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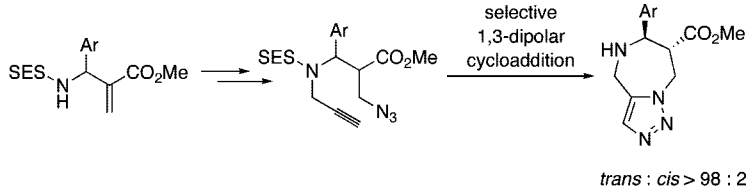
Selective [3 + 2] Huisgen Cycloaddition. Synthesis of *Trans*-Disubstituted Triazolodiazepines from *Aza*-Baylis−Hillman Adducts

Valérie Declerck,[†,‡] Loic Toupet,[§] Jean Martinez,[†] and Frédéric Lamaty*,[†]

Institut des Biomolécules Max Mousseron (IBMM), UMR 5247 CNRS-Université Montpellier 1-Université Montpellier 2, Place Eugène Bataillon, 34095 Montpellier Cedex 5, France, and Institut de Physique (IPR), UMR 6251 CNRS-Université de Rennes 1, Bâtiment 11A, 35042 Rennes Cedex, France

frederic.lamaty@univ-montp2.fr

Received November 14, 2008



The 1,3-dipolar cycloaddition of linear azido alkynes derived from protected β-amino esters proceeds *via* diastereomeric differentiation to provide *trans*-disubstituted triazolodiazepines in good yields.

Introduction

The *aza*-Baylis−Hilman reaction[1−3] is a powerful method for the preparation of densely functionalized small molecules which has attracted the attention of organic chemists. We have recently reported a three-component *aza*-Baylis−Hillman reaction involving a sulfonamide, an aldehyde, and an acrylate for the preparation of highly functionalized 2-(trimethylsilyl)ethanesulfonyl (or SES)-protected[4,5] α,β-unsaturated β-amino esters which can be used in further transformations.[6,7]

In an ongoing project dealing with the use of these α,β-unsaturated β-amino esters as building blocks for the synthesis of various heterocyclic structures, we reported the preparation of pyrroles,[6] pyrrolines,[8] pyrrolidines,[8] and benzazepines.[9,10] We describe herein the synthesis of triazolodiazepines from these β-amino esters involving an intramolecular [3 + 2] Huisgen cycloaddition[11] as a keystep.

Triazoles are important molecules due to their unique chemical properties. They possess a wide range of applications in organic, organometallic, medicinal, and material chemistry. Although no product containing the 1,2,3-triazole moiety has been found in nature, this scaffold constitutes an interesting class of pharmacophores since it shows a remarkable resistance to metabolic transformations such as oxidation, reduction, basic or acidic hydrolysis. The 1,2,3-triazole unit is present in various compounds exhibiting interesting antibacterial,[12] anti-HIV,[13] and antiallergic[14] activities. As examples, cefmatilen[15] exhibit antibacterial activities and tazobactam[16] is a β-lactamase inhibi-

* To whom correspondence should be addressed. Fax: +33 (0) 4 67 14 48 66.

† IBMM, Université de Montpellier 2.

‡ Present address: Laboratoire de Synthèse Organique et Méthodologie, ICMMO, Université Paris-Sud 11, 15 Rue Georges Clemenceau, 91405 Orsay Cedex, France.

§ IPR, Université de Rennes 1.

(1) Balan, D.; Adolfsson, H. *J. Org. Chem.* **2001**, *66*, 6498–6501. (a) Balan, D.; Adolfsson, H. J. *Org. Chem.* **2002**, *67*, 2329–2334.

(2) Declerck, V.; Martinez, J.; Lamaty, F. *Chem. Rev.* **2009**, *109*, 1–48.

(3) Shi, Y.-L.; Shi, M. *Eur. J. Org. Chem.* **2007**, 2905–2916.

(4) Weinreb, S. M.; Demko, D. M.; Lessen, T. A.; Demers, J. P. *Tetrahedron Lett.* **1986**, *27*, 2099–2102.

(5) (a) Ribière, P.; Declerck, V.; Martinez, J.; Lamaty, F. *Chem. Rev.* **2006**, *106*, 2249–2269. (b) Declerck, V.; Ribière, P.; Martinez, J.; Lamaty, F.; Weinreb, S. M.; Ralbovsky, J. L. β-(Trimethylsilyl)ethanesulfonyl Chloride (17 September 2007). *Encyclopedia of Reagents for Organic Synthesis [Online]*; John Wiley & Sons Ltd., www.mrw.interscience.wiley.com/eros/, accessed 20 November 2007, DOI: 10.1002/047084289X.rt300.pub2.

(6) Declerck, V.; Ribière, P.; Martinez, J.; Lamaty, F. *J. Org. Chem.* **2004**, *69*, 8372–8381.

(7) (a) Ribière, P.; Enjalbal, C.; Aubagnac, J.-L.; Yadav-Bhatnagar, N.; Martinez, J.; Lamaty, F. *J. Comb. Chem.* **2004**, *6*, 464–467. (b) Ribière, P.; Yadav-Bhatnagar, N.; Martinez, J.; Lamaty, F. *QSAR Comb. Sci.* **2004**, *23*, 911–914.

(8) Declerck, V.; Allouchi, H.; Martinez, J.; Lamaty, F. *J. Org. Chem.* **2007**, *72*, 1518–1521.

(9) Ribière, P.; Declerck, V.; Nédellec, Y.; Yadav-Bhatnagar, N.; Martinez, J.; Lamaty, F. *Tetrahedron* **2006**, *62*, 10456–10466.

(10) Declerck, V.; Ribière, P.; Nédellec, Y.; Allouchi, H.; Martinez, J.; Lamaty, F. *Eur. J. Org. Chem.* **2007**, 201–208.

(11) For examples of 7-membered rings, see: (a) Padwa, A.; Ku, A.; Ku, H.; Mazzu, A. *J. Org. Chem.* **1978**, *43*, 66–72. (b) Akritopoulou-Zanze, I.; Gracias, V.; Djuric, S. W. *Tetrahedron Lett.* **2004**, *45*, 8439–8441. (c) Tezuka, K.; Compain, P.; Martin, O. R. *Synlett* **2000**, 1837–1839. (d) Dolhem, F.; Al Tahli, F.; Lievre, C.; Demailly, G. *Eur. J. Org. Chem.* **2005**, 5019–5023. (e) Röper, S.; Franz, M. H.; Wartchow, R.; Hoffmann, H. M. R. *Org. Lett.* **2003**, *5*, 2773–2776. (f) Mohapatra, D. K.; Maity, P. K.; Chorghade, M. S.; Gurjar, M. K. *Heterocycles* **2007**, *73*, 269–274.

10.1021/jo802533d CCC: $40.75 © 2009 American Chemical Society
Published on Web 02/06/2009

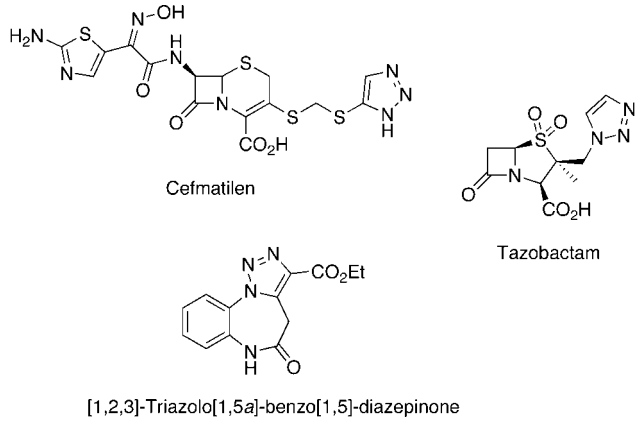
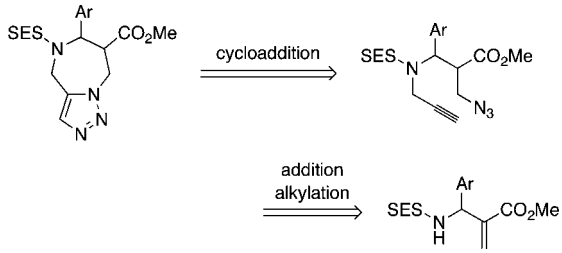


FIGURE 1. Biologically active 1,2,3-triazole containing compounds.

SCHEME 1. Retrosynthetic Analysis



tor. Triazolobenzodiazepines[17] have high affinity for the benzodiazepine receptors (Figure 1).

Results and Discussion

As described in the retrosynthetic scheme (Scheme 1), the triazolodiazepines can be obtained by an intramolecular 1,3-dipolar cycloaddition of a linear precursor possessing an azide function and a triple bond. This precursor can be obtained by sequential Michael addition of HN_3 on the α,β-unsaturated β-amino esters and alkylation with propargyl bromide.

Starting from the SES-protected amino ester, we had the choice to perform first either the Michael addition of HN_3 or the alkylation reaction. A disubstituted SES-sulfonamide, which would be obtained after alkylation by propargyl bromide, owns a leaving group character similar to that of acetate[18] and is not suitable for a 1,4-addition (it would provide mainly an elimination product). Consequently, we have chosen to introduce first the azide function and then the propargyl moiety. Introduction of the azido group on the α,β-unsaturated β-amino ester was realized according to the procedure described by Miller[19] to avoid the use of a toxic and explosive HN_3 solution. This procedure is well-adapted for the 1,4-addition of N_3 to unsaturated ketones, but an intramolecular amine-mediated activation is necessary in the case of α,β-unsaturated esters. Furthermore, to our knowledge no example of the azide addition on a 1,1-disubstituted acrylate has been described. Thus, treatment of the α,β-unsaturated β-amino esters **1a** with an excess of TMS-N_3 in the presence of acetic acid and triethylamine at 40 °C for 24 h allowed a complete conversion and the azido-β-amino esters **2** were obtained in high yields as a mixture of *anti* and *syn* diastereoisomers, which could not be separated by column chromatography. X-ray analysis of the cyclic compound **5a** obtained after the cycloaddition step confirmed that the *anti* isomer was the major one (Scheme 2, Table 1).

SCHEME 2. Conjugate Addition of HN_3

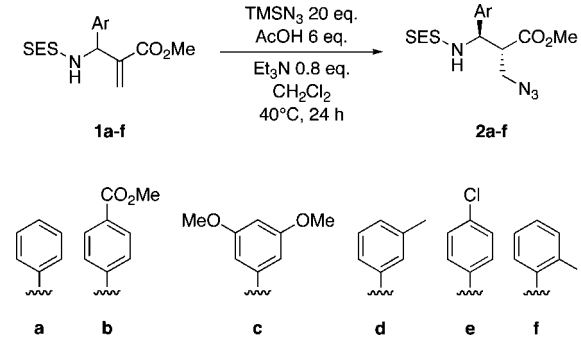


TABLE 1. Yields and Stereoselectivities of Isolated Compounds 2, 3, 5, and 6

	azido-β-amino esters **2**		precursors **3**	SES-triazoles **5**		triazoles **6**
substituent	yield (%)	anti/syn[a]	**3**:**4**	yield (%)[b]	trans/cis[a]	yield (%)
a	98	83:17	96:4	77	>99	100
b	96	81:19	90:10	68	98:2	100
c	99	83:17	95:5	70	98:2	100
d	94	83:17	96:4	69	>99	100
e	99	78:22	93:7	69	99:1	100
f	95	71:29	96:4	70	99:1	100

[a] Determined by ^{1}H NMR. [b] Yield in two steps: alkylation and 1,3-dipolar cycloaddition.

The stereochemical outcome of this reaction was governed by the reprotonation of the enolate intermediate formed after the 1,4-addition (Scheme 2). According to the studies of Perlmutter et al. on 1,4-addition of amines to 2-hydroxyalkylpropenoates,[20] the two possible conformers A and B of the enolate resulting from the addition of HN_3 are depicted in Scheme 3. Since the bulky SES-NH group does not accommodate easily an interaction with the azidomethylene moiety, conformer A is preferred, leading to the formation of the *anti* product.

The next step was the alkylation of the azido-β-amino ester **2a** by propargyl bromide (Table 2). Under classical alkylation conditions using K_2CO_3 in DMF for 6 h (entry 1),[6] we observed

(12) Genin, M. J.; Allwine, D. A.; Anderson, D. J.; Barbachyn, M. R.; Emmert, D. E.; Garmon, S. A.; Graber, D. R.; Grega, K. C.; Hester, J. B.; Hutchinson, D. K.; Morris, J.; Reischer, R. J.; Ford, C. W.; Zurenko, G. E.; Hamel, J. C.; Schaadt, R. D.; Stapert, D.; Yagi, B. H. *J. Med. Chem.* **2000**, *43*, 953–970.

(13) Alvarez, R.; Velázquez, S.; San-Félix, A.; Aquaro, S.; De Clercq, E.; Perno, C.-F.; Karlsson, A.; Balzarini, J.; Camarasa, M. J. *J. Med. Chem.* **1994**, *37*, 4185–4194.

(14) Brockunier, L. L.; Parmee, E. R.; Ok, H. O.; Candelore, M. R.; Cascieri, M. A.; Colwell, L. F.; Deng, L.; Feeney, W. P.; Forrest, M. J.; Hom, G. J.; MacIntyre, D. E.; Tota, L.; Wyvratt, M. J.; Fisher, M. H.; Weber, A. E. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 2111–2114.

(15) (a) Kume, M.; Kubota, T.; Kimura, Y.; Nakashimizu, H.; Motokawa, K.; Nakano, M. *J. Antibiot.* **1993**, *46*, 177–192. (b) Kume, M.; Kubota, T.; Kimura, Y.; Nakashimizu, H.; Motokawa, K. *J. Antibiot.* **1993**, *46*, 316–330. (c) Kume, M.; Kubota, T.; Kimura, Y.; Nakashimizu, H.; Motokawa, K. *Chem. Pharm. Bull.* **1993**, *41*, 758–762.

(16) Tanaka, M.; Yamazaki, T.; Kajitani, M. "Penam Derivatives" Eur. Pat. 158494, 1985; *Chem. Abstr.* **1986**, *104*, 186239d.

(17) (a) Smalley, R. K.; Teguiche, M. *Synthesis* **1990**, 654–666. (b) Bertelli, L.; Biagi, G.; Giorgi, I.; Livi, O.; Manera, C.; Scartoni, V.; Martini, C.; Giannaccini, G.; Trincavelli, L.; Barili, P. L. *Farmaco* **1998**, *53*, 305–311.

(18) Declerck, V.; Martinez, J.; Lamaty, F. Unpublished results.

(19) Guerin, D. J.; Horstmann, T. E.; Miller, S. J. *Org. Lett.* **1999**, *1*, 1107–1109.

(20) Perlmutter, P.; Tabone, M. *Tetrahedron Lett.* **1988**, *29*, 949–952.

SCHEME 3. Transition Structure Analysis of the Addition of HN_3 on β-Amino Esters 1

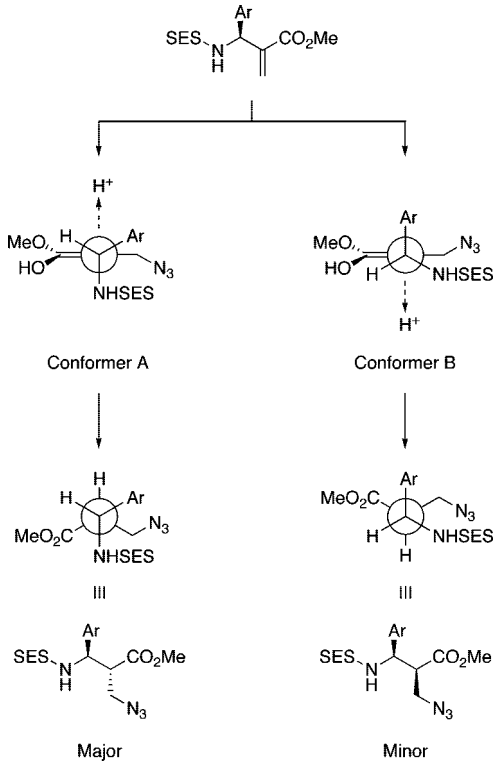
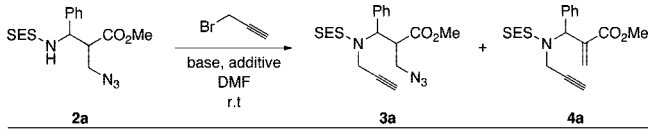


TABLE 2. Optimization of Alkylation of 2a with Propargyl Bromide



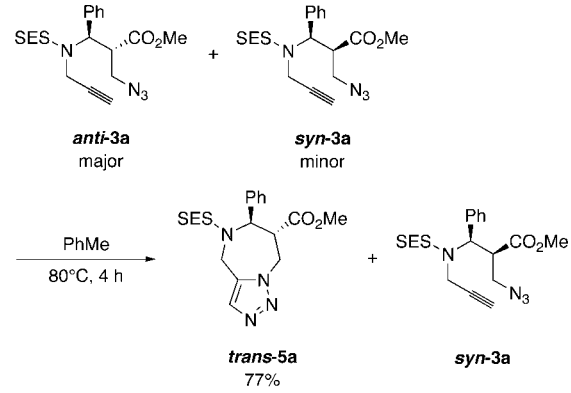
entry	RBr (equiv)	base (equiv)	time (h)	additive (equiv)	proportions[a] 2a	3a	4a
1	4	K_2CO_3 (10)	6		0	70	30
2	4	K_2CO_3 (10)	4	18-C-6 (1)	0	82	18
3	4	Cs_2CO_3, 10)	0.5		0	91	9
4	4	Cs_2CO_3 (10)	0.5	NaI (8)	13	83	4
5	8	Cs_2CO_3 (10)	1	NaI (16)	0	96	4

[a] Determined by ^{1}H NMR.

the formation of compound **4a** resulting from elimination of HN_3. The use of a crown ether to accelerate the alkylation decreased the elimination (entry 2). Changing K_2CO_3 for the more basic Cs_2CO_3 decreased the elimination to 9% and the reaction time to 30 min (entry 3). Addition of NaI slowed down the reaction, but the elimination was decreased (entry 4). Finally, using Cs_2CO_3 with NaI in the presence of an excess of propargyl bromide in DMF was a good compromise to obtain compound **3a** in 1 h at rt, along with only 4% of elimination product **4a**. For the other substrates, the linear precursors **3** were obtained along with the elimination compounds **4** in similar proportions except for substrates **2b** and **2e** bearing an electron-withdrawing group on the aryl moiety, for which the elimination was slightly more significant (Table 1). Compounds **3** were obtained as an unseparable mixture of *anti* and *syn* isomers together with compound **4**.

With the compounds **3** in hand, we started to explore the thermal 1,3-dipolar cycloaddition.[21,22] A first experiment realized by heating the linear precursor **3a** at 80 °C in toluene for 12 h allowed the preparation of the bicyclic triazole **5a**, which was easily separated from the elimination compound **4a** by silica gel chromatography and obtained in a 45% yield. The prolonged reaction time resulted in the degradation of the product. We speculated on the use of the microwave heating to reduce reaction time and probably diminish the degradation. Heating compound **3a** in toluene at 100 °C under microwave irradiation for 30 min did not yield a complete conversion but showed that the linear precursor ***anti*-3a** cyclized more rapidly than the *syn* isomer. By carefully monitoring by ^{1}H NMR the reaction under classical heating conditions, we found that after 4 h in toluene at 80 °C, only the *anti* diastereoisomer had fully cyclized while the *syn* one did not react. The reaction gave a mixture of bicyclic triazole ***trans*-5a**, linear precursor ***syn*-3a**, and elimination compound **4a** (present in the starting material). The triazolodiazepine ***trans*-5a** was obtained in 77% yield after purification by chromatography on silica gel (Scheme 4). An NOE NMR experiment performed on **5a** did not show any effect between the phenyl group protons and those of the ester group, which implies a *trans* relationship between these substituents. Furthermore, X-ray analysis of **5a** showed that the two substituents are in a trans configuration, thus confirming the formation of the *anti* diastereoisomer during the addition of HN_3. Similar results were obtained with the other substrates which allowed the preparation of bicyclic triazoles **5** in good yields with a selectivity higher than 98% for the *trans* isomer (Table 1).

SCHEME 4. 1,3-Dipolar Cycloaddition of Compound 3a



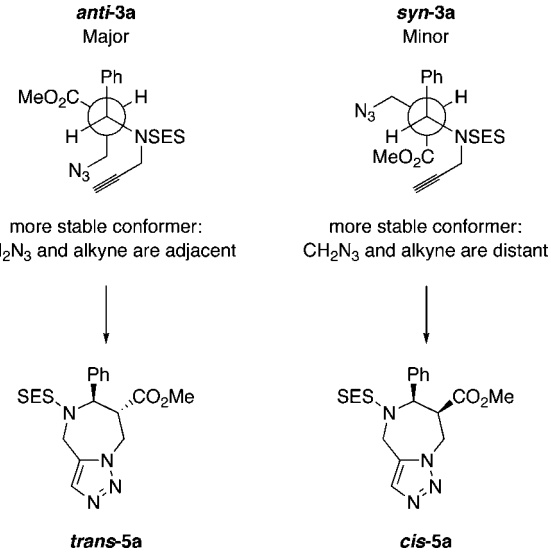
The difference of reactivity between ***anti*-3a** and ***syn*-3a** could be explained by unfavorable interactions between substituents. Newman projections showed that the conformer presenting weaker interactions possess the alkyne and azido substituents in close proximity in the diastereoisomer ***anti*-3a**, whereas these two substituents are in opposite directions in the diastereoisomer ***syn*-3a** (Scheme 5). Diastereomeric differentiation of the two linear diastereomers provided only ***trans*-5a** as a cyclic product.

The last step consisted of the cleavage of the SES group to obtain the free amine. The use of CsF at 80 °C in DMF or *n*-Bu_4NF,[4] usually employed to deprotect the SES group, yielded only degradation products. We turned our attention to anhydrous HF, a nonbasic fluoride source which has proved to be a very efficient reagent for the deprotection of the SES group in other cyclic β-amino esters.[8,10] Deprotection of the SES group by anhydrous HF followed by neutralization of the hydrofluoride

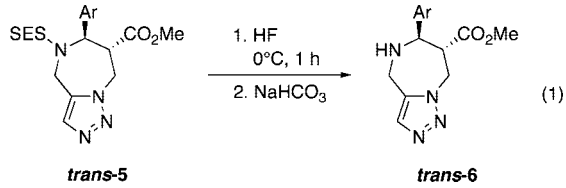
(21) (a) Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 565–598. (b) Huisgen, R. *Angew. Chem.* **1963**, *75*, 604–637.

(22) Huisgen, R.; Knorr, R.; Möbius, L.; Szeimies, G. *Chem. Ber.* **1965**, *98*, 4014–4021.

SCHEME 5. Conformational Analysis of Compound 3a



salt by $NaHCO_3$ yielded the deprotected bicyclic triazoles quantitatively (eq 1, Table 1).



In conclusion, we have described an efficient synthesis of new bicyclic triazoles by sequential azidation/alkylation/1,3-dipolar cycloaddition/deprotection starting from SES-protected *aza*-Baylis−Hillman β-amino esters. To our knowledge, we have reported the first example of selective Huisgen cycloaddition, starting from a mixture of diasteroisomers. The bicyclic triazoles are obtained in their *trans* form in good yields and very high diastereomeric ratios.

Experimental Section

General Procedure for HN_3 Addition on β-Amino Esters 1. To a solution of β-amino ester **2** (0.4 mmol, 1 equiv) in toluene were added azidotrimethylsilane (1.06 mL, 8 mmol, 20 equiv), acetic acid (137 μL, 2.4 mmol, 6 equiv), and triethylamine (45 μL, 0.32 mmol, 0.8 equiv). The solution was heated for 24 h at 40 °C, and the solvent was evaporated. Silica gel chromatography (Et_2O/cyclohexane) yielded the corresponding azido-β-amino ester **2** as a mixture of *anti* and *syn* diastereoisomers.

Methyl 2-(Azidomethyl)-3-phenyl-3-(2-trimethylsilylethanesulfonylamino)propanoate (2a). Addition of HN_3 on the β-amino ester **1a** yielded 156.1 mg (98%) of the title compound as a white solid (mixture anti:syn = 81:19) after silica gel chromatography (Et_2O/cyclohexane = 3/7): IR cm^{-1} 2955 (m), 2108 (s), 1740 (s), 1265 (s); ESIMS *m*/*z* 399.0 $(M + H)^+$, 421.2 $(M + Na)^+$; FAB+ *m*/*z* 398 $(M + H)^+$; HRMS calcd for $C_{16}H_{27}N_4O_4SSi$ 399.1522, found 399.1518. ***Anti* isomer:** ^1H NMR ($CDCl_3$, Me_4Si) δ −0.21 (s, 9H), 0.45−0.85 (m, 2H), 2.40−2.75 (m, 2H), 3.00−3.15 (m, 1H), 3.53 (s, 3H), 3.60−3.75 (m, 2H), 4.70 (dd, 1H, J_3 = 9.8 Hz, J_3 = 8.3 Hz), 6.03 (d, 1H, J_3 = 9.9 Hz), 7.20−7.40 (m, 5H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ –2.2, 10.1, 49.9, 50.2, 51.8, 52.3, 57.4, 127.0, 128.7, 129.1, 138.4, 171.1. ***Syn* isomer:** ^1H NMR ($CDCl_3$, Me_4Si) δ −0.20 (s, 9H), 0.45−0.85 (m, 2H), 2.40−2.75 (m, 2H), 2.95−3.10 (m, 1H), 3.35−3.65 (m, 2H), 3.70 (s, 3H), 4.65−4.75 (m, 1H), 6.07 (d, 1H, J_3 = 10.0 Hz), 7.20−7.40 (m, 5H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ −2.2, 10.2, 50.0, 50.7, 51.8, 52.6, 57.1, 126.7, 128.7, 129.2, 138.8, 172.1.

General Procedure for Alkylation of Azido-β-amino Esters 2 and 1,3-Dipolar Cycloaddition of the Intermediate 3. To a mixture of azido-β-amino ester **2** (0.35 mmol, 1 equiv), Cs_2CO_3 (1.14 g, 3.5 mmol, 10 equiv), and NaI (839 mg, 5.6 mmol, 5.6 equiv) in 9.8 mL of DMF was added propargyl bromide (210 μL, 2.8 mmol, 8 equiv). The mixture was stirred at room temperature for 1 h and then filtered through Celite. The residue was diluted in AcOEt, washed successively with water and brine, dried over $MgSO_4$, and evaporated to give the alkylated azido-β-amino ester **3** as a mixture of *anti* and *syn* diastereoisomers and enyne **4**. A solution of crude azido-β-amino ester **3** in 10 mL of toluene was heated at 80 °C for 4 h. The solvent was evaporated. Silica gel chromatography (AcOEt/CH_2Cl_2) yielded the SES-triazoldiazepine ***trans*-5**.

Methyl 6-Phenyl-5-(2-trimethylsilylethanesulfonyl)-5,6,7,8-tetrahydro-4*H*-[1,2,3]triazolo[1,5-*a*][1,4]diazepine-7-carboxylate (*trans*-5a). Alkylation of azido-β-amino ester **2a** with propargyl bromide yielded 149.3 mg (quant) of the linear precursor as a yellow oil (mixture *anti*/*syn*/**4a** = 79/17/4). Cyclization of the linear precursor **3a** yielded 118.3 mg (77%, two steps) of the title compound as a white solid (mixture *trans*/*cis* = >99:1) after silica gel chromatography (CH_2Cl_2/AcOEt = 9/1): mp 130−133 °C; IR cm^{-1} 2956 (m), 1742 (s), 1266 (s); ^1H NMR ($CDCl_3$, Me_4Si) δ −0.09 (s, 9H), 0.60−0.90 (m, 2H), 2.65−2.90 (m, 2H), 3.64 (s, 3H), 3.79 (dt, 1H, J_3 = 8.2 Hz, J_3 = 5.0 Hz), 4.47 (d, 1H, J_2 = 17.6 Hz), 4.98 (d, 2H, J_3 = 5.0 Hz), 5.00 (d, 1H, J_2 = 17.6 Hz), 5.74 (d, 1H, J_3 = 8.2 Hz), 7.30−7.50 (m, 5H), 7.49 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ −2.0, 10.2, 38.5, 46.8, 48.5, 50.6, 52.9, 61.3, 127.5, 129.2, 129.7, 131.4, 134.1, 136.3, 169.8; ESIMS *m*/*z* 437.2 $(M + H)^+$, 459.1 $(M + Na)^+$; FAB+ *m*/*z* 437 $(M + H)^+$; HRMS calcd for $C_{19}H_{29}N_4O_4SSi$ 437.1679, found 437.1704.

General Protocol for the Deprotection of the SES-triazole 5 with HF. SES-triazolodiazepine **5** (0.1 mmol) was treated with 1 mL of anhydrous HF at 0 °C for 1 h in a Teflon vessel. The HF was removed by distillation. The HF·triazolodiazepine thus obtained was neutralized with a saturated aqueous solution of $NaHCO_3$, and the aqueous phase was extracted three times with AcOEt, dried over $MgSO_4$, filtered, and evaporated to yield the triazolodiazepine **6**. Caution! HF is a harmful chemical.

Methyl 6-Phenyl-5,6,7,8-tetrahydro-4*H*-[1,2,3]triazolo[1,5-*a*]-[1,4]diazepine-7-carboxylate (*trans*-6a). Deprotection of the compound ***trans*-5a** according to the general procedure yield 27.2 mg (100%) of the title compound as a white solid (mixture *trans*/*cis* = >99:1): mp >230 °C; IR cm^{-1} 2982 (m), 1732 (s), 1372 (s); ^1H NMR ($CDCl_3$, Me_4Si) δ 1.89 (sl, 1H), 3.00 (ddd, 1H, J_3 = 10.4 Hz, J_3 = 9.1 Hz, J_3 = 2.1 Hz), 3.36 (s, 3H), 3.95 (d, 1H, J_2 = 15.6 Hz), 4.23 (d, 1H, J_3 = 9.1 Hz), 4.33 (d, 1H, J_2 = 15.6 Hz), 4.57 (dd, 1H, J_2 = 14.6 Hz, J_3 = 10.4 Hz), 5.09 (dd, 1H, J_2 = 14.6 Hz, J_3 = 2.1 Hz), 7.20−7.40 (m, 5H), 7.52 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 41.8, 50.4, 51.7, 52.0, 69.0, 127.2, 128.6, 128.9, 132.0, 137.7, 141.0, 171.2; ESIMS *m*/*z* 273.1 $(M + H)^+$; FAB+ *m*/*z* 273 $(M + H)^+$; HRMS calcd for $C_{14}H_{17}N_4O_2$ 273.1352, found 273.1360.

Acknowledgment. We thank the MENRT and the CNRS for financial support.

Supporting Information Available: Experimental details, spectral data, and copies of ^1H and ^{13}C NMR spectra for all new compounds and X-ray structure and crystal data for compound **5a**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO802533D