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Radical Carboazidation: Expedient Assembly of the Core Structure of Various Alkaloid Families

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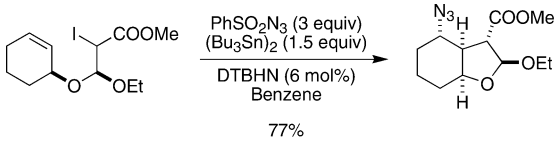
Received December 19, 2003

A procedure for one-pot intermolecular radical addition of 2-iodoesters to terminal alkenes followed by azidation of the radical adduct has been developed. This sequential reaction represents an alkene carboazidation process. Its efficacy is demonstrated by the two-step preparation of various lactams such as pyrrolidinones, pyrrolizidinones, and indolizidinones. An easy access to spirolactams bearing an amino-substituted quaternary carbon center is also described. These compounds are important building blocks for the synthesis of numerous alkaloids such as, for instance, FR901483.

Introduction

The use of free-radical reactions in multistep synthesis has steadily increased over the last years, mainly because of their compatibility with a large number of functional groups and their high potential to perform sequential transformations.[1] Much effort has been concentrated on the development of chain reactions for the formation of carbon−carbon bonds under reducing (Giese reaction)[1b,2] or atom-transfer (Kharasch−Curran)[3,4] conditions. Formation of carbon−nitrogen bonds via a radical pathway is highly attractive for the synthesis of alkaloids and related heterocyclic compounds. Most of the efforts reported in this field deal with the addition of nitrogen-centered radicals to olefins.[5,6] The reverse process, i.e., addition of a carbon-centered radical to a nitrogen-containing trap, is much less developed.[7] Recently, we have proposed a novel method allowing the efficient formation of carbon−nitrogen bonds via reaction of carbon radicals with sulfonyl azides.[8,9] Since sulfonyl azides possess an electrophilic character, it was shown that this azidation process is particularly efficient with nucleophilic radicals and does not occur with ambiphilic or electrophilic radicals. For instance, we have demonstrated that the cyclization depicted in eq 1 can be performed by mixing all reagents under relatively concentrated conditions (0.5 M in substrate) without observing even traces of noncyclized azidated products.[8]



(1)

This observation let us speculate that the reaction could eventually also be accomplished in intermolecular processes.[9] Here, we report a complete study of the intermolecular radical addition to unactivated alkenes followed by azidation. This reaction sequence represents a formal carboazidation of alkenes. Based on this reaction, efficient three-component syntheses of simple lactams such as pyrrolidinones, pyrrolizidinones, and indolizidinones have been performed. The utility of the carboazidation procedure is further demonstrated by the synthesis of a known spirolactam building block used in the total synthesis of (±)-desmethylamino FR901483.

Results and Discussion

Carboazidation Reactions. In a first series of experiments, we decided to test the feasibility of the reaction starting from terminal alkenes and different radical precursors that are known to be efficient in

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(4) Byers, J. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 1; p 72.

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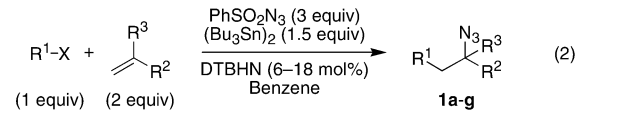
(9) Renaud, P.; Ollivier, C.; Panchaud, P. *Angew. Chem., Int. Ed.* **2002**, *41*, 3460.

10.1021/jo035843y CCC: $27.50
Published on Web 03/16/2004

TABLE 1. Radical Carboazidation of Terminal Alkenes According to Equation 2

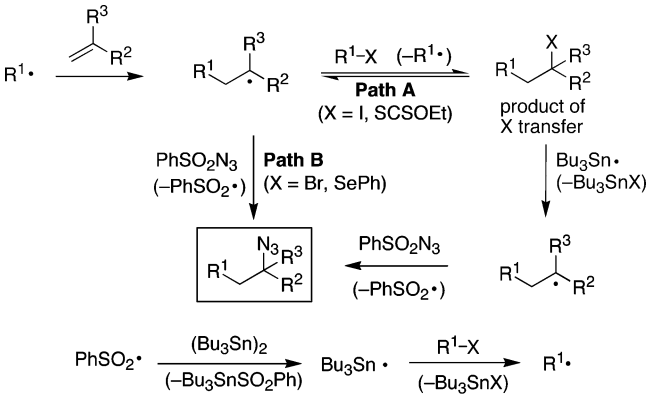


entry	X	R^1	R^2	R^3	product, yield (%)
1	I	$EtOOCCH_2$	C_6H_{13}	H	**1a**, 79
2	I	$EtOOCCH_2$	$(CH_2)_5$		**1b**, 89
3	I	$EtOOCCH_2$	$(CH_2)_3OTBDMS$	H	**1c**, 77
4	Br	$EtOOCCH_2$	C_6H_{13}	H	**1a**, 66
5	SC(S)OEt	$EtOOCCH_2$	C_6H_{13}	H	**1a**, 70
6	SC(S)OEt	$EtOOCCH_2$	CH_2SiMe_3	H	**1d**, 80
7	I	(EtOOC)(Me)CH	C_6H_{13}	H	**1e**, 75[a]
8	Br	$(EtOOC)_2CH$	C_6H_{13}	H	**1f**, 46
9	SePh	$(EtOOC)_2CH$	C_6H_{13}	H	**1f**, 50
10	SC(S)OEt	$(EtOOC)_2CH$	C_6H_{13}	H	**1f**, 76
11	Br	Cl_3C	$(CH_2)_5$		**1g**, 40

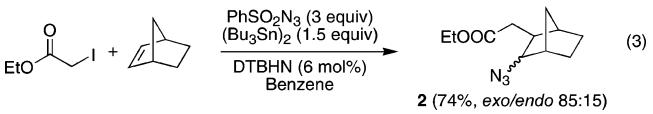
[a] As a 1:1 mixture of diastereomers.

radical atom or group transfer reactions (eq 2).[4] A one-pot procedure similar to the one used for intramolecular reactions gave promising results: the radical precursors are treated with terminal olefins (2 equiv), benzenesulfonyl azide (3 equiv), hexabutyldistannane (1.5 equiv) and di-*tert*-butylhyponitrite (DTBHN, 6−18 mol %) as initiator in refluxing benzene.[10] Slow addition of the benzenesulfonyl azide is not necessary because this electrophilic reagent does not react with the initial electrophilic or ambiphilic radicals, such as enolate radicals and the trichloromethyl radical. The results are reported in Table 1. Reactions of 1-octene, methylenecyclohexane, and silylated 5-pentene-1-ol with ethyl 2-iodoacetate give the expected azides **1a**−**c** in good yields (entries 1−3). Reactions of ethyl 2-bromoacetate and ethyl 2-ethoxythiocarbonylsulfanylethanoate with 1-octene (entries 4 and 5) furnish azide **1a** in 66% and 70% yield, respectively.[11] Reaction of the same dithiocarbonate with allyltrimethylsilane delivers the carboazidation product **1d** in 80% yield (entry 6). As expected, other enolate radicals react with similar efficiency, as demonstrated by the reaction of ethyl 2-iodopropionate with 1-octene affording azide **1e** in 75% yield (entry 7). The reaction of the malonyl radical, generated from diethyl bromomalonate and diethyl phenylselenomalonate, with 1-octene gives the carboazidation product **1f** in only 46% and 50% yield, respectively (entries 8 and 9). The products of bromine atom and phenylseleno group transfer were identified as the major side products. Interestingly, when the malonyl radical is generated from diethyl ethoxythiocarbonylsulfanylmalonate, the desired compound **1f** is obtained in higher yield (76%, entry 10). Finally, the use of bromotrichloromethane, a reagent known to be very efficient for bromine atom transfer reactions,[12] was investigated. Reaction with methylenecyclohexane furnishes the azide **1g** in 40% yield (entry 11). In this last example, the only identified side product is again the product of bromine atom transfer.

SCHEME 1. Proposed Mechanism



By analogy to iodine atom transfer, we were expecting that the radical addition−azidation process would be limited to terminal alkenes. Indeed, Curran showed that olefins substituted at both carbon atoms give low yields in atom-transfer processes with iodoacetate derivatives.[3] We tested the reaction with dimethyl cyclohex-4-ene-1,2-dicarboxylate, and we observed only traces of the desired azide. Interestingly, norbornene, a more reactive 1,2-disubstituted alkene, reacted cleanly with ethyl 2-iodoacetate to afford the azide **2** in 74% yield (eq 3).



Mechanism. Two reaction pathways (Scheme 1, paths A and B) can operate in the carboazidation of olefins. Path A is a stepwise mechanism involving formation of an intermediate via transfer of the X group. This pathway is operative when the atom or group transfer is fast. For instance, iodides and xanthates react along this pathway, and both steps, i.e., carbon−carbon bond formation via atom/group transfer and azidation of the intermediate iodide/xanthate, are efficient. The second pathway, path B, is a direct radical addition−azidation process that takes place when the atom-transfer step is slower than the azidation step. Bromides activated by a single ester group are expected to follow this reaction pathway. For instance, with ethyl 2-bromoacetate, no product of bromine atom transfer was detected during the reaction and the overall yield was good. With more activated bromides and selenides such as diethyl bromomalonate, diethyl phenylselenomalonate, and bromotrichloromethane, the atom/group transfer process is accelerated and path A becomes again operative.[13,14] The desired carboazidation products, isolated in moderate yields only, are presumably resulting from a competing direct azidation reaction

(10) Kiefer, H.; Traylor, T. G. *Tetrahedron Lett.* **1966**, *49*, 6163. DTBHN decomposes with a half-life time of 29 min. at 65 °C to give *tert*-butoxyl radicals and nitrogen. It is a stable solid, easily prepared from *tert*-butyl bromide and commercially available sodium hyponitrite (Aldrich): Mendenhall, G. D. *Tetrahedron Lett.* **1983**, *24*, 451. For further preparation details, see: Banks, J. T.; Scaiano, J. C.; Adam, W.; Oestrich, R. S. *J. Am. Chem. Soc.* **1993**, *115*, 2473. For a previous use of DTBHN to generate stannyl radicals, see: Dang, H. S.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 1* **1996**, 769.

(11) For general reviews on the use of dithiocarbonates in radical reactions, see: (a) Zard S. Z. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds; Wiley-VCH: Weinheim, 2001; Vol. 1, p 90. (b) Zard, S. Z. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 672.

(12) Bellus, D. *Pure Appl. Chem.* **1985**, *57*, 1827.

(13) For rate of bromine atom transfers, see: Curran, D. P.; Bosch, E.; Kaplan, J.; Newcomb, M. *J. Org. Chem.* **1989**, *54*, 1826.

(14) For rate of phenylseleno group transfers, see: Curran, D. P.; Martin-Esker, A. A.; Ko, S. B.; Newcomb, M. *J. Org. Chem.* **1993**, *58*, 4691.

SCHEME 2. Preparation of Pyrrolidinone, Pyrrolizidinone, and Indolizidinone Derivatives

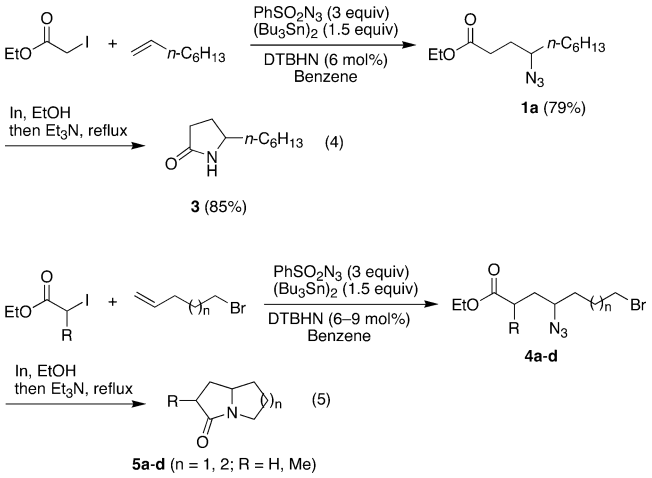
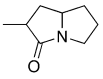
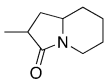


TABLE 2. Two-Step Preparation of Pyrrolizidinones and Indolizidinones According to Equation 5

entry	R	n	azide **4**, yield	lactam **5**,	yield
1	H	1	**4a**, 77%		**5a**, 82%
2	Me	1	**4b**, 72%[a]		**5b**, 84%[a]
3	H	2	**4c**, 74%		**5c**, 72%
4	Me	2	**4d**, 69%[a]		**5d**, 83%[a]

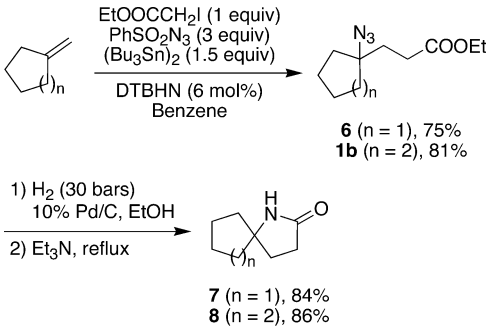
[a] As a 1:1 mixture of diastereomers.

according to path B since the intermediate bromides/selenides formed are not efficiently azidated under these reaction conditions.

Synthesis of Pyrrolidinone, Pyrrolizidinone, and Indolizidinone Derivatives. The radical carboazidation of alkenes with 2-iodoesters can be coupled with the reduction of azides to afford 3-amino esters that cyclize to pyrrolidinones (Scheme 2, eq 4). For example, 5-hexylpyrrolidinone **3** is prepared in 67% overall yield from ethyl 2-iodoacetate and 1-octene. The carboazidation of 1-octene affords the azidoester **1a** in 79% yield. Reduction of **1a** with indium in ethanol[15] affords the corresponding amino ester that cyclizes spontaneously to **3**. The lactamization process can be promoted by adding triethylamine and by heating the reaction mixture under reflux. Starting from 5-bromopent-1-ene, the carboazidation with ethyl 2-iodoacetate and ethyl 2-iodopropionate affords the azido esters **4a** and **4b** (Scheme 2, eq 5). Reduction with indium followed by treatment with triethylamine gives the pyrrolizidinones **5a** and **5b** via a double-cyclization reaction (Table 2, entries 1 and 2). The same reaction sequence starting with 6-bromohex-1-ene gives the azides **4c** and **4d** and the indolizidinones

(15) Reddy, G. V.; Rao, G. V.; Iyengar, D. S. *Tetrahedron Lett.* **1999**, *40*, 3937.

SCHEME 3. Rapid Access to Spirolactams 7 and 8



5c and **5d** in good yields (Table 2, entries 3 and 4). It is interesting to note that the carboazidation process with iodoesters proceeds in good yields in the presence of primary bromides, demonstrating further the high chemoselectivity of radical reactions.

Synthesis of Spirolactams. 1-Azaspiro[4,4]nonan-2-ones and 1-azaspiro[4,5]decan-2-ones are important spirolactam building blocks for the synthesis of a wide range of alkaloids. Their preparation is not trivial since they contain an amino-substituted quaternary carbon center. Since the radical carboazidation reaction is particularly suitable for the preparation of such moieties, we examined a rapid two-step synthesis of spirolactams starting from methylenecycloalkanes (Scheme 3).

The carboazidation of methylenecyclopentane and methylenecyclohexane affords azides **6** and **1b** in 75% and 81% yield, respectively (Scheme 3). These two reactions have been performed with one equivalent of the alkene and one equivalent of ethyl 2-iodoacetate. This procedure is important for many potential applications of the method since the alkene part will be the more complex and expensive reaction partner. Interestingly, under these conditions, we obtain similar yield for the preparation of **1b** relative to the case where two equivalents of methylenecyclohexane are used (Table 1, entry 2). Hydrogenation of azides **6** and **1b** (30 bar, 10% Pd/C) gives the amino esters that cyclize under heating in ethanol in the presence of triethylamine to afford the desired spirolactams **7** and **8**.

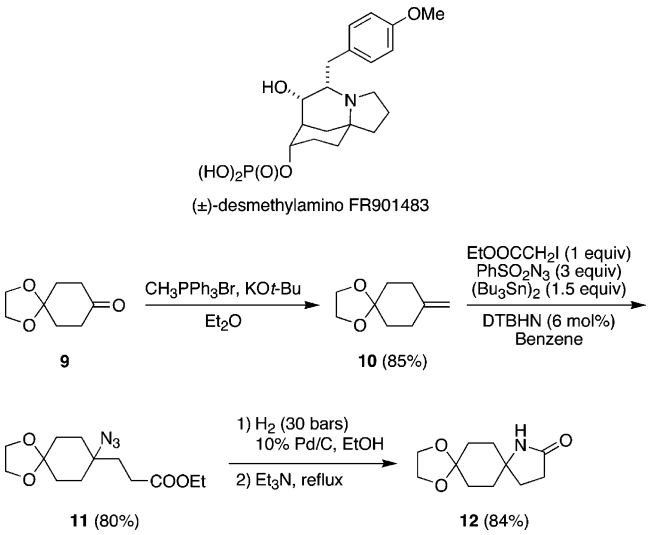
To show the utility of our approach for the synthesis of spirolactams, we decided to prepare compound **12**, an advanced intermediate in Wardrop's total synthesis of (±)-desmethylamino FR901483 (Scheme 4).[16] The synthesis started from commercially available monoprotected 1,4-cyclohexanedione **9**, which was first converted to the corresponding methylenecyclohexane **10**. Carboazidation of **10** afforded the azido ester **11** in 80% yield that was readily converted by hydrogenation−lactamization to the desired spirolactam **12**. This procedure for the preparation of **12** (3 steps, 57% overall yield) compares favorably with Wardrop's synthesis (five steps, 53% overall yield).[17]

Conclusion

A one-pot intermolecular radical addition−azidation procedure has been developed. Remarkably, this reaction

(16) Wardrop, D. J.; Zhang, W. M. *Org. Lett.* **2001**, *3*, 2353.
(17) For another synthesis of this intermediate, see: Bonjoch, J.; Diaba, F.; Puigbo, G.; Peidro, E.; Sole, D. *Tetrahedron Lett.* **2003**, *44*, 8387.

SCHEME 4. Preparation of Spirolactam 12, a Building Block for the Synthesis of (±)-Desmethylamino FR901483



is efficient with nonactivated terminal alkenes and takes advantage of radical atom or group-transfer processes. The synthetic utility of this method is demonstrated by the preparation of various pyrrolidinones, pyrrolizidinones, indolizidinones, and spirolactams, which are important building blocks for alkaloid synthesis. The reaction proves to be particularly efficient for the formation of aminated quaternary carbon centers.

Experimental Section

Caution: Since sulfonyl azides are capable of exploding, it is strongly recommended to apply standard safety rules and to use a safety shield.

General Procedure A. DTBHN (5 mg, 0.03 mmol) was added every 2 h to a solution of radical precursor (1.0 mmol), olefin (1.0 or 2.0 mmol), $PhSO_2N_3$ (550 mg, 3.0 mmol), and Bu_6Sn_2 (0.76 mL, 1.5 mmol) in dry C_6H_6 (2.0 mL) at reflux under N_2. The reaction was monitored by TLC. Upon completion of the reaction (4−12 h), the solvent was removed under reduced pressure and the crude product was filtered through silica gel. Elution with hexane allowed the removal of unchanged Bu_6Sn_2, and further elution with hexane/Et_2O or hexane/EtOAc gave a crude product that was purified by FC (hexane/Et_2O or hexane/EtOAc).

General Procedure B. Indium powder (230 mg, 2.0 mmol) and NH_4Cl (107 mg, 2.0 mmol) were added to a solution of azide (2.0 mmol) in dry EtOH (6.0 mL). The reaction mixture was stirred under reflux for 2 h. Et_3N (1.4 mL, 10.0 mmol) was added, and the reaction mixture was further stirred under reflux for 4 h. The cooled reaction mixture was then diluted with EtOAc (10 mL), stirred for 10 min, and filtered through a short pad of Celite. The solvent was removed under reduced pressure, and the crude product was purified by FC (CH_2Cl_2/MeOH).

General Procedure C. A solution of azide (2.0 mmol) and 10% Pd/C (10% w/w) in dry EtOH (12.0 mL) was stirred for 36 h at rt under H_2 (30 bar). Et_3N (1.4 mL, 10.0 mmol) was added, and the reaction mixture was stirred under reflux for 4 h. The catalyst was filtered off, the solvent removed under reduced pressure, and the crude product purified by CC (EtOAc or CH_2Cl_2/MeOH).

Ethyl 4-Azidodecanoate (1a). (a) Prepared according to general procedure A from ethyl 2-iodoacetate (214 mg, 1.0 mmol), 1-octene (0.31 mL, 2.0 mmol), $PhSO_2N_3$ (550 mg, 3.0 mmol), Bu_6Sn_2 (0.76 mL, 1.5 mmol), and DTBHN (10 mg, 0.06 mmol). Filtration (hexane then hexane/EtOAc 90:10) and FC (hexane/EtOAc 95:5) gave **1a** (191 mg, 79%) as a colorless oil: ^{1}H NMR (360 MHz, $CDCl_3$) δ 4.15 (q, J = 7.3 Hz, 2H), 3.35−3.27 (m, 1H), 2.50−2.31 (m, 2H), 1.95−1.81 (m, 1H), 1.80−1.64 (m, 1H), 1.62−1.21 (m, 10H), 1.26 (t, J = 7.3 Hz, 3H), 0.89 (t, J = 6.8 Hz, 3H); ^{13}C NMR (90 MHz, $CDCl_3$) 173.0, 62.2, 60.5, 34.4, 31.6, 30.9, 29.5, 29.0, 26.0, 22.5, 14.2, 14.0; IR (film) 2099, 1738 cm^{-1}; MS (CI, CH_4) m/z 242 (MH^+, 20), 214 (100), 199 (88), 168 (30), 143 (27), 126 (13), 113 (7), 70 (18). Anal. Calcd for $C_{12}H_{23}N_3O_2$ (241.33): C, 59.72; H, 9.61; N, 17.41. Found: C, 59.77; H, 9.56; N, 17.36.

(b) Prepared according to general procedure A from ethyl 2-bromoacetate (167 mg, 1.0 mmol), 1-octene (0.31 mL, 2.0 mmol), $PhSO_2N_3$ (550 mg, 3.0 mmol), Bu_6Sn_2 (0.76 mL, 1.5 mmol), and DTBHN (16 mg, 0.09 mmol). Filtration (hexane then hexane/EtOAc 90:10) and FC (hexane/EtOAc 95:5) gave **1a** (158 mg, 66%).

(c) Prepared according to general procedure A from ethyl 2-[[(ethyloxy)carbothioyl]sulfanyl]acetate (208 mg, 1.0 mmol, prepared from ethyl 2-iodoacetate and potassium ethyl xanthogenate according to a literature procedure),[18] 1-octene (0.31 mL, 2.0 mmol), $PhSO_2N_3$ (550 mg, 3.0 mmol), Bu_6Sn_2 (0.76 mL, 1.5 mmol), and DTBHN (31 mg, 0.18 mmol) added by 3% portions every 90 min. Filtration (hexane then hexane/EtOAc 90:10) and FC (hexane/EtOAc 95:5) gave **1a** (168 mg, 70%).

Ethyl 4-Azido-7-bromoheptanoate (4a). Prepared according to general procedure A from ethyl 2-iodoacetate (642 mg, 3.0 mmol), 5-bromo-1-pentene (0.71 mL, 6.0 mmol), $PhSO_2N_3$ (1.65 g, 9.0 mmol), Bu_6Sn_2 (2.25 mL, 4.5 mmol), and DTBHN (31 mg, 0.18 mmol). Filtration (hexane then hexane/EtOAc 90:10) and CC (hexane/Et_2O 95:5) gave **4a** (645 mg, 77%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.15 (q, J = 7.3 Hz, 2H), 3.44 (t, J = 6.4 Hz, 2H), 3.41−3.32 (m, 1H), 2.53−2.36 (m, 2H), 2.12−1.60 (m, 6H), 1.27 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.7, 61.2, 60.5, 33.0, 32.8, 30.6, 29.4, 29.0, 14.1; IR (film) 2102, 1732 cm^{-1}; MS (EI, 70ev) m/z 280 (M^+, 0.1), 278 (M^+, 0.1), 232 (2), 189 (1), 162 (10), 143 (17), 124 (18), 100 (15), 81 (39), 70 (100), 55 (45), 41 (98). Anal. Calcd for $C_9H_{16}BrN_3O_2$ (278.15): C, 38.86; H, 5.80; N, 15.11. Found: C, 38.94; H, 5.87; N, 15.17.

Hexahydro-3*H*-pyrrolizin-3-one (5a). Prepared according to general procedure B from azide **4a** (556 mg, 2.0 mmol). CC (CH_2Cl_2/MeOH 97:3) gave **5a** (205 mg, 82%) as a yellowish oil. Physical and spectral data were in accordance with literature data.[19]

Ethyl 3-(1-Azidocyclopentyl)propanoate (6). Prepared according to general procedure A from methylenecyclopentane (411 mg, 5.0 mmol), ethyl 2-iodoacetate (1.07 g, 5.0 mmol), $PhSO_2N_3$ (2.75 g, 15.0 mmol), Bu_6Sn_2 (3.79 mL, 7.5 mmol), and DTBHN (52 mg, 0.30 mmol). Filtration (hexane then hexane/EtOAc 90:10) and FC (hexane/EtOAc 98:2) gave **6** (790 mg, 75%) as a yellowish oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.09 (q, J = 7.0 Hz, 2H), 2.39−2.36 (m, 2H), 1.95−1.89 (m, 2H), 1.81−1.65 (m, 6H), 1.55−1.48 (m, 2H), 1.22 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 72.7, 60.4, 36.7, 33.9, 30.3, 23.6, 14.1; IR (film) 2101, 1727 cm^{-1}; HRMS (ESI) for $C_{10}H_{17}N_3O_2Na$ calcd 234.1218, found 234.1228.

1-Azaspiro[4.4]nonan-2-one (7). Prepared according to general procedure C from azide **6** (211 mg, 1 mmol) and 10% Pd/C (63 mg, 30% w/w). FC (EtOAc) gave **7** (115 mg, 84%) as a pale brown solid: mp 142−144 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.72 (br s, 1H), 2.41−2.36 (m, 2H), 2.04−1.98 (m, 2H), 1.72−1.65 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 66.9, 39.1, 33.8, 30.7, 29.7, 23.1; HRMS (ESI) for $C_8H_{14}NO$ calcd 140.1075, found 140.1071.

8-Methylene-1,4-dioxaspiro[4.5]decane (10). *t*-BuOK (3.67 g, 30.0 mmol) was added to a solution of CH_3PPh_3Br (10.72 g, 30.0 mmol) in Et_2O (60.0 mL) at rt under N_2. The resulting

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deep yellow suspension was stirred for 0.5 h at rt. Then a solution of ketone **9** (3.12 g, 20.0 mmol) in Et_2O (40.0 mL) was added dropwise to the reaction mixture. The suspension was stirred under reflux for 1 h, cooled to rt, and further stirred for 18 h. The reaction mixture was then washed with brine (2 × 20 mL**)** and dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was dissolved in EtOAc and $Ph_3P{=}O$ was precipitated by adding hexane slowly. The mixture was filtered through a short silica pad and the solvent removed under reduced pressure. FC (hexane/EtOAc 93:7) gave **10** (2.62 g, 85%) as a yellowish oil. Physical and spectral data were in accordance with literature data.[20]

Ethyl 3-(8-Azidodioxaspiro[4.5]dec-8-yl)propanoate (11). Prepared according to general procedure A from **10** (462 mg, 3.0 mmol), ethyl 2-iodoacetate (642 mg, 3.0 mmol), $PhSO_2N_3$ (1.65 g, 9.0 mmol), Bu_6Sn_2 (2.27 mL, 4.5 mmol), and DTBHN (32 mg, 0.18 mmol). Filtration (hexane then hexane/EtOAc 80:20) and FC (hexane/EtOAc 85:15) gave **11** (678 mg, 80%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.13 (q, J = 7.0 Hz, 2H), 3.97−3.87 (m, 4H), 2.42−2.37 (m, 2H), 1.94−1.88 (m, 2H), 1.82−1.57 (m, 8H), 1.25 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 107.9, 64.3, 64.2, 62.3, 60.6, 34.4, 31.8, 30.6, 28.9, 14.1; IR (film) 2094, 1735 cm^{-1}; HRMS (ESI) for $C_{13}H_{21}N_3O_4Na$ calcd 306.1429, found 306.1410.

1,4-Dioxa-9-azadispiro[4.2.4.2]tetradecan-10-one (12). Prepared according to general procedure C from azide **11** (283 mg, 1 mmol) and 10% Pd/C (90 mg, 30% w/w). FC (EtOAc/MeOH 99:1) gave **12** (177 mg, 84%) as a white solid. Physical and spectral data were in accordance with literature data.[16]

Acknowledgment. We thank the Swiss National Science Foundation and the University of Berne for support of this research.

Supporting Information Available: Experimental procedures in addition to ^{1}H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO035843Y

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