DOI: 10.1002/ejoc.200701072

Synthesis of Highly Substituted 2*H*-Azirine-2-carboxylates via 3-Azido-4-oxobut-2-enoates[‡]

Tamás Patonay,*[a] József Jekő,[b] and Éva Juhász-Tóth[a]

Dedicated to Professor Kálmán Medzihradszky on the occasion of his 80th birthday

Keywords: Azides / Azirines / C–C coupling / Nitrenes / Thermolysis

Phenacyl azides have been transformed into ethyl 4-aryl-3-azido-2-methyl-4-oxobut-2-enoates by base-induced coupling of the starting α-azido ketone with ethyl pyruvate followed by elimination of methanesulfonic acid from the mesylate generated in situ from the labile aldol-type intermediates ethyl 4-aryl-3-azido-2-hydroxy-2-methyl-4-oxobutanoates. Thermolysis of ethyl 4-aryl-3-azido-2-methyl-4-oxobut-2-enoates resulted in the formation of the hitherto unknown 3-aroyl-2-ethoxycarbonyl-2-methyl-2*H*-azirines.

Introduction

Vinyl azides are an important and synthetically useful class of nitrogen-containing derivatives.[1] The strong interest in this class of compounds is related to their high reactivity in pyrolysis and cycloaddition reactions, and their easy attack by both electrophiles and nucleophiles. The chemistry of related allenyl azides has also been reviewed.[1e] 2-Azido-1,3-diaryl-2-propen-1-ones (α-azidochalcones) represent an interesting subclass of vinyl azides; their transformations can give various products including heterocycles depending on the reagents and the reaction conditions used. Nitrenes generated by thermolysis have led to the formation of various insertion products;[2] in some cases azirines have also been obtained among other products in photolytic[3] or microwave-assisted reactions.[4] Cycloadditions to the azide function,[5] aza-Wittig reactions[6] and their electrolytical properties[7] have also been studied. Ring-closure of 3-aryl-2-azido-1-(2-hydroxy- or 2-aminophenyl)-2-propen-1-ones by intramolecular conjugate addition followed by various secondary reactions has led to the formation of various 3-substituted chromones, flavones or 4(1*H*)-quinolones.[8]

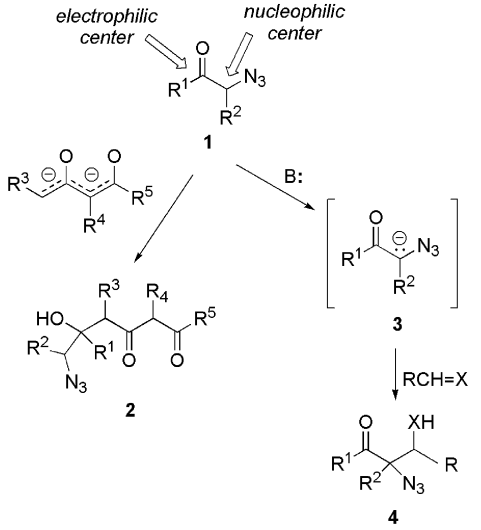
Several methods describing the preparation of these unsaturated azides have been published in the literature.[1] The most important procedures for the synthesis of α- or β-azido-α,β-unsaturated ketones involve the Knoevenagel-type condensation of phenacyl azides,[2a,9] iodine azide addition to an α,β-unsaturated ketone,[10] treatment of α,β-dihalo ketones or the intermediate α-halo-α,β-unsaturated ketones with sodium azide[8b,8d,11] and ammonium cerium(IV) nitrate mediated oxidative addition of sodium azide to α,β-unsaturated ketones followed by treatment with sodium acetate.[12]

α-Azido ketones **1** are a synthetically valuable group of azides that exhibit double reactivity in C–C bond formation. The electrophilic carbonyl function provides a target for the attack of carbanions leading to adducts such as compounds **2**; this chemistry has been utilized by Langer and co-workers[13] (Scheme 1). On the other hand, α-azido ketones possessing an α-hydrogen show enhanced C–H acidity due to the anion-stabilizing effect of the azido group. The controlled generation of carbanions **3** followed by trapping with various carbon electrophiles results in the formation of aldol-type products **4** (Scheme 1).

In our previous work[14] we have demonstrated that base-induced reactions between α-azido ketones **1** and either simple aldehydes or more complex carbonyl compounds like α-oxo aldehydes provide an efficient method for the preparation of valuable tri- and tetrafunctionalized synthons. Our method has been successfully used by other research groups. Thus, α-azido ketones have been coupled with Michael acceptors,[15] aldehydes[16] and various in situ generated imines.[17] This latter reaction was performed by using a proline-based organocatalyst as base and gave enantiomerically enriched 2-amino-3-azido-4-oxoalkanoates and 3-amino-2-azido ketones. This pathway represents a new approach towards chiral, non-racemic 1,2-diamines.

[‡] α-Azido Ketones, Part 5. Part 4: É. Juhász-Tóth, T. Patonay, *Eur. J. Org. Chem.* **2002**, 3055–3064.

[a] Department of Organic Chemistry, University of Debrecen, Egyetem tér 1, 4032 Debrecen, Hungary
Fax: +36-52-453-836
E-mail: tpatonay@puma.unideb.hu
[b] Department of Chemistry, College of Nyíregyháza, Sóstói út 31/b, 4400 Nyíregyháza, Hungary



Scheme 1. Reactivity of α-azido ketones in C–C bond formation reactions.

In a previous publication[14c] we reported on the reaction of phenacyl azides and ethyl pyruvate in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) which afforded the expected coupling products 3-azido-2-hydroxy-4-oxoalkanoates in high yield according to TLC and ^{1}H NMR studies. However, only one stable product, namely ethyl 3-azido-2-hydroxy-4-(4-methoxyphenyl)-2-methyl-4-oxobutanoate (**6b**, see Scheme 2), was isolated in 69% yield. In the other cases, all attempts to isolate the products by column chromatography failed. The lability of the adducts was explained in terms of their increased ability to undergo a retro-aldol reaction, probably due to the crowdedness around the quaternary C-2 atom. In this contribution we wish to demonstrate that these valuable but not isolable tetrafunctionalized synthons **6** can be simply transformed into the corresponding stable 3-azido-4-oxoalk-2-enoates **7** which can then be converted into the hitherto unknown 2-alkyl-3-aroyl-2*H*-azirine-2-carboxylates **9** (see Scheme 3).

Results and Discussion

The reaction of 2-azido-4′-methoxyacetophenone (**5b**) and ethyl pyruvate resulted in the formation of adduct **6b** as a mixture of *syn* and *anti* diastereomers in a ratio of 67:33. The low diastereoselectivity seems to be typical in the coupling of α-azido ketones with carbon electrophiles[14–17] and can be interpreted in terms of thermodynamic control during the formation of the adducts. The diastereomers of ethyl 3-azido-2-hydroxy-4-(4-methoxyphenyl)-2-methyl-4-oxobutanoate (**6b**) were separated by column chromatography, and single-crystal X-ray analysis of the minor product revealed its *anti* relative configuration (Figure 1). Note that a strong hydrogen bond was observed in the crystals of *anti*-**6b**; the crystal packing is shown in Figure 2. The observed preference for the formation of the *syn* configuration during C–C bond coupling is in accordance with both our previous observations[14] and other reported results.[16,17]

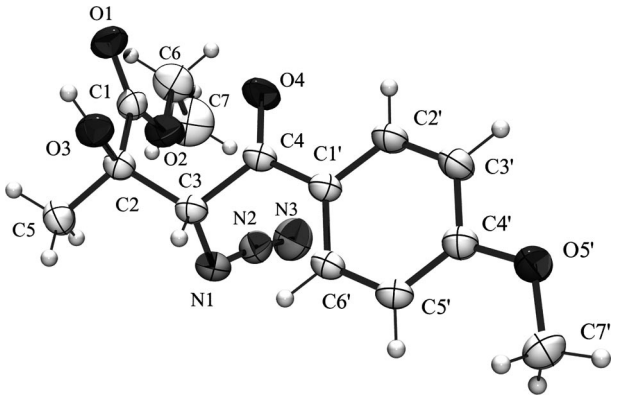


Figure 1. Crystal structure of *anti*-**6b**.

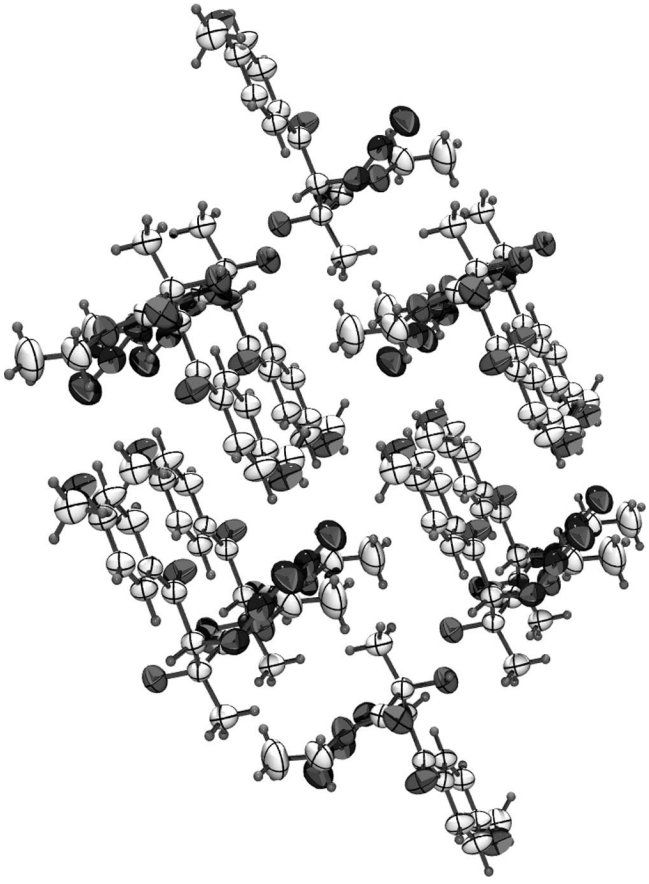
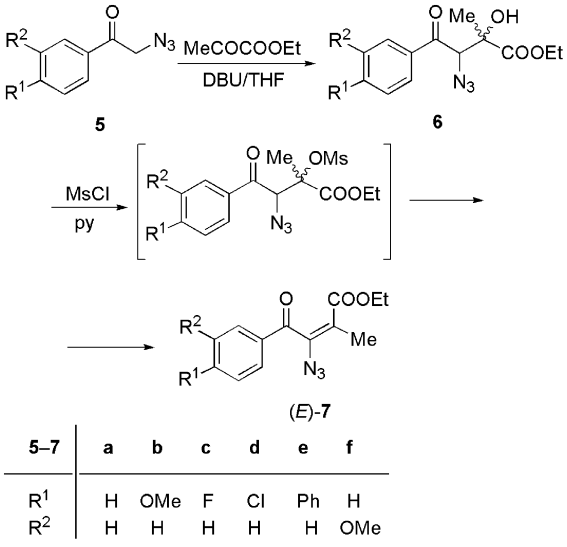


Figure 2. Crystal packing of *anti*-**6b**, view normal to (010).

We also demonstrated previously that treatment of a mixture *syn*/*anti*-**6b** with mesyl chloride (MsCl) in pyridine resulted in the formation of the corresponding stable ethyl 3-azido-4-(4-methoxyphenyl)-2-methyl-4-oxo-2-butenoate (**7b**) in diastereopure form and in moderate (50%) yield.[14c] When the reaction was repeated with pure diastereomers of azido alcohol **6b** (see Experimental Section), we found that both stereoisomers show similar reactivity and give the

same vinyl azide (*E*)-**7b** with complete diastereoselectivity and in nearly the same yields (*anti*: 75% yield, 81% conversion; *syn*: 63% yield, 75% conversion).

Since the stereochemical outcome of the elimination from the in situ generated intermediates ethyl 3-azido-2-mesyloxy-4-(4-methoxyphenyl)-2-methyl-4-oxobutanoates did not seem to depend on their relative configuration, we decided to develop a direct methodology for the synthesis of vinyl azides **7**. Direct treatment of the crude mixture of the coupling reaction of phenacyl azides **5a**–**f** giving adducts **6a**–**f** with mesyl chloride after removal of the solvent and without isolation of the products **6** resulted in the formation of diastereopure vinyl azides (*E*)-**7a**–**f** in good overall yields (36–51%, Scheme 2, Table 1). No marked substituent effect was observed.



5–7	a	b	c	d	e	f
R^1	H	OMe	F	Cl	Ph	H
R^2	H	H	H	H	H	OMe

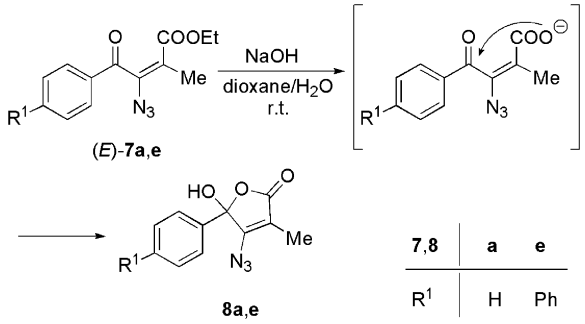
Scheme 2. Synthesis of vinyl azides (*E*)-**7**.

Table 1. Results of the two-step synthesis of vinyl azides (*E*)-**7**.

Entry	Starting material	Product	R^1	R^2	*t*[a] [h]	Overall yield [%]
1	**5a**	**7a**	H	H	5.5/40	44
2	**5b**	**7b**	OMe	H	27/47	43
3	**5c**	**7c**	F	H	6.5/40.5	44
4	**5d**	**7d**	Cl	H	24/91	36
5	**5e**	**7e**	Ph	H	26.5/90	49
6	**5f**	**7f**	H	OMe	5/41	51

[a] Reaction time for the C–C coupling (Step 1)/reaction time for the formation of the vinyl azide (Step 2).

Determination of the relative configuration of the prepared vinyl azides **7** was quite troublesome due to the lack of $^3J_{H,H}$ coupling constants in the vinyl azide unit. The β-azido-α,β-unsaturated esters **7** were isolated as oils which prevented us from using X-ray crystallography. To obtain crystallizable solids, azides **7a**,**e** were treated with sodium hydroxide in dioxane/water solution. Structure elucidation of the products isolated in moderate yields (50–59%) revealed that no carboxylic acids but 2,5-dihydro-5-hydroxy-2-oxofurans **8a**,**e** were obtained (Scheme 3). X-ray analysis of lactone **8e** provided further support for the structure of the products (Figure 3). Again, strong hydrogen bonds were found between the hydroxy group and the carbonyl oxygen atom; the crystal packing is shown in Figure 4.



7,8	a	e
R^1	H	Ph

Scheme 3. Formation of lactones **8**.

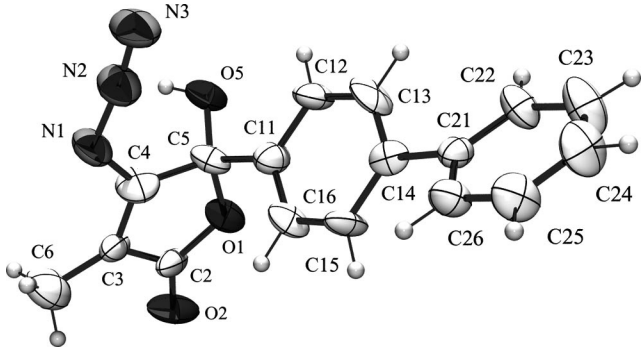


Figure 3. Crystal structure of lactone **8e**.

The formation of lactones **8a**,**e** can only be explained by an internal attack by the carboxylate anions of β-aroyl-α,β-unsaturated carboxylic acids having an (*E*) relative configuration on the carbonyl unit: the appropriate β-aroyl-α,β-unsaturated esters **7a**,**e** should therefore also be (*E*) diastereomers. This ring/chain tautomerism of β-aroyl-α,β-unsaturated carboxylic acids is documented in the literature.[18]

Having the β-azido-α,β-unsaturated esters **7** in our hands, we examined their thermolysis. After refluxing in toluene for 1 h, the starting vinyl azides **7a**–**f** were completely transformed, and 3-aroyl-2-ethoxycarbonyl-2*H*-azirines **9a**–**f** were isolated from the reaction mixtures in moderate to good yields (33–70%, Scheme 4, Table 2). All the azirines **9a**–**f** are stable compounds and were identified by their spectral characteristics. In the IR spectra, 2*H*-azirines **9** showed a strong C=N stretch in the region of 1739–1742 cm^{-1}. Further diagnostic tools were the chemical shifts of the signals of the carbon atoms C-2 (δ = 38.6–39.0 ppm) and C-3 (δ = 164.4–166.0) in their ^{13}C NMR spectra.[19]

The synthesis of 2*H*-azirines by the thermal or photochemical treatment of vinyl azides is well documented.[19,20] However, the formation of 2*H*-azirines by thermolysis depends largely on the structure of the vinyl azide.[21] When a

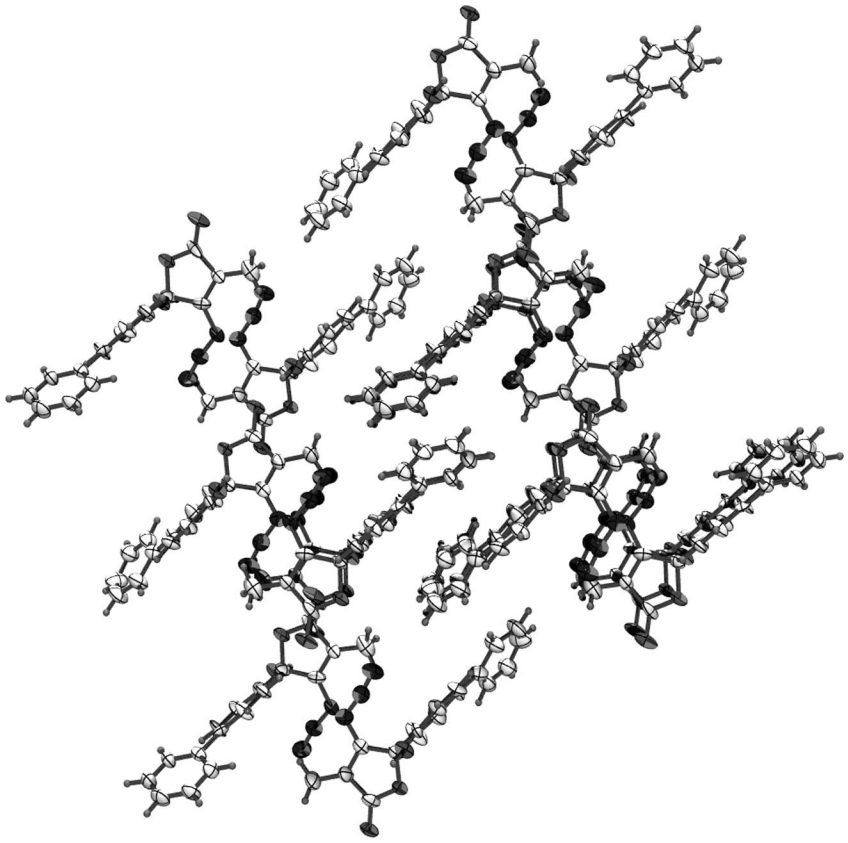
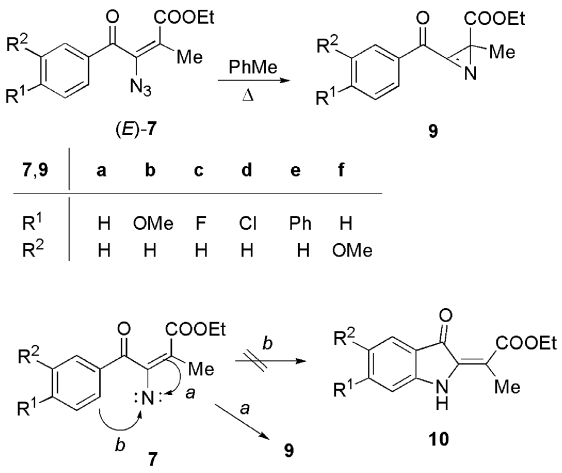


Figure 4. Crystal packing for lactone **8e**.



Scheme 4. Synthesis of 2*H*-azirines **9**.

Table 2. Synthesis of 2*H*-azirines **9** by the thermolysis of vinyl azides **7**.

Entry	Starting material	Product	R^1	R^2	Yield [%]
1	**7a**	**9a**	H	H	68
2	**7b**	**9b**	OMe	H	70
3	**7c**	**9c**	F	H	49
4	**7d**	**9d**	Cl	H	33
5	**7e**	**9e**	Ph	H	54
6	**7f**	**9f**	H	OMe	70

carbonyl group is present in the vinyl azide, isoxazoles, oxazoles or nitriles may be formed from the nitrene intermediate. In the presence of a β-aryl group, ring-closure leading to indoles may also take place. The structure of the formed product also depends on the relative configuration of the acyl and the azido groups in the vinyl azide.[1a–1d,2–4,11a,21,22] The thermolysis of 2-azidoalk-2-en-1-ones usually gives 2-cyanoalkan-1-ones by rearrangement of the nitrene intermediate; however, the formation of 3-acyl-2*H*-azirines in low yields has also been reported in some cases.[4,21,23] Changing the 3-aryl group to an alkyl unit tends to increase the stability of the azirine.[23]

Our substrates **7** can be considered as either 2-azidoalk-2-en-1-ones or 3-azidoalk-2-enoates, but their (*E*) stereochemistry prevents the nitrene from attacking the electron-rich carbonyl oxygen atom of the ester function. Thus, the formation of an isoxazolone-type product is excluded. From the alternative routes *a* and *b* (Scheme 4), the migration of the π-electrons of the double bond to the electron-deficient nitrene (route *a*) takes place instead of indolone formation (route *b*) which would require temporary dearomatization. Since the similar 2,3-diacetyl-2*H*-azirine was found to be unstable and gave 2-acetyl-5-methyloxazole on irradiation,[3] the observed stability of our 2*H*-azirines **9a**–**f** can be explained by the presence of the quaternary C-2 atom and/or by the stabilizing effect of the methyl and carboxylate groups. To the best of our knowledge, this is the first general synthesis of 3-acyl-2*H*-azirine-2-carboxylic

acid derivatives. Up to now, only one compound, namely, methyl 3-benzoyl-2-chloro-2*H*-azirine-2-carboxylate had been synthesized in an independent way.[24]

Conclusions

We have presented a further example to demonstrate the synthetic usefulness of our previously developed methodology based on the trapping of carbanions generated in situ from the reaction of α-azido ketones with carbon electrophiles. It has been pointed out that the reaction of phenacyl azides with an α-oxo carboxylate, ethyl pyruvate, resulted in the formation of 4-aryl-3-azido-2-hydroxy-4-oxobutanoates that are somewhat unstable due to their ability to undergo an easy retro-aldol cleavage. A convenient method has been developed for the conversion of these intermediates into ethyl 4-aryl-3-azido-2-methyl-4-oxobut-2-enoates. Thermolysis of these unique vinyl azides led to the rare 3-aroyl-2*H*-azirine-2-carboxylic acid esters. The relative configurations of the aldol-type adduct and the vinyl azide have been determined by X-ray analysis.

Experimental Section

General: All chemicals were used as purchased unless otherwise stated. THF was distilled from benzophenone ketyl. α-Azido ketones **5** were prepared according to the procedure reported previously.[14b] Column chromatography was performed on Kieselgel 60. Melting points: Boetius hot-stage apparatus, uncorrected values. IR: Perkin-Elmer 16 PC-FT-IR spectrometer; KBr pellets unless otherwise stated. NMR: Varian Gemini 200, Bruker WP 200 SY, Bruker AM 360, Bruker AM 400 spectrometers (200, 360 or 400 MHz for ^{1}H; 50, 90 or 100 MHz for ^{13}C). Spectra were recorded in $CDCl_3$ solution, unless otherwise stated. Chemical shifts are given in δ relative to an internal standard TMS (δ = 0 ppm) or to the residual $CHCl_3$ (δ = 7.26 ppm for ^{1}H NMR and δ = 77.0 ppm for ^{13}C NMR). Elemental analysis: Carlo Erba. X-ray quality crystals of *anti*-**6b** or **8e** were mounted onto a glass fibre by using epoxy resin. Data were collected at 293(1) K with an Enraf–Nonius MACH3 diffractometer using monochromated Mo-K_α radiation (λ = 0.71073 Å), ω-motion. Absorption correction was made using ψ-scans. The structure was solved by direct methods using the SIR-92 software[25] and refined on F^2 by full-matrix least-squares methods using the SHELX-97 program.[26] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included at geometric positions using a riding model except for hydroxy protons which could be found on the difference electron-density map, and their distance to the oxygen atom was constrained. Strong hydrogen bonds were observed between the hydroxy group and the carbonyl oxygen atom in both cases. Material for publication was prepared with the WINGX-97 suite of programs.[27] CCDC-664649 (*anti*-**6b**) and -664650 (**8e**) contain the supplementary crystallography data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.au.uk/data_request/cif.

Ethyl 3-Azido-2-hydroxy-4-(4-methoxyphenyl)-2-methyl-4-oxobutanoate (6b): A solution of 2-azido-4′-methoxyacetophenone (**5b**) (1.00 g, 5.25 mmol) in dry THF (50 mL) was cooled to 0 °C. Ethyl 2-oxopropionate (1.73 mL, 15.75 mmol) and DBU (84 μL, 0.56 mmol) were added, and the mixture was allowed to stand at 0 °C. After 43 h, the reaction mixture was concentrated in vacuo, and the residue was purified by column chromatography (eluent: toluene/ethyl acetate = 9:1, v/v) to give pure **6b** (982 mg, conversion: 88%, yield: 69%, normalized to 100% conversion) as a colourless oil which was a 67:33 mixture of the *syn*/*anti* diastereomers (based on ^{1}H NMR). Repeated column chromatography (eluent: toluene/ethyl acetate = 9:1, v/v) of the diastereomeric mixture resulted in pure isomers.

***syn*-6b:** Colourless oil. IR (neat): $\tilde{\nu}$ = 3500 (OH), 2100 (N_3), 1746, 1732, 1682, 1674, 1600, 1312, 1266, 1224, 1174, 1020 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.13 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 1.57 (s, 3 H, 2-Me), 3.86 (s, 3 H, 4′-OMe), 4.09 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 4.55 (s, 1 H, 3-H), 6.95 (d, ^3J = 9.1 Hz, 2 H, 3′,5′-H), 7.97 (d, ^3J = 9.1 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 13.6 (OCH_2CH_3), 23.0 (2-Me), 55.3 (4′-OMe), 61.6 (OCH_2CH_3), 64.5 (C-3), 77.0 (C-2), 113.8 (C-3′,5′), 127.2 (C-1′), 131.4 (C-2′,6′), 164.4 (C-4′), 173.8 (C-1) 194.3 (C-4) ppm. $C_{14}H_{17}N_3O_5$ (307.3): calcd. C 54.72, H 5.58, N 13.67; found C 54.59, H 5.56, N 13.72.

***anti*-6b:** White prisms, m.p. 87–90 °C. IR: $\tilde{\nu}$ = 3470 (OH), 2101 (N_3), 1723, 1672, 1600, 1264, 1180 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.35 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 1.48 (s, 3 H, 2-Me), 3.88 (s, 3 H, 4′-OMe), 4.33 (dq, ^3J = 7.2, 2.2 Hz, 2 H, OCH_2CH_3), 4.67 (s, 1 H, 3-H), 6.96 (dd, ^3J = 9.2, ^4J = 2.1 Hz, 2 H, 3′,5′-H), 7.99 (dd, ^3J = 9.2, ^4J = 2.1 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 13.9 (OCH_2CH_3), 24.0 (2-Me), 55.5 (4′-OMe), 61.9 (OCH_2CH_3), 66.2 (C-3), 76.2 (C-2), 114.1 (C-3′,5′), 128.6 (C-1′), 131.6 (C-2′,6′), 164.5 (C-4′), 174.3 (C-1) 192.7 (C-4) ppm. $C_{14}H_{17}N_3O_5$ (307.3): calcd. C 54.72, H 5.58, N 13.67; found C 54.51, H 5.56, N 13.64.

X-ray Crystallographic Data for *anti*-6b: Formula $C_{14}H_{17}N_3O_5$, M = 307.31, triclinic, space group $P\bar{1}$, a = 7.915(2), b = 8.080(2), c = 12.595(2) Å, α = 81.76(2), β = 79.306(10), γ = 81.39(2)°, V = 777.1(3) Å^3, Z = 2, $\rho_{calcd.}$ = 1.313, 2857 measured reflections of which 2051 were unique with $I > 2\sigma(I)$, decay 4%, R_1 = 0.057 and wR_2 = 0.167 for 2857 reflections and 203 parameters, GOF = 1.03. Residual electron density: 0.29/–0.22 e/Å^3. The configurations at C2 and C3 are (*R*,*R*) and its enantiomer pair (*S*,*S*). Hydrogen-bond geometries are shown in Table 3.

Table 3. Hydrogen-bond geometries in the crystals of *anti*-**6b**.

D–H···A	D–H [Å]	H···A [Å]	D···A [Å]	D–H···A [°]
O3–H1O···O1	0.79(3)	2.34(3)	2.693(2)	108(3)
O3–H1O···O1[a]	0.79(3)	2.12(3)	2.862(3)	157(3)

[a] Symmetry codes: $-x + 2$, $-y + 2$, $-z$.

Ethyl 3-Azido-4-(4-methoxyphenyl)-2-methyl-4-oxobut-2-enoate (7b): A solution of azido alcohol **6b** (*syn*/*anti* = 67:33, 203 mg, 0.66 mmol) in dry pyridine (5 mL) was cooled to –15 °C, and mesyl chloride (0.10 mL, 1.32 mmol) was added in one portion. The mixture was warmed to room temperature and stirred for 25 h. Then it was poured into water and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution (25 mL) and water, dried ($MgSO_4$), concentrated in vacuo and purified by column chromatography (eluent: hexane/ethyl acetate = 3:1, v/v) to give pure (*E*)-**7b** (66 mg, conversion: 69%, yield: 50%, normalized to 100% conversion) as a yellow oil. IR (neat): $\tilde{\nu}$ = 2108 (N_3), 1712 (ester), 1662 (C=O), 1598, 1290, 1264, 1244, 1172, 844 cm^{-1}. ^{1}H NMR (360 MHz, $CDCl_3$, 25 °C): δ = 0.98 (t, ^3J = 7.0 Hz, 3 H, OCH_2CH_3), 1.99 (s, 3 H, 2-Me), 3.89 (s, 3 H, 4′-OMe), 3.94 (q, ^3J = 7.0 Hz, 2 H, OCH_2CH_3), 6.98 (d, ^3J = 9.4 Hz,

2 H, 3′,5′-H), 7.92 (d, ^3J = 9.4 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 12.6, 13.5 (2-Me, OCH_2CH_3), 55.5 (4′-OMe), 61.0 (OCH_2CH_3), 114.3 (C-3′,5′), 116.5 (C-3), 127.9 (C-1′), 131.3 (C-2′,6′), 144.6 (C-2), 164.4 (C-4′), 166.0 (C-1), 188.6 (C-4) ppm. $C_{14}H_{15}N_3O_4$ (289.3): calcd. C 58.13, H 5.23, N 14.53; found C 57.91, H 5.20, N 14.49. The above procedure was extended to the pure diastereomers of the azido alcohol **6b**. With *anti*-**6b** (60 mg, 0.195 mmol), 35 mg (conversion: 81%, yield: 75%, normalized to 100% conversion) of vinyl azide (*E*)-**7b** was obtained. Reaction of *syn*-**6b** (60 mg) yielded the vinyl azide (*E*)-**7b** as a yellow oil (conversion: 75%, yield: 63%, normalized to 100% conversion).

General Procedure for the Synthesis of Ethyl 4-Aryl-3-azido-2-methyl-4-oxobut-2-enoates 7: A solution of α-azido ketone **5** (4.96 mmol) in dry THF (40 mL) was cooled to 0 °C. Ethyl 2-oxopropionate (1.63 mL, 14.90 mmol) and DBU (81 μL, 0.55 mmol) were added, and the mixture was allowed to stand at 0 °C. After completion of the reaction, the mixture was concentrated in vacuo, and the residue was dissolved in dry pyridine (20 mL). The solution was cooled to –15 °C, and mesyl chloride (MsCl, 0.40 mL, 5.07 mmol) was added in one portion. The mixture was stirred at room temperature and monitored by TLC. New batches of mesyl chloride were added until completion of the reaction. Then it was poured into water and extracted with CH_2Cl_2 (4 × 50 mL), and the organic layer was dried ($MgSO_4$), concentrated in vacuo and purified by column chromatography.

Ethyl 3-Azido-2-methyl-4-oxo-4-phenylbut-2-enoate (7a): From the α-azido ketone **5a** (800 mg, 4.96 mmol), after the coupling reaction (5.5 h) and the elimination (2 × 0.40 mL of MsCl, 40 h), 289 mg (overall yield: 44%) of (*E*)-**7a** was obtained (eluent: toluene/ethyl acetate = 10:1, v/v). Yellow oil. IR (neat): $\tilde{\nu}$ = 2112 (N_3), 1716 (ester), 1674 (C=O), 1596, 1450, 1288, 1234, 1184, 892 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 0.94 (t, ^3J = 7.4 Hz, 3 H, OCH_2CH_3), 2.00 (s, 3 H, 2-Me), 3.90 (q, ^3J = 7.4 Hz, 2 H, OCH_2CH_3), 7.45–7.59 (m, 2 H, 3′,5′-H), 7.64 (m, 1 H, 4′-H), 7.93 (dd, ^3J = 6.9, ^4J = 1.8 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 12.6, 13.5 (2-Me, OCH_2CH_3), 61.1 (OCH_2CH_3), 117.1 (C-3), 128.8, 129.0 (C-2′,3′,5′,6′), 134.2 (C-4′), 135.0 (C-1′), 144.3 (C-2), 166.0 (C-1), 190.1 (C-4) ppm. $C_{13}H_{13}N_3O_3$ (259.3): calcd. C 60.23, H 5.05, N 16.21; found C 60.20, H 5.04, N 16.22.

Ethyl 3-Azido-4-(4-methoxyphenyl)-2-methyl-4-oxobut-2-enoate (7b): From the α-azido ketone **5b** (427 mg, 2.23 mmol), after the coupling reaction (27 h) and the elimination (3 × 0.35 mL of MsCl, 47 h), 279 mg (overall yield: 43%) of (*E*)-**7b** was obtained (eluent: hexane/ethyl acetate = 3:1, v/v).

Ethyl 3-Azido-4-(4-fluorophenyl)-2-methyl-4-oxobut-2-enoate (7c): From the α-azido ketone **5c** (400 mg, 2.23 mmol), after the coupling reaction (6.5 h) and the elimination (3 × 0.35 mL of MsCl, 40.5 h), 274 mg (overall yield: 44%) of (*E*)-**7c** was obtained (eluent: toluene). Yellow oil. IR (neat): $\tilde{\nu}$ = 2112 (N_3), 1714 (ester), 1674 (C=O), 1598, 1288, 1236, 1154 cm^{-1}. ^{1}H NMR (360 MHz, $CDCl_3$, 25 °C): δ = 1.00 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 1.99 (s, 3 H, 2-Me), 3.95 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 7.16–7.20 (m, 2 H, 3′,5′-H), 7.95–7.99 (m, 2 H, 2′,6′-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 12.6, 13.6 (2-Me, OCH_2CH_3), 61.2 (OCH_2CH_3), 116.3 (d, $J_{C,F}$ = 22.2 Hz, C-3′,5′), 116.9 (C-3), 131.6 (d, $J_{C,F}$ = 9.8 Hz, C-2′,6′), 144.1 (C-1′,2), 166.4 (d, $J_{C,F}$ = 255 Hz, C-4′), 166.0 (C-1), 188.6 (C-4) ppm. $C_{13}H_{12}FN_3O_3$ (277.3): calcd. C 56.32, H 4.36, N 15.16; found C 56.28, H 4.38, N 15.15.

Ethyl 3-Azido-4-(4-chlorophenyl)-2-methyl-4-oxobut-2-enoate (7d): From the α-azido ketone **5d** (437 mg, 2.23 mmol), after the coupling reaction (24 h) and the elimination (2 × 0.35 mL of MsCl, 91 h), 238 mg (overall yield: 36%) of (*E*)-**7d** was obtained (eluent: toluene). Yellow oil. IR (neat): $\tilde{\nu}$ = 2110 (N_3), 1714 (ester), 1674 (C=O), 1588, 1290, 1234 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.01 (t, ^3J = 7.0 Hz, 3 H, OCH_2CH_3), 1.99 (s, 3 H, 2-Me), 3.95 (q, ^3J = 7.0 Hz, 2 H, OCH_2CH_3), 7.48 (d, ^3J = 8.6 Hz, 2 H, 3′,5′-H), 7.88 (d, ^3J = 8.6 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.6, 13.6 (2-Me, OCH_2CH_3), 61.3 (OCH_2CH_3), 117.3 (C-3), 129.5 (C-3′,5′), 130.1 (C-2′,6′), 133.4 (C-1′), 140.8 (C-4′) 143.9 (C-2), 165.9 (C-1), 188.9 (C-4) ppm. $C_{13}H_{12}ClN_3O_3$ (293.7): calcd. C 53.16, H 4.12, N 14.31; found C 53.18, H 4.11, N 14.35.

Ethyl 3-Azido-4-(biphenyl-4-yl)-2-methyl-4-oxobut-2-enoate (7e): From the α-azido ketone **5e** (530 mg, 2.23 mmol), after the coupling reaction (26.5 h) and the elimination (2 × 0.35 mL of MsCl, 90 h), 365 mg (overall yield: 49%) of (*E*)-**7e** was obtained (eluent: toluene). Yellow oil. IR (neat): $\tilde{\nu}$ = 2110 (N_3), 1712 (ester), 1668 (C=O), 1602, 1288, 1238, 1178, 748 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.00 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 2.02 (s, 3 H, 2-Me), 3.96 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 7.41–7.53 (m, 3 H, 3′′,4′′,5′′-H), 7.61–7.66 (m, 2 H, 2′′,6′′-H), 7.73 (d, ^3J = 8.3 Hz, 2 H, 3′,5′-H), 8.02 (d, ^3J = 8.3 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.6, 13.5 (2-Me, OCH_2CH_3), 61.1 (OCH_2CH_3), 116.9 (C-3), 127.2, 127.6, 128.4, 128.9, 129.3 (Ph, C-2′,3′,5′,6′), 133.6 (C-1′), 139.4 (C-4′) 144.3 (C-2), 146.8 (C-1′′), 165.9 (C-1), 189.6 (C-4) ppm. $C_{19}H_{17}N_3O_3$ (335.3): calcd. C 68.05, H 5.11, N 12.53; found C 68.06, H 5.10, N 12.56.

Ethyl 3-Azido-4-(3-methoxyphenyl)-2-methyl-4-oxobut-2-enoate (7f): From the α-azido ketone **5f** (427 mg, 2.23 mmol), after the coupling reaction (5 h) and the elimination (3 × 0.35 mL of MsCl, 41 h), 328 mg (overall yield: 51%) of (*E*)-**7f** was obtained (eluent: toluene/ethyl acetate = 10:1, v/v). Brownish oil. IR (neat): $\tilde{\nu}$ = 2110 (N_3), 1714 (ester), 1674 (C=O), 1596, 1486, 1290, 1262 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.00 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 2.02 (s, 3 H, 2-Me), 3.87 (s, 3 H, 3′-OMe), 3.94 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 7.17 (m, 1 H, 4′-H), 7.36–7.52 (m, 3 H, 2′,5′,6′-H) ppm. ^{13}C NMR (90 MHz, $CDCl_3$, 25 °C): δ = 12.5, 13.5 (2-Me, OCH_2CH_3), 55.4 (3′-OMe), 61.1 (OCH_2CH_3), 112.3 (C-2′), 117.0 (C-3), 120.8 (C-4′), 121.6 (C-6′), 130.0 (C-5′), 136.2 (C-1′), 144.2 (C-2), 160.1 (C-3′), 165.9 (C-1), 189.8 (C-4) ppm. $C_{14}H_{15}N_3O_4$ (289.3): calcd. C 58.13, H 5.23, N 14.53; found C 57.91, H 5.20, N 14.49.

4-Azido-5-hydroxy-3-methyl-2-oxo-5-phenyl-2,5-dihydrofuran (8a): An 8% sodium hydroxide solution (0.43 mL, 0.89 mmol) was added to a stirred solution of vinyl azide (*E*)-**7a** (231 mg, 0.89 mmol) in a mixture of dioxane (13 mL) and water (6.5 mL) at room temperature. Two further batches of sodium hydroxide solution (0.41 mmol) were added to the reaction mixture after 2 and 21 h. When the reaction was complete (25 h) the reaction mixture was acidified with 10% hydrochloric acid and diluted with water (50 mL). Then it was extracted with CH_2Cl_2 (3 × 30 mL), dried (Na_2SO_4) and concentrated in vacuo. The residue was purified as follows: it was dissolved in a mixture of water (21 mL) and 8% sodium hydroxide solution (2.0 mL), and the alkaline phase was extracted with CH_2Cl_2 (2 × 20 mL). The basic solution was acidified with 10% hydrochloric acid. White crystals precipitated and were filtered off to give pure **8a** (104 mg, yield: 50%). M.p. 95–105 °C. IR: $\tilde{\nu}$ = 3298 (OH), 2124 (N_3), 1730 (C=O), 1662, 1336 cm^{-1}. ^{1}H NMR (360 MHz, [D$_6$]DMSO, 25 °C): δ = 1.76 (s, 3 H, 2-Me), 7.47–7.51 (m, 5 H, Ph), 8.87 (br. s, 1 H, 5-OH) ppm. ^{13}C NMR (90 MHz, [D$_6$]DMSO, 25 °C): δ = 7.3 (2-Me), 102.0 (C-5), 110.5 (C-3), 125.9 (C-2′,6′), 128.9 (C-3′,5′), 130.0 (C-4′), 135.8 (C-1′), 155.0 (C-4), 169.9 (C-2) ppm.

4-Azido-5-(biphenyl-4-yl)-5-hydroxy-3-methyl-2-oxo-2,5-dihydrofuran (8e): An 8% sodium hydroxide solution (0.43 mL, 0.89 mmol)

was added to a stirred solution of vinyl azide (*E*)-**7e** (300 mg, 0.89 mmol) in a mixture of dioxane (13 mL) and water (6.5 mL) at room temperature. Another batch of sodium hydroxide solution (0.89 mmol) was added to the reaction mixture after 2 h. When the reaction was complete (4 h), the mixture was acidified with 10% hydrochloric acid and diluted with water (50 mL). Then it was extracted with CH_2Cl_2 (3 × 30 mL), dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography (eluent: hexane/ethyl acetate = 2:1, v/v) to give pure **8e** (162 mg, yield: 59%) as a yellow crystalline solid. M.p. 214 °C (recrystallization at ca. 120 °C). IR: $\tilde{\nu}$ = 3278 (OH), 2118 (N_3), 1738 (C=O), 1662, 1336 cm^{-1}. ^1H NMR (360 MHz, [D$_6$]DMSO, 25 °C): δ = 1.79 (s, 3 H, 2-Me), 7.40 (m, 1 H, 4′′-H), 7.47–7.51 (m, 2 H, 3′′,5′′-H), 7.60 (d, ^3J = 8.4 Hz, 2 H, 2′,6′-H), 7.71 (d, ^3J = 7.6 Hz, 2 H, 2′′,6′′-H), 7.78 (d, ^3J = 8.4 Hz, 2 H, 3′,5′-H), 8.93 (br. s, 1 H, 5-OH) ppm. ^{13}C NMR (90 MHz, [D$_6$]DMSO, 25 °C): δ = 7.2 (2-Me), 101.9 (C-5), 110.6 (C-3), 126.5, 126.8, 127.1, 127.9, 129.0 (C-2′,6′, C-3′,5′, C-2′′,6′′, C-3′′,5′′, C-4′′), 134.8 (C-4′), 139.2 (C-1′′), 141.6 (C-1′), 155.0 (C-4), 169.8 (C-2) ppm.

X-ray Crystallographic Data for 8e: Formula $C_{17}H_{13}N_3O_3$, M = 307.3, monoclinic, space group $P2_1$, a = 14.140(2), b = 7.351(2), c = 15.864(2) Å, β = 108.117(10)°, V = 1567.1(5) Å^3, Z = 4, $\rho_{calcd.}$ = 1.302, 3295 measured reflections of which 1312 were unique with $I > 2\sigma(I)$, decay 8%, R_1 = 0.078 and wR_2 = 0.184 for 3295 reflections and 423 parameters, GOF = 0.96. Residual electron density: 0.18/–0.18 e/Å^3. The structure shows pseudosymmetry. However, when the structure was solved in the centrosymmetric space group $P2_1/c$ there was a disorder of the phenyl rings with an occupancy of 50:50 and with a significantly higher R factor. In a non-centrosymmetric space group this was perfectly solved. For this reason $P2_1$ was chosen as the symmetry group. The angle between the mean-square planes of the C11–C16 and C21–C26 rings and that of the pseudosymmetric related rings C51–C56 and C61–C66 were 33 and 20°, respectively. The crystal was a rather weakly diffracting one, and the absolute configuration could not be assigned. Hydrogen-bond geometries are shown in Table 4.

Table 4. Hydrogen bond geometry in the crystals of **8e**.

D–H···A	D–H [Å]	H···A [Å]	D···A [Å]	D–H···A [°]
O5–H5···O2[a]	0.86(2)	1.99(6)	2.726(9)	142(8)
O45–H45···O42[b]	0.79(3)	2.12(3)	2.862(3)	157(3)

[a] Symmetry codes: $-x + 2$, $-y + ½$, $-z + 2$. [b] Symmetry codes: $-x$, $y - ½$, $-z + 1$.

General Procedure for the Synthesis of 3-Acyl-2-(ethoxycarbonyl)-2-methyl-2*H*-azirines 9: A solution of ethyl 4-aryl-3-azido-2-methyl-4-oxobut-2-enoate (*E*)-**7** (0.70 mmol) in toluene (10 mL) was refluxed for 1 h. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (eluent: hexane/acetone = 5:1, v/v).

3-Benzoyl-2-(ethoxycarbonyl)-2-methyl-2*H*-azirine (9a): From the vinyl azide (*E*)-**7a** (300 mg, 1.16 mmol), 182 mg (68%) of **9a** was obtained. Yellow liquid. IR (neat): $\tilde{\nu}$ = 1742 (C=N), 1722 (ester), 1668 (C=O), 1276, 1132, 706 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$, 25 °C): δ = 1.25 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 1.68 (s, 3 H, 2-Me) 4.19 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 7.56–7.60 (m, 2 H, 3′,5′-H), 7.72–7.75 (m, 1 H, 4′-H), 8.28 (d, ^3J = 8.1 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR (90 MHz, $CDCl_3$, 25 °C): δ = 14.01 (OCH_2CH_3), 17.7 (2-Me), 38.9 (C-2), 61.8 (OCH_2CH_3), 129.2, 129.7 (C-2′,3′,5′,6′), 134.2 (C-1′), 135.6 (C-4′), 164.4 (C-3), 171.2 (CO_2Et), 181.7 (C=O) ppm. MS (EI, 70 eV): m/z (%) = 158 (2.4) [M – CO_2Et]$^{+\cdot}$, 105 (100) [PhCO]$^+$, 77 (47) [Ph]$^+$, 51 (17). $C_{13}H_{13}NO_3$ (231.3): calcd. C 67.52, H 5.67, N 6.06; found C 66.95, H 5.49, N 6.14.

2-(Ethoxycarbonyl)-3-(4-methoxybenzoyl)-2-methyl-2*H*-azirine (9b): From the vinyl azide (*E*)-**7b** (200 mg, 0.69 mmol), 127 mg (70%) of **9b** was obtained. Yellow oil. IR (neat): $\tilde{\nu}$ = 1740 (C=N), 1717 (ester), 1650 (C=O), 1600, 1511, 1269, 1171, 668 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.24 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 1.67 (s, 3 H, 2-Me), 3.92 (s, 3 H, 4′-OMe), 4.18 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 7.04 (d, ^3J = 8.8 Hz, 2 H, 3′,5′-H), 8.26 (d, ^3J = 8.8 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR (90 MHz, $CDCl_3$, 25 °C): δ = 13.9 (OCH_2CH_3), 17.6 (2-Me), 38.6 (C-2), 55.6 (OCH_3), 61.7 (OCH_2CH_3), 114.7 (C-3′,5′), 127.7 (C-1′), 132.5 (C-2′,6′), 164.6 (C-4′), 166.0 (C-3), 171.8 (CO_2Et), 180.1 (C=O) ppm. MS (EI, 70 eV): m/z (%) = 188 (5.4) [M – CO_2Et]$^{+\cdot}$, 135 (100) [ArCO]$^+$, 107 (4.8) [Ar]$^+$, 92 (12) [Ar – Me]$^+$, 77 (17) [Ph]$^+$, 64 (7.3). $C_{14}H_{15}NO_4$ (261.3): calcd. C 64.36, H 5.79, N 5.36; found C 64.25, H 5.73, N 5.32.

2-(Ethoxycarbonyl)-3-(4-fluorobenzoyl)-2-methyl-2*H*-azirine (9c): From the vinyl azide (*E*)-**7c** (200 mg, 0.72 mmol), 88 mg (49%) of **9c** was obtained. Yellow oil. IR (neat): $\tilde{\nu}$ = 1743 (C=N), 1717 (ester), 1674 (C=O), 1599, 1507, 1241, 1158, 851 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.26 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 1.68 (s, 3 H, 2-Me), 4.20 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 7.23–7.31 (m, 2 H, 3′,5′-H), 8.31–8.38 (m, 2 H, 2′,6′-H) ppm. ^{13}C NMR (90 MHz, $CDCl_3$, 25 °C): δ = 13.9 (OCH_2CH_3), 17.5 (2-Me), 38.9 (C-2), 61.9 (OCH_2CH_3), 116.8 (d, $J_{C,F}$ = 22.1 Hz, C-3′,5′), 131.0 (C-1′), 132.9 (d, $J_{C,F}$ = 10.0 Hz C-2′,6′), 164.8 (C-3), 167.7 (d, $J_{C,F}$ = 259 Hz, C-4′), 171.5 (CO_2Et), 180.5 (C=O) ppm. MS (EI, 70 eV): m/z (%) = 176 (2.8) [M – CO_2Et]$^{+\cdot}$, 123 (100) [ArCO]$^+$, 95 (35) [Ar]$^+$, 75 (9.3). $C_{13}H_{12}FNO_3$ (249.2): calcd. C 62.65, H 4.85, N 5.62; found C 62.58, H 4.85, N 5.63.

3-(4-Chlorobenzoyl)-2-(ethoxycarbonyl)-2-methyl-2*H*-azirine (9d): From the vinyl azide (*E*)-**7d** (150 mg, 0.51 mmol), 45 mg (33%) of **9d** was obtained. Yellow oil. IR (neat): $\tilde{\nu}$ = 1739 (C=N), 1723 (ester), 1673 (C=O), 1588, 1403, 1280, 1135, 1014, 748 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.25 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.67 (s, 3 H, 2-Me), 4.19 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 7.56 (d, ^3J = 8.9 Hz, 2 H, 3′,5′-H), 8.24 (d, ^3J = 8.9 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR (90 MHz, $CDCl_3$, 25 °C): δ = 13.9 (OCH_2CH_3), 17.5 (2-Me), 39.0 (C-2), 62.0 (OCH_2CH_3), 129.9 (C-3′,5′), 131.3 (C-2′,6′), 132.8 (C-1′), 142.9 (C-4′), 164.8 (C-3), 171.4 (CO_2Et), 180.9 (C=O) ppm. MS (EI, 70 eV): m/z (%) = 192 (2.4) [M – CO_2Et]$^{+\cdot}$, 139 (100) [ArCO]$^+$, 111 (27) [Ar]$^+$, 75 (19) [Ar – HCl]$^+$, 50 (6.9). $C_{13}H_{12}ClNO_3$ (265.7): calcd. C 58.77, H 4.55, N 5.27; found C 58.63, H 4.58, N 5.30.

2-(Ethoxycarbonyl)-2-methyl-3-(4-phenylbenzoyl)-2*H*-azirine (9e): From the vinyl azide (*E*)-**7e** (224 mg, 0.67 mmol), 110 mg (54%) of **9e** were obtained. Yellow oil. IR (neat): $\tilde{\nu}$ = 1739 (C=N), 1722 (ester), 1669 (C=O), 1602, 1449, 1280, 1134, 743 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.26 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.70 (s, 3 H, 2-Me), 4.20 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 7.42–7.53 (m, 3 H, 3′′,4′′,5′′-H), 7.63–7.67 (m, 2 H, 2′′,6′′-H), 7.79 (d, ^3J = 8.5 Hz, 2 H, 3′,5′-H), 8.35 (d, ^3J = 8.5 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR (90 MHz, $CDCl_3$, 25 °C): δ = 13.9 (OCH_2CH_3), 17.6 (2-Me), 38.8 (C-2), 61.9 (OCH_2CH_3), 127.4 (C-4′′), 127.5, 128.0, 129.0, 129.2, 130.5 (C-2′,6′, C-3′,5′, C-2′′,6′′, C-3′′,5′′), 133.2 (C-1′), 139.4 (C-1′′), 148.7 (C-4′), 164.8 (C-3), 171.6 (CO_2Et), 181.5 (C=O) ppm. MS (EI, 70 eV): m/z (%) = 207 (4) [ArCOCN]$^+$, 196 (42), 181 (100) [ArCO]$^+$, 152 (63), 129 (40), 101 (21), 73 (52), 57 (47), 43 (98). $C_{19}H_{17}NO_3$ (307.3): calcd. C 74.25, H 5.58, N 4.56; found C 74.11, H 5.57, N 4.57.

2-(Ethoxycarbonyl)-3-(3-methoxybenzoyl)-2-methyl-2*H*-azirine (9f): From the vinyl azide (*E*)-**7f** (203 mg, 0.70 mmol), 127 mg (70%) of **9f** was obtained. Yellow oil. IR (neat): $\tilde{\nu}$ = 1741 (C=N), 1722 (ester), 1669 (C=O), 1597, 1487, 1268, 1134, 1035, 744 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.26 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.68 (s, 3 H, 2-Me), 3.90 (s, 3 H, 3′-OMe), 4.19 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 7.28 (m, 1 H, 4′-H), 7.47 (m, 1 H, 5′-H), 7.73 (m, 1 H, 2′-H), 7.92 (m, 1 H, 6′-H) ppm. ^{13}C NMR (90 MHz, $CDCl_3$, 25 °C): δ = 13.9 (OCH_2CH_3), 17.6 (2-Me), 39.0 (C-2), 55.5 (OCH_3), 61.8 (OCH_2CH_3), 112.9 (C-2′), 123.0 (C-4′,6′), 130.4 (C-5′), 135.7 (C-1′), 160.5 (C-3′), 164.8 (C-3), 171.5 (CO_2Et), 181.9 (C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 261 (1) $[M]^{+\cdot}$, 188 (2.8) $[M - CO_2Et]^{+\cdot}$, 135 (100) $[ArCO]^+$, 123 (9.2), 107 (19) $[Ar]^+$, 92 (15) $[Ar - Me]^+$, 77 (19) $[Ph]^+$, 64 (8.9). $C_{14}H_{15}NO_4$ (261.3): calcd. C 64.36, H 5.79, N 5.36; found C 64.28, H 5.75, N 5.39.

Acknowledgments

Financial support from the Hungarian Scientific Research Fund (OTKA T46946) is highly appreciated. The authors thank Dr. Attila Bényei, University of Debrecen, for X-ray measurements.

[1] a) G. Smolinsky, C. A. Pride, "The Chemistry of Vinyl Azides" in *The Chemistry of the Azido Group* (Ed.: S. Patai), Wiley-Interscience, New York, **1971**, pp. 555–585; b) A. Hassner, "Vinyl Azides and Nitrenes" in *Azides and Nitrenes; Reactivity and Utility* (Ed.: E. F. V. Scriven), Academic Press, Orlando, **1984**, pp. 35–94; c) G. L'abbé, *Chem. Rev.* **1968**, *68*, 345–363; d) G. L'abbé, *Angew. Chem.* **1975**, *87*, 831–838; *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 775–782; e) K. Banert, *Liebigs Ann./Recueil* **1997**, 2005–2018.

[2] a) G. Knittel, H. Hemetsberger, R. Leipert, H. Weidman, *Tetrahedron Lett.* **1970**, *11*, 1459–1462; b) H. Hemetsberger, D. Knittel, *Monatsh. Chem.* **1972**, *103*, 194–204; c) C. Vogel, P. Delavier, *Tetrahedron Lett.* **1989**, *30*, 1789–1792; d) P. Molina, A. Tárraga, A. Ferao, C. Gaspar, *Heterocycles* **1993**, *35*, 427–432.

[3] R. S. Sauers, S. D. Van Arnum, *Tetrahedron Lett.* **1987**, *28*, 5795–5800.

[4] P. N. D. Singh, C. L. Carter, A. D. Gudmundsdóttir, *Tetrahedron Lett.* **2003**, *44*, 6763–6765.

[5] a) P. Ykman, G. Mathys, G. L'abbé, G. Smets, *J. Org. Chem.* **1972**, *37*, 3213–3216; b) G. L'abbé, G. Mathys, *J. Heterocycl. Chem.* **1974**, *11*, 613–614.

[6] P. Molina, E. Aller, A. López-Lázaro, M. Alajarín, A. Lorenzo, *Tetrahedron Lett.* **1994**, *35*, 3817–3820.

[7] a) D. Knittel, V. S. Rao, *Monatsh. Chem.* **1986**, *117*, 1185–1193; b) D. Knittel, V. S. Rao, *Monatsh. Chem.* **1988**, *119*, 223–232.

[8] a) G. Litkei, T. Mester, T. Patonay, R. Bognár, *Liebigs Ann. Chem.* **1979**, 174–180; b) T. Patonay, R. Bognár, G. Litkei, *Tetrahedron* **1984**, *40*, 2555–2562; c) A. L. Tőkés, G. Litkei, L. Szilágyi, *Synth. Commun.* **1992**, *22*, 2433–2445; d) T. Patonay, J. Jekő, É. Rimán, *Synth. Commun.* **2002**, *32*, 2403–2415.

[9] a) H. Hemetsberger, D. Knittel, H. Weidmann, *Monatsh. Chem.* **1969**, *100*, 1599–1603; b) D. Knittel, G. Weber, *Z. Naturforsch.* **1980**, *35b*, 1326–1327.

[10] a) F. W. Fowler, A. Hassner, L. A. Levy, *J. Am. Chem. Soc.* **1967**, *89*, 2077–2082; b) G. L'abbé, A. Hassner, *J. Org. Chem.* **1971**, *36*, 258–260.

[11] a) A. Hassner, G. L'abbé, M. J. Miller, *J. Am. Chem. Soc.* **1971**, *93*, 981–985; b) V. A. Reznikov, G. I. Roschupkina, T. V. Rybalova, Yu. V. Gatilov, *Russ. Chem. Bull.* **2001**, *50*, 874–881; c) G. I. Roschupkina, Yu. V. Gatilov, T. V. Rybalova, V. A. Reznikov, *Eur. J. Org. Chem.* **2004**, 1765–1773.

[12] V. Nair, T. G. George, *Tetrahedron Lett.* **2000**, *41*, 3199–3201.

[13] a) P. Langer, I. Freifeld, H. Shojaei, *Chem. Commun.* **2003**, 3044–3045; b) I. Freifeld, H. Shojaei, P. Langer, *J. Org. Chem.* **2006**, *71*, 4965–4968; c) I. Freifeld, H. Shojaei, R. Dede, P. Langer, *J. Org. Chem.* **2006**, *71*, 6165–6170.

[14] a) T. Patonay, R. V. Hoffman, *J. Org. Chem.* **1995**, *60*, 2368–2377; b) T. Patonay, É. Juhász-Tóth, A. Bényei, *Eur. J. Org. Chem.* **2002**, 285–295; c) É. Juhász-Tóth, T. Patonay, *Eur. J. Org. Chem.* **2002**, 3055–3064.

[15] J. L. Marco, A. Martínez-Grau, N. Martín, C. Seoane, *Tetrahedron Lett.* **1995**, *36*, 5393–5396.

[16] A. Padwa, M. M. Sá, M. D. Weingarten, *Tetrahedron* **1997**, *53*, 2371–2386.

[17] N. S. Chowdari, M. Ahmad, K. Albertshofer, F. Tanaka, C. F. Barbas III, *Org. Lett.* **2006**, *8*, 2839–2842.

[18] a) W. M. F. Fabian, K. Bowden, *Eur. J. Org. Chem.* **2001**, 303–309; b) A. M. Doherty, W. C. Pratt, J. J. Edmunds, K. A. Berryman, B. R. Reisdorph, M. S. Plummer, A. Shahripour, C. Lee, X.-M. Cheng, D. M. Walker, S. J. Haleen, J. A. Keiser, M. A. Flynn, K. M. Welch, H. Hallak, D. G. Taylor, E. E. Reynolds, *J. Med. Chem.* **1995**, *38*, 1259–1263; c) H. Cousse, G. Mouzin, J. P. Rieu, A. Delhon, F. Bruniquel, F. Fauran, *Eur. J. Med. Chem.* **1987**, *22*, 45–57.

[19] F. Palacios, A. M. O. Retana, E. M. Marigorta, J. M. Santos, *Org. Prep. Proced. Int.* **2002**, *34*, 221–269.

[20] a) F. Palacios, A. M. O. Retana, E. M. Marigorta, J. M. Santos, *Eur. J. Org. Chem.* **2001**, 2401–2414; b) F. W. Fowler, "Synthesis and Reactions of 1-Azirines" in *Advanced Heterocyclic Chemistry*, vol. 13 (Eds.: A. R. Katritzky, A. J. Boulton), Academic Press, New York, **1971**, pp. 45–76.

[21] A. Hassner, N. H. Wiegand, H. E. Gottlieb, *J. Org. Chem.* **1986**, *51*, 3176–3180.

[22] a) G. L'abbé, A. Hassner, *Angew. Chem.* **1971**, *83*, 103–109; *Angew. Chem. Int. Ed. Engl.* **1971**, *10*, 98–104; b) G. L'abbé, A. Hassner, *J. Org. Chem.* **1971**, *36*, 258–260; c) H. Hemetsberger, I. Spira, W. Schönfelder, *J. Chem. Res. (S)* **1977**, 247; *J. Chem. Res. (M)* **1977**, 2701–2719; d) L. Henn, D. M. B. Hickey, C. J. Moody, C. W. Rees, *J. Chem. Soc. Perkin Trans. 1* **1984**, 2189–2196; e) Y. S. P. Álvares, M. J. Alves, N. G. Azoia, J. F. Bickley, T. L. Gilchrist, *J. Chem. Soc. Perkin Trans. 1* **2002**, 1911–1919.

[23] H. Hemetsberger, D. Knittel, *Monatsh. Chem.* **1972**, *103*, 205–209.

[24] T. M. V. D. P. Melo, A. M. A. R. Gonsalves, C. S. J. Lopes, T. L. Gilchrist, *Tetrahedron Lett.* **1999**, *40*, 789–792.

[25] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, *J. Appl. Crystallogr.* **1993**, *26*, 343–350.

[26] G. M. Sheldrick, *SHELX-97*, *Programs for Crystal Structure Analysis*, release 97-2, University of Göttingen, Göttingen, **1997**.

[27] L. J. Farrugia, *J. Appl. Crystallogr.* **1999**, *32*, 837–838.

Received: November 12, 2007
Published Online: January 17, 2008

