(Azidosulfonyl)ethanoate. The desulfonylative carboazidation process was first tested with the ethoxycarbonylmethyl radical using ethyl 2-(azidosulfonyl)-ethanoate (**1**). Sulfonyl azide **1** was prepared on a multigram scale in two steps from ethyl 2-mercaptoethanoate according to Scheme 4.[11] Before this reagent was tested in a carboazidation process, its stability was probed by differential scanning calorimetry. It starts to decompose at 110 °C with a peak at 124 °C, and therefore, for safety reasons the carboazidation optimization was carried out in benzene at ambient pressure to avoid temperatures exceeding 80 °C.

The carboazidation of 1-octene with 2 equiv of **1** was chosen for the optimization experiments (eq 1), and the results are summarized in Table 1. Initiation with azobis(isobutyronitrile) (AIBN) afforded the carboazidation product in very low yield (<5%; entry 1). This result is not surprising, as the 2-cyanoprop-2-yl radical, because of its electrophilic character, probably does not directly react with the sulfonyl azide. The use of the

Scheme 4. Synthesis of Ethyl 2-(Azidosulfonyl)acetate (**1**)

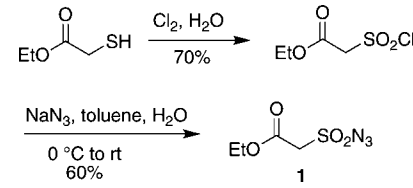
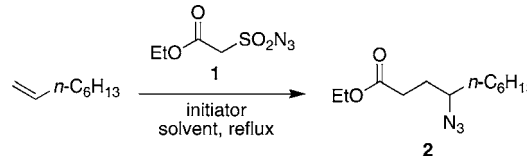


Table 1. Optimization of Reaction Conditions for Equation 1

entry	initiator	solvent	equiv of **1**	time (h)	yield (%)
1	AIBN	benzene	2	12	<5
2	Et_3B/air	benzene	2	6	<5
3	$(c\text{-}C_6H_{11})_3B$/air	benzene	2	4	52
4	*t*-BuN=N*t*-Bu, sun lamp, 300 W	benzene	2	24	67
5	*t*-BuN=N*t*-Bu, sun lamp, 300 W	*tert*-butyl alcohol	2	2	86
6	*t*-BuN=N*t*-Bu, sun lamp, 300 W	*tert*-butyl alcohol	1.5	2	85

triethylborane/air system provided only trace amounts of the desired carboazidation product (entry 2). In this case again, the nucleophilicity of the ethyl radical is probably not sufficient to ensure an efficient azidation. This was confirmed by the experiment with the tricyclohexylborane/air system (entry 3). An encouraging yield of 52% was obtained using this initiator. However, the purification of the product proved to be difficult, and this system was not further investigated. A clean reaction was obtained when the reaction was initiated with di-*tert*-butyldiazene (*t*-BuN=N*t*-Bu) under irradiation (sun lamp, 300 W) (entry 4), and the product was isolated in 67% yield.[12] Finally, replacement of benzene by *tert*-butyl alcohol increased the yield to 86% and allowed the reaction time to be shortened to 2 h. The use of a smaller excess of the carboazidating reagent (1.5 equiv; entry 6) afforded **2** in a very similar yield. Further optimization by increasing or decreasing the concentration of the reagents and the amount of initiator did not result in a further increase in yield. Therefore, the reaction conditions described in entry 5 were deemed to be optimal and were selected for the next series of experiments.



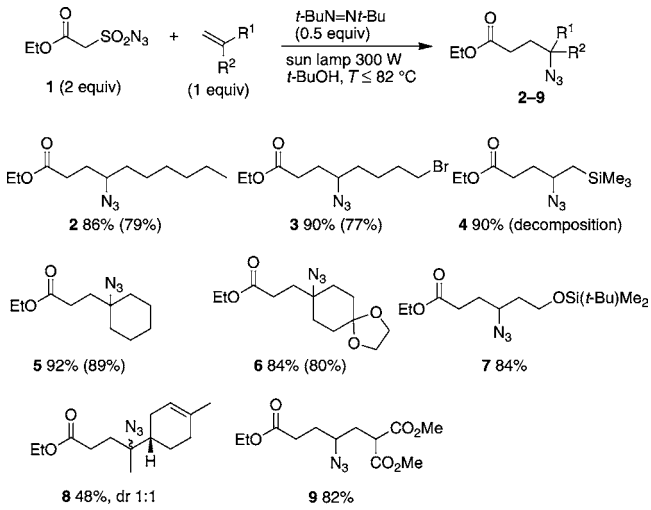
(1)

The carboazidation of a series of terminal alkenes using our optimized reaction conditions was examined (Scheme 5). Good to excellent yield were obtained when secondary and tertiary alkyl radicals were involved in the final azidation step (products **2**−**9**). Interestingly, the carboazidation of allyltrimethylsilane, which does not work with ethyl iodoacetate,[13,14] was possible with reagent **1** and gave **4** in 90% yield. Indeed, the secondary alkyl radical reacts directly with the azide **1** without formation of an unstable α-iodosilane intermediate. Different functional groups such as acetals (product **6**), silyl ethers (product **7**), alkenes (product **8**), and malonates (product **9**) were tolerated. Interestingly, the tin-free procedure affords slightly higher yields

(10) Kim, S.; Otsuka, N.; Ryu, I. *Angew. Chem., Int. Ed.* **2005**, *44*, 6183.
(11) Szymonifka, M. J.; Heck, J. V. *Tetrahedron Lett.* **1989**, *30*, 2869.

(12) Di-*tert*-butyldiazene is a stable radical initiator that efficiently gives *tert*-butyl radicals upon irradiation with a sun lamp (see the Supporting Information for UV absoption spectra). It is commercially available from Sigma-Aldrich.

Scheme 5. Carboazidation of Terminal Olefins [Reported Yields[2] for the Carboazidation Using $EtO_2CCH_2I/PhSO_2N_3/(Bu_3Sn)_2$ Are Given in Parentheses]



than the method involving benzenesulfonyl azide/ethyl iodoacetate/hexabutylditin (yields obtained using this method are given in parentheses in Scheme 5).[2]

Since the azidation step is an efficient but relatively slow process for secondary and tertiary alkyl radicals, it was possible to run ring-opening and cyclization reactions as shown in Scheme 6. Reaction of **1** with (−)-β-pinene afforded product **10** resulting from the cyclobutane ring opening with a yield of 82% (eq 2 in Scheme 6). Starting from 1,6-dienes **11**−**13** (eq 3 in Scheme 6), it was possible to prepare the corresponding five-membered ring systems **14**−**16** in good yields.

Carboazidation with (*N*-Methoxy-*N*-methyl)-2-(azidosulfonyl)-ethanamide (Weinreb Amide). Running the carboazidation with a Weinreb amide derivative should open the possibility of direct transformation of the carboazidation products into azido ketones and aldehydes (see below).[15,16] Therefore, sulfonyl azide **17** was prepared from chloroacetyl chloride according to Scheme 7. Reaction of the acetyl chloride with *N*,*O*-dimethylhydroxylamine hydrochloride afforded 2-chloro-*N*-methylacetamide, which was converted to sulfonyl azide **17** via the corresponding sulfonyl chloride. Reaction of **17** with different terminal alkenes afforded the expected carboazidation products **18**−**21** in high yields (Scheme 8).

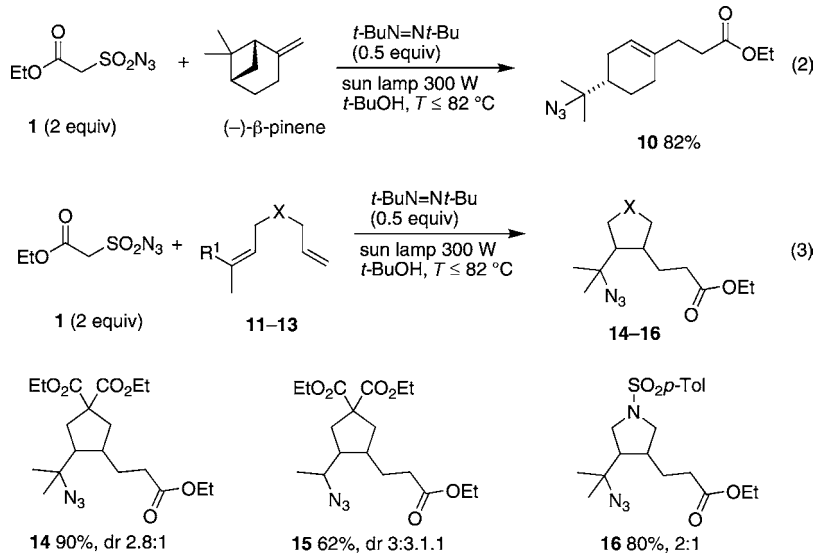
Carboazidation with Trichloromethanesulfonyl Azide. Trichloromethanesulfonyl azide (**22**) can be readily prepared by treating commercially available trichloromethanesulfonyl chloride with sodium azide.[17] Since trichloromethyl radicals are known to add very efficiently to a wide range of alkenes (see, e.g., the classical Kharasch reaction involving CCl_4 and CCl_3Br[18]), an efficient carboazidation process was expected. Indeed, treatment of different terminal alkenes with **22** under the standard reaction conditions developed for **1** and **17** afforded the carboazidation products in excellent yields (Scheme 9). This approach proved to be much more efficient than our previously reported method based on the $CCl_3Br/PhSO_2N_3/Bu_6Sn_2$ system, which gave **23** in only 40% yield.[2] This reaction is very attractive since the trichloromethyl group easily can be partially reduced to a chloromethyl group,[19] fully reduced to a methyl group,[20] or hydrolyzed to the corresponding carboxylate.[21]

Synthesis of Alkaloids. The synthetic utility of Weinreb amide **17** was highlighted in a very short synthesis of *cis*-2-butyl-5-heptylpyrrolidine (*cis*-**29**). *trans*-2-Butyl-5-heptylpyrrolidine (*trans*-**29**) and related 2,5-disubstituted pyrrolidines have been isolated from ant venom toxins of the genus *Solenopisis punctaticeps*.[22] The *trans*-2,5-disubstituted pyrrolidines are the major components of the ant venom. More recently, a potent σ-receptor ligand was isolated from the culture broth of *Streptomyces longispororuber*, and the active compound was identified to be *trans*-(2*R*,5*R*)-**29**.[23] Interestingly, *trans*-(2*S*,5*S*)- and (±)-*cis*-**29** also show high affinity to σ receptors. The cis and trans isomers of **29** have been synthesized in racemic and optically pure form.[24] Therefore, it was of interest to investigate whether an approach based on Weinreb amide **17** could compete favorably with these syntheses. Carboazidation of 1-nonene with **17** afforded azido amide **27**, which was converted to azido ketone **28** by reaction with *n*-butyllithium (Scheme 10). Hydrogenation of **28** using Pd on charcoal as a catalyst afforded the desired racemic pyrrolidine **29** in 98% yield as a 3:1 cis/trans mixture of diastereomers.[25] This synthesis is not only very short but also allows easy variation of the two side chains by appropriate choice of the alkene and the organolithium reagent.

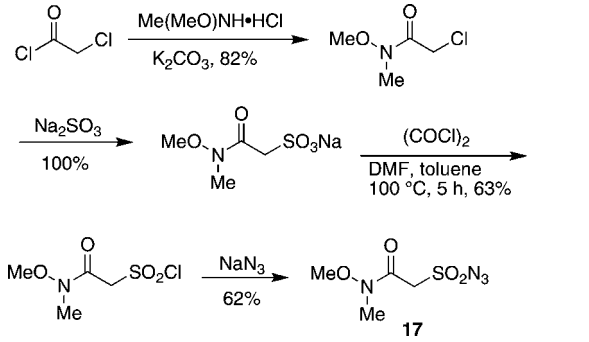
As a second illustration of the synthetic usefulness of **17**, a very concise formal synthesis of lepadiformine C was performed. Lepadiformine C was recently isolated from *Clavelina moluccensis*.[26] Interestingly, lepadiformines A and B and to a lesser degree lepadiformine C are inwardly rectifiying K^+ channel blockers. This is of physiological interest in the cardiac muscle since there are not many blockers specific for this K^+ channel. Recently, the syntheses of racemic and enantiomerically pure lepadiformine C have been reported.[27,28] Our synthesis started with Weinreb amide

(13) The reaction led to the allylated product via an iodine atom transfer process followed by a rapid Peterson olefination process.
(14) Porter, N. A.; Feng, H.; Kavrakova, I. K. *Tetrahedron Lett.* **1999**, *40*, 6713.
(15) Radicals involving 2-ethoxythiocarbonylthiyl Weinreb amides have been reported.
(16) (a) Briggs, M. E.; Zard, S. Z. *Synlett* **2005**, 334. (b) Chabaud, L.; Landais, Y.; Renaud, P.; Robert, F.; Castet, F.; Lucarini, M.; Schenk, K. *Chem.—Eur. J.* **2008**, *14*, 2744.
(17) For safety reasons, this azide was not purified; the crude solution in benzene was directly used for the carboazidation reactions.
(18) Bellus, D. *Pure Appl. Chem.* **1985**, *57*, 1827.
(19) Vo Quang, Y.; Carniato, D.; Vo Quang, L.; Goffic, F. L. *Synthesis* **1985**, 62.
(20) (a) Vanhessche, K. P. M.; Sharpless, K. B. *Chem.—Eur. J.* **1997**, *3*, 517. (b) Porter, N. A.; Breyer, R.; Swann, E.; Nally, J.; Pradhan, J.; Allen, T.; McPhail, A. T. *J. Am. Chem. Soc.* **1991**, *113*, 7002.
(21) Joyce, R. M.; Hanford, W. E.; Harmon, J. *J. Am. Chem. Soc.* **1948**, *70*, 2531.
(22) (a) Pedder, D. J.; Fales, H. M.; Jaouni, T.; Blum, M.; MacConnell, J.; Crewe, R. M. *Tetrahedron* **1976**, *32*, 2275. (b) Jones, T. H.; Blum, M. S.; Fales, H. M. *Tetrahedron Lett.* **1979**, *20*, 1031.
(23) Kumagai, K.; Shono, K.; Nakayama, H.; Ohno, Y.; Saji, I. *J. Antibiot.* **2000**, *53*, 467.
(24) (a) Shiosaki, K.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 1229. (b) Huang, P. Q.; Arseniyadis, S.; Husson, H. P. *Tetrahedron Lett.* **1987**, *28*, 547. (c) Arseniyadis, S.; Huang, P. Q.; Piveteau, D.; Husson, H. P. *Tetrahedron* **1988**, *44*, 2457. (d) Wistrand, L.-G.; Skrinjar, M. *Tetrahedron* **1991**, *47*, 573. (e) Oppolzer, W.; Bochet, C. G.; Merifield, E. *Tetrahedron Lett.* **1994**, *35*, 7015. (f) Duebon, P.; Farwick, A.; Helmchen, G. *Synlett* **2009**, 1413. (g) Arredondo, V. M.; Tian, S.; McDonald, F. E.; Marks, T. J. *J. Am. Chem. Soc.* **1999**, *121*, 3633. (h) Bäckvall, J.-E.; Schink, H. E.; Renko, Z. D. *J. Org. Chem.* **1990**, *55*, 826.
(25) No effort to optimize the diastereoselectivity of the reductive amination was made. However, a higher diastereoselectivty (9:1 cis/trans) was obtained for a very closely related system when the hydrogenation was performed with Raney nickel as a catalyst.
(26) Sauviat, M.-P.; Vercauteren, J.; Grimaud, N.; Juge, M.; Nabil, M.; Petit, J.-Y.; Biard, J.-F. *J. Nat. Prod.* **2006**, *69*, 558.

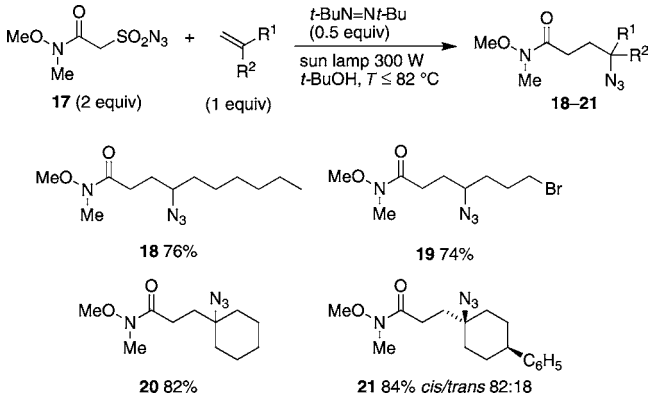
Scheme 6. Ring-Opening and Cyclization Reactions



Scheme 7. Preparation of Azidosulfonylated Weinreb Amide **17**

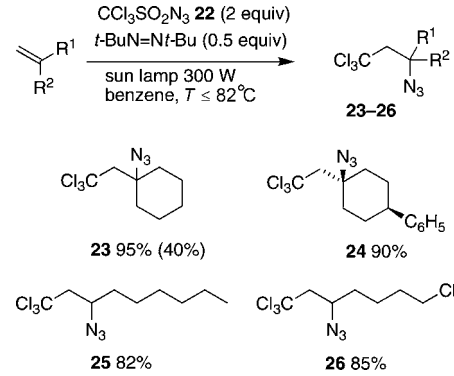


Scheme 8. Carboazidation Using Azidosulfonylated Weinreb Amide **17**

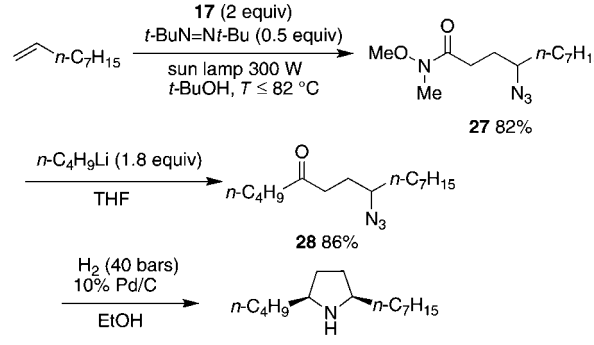


30, which was easily prepared in three steps (76% overall yield) from commercially available 1-pyrrolidinocyclohexene (Scheme 11).[3] Treatment of **30** with *n*-butyllithium afforded ketone **31**, which was engaged in the carboazidation reaction with sulfonyl azide **1**. Azido ester **32** was obtained in 82% yield as a 3:2 trans/cis mixture. Hydrogenation using Pd on calcium carbonate promoted the reduction of the azide, which was followed by

Scheme 9. Azidotrichloromethylation of Alkenes with Trichloromethylsulfonyl Azide **22** [The Reported Yield[2] for the Carboazidation of Methylenecyclohexene Using $CCl_3Br/PhSO_2N_3$/$(Bu_3Sn)_2$ Is Given in Parentheses]



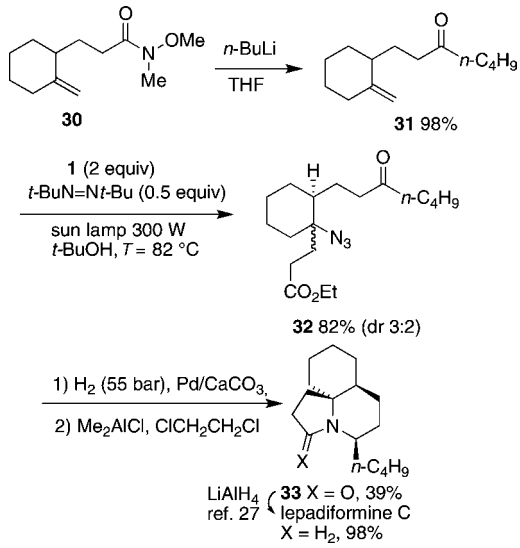
Scheme 10. Synthesis of 2-Butyl-5-heptylpyrrolidine **29**



stereoselective reductive amination of the ketone to give a decahydroquinoline. Treatment of this crude amino ester with dimethylaluminum chloride afforded lactam **33** in 39% overall yield from **32** (mixture of diastereomers) as a 10:1 mixture of diastereomers. The minor diastereomer was partly lost during this process, as reported previously during our recent synthesis of lepadiformine A.[3] Physical and spectroscopic data of lactam **33** were identical with literature data.[27] Aubé and collaborators reported that lactam **33** is converted in 96% yield to lepadiformine C by reduction with lithium aluminum hydride. Our synthetic approach of lepadiformine

(27) Meyer, A. M.; Katz, C. E.; Li, S.-W.; Vander Velde, D.; Aubé, J. *Org. Lett.* **2010**, *12*, 1244.
(28) Perry, M. A.; Morin, M. D.; Slafer, B. W.; Wolckenhauer, S. A.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **2010**, *132*, 9591.

Scheme 11. Synthesis of Lepadiformine C



C is not only extremely short (four steps involving three purifications from **30** and seven steps from commercially available pyrrolidinocyclohexene) but also high-yielding (23% overall yield from pyrrolidinocyclohexene).

Conclusions

By combining the radical precursors and the azidating agent into a single compound, a highly efficient and atom-economical carboazidation of alkenes has been accomplished. The desulfonylative azide transfer reaction proved to be very efficient with three sulfonyl azides as well as a large number of terminal alkenes. Moreover, the reaction takes place under mild conditions with short reaction times. Interestingly, the yields were noticeably higher than those obtained using previous methods. The synthetic potential of the process has been demonstrated by the synthesis of two alkaloids. The extension of this approach to a broad range of carbon-centered radicals possessing electrophilic character (activation by one electron-withdrawing substituent is sufficient) is under investigation and will be applied to the synthesis of useful scaffolds of biological interest.

Experimental Section

Caution! Sulfonyl azides are capable of explosion. It is strongly recommended that standard safety rules be applied and a safety shield be used.

General Procedure (GP) for the Carboazidation of Alkenes. To a stirred solution of sulfonyl azide (2.0 equiv) in *tert*-butyl alcohol or benzene was added alkene (1.0 equiv) and di-*tert*-butyldiazene (0.5 equiv) in a quartz round-bottom flask. The resulting mixture was irradiated with a 300 W sun lamp and stirred under reflux. The reaction was monitored by TLC. Upon completion, the organic phase was washed with saturated aqueous Na_2CO_3 solution, dried with Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel.

Ethyl 3-(1-Azidocyclohexyl)propanoate (5). Compound **5** was obtained according to the GP from ethyl 2-(azidosulfonyl)acetate **1** (309 mg, 1.6 mmol), methylenecyclohexane (84 mg, 0.8 mmol), and di-*tert*-butyldiazene (57 mg, 0.4 mmol) in *tert*-butyl alcohol (2 mL). The crude product was purified by flash chromatography (95:5 pentane/EtOAc) to afford **5** (166 mg, 92%) as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.14 (q, J = 7.2 Hz, 2H), 2.42−2.38 (m, 2H), 1.90−1.87 (m, 2H), 1.71−1.65 (m, 2H), 1.62−1.51 (m, 5H), 1.40−1.24 (m, 3H), 1.27 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.3, 63.3, 60.5, 34.7, 34.4, 28.6, 25.3, 22.1, 14.2. IR (neat): 2936, 2861, 2101, 1738, 1451, 1377, 1302, 1258, 1174, 1024, 895 cm^{-1}. MS (EI) *m*/*z* (%): 226 (8, $[MH]^+$), 198 (37), 183 (100), 168 (7), 152 (17), 137 (21), 125 (20), 109 (14), 96 (37), 82 (10), 67 (13), 56 (20). Anal. Calcd for $C_{11}H_{19}N_3O_2$: C, 58.64; H, 8.50; N, 18.65. Found: C, 58.70; H, 8.47; N, 18.55.

3-Azido-1,1,1-trichlorodecane (25). Compound **25** was obtained according to the GP from **22** (269 mg, 1.2 mmol), 1-octene (67 mg, 0.6 mmol), and di-*tert*-butyldiazene (43 mg, 0.3 mmol) in benzene. The crude product was purified by flash chromatography (pentane) to afford **25** (134 mg, 82%) as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.32−4.23 (m, 1H), 3.27 (dd, J = 5.8, 15.7 Hz, 1H), 3.12 (dd, J = 4.2, 15.7 Hz, 1H), 2.01−1.77 (m, 2H), 1.61−1.27 (m, 8H), 0.97−0.85 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 97.2, 60.4, 58.9, 35.7, 31.6, 28.8, 25.7, 22.5, 14.0. IR (diamond ATR): 2928, 2857, 2096, 1467, 1275, 780 cm^{-1}. MS (EI) *m*/*z* (%) 274 (20, $[M^+]$), 273 (11, $[M^+]$), 272 (0.2, $[M^+]$), 271 (0.9, $[M^+]$), 255 (M^+, 0.9), 199 (20), 154 (25), 126 (20), 114 (24), 112 (49), 84 (22), 71 (20), 70 (56), 69 (68), 57 (100), 55 (50). HRMS (ESI) for $C_9H_{17}Cl_3N_3$: calcd, 272.0470; found, 272.0483.

Ethyl 3-[(1*RS*,2*RS*)-1-Azido-2-(3-oxoheptyl)cyclohexyl]propanoate (32). Compound **32** was obtained according to the GP from ethyl 2-(azidosulfonyl)acetate **1** (1.1 g, 5.76 mmol), **31** (600 mg, 2.88 mmol), and di-*tert*-butyldiazene (204 mg, 1.44 mmol) in *tert*-butyl alcohol (9 mL). The crude product was purified by flash chromatography (8:1 pentane/Et_2O) to afford **32** (863 mg, 82%) as a light-yellow oil containing a 3:2 mixture of diastereomers in favor of the desired *trans*-(1*RS*,2*RS*) isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.17−4.06 (m, 2H), 2.51−2.22 (m, 6H), 2.12−2.03 (m, 1H), 1.94−1.15 (m, 20H), 0.89 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 210.9, 210.8, 173.4, 173.0, 66.4, 65.9, 60.6, 60.5, 43.4, 42.5, 42.5, 42.1, 40.9, 40.0, 33.0, 32.8, 32.2, 32.2, 29.4, 28.4, 27.1, 26.6, 26.0, 24.8, 23.8, 23.1, 22.8, 22.3, 22.2, 21.8. IR (neat): 2933, 2863, 2093, 1732, 1712, 1455, 1377, 1254, 1177, 1024, 860 cm^{-1}. MS (EI) *m*/*z* (%): 309 (1, $[M - N_2]^+$), 263 (10), 245 (12), 224 (21), 210 (26), 197 (18), 164 (90), 150 (38), 136 (52), 124 (26), 106 (25), 85 (39), 67 (31), 57 (84), 55 (100). HRMS (ESI): calcd for $C_{18}H_{31}O_3N_3Na$, 360.22576; found, 360.22647.

(5*RS*,7a*SR*,11a*SR*)-5-Butyldecahydro-3*H*-pyrrolo[2,1-*j*]quinolin-3-one (33). A mixture of **32** (dr = 3:2, 600 mg, 1.64 mmol) in ethanol (16 mL) was hydrogenated at a pressure of 55 bar in the presence of Pd/$CaCO_3$ (164 mg, 5% w/w) at 100 °C for 3 days. The catalyst was removed by filtration over Celite, and the solvent was removed under reduced pressure. The crude product was diluted in $(CH_2Cl)_2$ (15 mL). To this solution was added Me_2AlCl (8.2 mL of a 2.4 M solution in 1,2-dichloroethane, 12 mmol), and the reaction mixture was heated under reflux for 3 days and then cooled to room temperature. Next, the reaction mixture was diluted in ice-cold EtOAc (100 mL), and 0.5 M aqueous Na_2HPO_4 (4 mL) was cautiously added. The organic layer was dried, and the solvent was removed under reduced pressure. The crude product was purified by chromatography (2:1 pentane/Et_2O) to afford **33** (160 mg, 0.64 mmol, 39%) as a colorless liquid containing a 10:1 (5*RS*,7a*SR*,11a*SR*)/(5*SR*,7a*SR*,11a*SR*) mixture of diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$) (mixture of diastereomers): δ 3.21−3.08 (m, 1H), 2.55−2.38 (m, 2H), 2.11 (dd, J = 8.7, 16.1 Hz, 1H), 1.92−1.83 (m, 1H), 1.82−1.21 (m, 20 H), 1.20−1.12 (m, 1H), 0.88 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): (major, 5*RS*,7a*SR*,11a*SR*) δ 176.3, 66.2, 51.7, 42.5, 33.3, 31.6, 30.5, 30.0, 27.2, 26.1, 24.4, 23.5, 22.6, 22.1, 14.1; (minor, 5*SR*,7a*SR*,11a*SR*, selected peaks) δ 174.8, 64.9, 53.9, 39.9. The ^{1}H and ^{13}C NMR data are in excellent agreement with those reported in the literature.[27]

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Supporting Information Available: Experimental procedures, characterization data, and copies of ^{1}H and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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