A simple method of preparing trimethylsilyl- and *tert*-butyldimethylsilyl-enol ethers of α-diazoacetoacetates and their use in the synthesis of a chiral precursor to thienamycin analogs

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A simple method of preparing trimethylsilyl- and *tert*-butyldimethylsilyl-enol ethers of various esters of α-diazoacetoacetic acid is described. Displacement reaction of 4-acetoxyazetidinone **8** with *tert*-butyldimethylsilylenol ethers **7***a*, followed by desilylation, afforded the key chiral precursor **2***a* for the synthesis of thienamycin analogs.

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On décrit une méthode simple de préparer des éthers énoliques triméthylsilylés et *tert*-diméthylsilylés de divers esters de l'acide α-diazoacétoacétique. La réaction de substitution de l'acétoxyazétidinone (**8**) par les éthers énoliques *tert*-butyldiméthylsilyles (**7***a*), suivie d'une réaction de désilylation, conduit au précurseur chiral **2***a* qui est un produit clé dans la synthèse d'analogues de la thiènamycine.

[Traduit par le journal]

Since the discovery of thienamycin **1** (R = $CH_2CH_2NH_2$), intense efforts have been directed toward the synthesis of thienamycin analogs **1** (1). While many methods are available for carbapenem synthesis, the most widely used process goes through a common intermediate, diazoazetidinone **2** (2, 3).

Recently two groups of scientists reported (3*a*, *b*) elegant ways of constructing this type of intermediate by direct introduction of the α-diazoacetoacetate moiety into the 4-position of 2-azetidinones. Karady *et al.* (3*a*) described the preparation of a chiral diazo intermediate **2** (R = CH_2Ph) by the displacement reaction of an optically active 4-chloroazetidinone **3** (R = Si*t*BuMe$_2$, X = Cl) with trimethylsilylenol ether of benzyl α-diazoacetoacetate (**4**) in the presence of silver tetrafluoroborate followed by desilylation. Similarly Reider and Grabowski (3*b*) employed a displacement reaction (4) of a chiral 4-acetoxyazetidinone **3** (R = H, X = OAc) with **4** in the presence of Lewis acid (zinc iodide) for their synthesis of an optically active diazoazetidinone **2** (R = CH_2Ph).

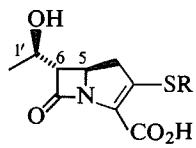
In both cases, the α-diazoacetoacetate unit they employed carried a benzyl group to protect the carboxylic acid. Although the benzyl ester is reported (3*a*) to be useful as a carboxyl protecting group, it has been recognized (2) and recently demonstrated (2*e*) that the *p*-nitrobenzyl ester is far superior to the benzyl ester in the synthesis of thienamycin analogs.

Karady *et al.* prepared trimethylsilylenol ether of benzyl α-diazoacetoacetate (**4**) from benzyl α-diazoacetoacetate (**5**, R = CH_2Ph) by generating the enolate with a strong base such as lithium hexamethyldisilazide, followed by trapping with trimethylsilyl chloride. While successful for the benzyl ester, unfortunately this method, which required a strong base, was not compatible with the *p*-nitrobenzyl ester, producing an intractable mixture with only a little of the desired material **6***a* (Scheme 1).

Here we wish to report (1) a facile preparation of trimethylsilylenol ether and *tert*-butyldimethylsilylenol ether of *p*-nitrobenzyl α-diazoacetoacetate (**6***a* and **7***a*) as well as some other corresponding esters (**6***b*−**6***d* and **7***b*−**7***d*), and (2) subsequent synthesis of a chiral carbapenem intermediate **2** (R = $-CH_2-C_6H_4-NO_2$) as shown in Scheme 1.

Thus, the trimethylsilylenol ether of *p*-nitrobenzyl α-diazoacetoacetate (**6***a*) was prepared in good yield from *p*-nitrobenzyl α-diazoacetoacetate (**5***a*)[3] by using trimethylsilyl trifluoromethanesulfonate as a silylating agent (5*a*) and triethylamine as a base. The reaction was complete within a few minutes in CH_2Cl_2 at 0−5°C. Although several other methods are available for the preparation of silylenol ethers (5*b*, *c*), we find this method simplest and most successful for the preparation of **6***a*. The structural assignment of this silylenol ether was made by means of its ^{1}Hmr spectrum, which showed disappearance of the acetyl group at 2.50 ppm (in compound **5***a*) and appearance of two sharp doublets at 4.23 and 4.93 ppm with a coupling constant of 2 Hz for the vinyl protons.

Although readily prepared, the trimethylsilylenol ether was somewhat labile and easily hydrolyzed to *p*-nitrobenzyl α-diazoacetoacetate (**5***a*) on contact with water or simply atmospheric moisture, thereby creating difficulty in handling. To overcome this problem, we prepared the corresponding *tert*-butyldimethylsilylenol ether **7***a* by the method described above using *tert*-butyldimethylsilyl trifluoromethanesulfonate (7) in place of trimethylsilyl trifluoromethanesulfonate (see Scheme 1). In contrast to the trimethylsilylenol ether **6***a*, the *tert*-butyldimethylsilylenol ether **7***a* was more stable towards neutral water, permitting aqueous work-up. The *tert*-butyldi-



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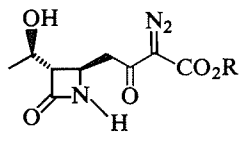

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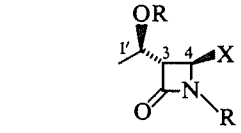

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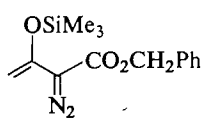

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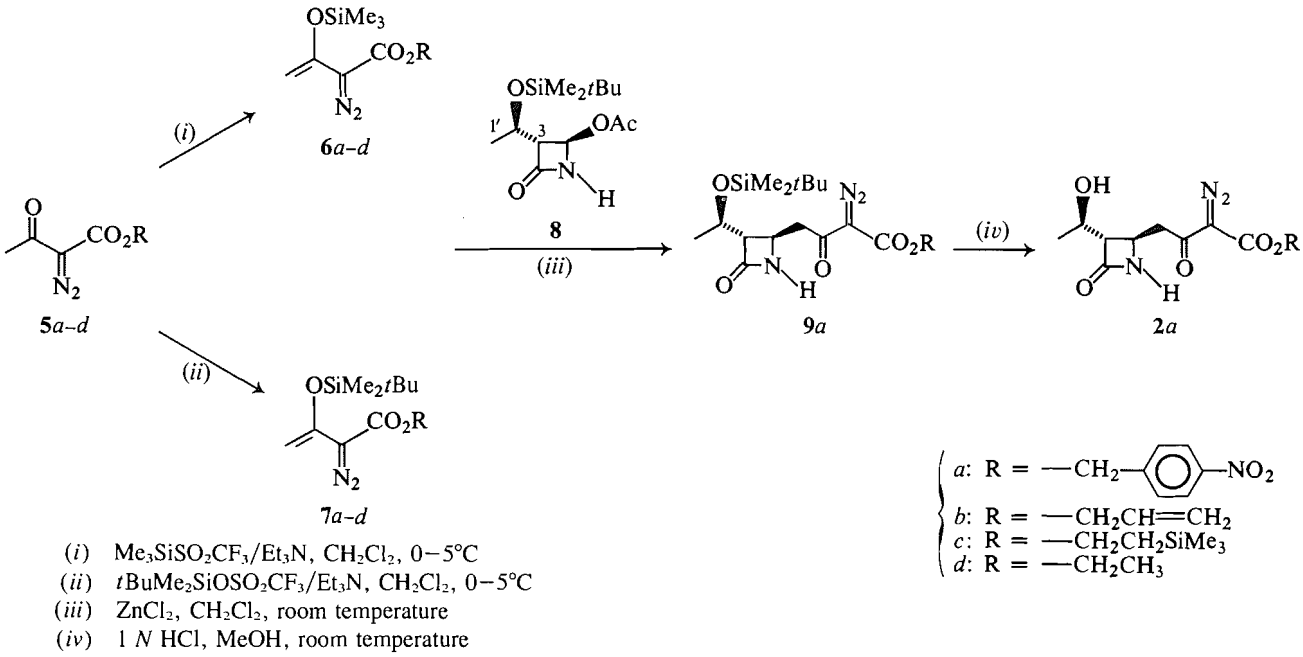
[3]All esters of α-diazoacetoacetic acid described here were prepared from the corresponding acetoacetate esters by the method of Regitz (6) (see Experimental).



(*i*) $Me_3SiSO_2CF_3/Et_3N$, CH_2Cl_2, 0–5°C
(*ii*) $tBuMe_2SiOSO_2CF_3/Et_3N$, CH_2Cl_2, 0–5°C
(*iii*) $ZnCl_2$, CH_2Cl_2, room temperature
(*iv*) 1 *N* HCl, MeOH, room temperature

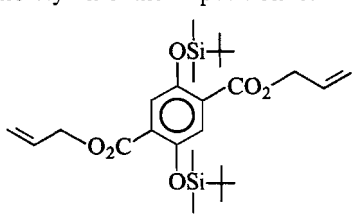
SCHEME 1.

methylsilylenol ether **7***a* (a yellow solid) has been stored in a capped bottle in a refrigerator (0–5°C) for more than 1 year without any hydrolysis to diazoacetoacetate **5***a*.

This method was found to be quite general. Thus, we prepared trimethylsilylenol ethers and *tert*-butyldimethylsilylenol ethers of allyl (**6***b* and **7***b*), trimethylsilylethyl (**6***c* and **7***c*), and ethyl (**6***d* and **7***d*) esters of α-diazoacetoacetic acid from α-diazoacetoacetates,[3] **5***b*–**5***d*. Some of these esters (e.g. allyl (8) and trimethylsilylethyl (9)) have been demonstrated to be useful carboxyl protecting groups in the synthesis of labile molecules such as penems and carbapenems.

The facile preparation of the *tert*-butyldimethylsilylenol ethers (**7***a*–**7***b*) is of particular interest, because generally the *tert*-butyldimethylsilylenol ether of α-diazoacetoacetates **7** could not be prepared, in our hands, by the method of Karady *et al.* (3*a*) which was successful for the preparation of the corresponding trimethylsilylenol ethers **6**. For example, the enolate generated from allyl α-diazoacetoacetate by lithium hexamethyldisilazide in the presence of tetramethylethylenediamine did not react with *tert*-butyldimethylsilyl chloride at −78°C. The reaction at 0°C produced diallyl terephthalate **10**[4], not silylenol ether **7***b*. The compound **10** was formed,[4] presumably by dimerization of the enolate of α-diazoacetoacetate followed by oxidation.

We investigated a direct introduction of the α-diazoacetoacetate moiety into the 4-position of 2-azetidinone by



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displacement reaction of azetidinone **3** with these silylenol ethers under the conditions of Reider *et al.* (4). An optically active 4-acetoxyazetidinone **8** was chosen as an azetidinone counterpart, for it was available from 6-aminopenicillanic acid (11) and it had the correct stereoconfigurations at the 3- and 1′-positions, for the synthesis of thienamycin analogs **1**.

As expected, the trimethylsilylenol ether **6***a* gave, stereospecifically, *trans*-azetidinone **9***a* in 54% yield. Interestingly, the *tert*-butyldimethylsilylenol ether **7***a* also reacted smoothly with 4-acetoxyazetidinone **8** in the presence of zinc chloride to produce, stereospecifically, *trans*-diazoazetidinone **9***a* in 84% yield. The assignment of the *trans*-stereochemistry was readily achieved on the basis of a small coupling constant between H3 and H4 (J_{3-4} = 1.5 Hz).

This stereospecific formation of *trans*-azetidinone, combined with the fact that the starting 4-acetoxyazetidinone has the *tert*-butyldimethylsiloxyethyl group at the 3-position with the *S*-configuration, establishes the stereochemistry at the 4-position of the product as the one found in the natural series such as thienamycin.

Finally, desilylation of this diazoazetidinone **9***a* with 1 *N* aqueous HCl in MeOH afforded key thienamycin precursor **2***a* in 84% yield. The key intermediate, **2***a*, has spectroscopic properties (^{1}Hmr, ir) consistent with data reported by Christensen *et al.* (2*b*). This compound was previously converted to thienamycin **1** (R = $CH_2CH_2NH_2$) and its analogs (2).

This whole sequence, starting from *p*-nitrobenzyl α-diazoacetoacetate (**5***a*) via the *tert*-butyldimethylsilylenol ether **7***a* constitutes an improved and practical method for the synthesis of thienamycin analogs **1**.

In summary, the trimethylsilyl- and *tert*-butyldimethylsilylenol ethers of various esters (including *p*-nitrobenzyl ester) of α-diazoacetoacetic acid were prepared by use of trimethylsilyl trifluoromethanesulfonate and *tert*-butyldimethylsilyl trifluoromethanesulfonate respectively, and they were found to be useful synthons for the synthesis of key carbapenem precursors **2**.

Experimental

Melting points were determined on a Gallenkamp melting point

[4]The structure **10** was tentatively assigned, based on the mechanistic considerations and its spectroscopic data. Ethyl γ-chloroacetoacetate was also reported to produce diethyl 2,5-dihydroxyterephthalate by base treatment.

apparatus and are not corrected. The infrared spectra were recorded on a Perkin-Elmer 267 grating infrared spectrometer. The ^{1}H nuclear magnetic resonance spectra were taken with either the Varian EM-360 (60 MHz), unless specified, or a Varian CFT-20 (80 MHz) nmr spectrometer. Tetramethylsilane was used as an internal standard and chemical shifts are reported in parts per million (δ) relative to the internal standard. The ultraviolet spectra were recorded on a Unicam SP8-100 uv spectrometer. Optical rotations were measured with a Perkin–Elmer Model 141 polarimeter. Tetrahydrofuran was freshly distilled from lithium aluminum hydride. Anhydrous diethyl ether (Fisher) was used without further treatment. All other solvents were reagent grade and had been stored over molecular sieves before use. Triethylamine and tetramethylethylenediamine were distilled from CaH_2 and stored over NaOH. Anhydrous zinc chloride was fused under reduced pressure and pulverized prior to use. Allyl diazoacetoacetate (**5***b*) (12) and ethyl diazoacetate (**5***d*) (6*a*) were prepared by the general procedure of Regitz (6). Analytical thin layer chromatography (tlc) was conducted on precoated plates (Silica Gel 60F-254, E. Merck). Visualization was effected by uv light, and iodine or ammonium molybdate (VI). Preparative layer chromatography (plc) was performed on silica gel plates prepared from Silica Gel 60 GF-254 (E. Merck). For column chromatography, 70–230 mesh Silica Gel (E. Merck) was used. The analyses were performed by Micro-Tech Laboratories, Skokie, Illinois, U.S.A.

p-*Nitrobenzyl acetoacetate*

A mixture of ethyl acetoacetate (140 g, 1.08 mol; Aldrich) and *p*-nitrobenzyl alcohol (153 g, 1.00 mol; Aldrich) in toluene (1 L) was heated and slowly distilled, removing 900 mL of the distillate over a period of 15 h. After cooling, any insoluble material was removed by filtration over Celite, washed with toluene. The filtrate and washings were combined and evaporated *in vacuo* to obtain 280 g of a crude oil. This oil was crystallized at 5°C from diethyl ether (280 mL) to yield 181.55 g (0.766 mol, yield 76.6%) of the title compound as off-white crystals, mp 40–42°C; R_f 0.45 (Et_2O); ir (film) ν_{max}: 1740 (ester), 1715 (ketone), 1515 and 1345 (NO_2) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 1.98 (0.3H, s, *Me*(OH)═), 2.32 (2.7H, s, CH_3), 3.62 (1.8H, s, —CO*CH*$_2$CO$_2$—), 5.08 (0.1H, s, vinyl proton of the enol form), 5.28 (2H, s, —CO$_2$*CH*$_2$Ar), 7.53 (2H, 'd', *J* = 9 Hz, ArH's), and 8.23 (2H, 'd', *J* = 9 Hz, ArH's) ppm. An analytical sample was obtained by recrystallization from toluene–hexanes, mp 44–45°C; uv (CH_2Cl_2)λ_{max}: 267 nm (ε 10 800), *Anal.* calcd. for $C_{11}H_{11}NO_5$: C 55.70, H 4.67, N 5.91; found: C 55.59, H 4.62, N 5.85.

Trimethylsilylethyl acetoacetate

A solution of ethyl acetoacetate (2.60 g, 20 mmol; Aldrich) and trimethylsilylethanol (2.51 g, 21.1 mmol; Fluka) in toluene (100 mL) was heated and slowly distilled at 80–100°C with a Vigreux column (1.7 cm × 7 cm), removing most of the solvent over a period of 10 h. The residue was distilled under reduced pressure with a Vigreux column (1.7 cm × 7 cm) to obtain 3.34 g (16.5 mmol, yield 82.7%) of the title compound as a colourless oil; R_f 0.32 (20% EtOAc/hex); bp 85–88°C (0.3 Torr; 1 Torr = 133.3 Pa) (lit. (13) bp 77–80°C (1 Torr)); ir (neat) ν_{max}: 1740 (ketone) and 1720 (ester) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.07 (9H, s, $SiMe_3$), 1.00 (2H, 't' *J* = 8 Hz, $SiCH_2$), 1.93 (0.45H, s, *Me*C(OH)═), 2.28 (2.55H, s, MeCO), 3.12 (0.15H, s, OH of the enol form), 3.43 (1.7H, s, $COCH_2$), 4.2 (2H, 't', *J* = 8 Hz, CO_2CH_2), and 4.95 (0.15H, s, vinyl proton of the enol form) ppm; *Anal.* calcd. for $C_9H_{18}O_3Si$: C 53.43, H 8.97; found: C 53.19, H 8.82.

p-*Nitrobenzyl α-diazoacetoacetate* (*5*a)

To a solution of *p*-nitrobenzyl acetoacetate (134.6 g, 0.568 mol) and triethylamine (79.0 nL, 0.568 mol) in CH_3CN (340 mL) was added at 0–5°C under a nitrogen atmosphere *p*-toluenesulfonyl azide[5] (14) (130 g, 0.568 mol, estimated purity 86%) over a period of 15 min. During this period the title compound started precipitating. The cooling bath was removed and the mixture stirred at room temperature for 3 h. The mixture was cooled again in an ice bath for 30 min and the precipitate was filtered, washed with cold CH_3CN (75 mL), and then cold Et_2O (200 mL) to yield 135.06 g (0.514 mol, yield 90.4%) of the title compound as pale yellow powder; R_f 0.65 (EtOAc); ir (CH_2Cl_2) ν_{max}: 2130 (N_2), 1720 (ester), 1655 (ketone), 1520 and 1350 (NO_2) cm^{-1}; uv (CH_2Cl_2) λ_{max}: 260 nm (ε 17 400); ^{1}Hmr ($CDCl_3$) δ: 2.50 (3H, s, CH_3), 5.38 (2H, s, CO_2CH_2Ar), 7.53 (2H, 'd', *J* = 9 Hz, ArH's), and 8.27 (2H, 'd', *J* = 9 Hz, ArH's) ppm.

2-Trimethylsilylethyl α-diazoacetoacetate (*5*c)

To a solution of trimethylsilylethyl acetoacetate (10.6 g, 50.0 mmol) and triethylamine (7.10 mL, 51.5 mmol) in acetonitrile (85 mL) was added in an ice bath *p*-toluenesulfonyl azide[5] (14) (10.0 g, 50.7 mmol) and the reaction mixture stirred at room temperature for 20 h. After evaporation of the solvent *in vacuo*, the residue was extracted with Et_2O (90 mL) and this extract was washed with a solution of KOH (3.0 g) in H_2O (83 mL) and again a solution of KOH (0.9 g) in H_2O (30 mL), then brine, and dried (Na_2SO_4). Evaporation of the solvent *in vacuo* gave 11.6 g of a crude oil which was purified by column chromatography (SiO_2, 150 g) eluting with 20% EtOAc/hexanes, to obtain 9.65 g (42.3 mmol, yield 84.5%) of the title compound as yellowish oil; R_f 0.44 (20% EtOAc/hex); ir (neat) ν_{max}: 2130 (C═N_2), 1715 (ester), and 1660 (ketone) cm^{-1}; uv (CH_2Cl_2) λ_{max}: 257 nm (ε 7200); ^{1}Hmr ($CDCl_3$) δ: 0.07 (9H, s, $SiMe_3$), 1.03 (2H, 't' *J* = 8 Hz, CH_2Si), 2.47 (3H, s, $COCH_3$), and 4.30 (2H, 't' *J* = 8 Hz, CO_2CH_2) ppm.

2-Diazo-3-trimethylsilyloxy-3-butenoic acid esters (**6**a–**6**d) *(general procedure)*

To a stirred solution (or suspension for the *p*-nitrobenzyl ester) of α-diazoacetoacetic acid esters, **5***a*–**5***d*, (1 mmol) and triethylamine (0.20 mL, 1.4 mmol) in dry CH_2Cl_2 or CCl_4 (2 mL) was added at 0–5°C trimethylsilyl trifluoromethanesulfonate (0.22 mL, 1.1 mmol; Aldrich) under a dry nitrogen atmosphere and the mixture stirred (0–5°C, N_2) for 30 min. To this clear yellow solution was added anhydrous hexanes (30 mL for the *p*-nitrobenzyl ester or 5 mL for the other esters) and stirred for 10 min under a nitrogen atmosphere. After removing the oily deposit by gravity filtration, the hexanes solution was evaporated *in vacuo* and the residue was re-dissolved in anhydrous hexanes (50 mL for the *p*-nitrobenzyl ester or 10 mL for the other esters). The insoluble material was again removed by gravity filtration and the filtrate was evaporated *in vacuo* to obtain **6***a* as yellow crystals or **6***b*–**6***d* as orangish oil in 77–97% yield. The whole operation should be performed under an anhydrous atmosphere since the products are sensitive to moisture.

Compound **6**a: 90% yield: ir (film) ν_{max}: 2100 (C═N_2), 1705 (ester), 1520 and 1345 (NO_2) cm^{-1}; ^{1}Hmr (CCl_4) δ: 0.28 (9H, s, $SiMe_3$), 4.17 (1H, d, *J* = 2 Hz, vinyl proton), 4.93 (1H, d, *J* = 2 Hz, vinyl proton), 5.29 (2H, s, CO_2CH_2Ar), 7.50 (2H, 'd' *J* = 9 Hz, ArH's), and 8.20 (2H, 'd', *J* = 9 Hz, ArH's) ppm.

Compound **6**b: 77% yield: ir (neat) ν_{max}: 2100 (C═N_2), 1710 (ester), and 1605 (C═C) cm^{-1}; ^{1}Hmr (CCl_4) δ: 0.20 (9H, s, $SiMe_3$), 4.15 (1H, d, *J* = 2 Hz, vinyl proton), 4.63 (2H, d, *J* = 5 Hz, CO_2CH_2), 4.95 (1H, d, *J* = 2 Hz, vinyl proton), and 5–6.2 (3H, m, vinyl protons) ppm.

Compound **6**c: 97% yield; ir (neat) ν_{max}: 2090 (C═N_2), 1705 (ester), and 1605 (C═C) cm^{-1}; ^{1}Hmr (CCl_4) δ: 0.07 (9H, s, $SiMe_3$), 0.25 (9H, s, $OSiMe_3$), 1.00 (2H, 't', *J* = 8 Hz, CH_2Si), 4.15 (1H, d, *J* = 2 Hz, vinyl proton), 4.23 (2H, 't' *J* = 8 Hz, CO_2CH_2), and 4.98 (1H, d, *J* = 2 Hz, vinyl proton) ppm.

Compound **6**d: 78% yield; ir (neat) ν_{max}: 2090 (C═N_2), 1710 (ester), and 1605 (C═C) cm^{-1}; ^{1}Hmr (CCl_4) δ: 0.25 (9H, s, $SiMe_3$), 1.32 (3H, t, *J* = 7 Hz, CH_3), 4.17 (1H, d, *J* = 2 Hz, vinyl proton), 4.23 (2h, q, *J* = 7 Hz, CO_2CH_2), and 4.97 (1H, d, *J* = 2 Hz, vinyl proton) ppm.

[5]*p*-Toluenesulfonyl azide, when prepared from unpurified *p*-toluenesulfonyl chloride by warming (ca. 50°C) to dissolve in EtOH, was contaminated by ethyl *p*-toluenesulfonate (ca. 15%). *p*-Toluenesulfonyl azide, free from ethyl *p*-toluenesulfonate, can also be prepared in aqueous acetone.

p-*Nitrobenzyl 2-diazo-3-(*tert-*butyldimethylsiloxy)-3-butenoate (7a)*

To a stirred suspension of *p*-nitrobenzyl α-diazoacetoacetate (26.30 g, 0.100 mol) and triethylamine (20.0 mL, 0.140 mol) in CH_2Cl_2 (200 mL) was added at 2°C *tert*-butyldimethylsilyl trifluoromethanesulfonate (27.5 mL, 0.12 mol; Fluka), in 30 min, under a nitrogen atmosphere and the mixture stirred at 2°C for 1 h. The clear orange solution was diluted with CH_2Cl_2 (50 mL) and washed with water (3 × 200 mL) and then brine (100 mL), dried (Na_2SO_4), and evaporated, yielding 37.40 g (0.0991 mol, yield 99.1%) of the title compound as a yellow solid; R_f 0.44 (20% EtOAc/hex: partially decomposed to *p*-nitrobenzyl α-diazoacetoacetate on the plate); ir (film) ν_{max}: 2090 (br, C=N_2), 1694 (ester), 1600 (C=C), and 1344 (NO_2) cm^{-1}; uv (CH_2Cl_2) λ_{max}: 271 nm (ε 14 500); ^{1}Hmr ($CDCl_3$) δ: 0.26 (6H, s, $SiMe_2$), 0.96 (9H, s, Si-*t*Bu), 4.25 (1H, d, J = 2.5 Hz, vinyl proton), 4.97 (1H, d, J = 2.5 Hz, vinyl proton), 5.32 (2H, s, CO_2H_2), 7.48 (2H, 'd' J = 9 Hz, ArH's), and 8.22 (2H, 'd', J = 9 Hz, ArH's) ppm. This material was purified by crystallization from hexanes to obtain an analytical sample: uv (CH_2Cl_2) λ_{max} 270 nm (ε 15 500).

*2-Diazo-3-(*tert-*butyldimethylsiloxy)-3-butenoic acid esters (7b–7d) (general procedure)*

To a stirred solution of α-diazoacetoacetic acid esters, **5b–5d**, (1 mmol) and triethylamine (0.20 mL, 1.4 mmol) in dry CH_2Cl_2 (2 mL) was added, at 0–5°C, *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.28 mL, 1.2 mmol; Fluka) under a nitrogen atmosphere and the yellow mixture stirred at 0–5°C for 15 min. This was diluted with hexanes (20 mL), washed with a diluted $NaHCO_3$ solution and then brine, dried (Na_2SO_4), and evaporated to obtain **7b–7d** as orangish oil in 93–99% yield.

Compound **7b**: 96% yield; R_f 0.6 (20% EtOAc/hex; partially decomposed to α-diazoacetoacetate on the plate); ir (film) ν_{max}: 2100 (C=N_2), 1715 (ester), and 1610 (C=C) cm^{-1}; uv (CH_2Cl_2) λ_{max}: 280 nm (ε 6000); ^{1}Hmr ($CDCl_3$) δ: 0.23 (6H, s, $SiMe_2$), 0.93 (9H, s, Si-*t*Bu), 4.20 (1H, d, J = 5 Hz, J = 2 Hz, vinyl proton), 4.63 (2H, br d, J = 5 Hz, CO_2CH_2), 4.95 (1H, d, J = 2 Hz, vinyl proton), and 5–6.3 (3H, m, vinyl protons) ppm.

Compound **7c**: 94% yield; R_f 0.7 (20% EtOAc/hex; partially decomposed to α-diazoacetoacetate on the plate); ir (film) ν_{max}: 2100 (C=N_2), 1710 (ester), and 1610 (C=C) cm^{-1}; uv (CH_2Cl_2) λ_{max}: 280 nm (ε 7600); ^{1}Hmr (acetone-d_6; CFT-20) δ: 0.06 (9H, s, $SiMe_3$), 0.25 (6H, s, $SiMe_2$), 0.94 (9H, s, Si-*t*Bu), 1.05 (2H, t, J = 8.3 Hz, $CO_2CH_2CH_2SiMe_3$), 4.31 (1H, d, J = 1.8 Hz, vinyl proton), 4.32 (2H, t, J = 8.3 Hz, $CO_2CH_2CH_2SiMe_3$), and 5.03 (1H, d, J = 1.8 Hz, vinyl proton) ppm.

Compound **7d**: 99% yield; R_f 0.66 (20% EtOAc/hex; partially decomposed to α-diazoacetoacetate on the plate); ir (film) ν_{max}: 2090 (C=N_2), 1710 (ester), and 1610 (C=C) cm^{-1}; uv (CH_2Cl_2) λ_{max}: 282 nm (ε 7950); ^{1}Hmr (acetone-d_6; CFT-20) δ: 0.25 (6H, s, $SiMe_2$), 0.94 (9H, s, Si-*t*Bu), 1.26 (3H, t, J = 7.1 Hz, $CO_2CH_2CH_3$), 4.25 (2H, q, J = 7.1 Hz, $CO_2CH_2CH_3$), 4.28 (1H, d, J = 2 Hz, vinyl proton), and 5.02 (1H, d, J = 1.9 Hz, vinyl proton) ppm.

*Attempted preparation of allyl 3-*tert-*butyldimethylsiloxy-2-diazo-3-butenoate 7b through the enolate (formation of diallyl terephthalate 10*

To a stirred solution of lithium hexamethyldisilazide in THF (1 *M* solution, 1.2 mL, 1.2 mmol; Aldrich) and tetramethylethylenediamine (0.16 mL, 1.1 mmol) in THF (4 mL) was added slowly at −78°C, under a nitrogen atmosphere, allyl α-diazoacetoacetate (**5b**) (12) (168 mg, 1.00 mmol) and the mixture stirred (−78°C, N_2) for 1 h. To this solution was added a solution of *tert*-butyldimethylsilyl chloride (237 mg, 1,57 mmol; Aldrich) in THF (0.8 mL) and this was stirred at −78°C for 20 min. The mixture (1.2 ml) was partitioned between H_2O and hexanes. The hexanes phase was dried (Na_2SO_4) and evaporated to obtain 52 mg of a crude oil, the ^{1}Hmr ($CDCl_3$) spectrum of which indicated this to be mainly the starting diazoacetoacetate **5b**. The rest of the reaction mixture was warmed gradually to 0°C by replacing the Dry Ice − acetone bath with an ice bath over a period of 2 h. This was diluted with hexanes, washed with H_2O, dried (Na_2SO_4), and evaporated, yielding 241 mg of an oily solid. Purification of this material by plc (SiO_2, Et_2O/hex 1:1) gave 101 mg of diallyl 2,5-bis (*tert*-butyldimethylsiloxy)terephthalate (**10**) as a white solid; R_f 0.19 (Et_2O/hex 1:1); ir (film) ν_{max}: 1720 (ester) cm^{-1}: ^{1}Hmr ($CDCl_3$) δ: 0.15 (6H, s, $SiMe_2$), 0.95 (9H, s, Si-*t*Bu), 4.75 (2H, br d, J = 6 Hz, CO_2CH_2), 5–6.4 (2H, m, vinyl protons), and 7.27 (1H, s, ArH) ppm.

This material in EtOH was treated with 1 *N* aqueous HCl at room temperature to obtain diallyl 2,5-dihydroxyterephthalate, mp 85–87°C; R_f 0.47 (EtOAc); ir (film) ν_{max}: 3400 (OH) and 1700 (ester) cm^{-1}; ^{1}Hmr ($CDCl_3$, CFT-20) δ: 4.89 (2H, 'd', J = 5.81 Hz, CO_2CH_2), 5–6.4 (2H, m, vinyl protons), 7.34 (1H, s, ArH), and 8.20 (br, OH) ppm. This compound gave intense purple colour when treated with an aqueous solution of ferric chloride, indicating the presence of a phenolic hydroxy group (10).

*(3S)-{(1R)-(*tert-*butyldimethylsiloxy)ethyl}-(4R)-{3-(*p-*nitrobenzyloxy) carbonyl-2-oxo-3-diazopropan-1-yl}azetidin-2-one (9a)*

To a stirred mixture of (3*R*)-{(1*R*)-(*tert*-butyldimethylsiloxy)-ethyl)-(4*R*)-acetoxy-2-azetidinone (**8**) (144 mg, 0.50 mmol, mp 101–103°C) (11) and anhydrous $ZnCl_2$ (34 mg, 0.25 mmol) in CH_2Cl_2 (3 mL) was added at room temperature, under a nitrogen atmosphere, a solution of *p*-nitrobenzyl 2-diazo-3-trimethylsiloxy-3-butenoate (**6a**) (308 mg, 1.00 mmol) or *p*-nitrobenzyl 3-(*tert*-butyldimethylsiloxy)-2-diazo-3-butenoate (**7a**) (226 mg, 0.60 mmol) over a period of 2–3 h. The mixture was stirred another 1–2 h under the same conditions. This was diluted with EtOAc (20 mL), washed with H_2O and then brine, dried (Na_2SO_4), and evaporated, yielding a crude oil. This was purified by column chromatography (SiO_2, 20 g) eluting with 20% EtOAc in CH_2Cl_2 to obtain 132 mg (0.269 mmol, yield 53.8%) from the reaction with **6a**, or 207 mg (0.422 mmol, yield 84.4%) from the reaction with **7a**, of the title compound as a colourless oil; R_f 0.39 (20% EtOAc/CH_2Cl_2); ir (neat) ν_{max}: 3000 (br, NH), 2140 (C=N_2), 1755 (β-lactam), 1720 (ester), 1655 (C=O), 1525 and 1350 (NO_2) cm^{-1}; $[\alpha]_D^{20}$ +44.3° (*c* 1.0, CH_2Cl_2); ^{1}Hmr ($CDCl_3$, CFT-20) δ: 0.06 (6H, s, $SiMe_2$), 0.86 (9H, s, Si-*t*Bu), 1.21 (3H, d, J = 6.3 Hz, 1'-Me), 2.85 (1H, dd, $J_{3-1'}$ = 5Hz, J_{3-4} = 2.5 Hz, 3-H), 2.96 (1H, dd, J_{gem} = 18 Hz, $J_{1''-4}$ = 9.5 Hz, 1''–Ha), 3.41 (1H, dd, J_{gem} = 18 Hz, $J_{1''-4}$ = 3.5 Hz, 1''–Hb), 3.8–4.3 (2H, m, 4–H and 1'–H), 5.35 (2H, s, CO_2CH_2Ar), 5.95 (br, s, NH), 7.53 (2H, 'd', J = 8.8 Hz, ArH's), and 8.26 (2H, 'd', J = 8.8 Hz, ArH's) ppm.

The reaction with **7a** was also carried out on a large scale (0.25 mol of **8**) without lowering the yield.

*(3S)-{(1R)-Hydroxyethyl}-(4R)-{3-(*p-*nitrobenzyloxy)carbonyl-2-oxo-3-diazopropan-1-yl}azetidin-2-one (2a)*

To a stirred solution of **9a** (39.25 g, 80.0 mmol) in MeOH (240 mL) was added 1 *N* aqueous HCl (80 mL) and the mixture stirred at room temperature for 6 h. During this period the title compound was precipitated. This was cooled, filtered, and washed with cold MeOH–H_2O (9:1) and then cold Et_2O to obtain 25.26 g (67.2 mmol, yield 84.0%) of the title compound as white solid, mp 151–152°C (CH_3CN); $[\alpha]_D^{22}$ +21.8° (*c* 0.23, CH_3CN); R_f 0.19 (EtOAc); ir (Nujol) ν_{max}: 3390 (OH), 2130 (C=N_2), 1730 (β-lactam), 1705 (ester), 1660 (ketone), 1605 (Ar), 1520 and 1350 (NO_2) cm^{-1}; ^{1}Hmr ($CDCl_3$, CFT-20) δ: 1.33 (3H, d, J = 6.3 Hz, 1'–Me), 1.91 (br, OH), 2.88 (1H, dd, $J_{3-1'}$ = 7.3 Hz, J_{3-4} = 2.2 Hz, 3–H), 3.25 (2H, m, 1'–H's), 3.8–4.2 (1H, m, 4–H), 4.17 (1H, 'q', J = 6.7 Hz, 1'–H), 5.36 (2H, s, CO_2CH_2), 5.96 (1H, br, NH), 7.54 (2H, 'd', J = 8.6 Hz, ArH's), and 8.27 (2H, 'd', J = 8.7 Hz, ArH's) ppm.

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