Synthesis of Tetrafunctionalized 2-Azido-3-hydroxy-1,4-diones and Their Transformation into 5-Substituted 3-Acylisoxazoles[‡]

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Dedicated to Professor Waldemar Adam on the occasion of his 65th birthday

Keywords: Aldol reaction / Azides / C−C coupling / Diastereoselectivity / Nitrogen heterocycles

An efficient synthesis of 2-azido-3-hydroxy-1,4-diones, based on the base-induced coupling of α-azido ketones and α-oxo aldehydes, has been developed. The coupling reaction took place with moderate to good diastereoselectivity. The relative configurations of the adducts have been determined by X-ray analysis. Treatment of tetrafunctionalized synthons 2-azido-3-hydroxy-1,4-diones with mesyl chloride in the presence of base afforded 5-substituted 3-acylisoxazoles, through 2-azido-2-alkene-1,4-dione intermediates. Analogous treatment of α-azido ketones with α-oxo esters resulted in the formation of the unstable 3-azido-2-hydroxy-4-oxobutanoates.

Introduction

α-Azido ketones with α-hydrogen atoms are highly base-sensitive species and can undergo a smooth, base-promoted loss of nitrogen to give imines.[1] In our previous papers[2,3] we have demonstrated that various aldehydes and ketones can be used as electrophiles to trap the corresponding carbanion intermediate generated from α-azido ketones, to yield the valuable 1,2,3-trifunctionalized synthons 2-azido-3-hydroxy ketones. Both acyclic derivatives and α-azido-α-(1-hydroxyalkyl)benzocyclanones and -benzoheterocyclanones were found to be available by this new procedure. We were able to generate another anionic species − imino anion − by a subsequent loss of nitrogen, trapping of this latter nucleophile resulting in the formation of 2,5-dihydro-5-hydroxyoxazoles.

In this contribution we wish to demonstrate that it is not only simple aldehydes or ketones, but also other, more complex carbonyl compounds, that can be used as electrophiles. This extension allowed us to synthesize the valuable tetrafunctionalized synthons 2-azido-3-hydroxy-1,4-diketones, and to develop a new route to 3,5-disubstituted isoxazoles.

Results and Discussion

In continuation of our previous work,[2,3] we studied the reactions of 2-azido-1-(4-substituted phenyl)ethanones **1** and 3-azidochromanones **10** with α-keto aldehydes and α-keto esters as electrophiles under basic conditions. When 2-azido-4′-substituted-acetophenones **1a−d** were treated with various phenylglyoxal hydrates **2−4**[4] in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), previously found[3] to be the most effective base, we obtained 2-azido-3-hydroxy-1,4-diketones **6a−d**, **7d**, and **8d** in good yields (Scheme 1, Table 1).

The best yields could be achieved by use of 2−3 equiv. of the α-oxo aldehydes and a catalytic amount (10−11 mol %) of DBU at below ambient temperature. The synthetic value of this aldol-type reaction was also demonstrated by modification of the structure of the α-oxo aldehyde. Experiments with *tert*-butylglyoxal hydrate[5] as electrophile resulted in the desired product **9d** (Table 1, Entry 7). The data summarized in Table 1 show that the electronic effects of R groups in position 4′ have no influence on the conversion and yield of the C−C bond-forming reaction (Entries 1−4). Moreover, both aryl- and alkylglyoxals gave moderate to good yields (Entries 4−7), indicating the generality of the coupling reaction. Adducts **6a−d**, **7d**, **8d**, and **9d** were isolated as mixtures of *syn* and *anti* isomers in all cases. Repeated crystallization of the diastereomeric mixture of **6d** afforded the major component in a diastereopure form, and its *syn* relative configuration was unequivocally determined by X-ray analysis (Figure 1).

This allowed us to assign the diastereomers in the whole series on the basis of the characteristic differences in their NMR spectra. It is noteworthy that suitable separation of signals could be observed only in [D_6]acetone as solvent, and not in $CDCl_3$. The diagnostic tools were the chemical

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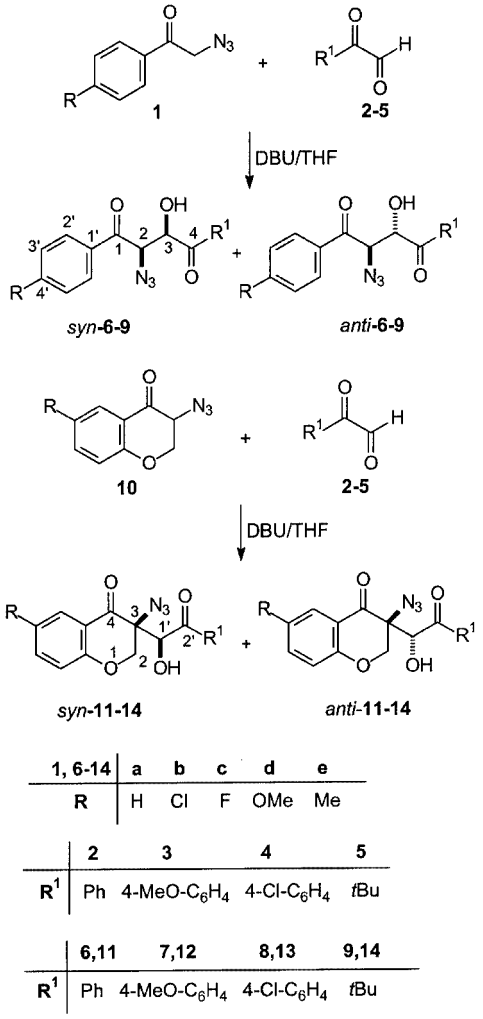
Table 1. Treatment of phenacyl azides **1** with α-oxo aldehydes **2**−**5**

Entry	Product[a]	R	R^1	*t* [h]	Conversion (%)[b]	Yield (%)[c]	*syn*/*anti*
1	**6a**	H	Ph	3	100	55	77:23
2	**6b**	Cl	Ph	6	100	52	76:24
3	**6c**	F	Ph	6	100	63	76:24
4	**6d**	OMe	Ph	4	100	62	87:13
5	**7d**	OMe	4-MeO-C_6H_4	24.5	52	84	80:20
6	**8d**	OMe	4-Cl-C_6H_4	24	84	82	77:23
7	**9d**	OMe	*t*Bu	4	100	52	89:11[d]

[a] Reactions were performed at 0 °C. [b] Determined by ^{1}H NMR analysis of the reaction mixture. [c] Isolated yields, normalized to 100% conversion. [d] An approximate 8:1 diastereomeric ratio was determined from the integrals of the *t*Bu signals in the ^{1}H NMR spectrum. No assignment of relative configuration of *syn* and *anti* diastereomers was feasible, due to the overlapping 2′-H and 3′-H signals of the isomers.



Scheme 1. Reactions between α-azido ketones **1** and **10** and α-oxo aldehydes **2**−**5**

shifts of the 2-H and 3-H hydrogen atoms of the *syn* isomers, whose signals appeared at lower field ($\Delta\delta$ = 0.03−0.06 ppm and $\Delta\delta$ = 0.12−0.15 ppm, respectively). Similarly, the signals of the C-2 carbon atoms of the *syn* isomers appeared in the ^{13}C NMR spectra at significantly lower field ($\Delta\delta$ = 1.8−2.7 ppm) than those of their counterparts in the *anti* diastereomers.

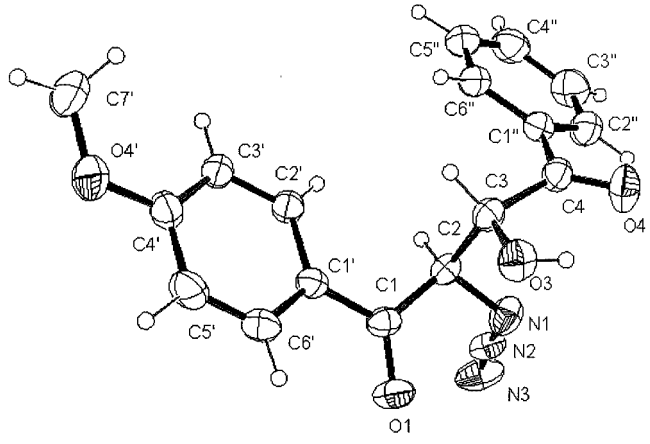


Figure 1. Crystal structure of azido alcohol *syn*-**6d**

A moderate to good diastereoselectivity (52−74% *de*) with a *syn* preference was observed in the formation of products **6a**−**d**, **7d**, and **8d**, these *de* values being markedly higher than the selectivities found[3] in the reactions between azido ketones **1** and simple aldehydes. On the other hand, excellent regioselectivity between the formyl and oxo carbonyl groups was observed in favor of the former, azides **6**−**9** being formed exclusively and no other aldol products being detected in the reaction mixtures. This selectivity could be explained in terms of the higher electrophilicity and the smaller steric hindrance of the formyl group.

As another point of interest, we also studied the coupling reactions of cyclic systems. Analogous reactions between 3-azidochromanones **10a**, **10b**, and **10e** and α-oxo aldehydes **2**−**5** in the presence of catalytic amounts of DBU afforded the desired 3-azido-3-(1-hydroxy-2-oxoalkyl)-4-chromanones **11a**, **11b**, **11e**, **12e**, **13e**, and **14e** in high (usually > 80%) yields (Scheme 1, Table 2). These yields were significantly higher than those found on treatment of the acyclic substrates **1**. This observation may be explained in terms of the lack of α-hydrogen moieties in the α-azido ketone unit, and hence the absence of retroaldol cleavage.

Again, azido alcohols **11**−**14** were isolated as mixtures of *syn* and *anti* diastereomers. The relative configuration of the diastereomers was assigned by X-ray structure determination. Recrystallization of the diastereomeric *anti*/*syn*

Table 2. Treatment of 3-azidochromanones **10** with α-oxo aldehydes **2**−**5**

Entry	Product[a]	R	R[1]	*t* [h]	Yield (%)[b]	*syn*/*anti*
1	**11a**	H	Ph	3	89	63:37
2	**11b**	Cl	Ph	3	65	60:40
3	**11e**	Me	Ph	3.5	80	62:38
4	**12e**	Me	4-MeO-C_6H_4	3	87	67:33
5	**13e**	Me	4-Cl-C_6H_4	3	87	58:42
6	**14e**	Me	*t*Bu	2.5	94	46:54

[a] Reactions were performed at 0 °C. [b] Isolated yields.

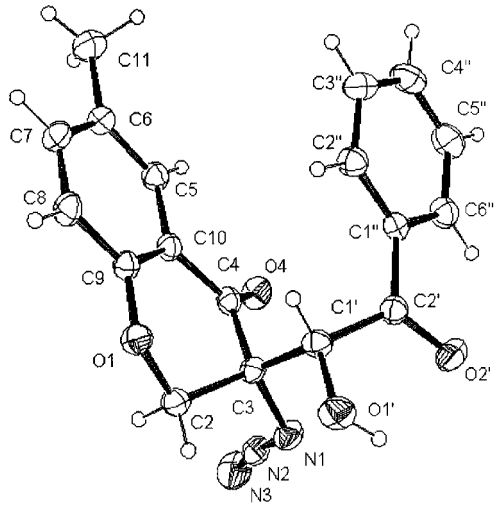
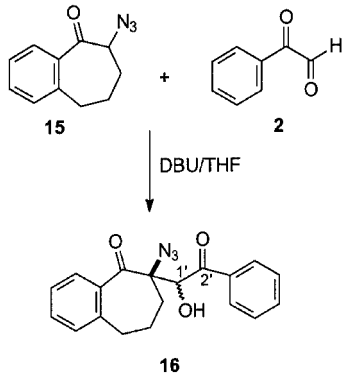


Figure 2. Crystal structure of azido alcohol *anti*-**11e**

mixture of compound **11e** afforded the minor product in a diastereopure form, and this proved on X-ray analysis to be the *anti*-**11e** isomer (Figure 2).

With the stereochemistry of the *syn*/*anti*-**11e** pair established, we were able to assign the isomers in the whole series, on the basis of their characteristic spectral differences. In good accordance with our previous results,[3] the characteristic feature in the ^{1}H NMR spectra of the *anti* diastereomers was the well-separated AX doublets representing the 2-methylene group of the chromanone ring (δ = 4.18−4.21 and 4.71−4.75 ppm, respectively), whereas the *syn* isomers showed a tight AB system ($\Delta\delta_{AB}$ = 0.17−0.23 ppm). Another diagnostic tool was the chemical shift of hydrogen atom 1′-H, this signal appearing at lower field (Δδ = 0.04−0.1 ppm) in the ^{1}H NMR spectrum of the *anti* isomer than in that of the *syn* diastereomer. Moreover, carbon atom C-1′ of the *syn* diastereomer appeared at lower field (Δδ = 1.5−1.7 ppm) than that of the *anti* isomer in the ^{13}C NMR. In contrast with the coupling reaction of acyclic azides **1**, products **11**−**13** were formed with low diastereoselectivity (16−34% *de*) and a *syn* preference. This selectivity is quite similar to the values and preferences observed[3] previously in the reactions between 3-azidochromanones **10** and simple aldehydes. The reaction between azide **10e** and *tert*-butylglyoxal hydrate (**5**) gave a different stereochemical outcome, as a weak *anti* preference (8% *de*) was observed.

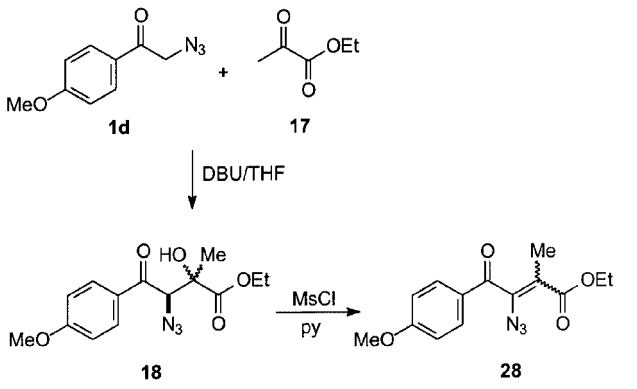
We also extended our experiments to another cyclic substrate, 2-azidobenzosuberone (**15**), which was synthesized from 2-bromobenzosuberone by our previously described PTC method.[3] When azide **15** was treated with phenylglyoxal hydrate (**2**) under our standard conditions, 2-azido-2-(1-hydroxy-2-oxo-2-phenylethyl)benzosuberone (**16**) was obtained in 86% yield (Scheme 2). Notably, the degree of conversion was only 54%, in spite of the long reaction period (4 d). It is very likely that the higher flexibility of the seven-membered ring results in greater steric hindrance in the attack of the intermediate carbanion on the carbonyl center and thus lowers the efficiency of the coupling reaction. Product **16** was isolated as a diastereomeric mixture (50% *de*), the ratio being determined from the integrals of the 1′-H hydrogen signals in the ^{1}H NMR spectrum, but no assignment of the relative configuration of the isomers was feasible.



Scheme 2. Reaction between 2-azidobenzosuberone (**15**) and phenylglyoxal (**2**)

To extend the range of electrophiles, we also investigated base-induced reactions between phenacyl azides **1** and α-oxo esters. When azides **1a**−**d** were treated with ethyl pyruvate (**17**) as a model electrophile in the presence of DBU, with the reaction being monitored by TLC and ^{1}H NMR spectroscopy, considerable amounts of the coupled products were detected, but attempts to isolate these compounds by column chromatography failed. Since chromatography of the crude product afforded the starting material **1** in high amounts, it is very likely that the instability of ethyl 4-aryl-3-azido-2-hydroxy-2-methyl-4-oxobutanoates can be explained in terms of their increased capability for decomposition by retroaldol cleavage, due to the increased steric interactions around the quaternary C-2 atom. The only stable product, ethyl 3-azido-2-hydroxy-4-(4-methoxyphenyl)-2-methyl-4-oxobutanoate (**18**), was isolated in 69% yield, confirming the efficiency and the usefulness of the coupling with α-oxo esters (Scheme 3). Further experiments to overcome this drawback are in progress.

2-Azido-3-hydroxy-1,4-diones and 3-azido-2-hydroxy-4-oxobutanoates, available from reactions between α-azido ketones and various α-oxo aldehydes or α-oxo esters, are useful tetrafunctionalized synthons. Their different functionalities allow selective manipulations even without the use of any protecting groups. Out of the many possible ap-

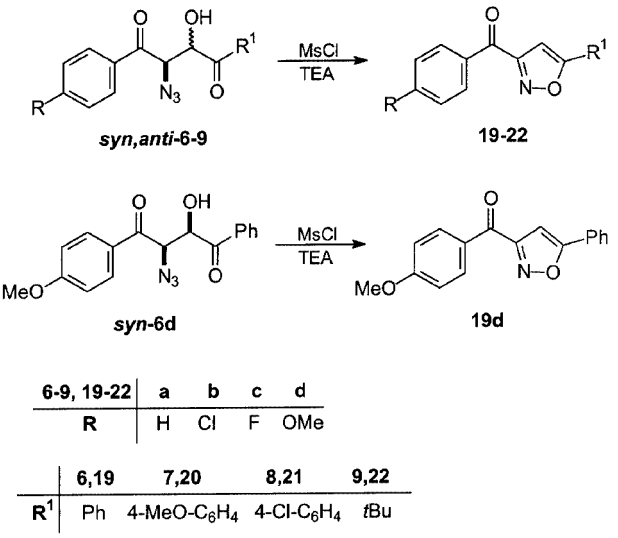


Scheme 3. Synthesis of α-oxo ester **18** and its transformation into vinyl azide **28**

plications, we investigated their transformation into vinyl azides in detail. Thanks to their high reactivity in pyrolysis, photolysis, and cycloadditions, and also in attack either by electrophiles or by nucleophiles, vinyl azides represent an important and synthetically useful class of organic compounds.[6] Several methods for the preparation of these unsaturated azides have been published in the literature.[6a,6b] The most reliable and general procedure involves dehydrohalogenation or dehydration from suitably substituted azides or related intermediates, and works well in the synthesis of simple vinyl azides and of α- or β-azido-α,β-unsaturated ketones or esters.[7] Since the hydroxy groups in adducts **6**−**9** and **18** can be converted into good leaving groups by conversion into sulfonates, we decided to study their reactions with mesyl chloride under basic conditions.

Treatment of *syn*/*anti*-1-aryl-2-azido-3-hydroxy-1,4-diones **6a**−**d** with mesyl chloride (MsCl, 2 equiv.) in dry pyridine resulted in the formation of the corresponding 3-aroyl-5-phenylisoxazoles **19a**−**d** in low yield (22−42%). We attempted to optimize the conditions by variation of bases and solvents, use of DBU, 1,4-diazabicyclo[2.2.2]octane (DABCO), or triethylamine (TEA) in dry dichloromethane, and adjustment of stoichiometry. The best results were achieved by use of a slight excess (1.1−1.25 equiv.) of mesyl chloride and 2.4−2.5 equiv. of TEA in dry dichloromethane. Treatment of *syn*/*anti*-**6a**−**d**, **7d**, **8d**, and **9d** and of *syn*-**6d** under the optimized conditions afforded the appropriate isoxazoles **19a**−**d**, **20d**, **21d**, and **22d** in moderate yields (Scheme 4, Table 3). Attempts to isolate the intermediate mesylate **23** and azide **24** (vide infra) failed. This new reaction offers a new route to the field of 3,5-disubstituted isoxazoles.

Products **19**−**22** were identified by their spectral characteristics (lack of OH and N_3 absorption bands in their IR spectra and any aliphatic proton or carbon signals in their ^1H and ^{13}C NMR spectra), microanalyses and chemical corroboration. 3-Benzoyl-5-phenylisoxazole (**19a**) was synthesized from *meso*-2,3-dibromo-1,4-diphenyl-1,4-butanedione (**26**) according to Hassner et al.[7f] and the product was completely identical with our sample obtained from *syn*/*anti*-**6a** (Scheme 5).

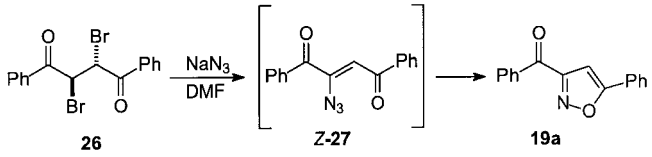


Scheme 4. Formation of isoxazoles **19**−**22** from azido alcohols **6**−**9**

Table 3. Synthesis of 5-substituted 3-acylisoxazoles **19**−**22** from 2-azido-3-hydroxy-1,4-diketones **6**−**9**

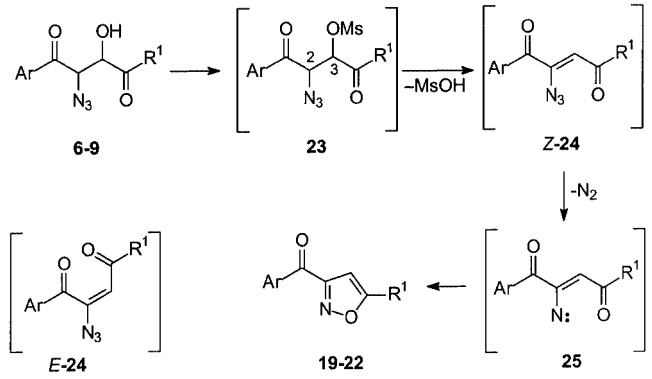
Entry	Starting material	Product	R	R^1	*t* [h]	Yield (%)[a]
1	**6a**	**19a**	H	Ph	1.5	39
2	**6b**	**19b**	Cl	Ph	4	46
3	**6c**	**19c**	F	Ph	4	48
4	**6d**	**19d**	OMe	Ph	5	42
5	**7d**	**20d**	OMe	4-MeO-C_6H_4	3.5	63
6	**8d**	**21d**	OMe	4-Cl-C_6H_4	4	48
7	**9d**	**22d**	OMe	*t*Bu	3.5	23

[a] Isolated yields.



Scheme 5. Independent route to isoxazole **19a**

The suggested pathway for the formation of isoxazoles **19**−**22** is shown in Scheme 6. The primary product mesylate **23** should smoothly give the elimination product **24**, thanks



Scheme 6. Postulated intermediates in the formation of isoxazoles **19**−**22**

to the activation by the two carbonyl groups. It is well documented that (*Z*)-β-azido-α,β-unsaturated ketones are highly unstable and give isoxazoles at room temperature, presumably via the corresponding nitrenes, while (*E*) isomers are more stable and yield oxazoles or nitriles under thermolytic conditions.[6][7e,8,9] Neither azides (*E*)-**24** nor their secondary products could be isolated or detected in our reaction mixtures. This observation may be explained in terms of a higher thermodynamic stability of isomer (*Z*)-**24**. The hydrogen atoms at both C-2 and C-3 should be highly acidic, due to the adjacent carbonyl functions. This feature results in easy epimerization at both centers and therefore allows thermodynamic control to predominate. The formation of the azide intermediate (*Z*)-**24** was also suggested by Hassner et al.[7f] Further support for the intermediacy of vinyl azides (*Z*)-**24** was provided by analogous treatment of pyruvate adduct **18** with MsCl in dry pyridine, which resulted in the formation of ethyl 3-azido-4-(4-methoxyphenyl)-2-methyl-4-oxo-2-butenoate (**28**, Scheme 3), which was inevitably stable due to the lack of the β-azido-α,β-unsaturated ketone unit.

In summary, base-induced reactions between α-azido ketones and α-oxo aldehydes and α-oxo esters constitute an efficient method for the preparation of the tetrafunctionalized 2-azido-3-hydroxy-1,4-dione and 3-azido-2-hydroxy-4-oxoalkanoate synthons. The reactions between acyclic α-azido ketones and α-oxo aldehydes take place with remarkable diastereoselectivity. Treatment of 2-azido-3-hydroxy-1,4-diones with mesyl chloride in the presence of an excess of base affords 3-acyl-5-substituted isoxazoles, providing a novel and synthetically valuable method for the preparation of this family of compounds.

Experimental Section

General: All chemicals were used as purchased unless otherwise stated. THF was distilled from benzophenone ketyl, triethylamine was distilled from LAH. Phenylglyoxal hydrates **2**−**4** were prepared as described by Rioux−Lacoste and Viel.[4] *tert*-Butylglyoxal hydrate (**5**) was prepared as described by Fuson et al.[5] α-Azido ketones **1a**−**d** and **10a**, **10b**, and **10e** were prepared by the procedure reported previously.[3] Column chromatography was performed on Kieselgel 60 or Kieselgel 40. Melting points: Boetius hot-stage, uncorrected values. IR: Perkin−Elmer 16 PC-FT-IR; KBr pellets unless otherwise stated. NMR: Varian Gemini 200, Bruker WP 200 SY, Bruker AM 360 (200 or 360 MHz for ^{1}H; 50 or 90 MHz for ^{13}C). Recorded in $CDCl_3$ solution unless otherwise stated. Chemical shifts are given in δ relative to an internal standard TMS (δ = 0) or to the residual $CHCl_3$ (δ = 7.26 ppm for ^{1}H NMR and δ = 77.0 ppm for ^{13}C NMR). Elemental analyses: Carlo−Erba apparatus.

2-Azido-3-hydroxy-1,4-diphenyl-1,4-butanedione (6a): Molecular sieves (4 Å, 1.00 g) were added to a solution of **1a** (300 mg, 1.86 mmol) in dry THF (20 mL) and the mixture was cooled to 0 °C. Then phenylglyoxal (**2**) (826 mg, 5.43 mmol)[10] and DBU (30 μL, 31 mg, 0.21 mmol) were added and the mixture was allowed to stand at 0 °C. After completion of the reaction (3 h), the molecular sieves were filtered off, the filtrate was concentrated in vacuo, and the residue was purified by column chromatography (toluene/ethyl acetate, 11:1, v/v) to give **6a** as a yellow oil (303 mg, 55%) made up of a 77:23 mixture of the *syn* and *anti* diastereomers (by ^{1}H NMR). The oil crystallized on standing with hexane to give yellow crystals. M.p. 82−84 °C. IR: $\tilde{\nu}$ = 3474 (OH), 2110 (N_3), 1686, 1676 (C=O), 1598, 1450, 1262, 686 cm^{-1}. ^{1}H NMR ***anti*-6a:** ([D_6]acetone): δ = 5.20 (d, *J* = 7.6 Hz, 1 H, 3-OH), 5.31 (d, *J* = 6.8 Hz, 1 H, 2-H), 5.58 (dd, *J* = 7.6, 6.8 Hz, 1 H, 3-H) ppm. ***syn*-6a:** δ = 5.14 (d, *J* = 6.3 Hz, 1 H, 3-OH), 5.34 (d, *J* = 4.6 Hz, 1 H, 2-H), 5.70 (dd, *J* = 6.3, 4.6 Hz, 1 H, 3-H) ppm. Inseparable signals: δ = 7.54−7.75 (m, 6 H, 3′,4′,5′,3′′,4′′,5′′-H), 7.98−8.11 (m, 4 H, 2′,6′,2′′,6′′-H) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. ^{13}C NMR: ***anti*-6a:** δ = 63.5 (C-2), 74.7 (C-3) ppm. ***syn*-6a:** δ = 65.6 (C-2), 74.4 (C-3) ppm. Inseparable signals: δ = 128.3, 128.8, 129.1, 129.2 (C-2′,3′,5′,6′,2′′,3′′,5′′,6′′), 133.2, 134.7 (C-1′,1′′), 134.0, 134.2, 134.5 (C-4′,4′′), 194.2 (C-1), 197.6 (C-4) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. $C_{16}H_{13}N_3O_3$ (295.3): C 65.08, H 4.44, N 14.23; found C 64.95, H 4.13, N 13.92.

2-Azido-1-(4-chlorophenyl)-3-hydroxy-4-phenyl-1,4-butanedione (6b): A solution of 2-azido-1-(4-chlorophenyl)ethanone (**1b**) (400 mg, 2.05 mmol) in dry THF (20 mL) was cooled to 0 °C. Then phenylglyoxal (**2**) (823 mg, 5.41 mmol)[10] and DBU (34 μL, 34 mg, 0.23 mmol) were added, and the mixture was allowed to stand at 0 °C. When the reaction was complete (6 h) the reaction mixture was concentrated in vacuo and the residue was purified by column chromatography (toluene/ethyl acetate, 9:1, v/v) to give pure **6b** (350 mg, 52%) as a yellow oil made up of a 76:24 mixture of the *syn* and *anti* diastereomers (by ^{1}H NMR). The oil crystallized on standing with hexane to give yellow crystals. M.p. 86−90 °C. IR: $\tilde{\nu}$ = 3440 (OH), 2112 (N_3), 1690, 1676 (C=O), 1596, 1258, 1092, 1010, 686 cm^{-1}. ^{1}H NMR ([D_6]acetone): ***anti*-6b:** δ = 5.26 (d, *J* = 7.5 Hz, 1 H, 3-OH), 5.32 (d, *J* = 6.4 Hz, 1 H, 2-H), 5.57 (dd, *J* = 7.5, 6.4 Hz, 1 H, 3-H) ppm. ***syn*-6b:** δ = 5.21 (d, *J* = 6.5 Hz, 1 H, 3-OH), 5.35 (d, *J* = 4.6 Hz, 1 H, 2-H), 5.71 (dd, *J* = 6.5, 4.6 Hz, 1 H, 3-H) ppm. Inseparable signals: δ = 7.53−7.75 (m, 5 H, 3′,5′,3′′,4′′,5′′-H), 7.98−8.12 (m, 4 H, 2′,6′,2′′,6′′-H) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. ^{13}C NMR: ***anti*-6b:** δ = 63.5 (C-2), 74.8 (C-3), 134.5 (C-4′′), 194.1 (C-1), 198.2 (C-4) ppm. ***syn*-6b:** δ = 65.9 (C-2), 74.3 (C-3), 134.6 (C-4′′), 193.3 (C-1), 197.6 (C-4) ppm. Inseparable signals: δ = 128.4, 128.9, 129.3, 129.4, 129.9, 130.2 (C-2′,3′,5′,6′,2′′,3′′,5′′,6′′), 133.3, 133.5 (C-1′,1′′), 140.6 (C-4′) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. $C_{16}H_{12}ClN_3O_3$ (329.7): C 58.28, H 3.67, N 12.74; found C 58.31, H 3.66, N 12.71.

2-Azido-1-(4-fluorophenyl)-3-hydroxy-4-phenyl-1,4-butanedione (6c): A solution of 2-azido-1-(4-fluorophenyl)ethanone (**1c**) (1.00 g, 5.58 mmol) in dry THF (36 mL) was cooled to 0 °C and phenylglyoxal (**2**) (1.50 g, 9.85 mmol)[10] and DBU (0.09 mL, 93 mg, 0.61 mmol) were added. After standing for 6 h at 0 °C, the mixture was worked up as described for **6b**, and column chromatography (toluene/ethyl acetate, 9:1, v/v) gave **6c** (1.10 g, 63%) as a yellow crystalline solid made up of a 76:24 mixture of the *syn* and *anti* diastereomers (by ^{1}H NMR). M.p. 112−113 °C. IR: $\tilde{\nu}$ = 3455 (OH), 2111 (N_3), 1689, 1674 (C=O), 1598, 1259, 1222 cm^{-1}. ^{1}H NMR ([D_6]acetone): ***anti*-6c:** δ = 5.26 (d, *J* = 8.1 Hz, 1 H, 3-OH), 5.32 (d, *J* = 7.6 Hz, 1 H, 2-H), 5.58 (dd, *J* = 8.1, 7.6 Hz, 1 H, 3-H). ***syn*-6c:** δ = 5.24 (d, *J* = 6.6 Hz, 1 H, 3-OH), 5.35 (d, *J* = 4.7 Hz, 1 H, 2-H), 5.72 (dd, *J* = 6.6, 4.7 Hz, 1 H, 3-H) ppm. Inseparable signals: δ = 7.31−7.45 (m, 2 H, 3′,5′-H), 7.56−7.73 (m, 3 H, 3′′,4′′,5′′-H), 8.03−8.23 (m, 4-H, 2′,6′,2′′,6′′-H) ppm. NMR

spectroscopic data were taken from the spectrum of the diastereomeric mixture. ^{13}C NMR: ***anti*-6c:** δ = 63.4 (C-2), 74.8 (C-3), 116.1 (d, $J_{C,F}$ = 22.0 Hz, C-3′,5′), 131.7 (d, $J_{C,F}$ = 9.4 Hz, C-2′,6′), 134.4 (C-4′′) ppm. ***syn*-6c:** δ = 65.8 (C-2), 74.3 (C-3), 116.3 (d, $J_{C,F}$ = 21.9 Hz, C-3′,5′), 131.3 (d, $J_{C,F}$ = 9.5 Hz, C-2′,6′), 134.5 (C-4′′) ppm. Inseparable signals: δ = 128.4, 128.9, 129.3 (C-2′′,3′′,5′′,6′′), 133.3 (C-1′,1′′), 166.2 (d, $J_{C,F}$ = 256 Hz, C-4′), 192.8 (C-1), 197.6 (C-4) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. $C_{16}H_{12}FN_3O_3$ (313.3): C 61.34, H 3.86, N 13.41; found C 61.30, H 3.84, N 13.39.

2-Azido-3-hydroxy-1-(4-methoxyphenyl)-4-phenyl-1,4-butanedione (6d): A solution of 2-azido-1-(4-methoxyphenyl)ethanone (**1d**) (356 mg, 1.86 mmol) in dry THF (20 mL) was cooled to 0 °C, phenylglyoxal (**2**) (749 mg, 4.92 mmol)[10] and DBU (31 μL, 32 mg, 0.21 mmol) were added, and the mixture was allowed to stand at 0 °C. When the reaction was complete (4 h), the reaction mixture was concentrated in vacuo and the residue was purified by column chromatography (toluene/ethyl acetate, 6:1, v/v) to give pure **6d** (378 mg, 62%) as a yellow crystalline solid made up of a 87:13 mixture of the *syn* and *anti* diastereomers (by ^{1}H NMR). M.p. 100−103 °C. IR: $\tilde{\nu}$ = 3471 (OH), 2126 (N_3), 1686 (C=O), 1604, 1264, 1248, 1176 cm^{-1}. Pure *syn*-**6d** diastereomer was obtained by crystallization from diisopropyl ether/ethyl acetate (2:1, v/v) mixture.

Isomer *syn*-6d: Colorless prisms, m.p. 103.5−106.5 °C. IR: $\tilde{\nu}$ = 3468 (OH), 2124 (N_3), 1686 (C=O), 1604, 1264, 1246, 1176, 956 cm^{-1}. ^{1}H NMR ([D$_6$]acetone): δ = 3.94 (s, 3 H, 4′-OMe), 5.19 (d, *J* = 6.5 Hz, 1 H, 3-OH), 5.25 (d, *J* = 4.7 Hz, 1 H, 2-H), 5.70 (dd, *J* = 6.5, 4.7 Hz, 1 H, 3-H), 7.14 (d, *J* = 9.0 Hz, 2 H, 3′,5′-H), 7.56−7.76 (m, 3 H, 3′′,4′′,5′′-H), 8.05−8.12 (m, 4 H, 2′,6′,2′′,6′′-H) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 56.0 (4′-OMe), 65.5 (C-2), 75.2 (C-3), 115.1 (C-3′,5′), 128.5 (C-1′), 129.6, 129.7 (C-2′′,3′′,5′′,6′′), 131.8 (C-2′,6′), 134.6 (C-4′′), 135.5 (C-1′′), 165.1 (C-4′), 193.4 (C-1), 198.7 (C-4) ppm. $C_{17}H_{15}N_3O_4$ (325.3): C 62.76, H 4.65, N 12.92; found C 62.72, H 4.67, N 12.94.

Isomer *anti*-6d: ^{1}H NMR ([D$_6$]acetone): δ = 3.91 (s, 3 H, 4′-OMe), 5.21 (d, *J* = 7.0 Hz, 1 H, 2-H), 5.55 (dd, *J* = 7.9, 7.0 Hz, 1 H, 3-H), 7.05 (d, *J* = 8.8 Hz, 2 H, 3′,5′-H), 7.54−7.74 (m, 3 H, 3′′,4′′,5′′-H), 7.98−8.11 (m, 4-H, 2′,6′,2′′,6′′-H) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. ^{13}C NMR: δ = 55.5 (4′-OMe), 62.8 (C-2), 74.7 (C-3), 114.0 (C-3′,5′), 127.2 (C-1′), 128.7, 128.8 (C-2′′,3′′,5′′,6′′), 131.3 (C-2′,6′), 133.4 (C-1′′), 134.2 (C-4′′), 164.2 (C-4′), 193.2 (C-1), 198.4 (C-4) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. $C_{17}H_{15}N_3O_4$ (325.3): C 62.76, H 4.65, N 12.92; found C 62.70, H 4.63, N 12.95.

Crystal Data of *syn*-6d: Colorless prism crystals (0.55 × 0.4 × 0.35 mm) of $C_{17}H_{15}N_3O_4$, *M* = 325.32, monoclinic, *a* = 8.135(1) Å, *b* = 8.8659(10) Å, *c* = 23.114(3) Å, β = 108.44(1)°, *V* = 1581.5(3) Å^3, *Z* = 4, space group: $P2_1/c$, $\rho_{calcd.}$ = 1.366 g cm^{-3}. Data were collected at 293(1) K, Enraf−Nonius MACH3 diffractometer, Mo-K_α radiation, λ = 0.71073 Å, ω-2θ motion, θ_{max} = 25.95°, 3077 measured, 2323 reflections were unique with $I > 2\sigma(I)$, decay: none. The structure was solved by use of SIR-92 software[13] and refined on F^2 with the SHELX-97[14] program, publication material was prepared with the WINGX-97 suite,[15] $R(F)$ = 0.049 and $wR(F^2)$ = 0.148 for 3077 reflections, 277 parameters. Residual electron density: 0.151/−0.204 e/Å^3. CCDC-182538 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Center, 12, Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

2-Azido-3-hydroxy-1,4-bis(4-methoxyphenyl)-1,4-butanedione (7d): A solution of 2-azido-1-(4-methoxyphenyl)ethanone (**1d**) (200 mg, 1.05 mmol) in dry THF (11 mL) was cooled to 0 °C, 4-methoxyphenylglyoxal (**3**) (571 mg, 3.14 mmol)[10] and DBU (17 μL, 18 mg, 0.12 mmol) were added, and the mixture was allowed to stand at 0 °C. After 24.5 h, the reaction mixture was concentrated in vacuo and the residue was purified by column chromatography (toluene/ethyl acetate, 4:1, v/v) to give pure **7d** (163 mg, conversion: 52%, yield: 84%, normalized to 100% conversion) as a yellow, crystalline solid made up of a 80:20 mixture of the *syn* and *anti* diastereomers (by ^{1}H NMR). M.p. 81−108 °C. IR: $\tilde{\nu}$ = 3446 (OH), 2102 (N_3), 1690, 1668 (C=O), 1600, 1570, 1260, 1174 cm^{-1}. ^{1}H NMR ([D$_6$]acetone): ***anti*-7d:** δ = 3.91, 3.92 (2 × s, 6 H, 4′,4′′-OMe), 5.02 (d, *J* = 8.1 Hz, 1 H, 3-OH), 5.16 (d, *J* = 6.5 Hz, 1 H, 2-H), 5.50 (dd, *J* = 8.1, 6.5 Hz, 1 H, 3-H) ppm. ***syn*-7d:** δ = 3.93, 3.94 (2 × s, 6 H, 4′,4′′-OMe), 5.05 (d, *J* = 6.7 Hz, 1 H, 3-OH), 5.22 (d, *J* = 4.8 Hz, 1 H, 2-H), 5.62 (dd, *J* = 6.7, 4.8 Hz, 1 H, 3-H) ppm. Inseparable signals: δ = 7.03−7.14 (m, 4 H, 3′,5′,3′′,5′′-H), 7.96−8.10 (m, 4 H, 2′,6′,2′′,6′′-H) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. ^{13}C NMR ([D$_6$]acetone): ***anti*-7d:** δ = 64.1 (C-2), 75.1 (C-3). ***syn*-7d:** δ = 66.5 (C-2), 75.7 (C-3) ppm. Inseparable signals: δ = 56.8 (4′,4′′-OMe), 115.8 (C-3′,5′,3′′,5′′), 128.8, 129.5 (C-1′,1′′), 132.5, 132.8, 133.0 (C-2′,6′,2′′,6′′), 165.9 (C-4′), 194.2 (C-1), 197.6 (C-4) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. $C_{18}H_{17}N_3O_5$ (355.4): C 60.84, H 4.82, N 11.82; found C 60.89, H 4.81, N 11.84.

2-Azido-4-(4-chlorophenyl)-3-hydroxy-1-(4-methoxyphenyl)-1,4-butanedione (8d): A solution of 2-azido-1-(4-methoxyphenyl)ethanone (**1d**) (300 mg, 1.57 mmol) in dry THF (15 mL) was cooled to 0 °C, 4-chlorophenylglyoxal (**4**) (879 mg, 4.71 mmol)[10] and DBU (26 μL, 26 mg, 0.17 mmol) were added, and the mixture was allowed to stand at 0 °C. After 24 h, the reaction mixture was concentrated in vacuo and the residue was purified by column chromatography (toluene/ethyl acetate, 9:1, v/v) to give 463 mg of **8d** (conversion: 84%, yield: 82%, normalized to 100% conversion) as a yellow oil made up of a 77:23 mixture of the *syn* and *anti* diastereomers (by ^{1}H NMR). The diastereomeric mixture was treated with hexane to afford pale yellow crystals, m.p. 117−136 °C. The *syn*/*anti* ratio was 74:26 by ^{1}H NMR. IR: $\tilde{\nu}$ = 3456 (OH), 2122 (N_3), 1682 (C=O), 1600, 1256, 1172, 1092, 958, 558 cm^{-1}. ^{1}H NMR ([D$_6$]acetone): ***anti*-8d:** δ = 3.90 (s, 3 H, 4′-OMe), 5.25 (d, *J* = 6.6 Hz, 1 H, 2-H), 5.52 (dd, *J* = 8.1, 6.6 Hz, 1 H, 3-H), 7.05 (d, *J* = 9.2 Hz, 2 H, 3′,5′-H) ppm. ***syn*-8d:** δ = 3.91 (s, 3 H, 4′-OMe), 5.29 (d, *J* = 5.3 Hz, 1 H, 2-H), 5.36 (d, *J* = 6.7 Hz, 1 H, 3-OH), 5.68 (dd, *J* = 6.7, 5.3 Hz, 1 H, 3-H), 7.11 (d, *J* = 8.7 Hz, 2 H, 3′,5′-H) ppm. Inseparable signals: δ = 7.55−7.63 (m, 2 H, 3′′,5′′-H), 7.99−8.13 (m, 4 H, 2′,6′,2′′,6′′-H) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. ^{13}C NMR ([D$_6$]acetone): ***anti*-8d:** δ = 63.5 (C-2), 74.9 (C-3), 114.9 (C-3′,5′). ***syn*-8d:** 65.3 (C-2), 75.2 (C-3), 115.0 (C-3′,5′). Inseparable signals: δ = 56.0 (4′-OMe), 128.5 (C-1′), 129.8 (C-3′′,5′′), 131.4, 131.5, 131.8, 132.1 (C-2′,6′,2′′,6′′), 134.3 (C-1′′), 140.2 (C-4′′), 165.1 (C-4′), 193.3 (C-1), 197.8 (C-4) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. $C_{17}H_{14}ClN_3O_4$ (359.8): C 56.76, H 3.92, N 11.68; found C 56.70, H 3.93, N 11.65.

2-Azido-3-hydroxy-1-(4-methoxyphenyl)-5,5-dimethyl-1,4-hexanedione (9d): A solution of 2-azido-1-(4-methoxyphenyl)ethanone (**1d**) (300 mg, 1.57 mmol) in dry THF (15 mL) was cooled to 0

°C, *tert*-butylglyoxal (**5**) (622 mg, 4.71 mmol)[10] and DBU (26 μL, 26 mg, 0.17 mmol) were added, and the mixture was allowed to stand at 0 °C. After 4 h, the reaction mixture was concentrated in vacuo and the residue was purified by column chromatography (hexane/ethyl acetate, 4:1, v/v) to give **9d** as a yellow oil (247 mg, 52%) made up of an 89:11 mixture of the **9d** and **9d′** diastereomers (by ^{1}H NMR). IR (neat): $\tilde{\nu}$ = 3452 (OH), 2110 (N_3), 1698, 1682 (C=O), 1600, 1264, 1172 cm^{-1}. ^{1}H NMR ([D$_6$]acetone): **9d:** δ = 1.27 (s, 9 H, *t*Bu), 8.01 (d, *J* = 9.1 Hz, 2 H, 2′,6′-H) ppm. **9d′:** δ = 1.24 (s, 9 H, *t*Bu), 8.05 (d, *J* = 8.7 Hz, 2 H, 2′,6′-H) ppm. Inseparable signals: δ = 3.91 (s, 3 H, 4′-OMe), 5.05−5.11, 5.16−5.23 (2 × m, 2 × 1 H, 2,3-H), 7.07−7.15 (m, 2 H, 3′,5′-H) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. ^{13}C NMR ([D$_6$]acetone): **9d:** 26.7 (C*Me*$_3$), 64.8 (C-2), 74.7 (C-3) ppm. **9d′:** δ = 26.0 (C*Me*$_3$), 62.0 (C-2), 71.4 (C-3) ppm. Inseparable signals: δ = 43.9 (C-5), 55.8 (4′-OMe), 114.8 (C-3′,5′), 128.2 (C-1′), 131.3, 131.5, 131.6 (C-2′,6′), 164.8 (C-4′), 193.4 (C-1), 213.1 (C-4) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. $C_{15}H_{19}N_3O_4$ (305.3): C 59.01, H 6.27, N 13.76; found C 59.04, H 6.26, N 13.78.

3-Azido-3-(1-hydroxy-2-oxo-2-phenylethyl)-4-chromanone (11a): A solution of 3-azido-4-chromanone (**10a**) (500 mg, 2.64 mmol) in dry THF (20 mL) was cooled to 0 °C. Phenylglyoxal (**2**) (709 mg, 4.66 mmol)[10] and DBU (43 μL, 44 mg, 0.29 mmol) were added, and the mixture was allowed to stand at 0 °C. When the reaction was complete (3 h), the reaction mixture was concentrated in vacuo and the residue was purified by column chromatography (toluene/ethyl acetate, 9:1, v/v) to give **11a** (763 mg, 89%) as a yellow oil made up of a 63:37 mixture of the *syn* and *anti* diastereomers (by ^{1}H NMR). The diastereomeric mixture was treated with hexane to afford pale yellow crystals, m.p. 88−89.5 °C. The *syn*/*anti* ratio was 59:41 by ^{1}H NMR. IR: $\tilde{\nu}$ = 3465 (OH), 2108 (N_3), 1685 (C=O), 1607, 1477, 1264 cm^{-1}. ^{1}H NMR: ***syn*-11a:** δ = 4.11, 4.29 (AB q, *J* = 12.5 Hz, 2 H, 2-H), 5.56 (s, 1 H, 1′-H) ppm. ***anti*-11a:** δ = 4.21, 4.75 (AB q, *J* = 11.7 Hz, 2 H, 2-H), 5.62 (s, 1 H, 1′-H) ppm. Inseparable signals: δ = 6.95−7.11 (m, 2 H, 6,8-H), 7.36−7.88 (m, 7 H, Ph, 5,7-H) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. ^{13}C NMR: ***syn*-11a:** δ = 67.7 (C-3), 69.3 (C-2), 72.8 (C-1′), 117.7 (C-8), 122.6 (C-6) 134.3 (C-4′′), 135.1 (C-1′′), 136.7 (C-7), 160.6 (C-8a), 188.2 (C-4), 198.1 (C-2′) ppm. ***anti*-11a:** δ = 67.2 (C-3), 69.6 (C-2), 71.1 (C-1′), 118.0 (C-8), 122.4 (C-6), 134.4 (C-4′′), 135.2 (C-1′′), 137.1 (C-7), 160.8 (C-8a), 187.5 (C-4), 198.9 (C-2′) ppm. Inseparable signals: δ = 119.6 (C-4a), 128.1, 128.2, 128.7, 128.8 (C-2′′,3′′,5′′,6′′,5) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. $C_{17}H_{13}N_3O_4$ (323.3): C 63.16, H 4.05, N 13.00; found C 63.22, H 4.04, N 12.98.

3-Azido-6-chloro-3-(1-hydroxy-2-oxo-2-phenylethyl)-4-chromanone (11b): A solution of 3-azido-6-chloro-4-chromanone (**10b)** (400 mg, 1.79 mmol) in dry THF (20 mL) was cooled to 0 °C. Phenylglyoxal (**2**) (720 mg, 4.73 mmol)[10] and DBU (29 μL, 30 mg, 0.20 mmol) were added, and the mixture was allowed to stand at 0 °C until completion of the reaction (3 h). The reaction mixture was concentrated in vacuo and the residue was purified by column chromatography (toluene/ethyl acetate, 9:1, v/v) to give **11b** (415 mg, 65%) as a yellow oil made up of a 60:40 mixture of the *syn* and *anti* diastereomers (by ^{1}H NMR). The diastereomeric mixture was treated with hexane to afford pale yellow crystals, m.p. 105−110 °C. The *syn*/*anti* ratio was 59:41 by ^{1}H NMR. IR: $\tilde{\nu}$ = 3462 (OH), 2124 (N_3), 1702 (C=O), 1683, 1474, 1261 cm^{-1}. ^{1}H NMR: ***syn*-11b:** δ = 4.10, 4.33 (AB q, *J* = 12.7 Hz, 2 H, 2-H), 5.51 (s, 1 H, 1′-H), 6.92 (d, *J* = 9.1 Hz, 1 H, 8-H), 7.80 (d, *J* = 7.5 Hz, 2 H, 2′′,6′′-H) ppm. ***anti*-11b:** δ = 4.19, 4.72 (AB q, *J* = 11.8 Hz, 2 H, 2-H), 5.60 (s, 1 H, 1′-H) 7.00 (d, *J* = 9.0 Hz, 1 H, 8-H), 7.74 (d, *J* = 7.5 Hz, 2 H, 2′′,6′′-H) ppm. Inseparable signals: δ = 7.39−7.51, 7.58−7.71 (2 × m, 3H + 2 H, 3′′,4′′,5′′,5,7-H) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. ^{13}C NMR: ***syn*-11b:** δ = 67.6 (C-3), 69.4 (C-2), 72.9 (C-1′), 119.4 (C-8), 128.2 (C-6), 134.4 (C-4′′), 134.9 (C-1′′), 136.6 (C-7), 159.1 (C-8a), 187.3 (C-4), 197.8 (C-2′) ppm. ***anti*-11b:** δ = 66.7 (C-3), 69.7 (C-2), 71.4 (C-1′), 119.8 (C-8), 128.1 (C-6), 134.6 (C-4′′), 135.1 (C-1′′), 137.0 (C-7), 159.2 (C-8a), 186.5 (C-4), 198.8 (C-2′) ppm. Inseparable signals: δ = 120.5 (C-4a), 127.2, 127.3, 128.7, 128.8 (C-2′′,3′′,5′′,6′′,5) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. $C_{17}H_{12}ClN_3O_4$ (357.8): C 57.07, H 3.38, N 11.75; found C 56.98, H 3.39, N 11.73.

3-Azido-3-(1-hydroxy-2-oxo-2-phenylethyl)-6-methyl-4-chromanone (11e): A solution of 3-azido-6-methyl-4-chromanone (**10e**) (863 mg, 4.25 mmol) in dry THF (50 mL) was cooled to 0 °C. Phenylglyoxal (**2**) (1.14 g, 7.49 mmol)[10] and DBU (0.07 mL, 71 mg, 0.47 mmol) were added to the solution and the mixture was allowed to stand at 0 °C. When the reaction was complete (3.5 h), the reaction mixture was concentrated in vacuo and the residue was purified by column chromatography (toluene/ethyl acetate, 6:1, v/v) to give pure **11e** (1.15 g, 80%) as a yellow crystalline solid made up of a 62:38 mixture of the *syn* and *anti* diastereomers (by ^{1}H NMR). M.p. 102.5−105.5 °C. IR: $\tilde{\nu}$ = 3434 (OH), 2126 (N_3), 1696 (C=O), 1666, 1618, 1492, 1288, 1256, 1216, 830 cm^{-1}. Pure ***anti*-11e** diastereomer was obtained by crystallization from hexane/ethyl acetate (2:1, v/v) mixture.

Isomer *anti*-11e: Colorless block crystals, m.p. 161−163 °C. IR: $\tilde{\nu}$ = 3458 (OH), 2124 (N_3), 1684 (C=O), 1616, 1490, 1290, 1262 cm^{-1}. ^{1}H NMR: δ = 2.32 (s, 3 H, 6-Me), 3.96 (br. s, 1 H, 1′-OH), 4.18, 4.72 (AB q, *J* = 11.7 Hz, 2 H, 2-H), 5.62 (br. s, 1 H, 1′-H) 6.94 (d, *J* = 8.4 Hz, 1 H, 8-H), 7.37−7.44 (m, 3 H, 3′′,5′′,7-H), 7.52 (s, 1 H, 5-H), 7.62 (m, 1 H, 4′′-H), 7.74 (d, *J* = 7.1 Hz, 2 H, 2′′,6′′-H) ppm. ^{13}C NMR: δ = 20.4 (6-Me), 67.2 (C-3), 69.6 (C-2), 71.4 (C-1′), 117.9 (C-8), 119.4 (C-4a), 127.7, 128.7 (C-5,2′′,3′′,5′′,6′′), 132.1 (C-6), 134.4 (C-4′′), 135.3 (C-1′′), 138.3 (C-7), 158.9 (C-8a), 187.6 (C-4), 199.0 (C-2′) ppm. $C_{18}H_{15}N_3O_4$ (337.3): C 64.09, H 4.48, N 12.46, found C 64.01, H 4.47, N 12.48.

Isomer *syn*-11e: ^{1}H NMR: δ = 2.24 (s, 3 H, 6-Me), 4.11, 4.30 (AB q, *J* = 12.3 Hz, 2 H, 2-H), 5.58 (s, 1 H, 1′-H) 6.87 (d, *J* = 8.4 Hz, 1 H, 8-H), 7.29 (dd, *J* = 8.4, 2.0 Hz, 1 H, 7-H), 7.35−7.45 [m, 3 H, 3′′,5′′-H, 7-H (*anti*)], 7.52 (br. s, 1 H, 5-H), 7.57 (m, 1 H, 4′′-H), 7.86 (d, *J* = 7.9 Hz, 2 H, 2′′,6′′-H) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. ^{13}C NMR: δ = 20.3 (6-Me), 67.8 (C-3), 69.3 (C-2), 72.9 (C-1′), 117.5 (C-8), 119.3 (C-4a), 127.6, 128.7, 128.9 (C-5,2′′,3′′,5′′,6′′), 132.2 (C-6), 134.2 (C-4′′), 135.2 (C-1′′), 137.9 (C-7), 158.7 (C-8a), 188.4 (C-4), 198.2 (C-2′) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. $C_{18}H_{15}N_3O_4$ (337.3): C 64.09, H 4.48, N 12.46; found C 65.16, H 4.49, N 12.45.

Crystal Data of *anti*-11e: Colorless block crystals (0.56 × 0.4 × 0.36 mm) of $C_{18}H_{15}N_3O_4$, *M* = 337.33, triclinic, *a* = 7.7112(10) Å, *b* = 8.6527(10) Å, *c* = 13.1405(10) Å, α = 76.07(1), β = 74.55(1), γ = 70.39(1)°, *V* = 784.93(15) Å^3, *Z* = 2, space group: $P\bar{1}$, $\rho_{calcd.}$ = 1.427 g cm^{-3}. Data were collected at 293(1) K, Enraf−Nonius MACH3 diffractometer, Mo-K_α radiation, λ = 0.71073 Å, ω-2θ motion, θ_{max} = 25.27°, 2684 measured, 2108 reflections were unique with $I > 2\sigma(I)$, decay: none. The structure was solved by use of SIR-92 software[13] and refined on F^2 with the SHELX-97[14] program,

publication material was prepared with the WINGX-97 suite,[15] $R(F) = 0.0397$ and $wR(F^2) = 0.1145$ for 2684 reflections, 230 parameters. Residual electron density: 0.212/−0.179 e/Å^3. CCDC-184120 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

3-Azido-3-[1-hydroxy-2-(4-methoxyphenyl)-2-oxoethyl]-6-methyl-4-chromanone (12e): A solution of 3-azido-6-methyl-4-chromanone (**10e**) (100 mg, 0.49 mmol) in dry THF (6 mL) was cooled to 0 °C. 4-Methoxyphenylglyoxal (**3**) (179 mg, 0.98 mmol)[10] and DBU (8.0 µL, 8.2 mg, 0.05 mmol) were added to the solution and the mixture was allowed to stand at 0 °C. When the reaction was complete (3 h), the reaction mixture was concentrated in vacuo and the residue was purified by column chromatography (toluene/ethyl acetate, 6:1, v/v) to give **12e** (157 mg, 87%) as a yellow oil made up of a 67:33 mixture of the *syn* and *anti* diastereomers (by ^{1}H NMR). The diastereomeric mixture was treated with hexane to afford yellow crystals, m.p. 115−118 °C. The *syn*/*anti* ratio was 65:35 by ^{1}H NMR. IR: $\tilde{\nu}$ = 3462 (OH), 2122 (N_3), 1680 (C=O), 1654, 1600, 1514, 1492, 1266, 1178, 1024, 828 cm^{-1}. ^{1}H NMR: ***syn*-12e:** δ = 2.28 (s, 3 H, 6-Me), 4.08, 4.28 (AB q, J = 12.5 Hz, 2 H, 2-H), 5.53 (s, 1 H, 1′-H), 7.31 (d, J = 9.0 Hz, 1 H, 7-H), 7.57 (br. s, 1 H, 5-H), 7.88 (d, J = 9.0 Hz, 2 H, 2′′,6′′-H) ppm. ***anti*-12e:** δ = 2.34 (s, 3 H, 6-Me), 4.18, 4.72 (AB q, J = 11.8 Hz, 2 H, 2-H), 5.59 (s, 1 H, 1′-H), 7.39 (d, J = 8.7 Hz, 1 H, 7-H), 7.59 (br. s, 1 H, 5-H), 7.77 (d, J = 8.6 Hz, 2 H, 2′′,6′′-H) ppm. Inseparable signals: δ = 3.89 (s, 3-H, 4′′-OMe), 6.87−6.96 (m, 3 H, 3′′,5′′,8-H) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. ^{13}C NMR: ***syn*-12e:** δ = 69.1 (C-2), 72.4 (C-1′), 117.4 (C-8), 131.4 (C-2′′,6′′), 137.7 (C-7), 158.6 (C-8a), 188.6 (C-4) ppm. ***anti*-12e:** δ = 69.5 (C-2), 70.8 (C-1′), 117.8 (C-8), 131.2 (C-2′′,6′′), 138.2 (C-7), 159.0 (C-8a), 187.6 (C-4) ppm. Inseparable signals: δ = 20.2 (6-Me), 55.5 (4′′-OMe), 67.7 (C-3), 113.9 (C-3′′,5′′), 119.2 (C-4a), 127.5 (C-5), 127.7 (C-1′′), 132.0 (C-6), 164.6 (C-4′′), 195.9 (C-2′) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. $C_{19}H_{17}N_3O_5$ (367.4): C 62.12, H 4.66, N 11.44; found C 61.97, H 4.68, N 11.40.

3-Azido-3-[2-(4-chlorophenyl)-1-hydroxy-2-oxoethyl]-6-methyl-4-chromanone (13e): A solution of 3-azido-6-methyl-4-chromanone (**10e**) (100 mg, 0.49 mmol) in dry THF (6 mL) was cooled to 0 °C. (4-Chlorophenyl)glyoxal (**4**) (184 mg, 0.98 mmol)[10] and DBU (8.0 µL, 8.2 mg, 0.05 mmol) were added, and the mixture was allowed to stand at 0 °C. When the reaction was complete (3 h), the reaction mixture was concentrated in vacuo and the residue was purified by column chromatography (toluene/ethyl acetate, 6:1, v/v) to give **13e** (159 mg, 87%) as a yellow oil made up of a 58:42 mixture of the *syn* and *anti* diastereomers (by ^{1}H NMR). The diastereomeric mixture was treated with diisopropyl ether to afford yellow crystals, m.p. 146−153 °C. The *syn*/*anti* ratio was 51:49 by ^{1}H NMR. IR: $\tilde{\nu}$ = 3450 (OH), 2122 (N_3), 1684 (C=O), 1616, 1492, 1290, 1094 cm^{-1}. ^{1}H NMR: ***syn*-13e:** δ = 2.27 (s, 3 H, 6-Me), 4.13, 4.34 (AB q, J = 12.1 Hz, 2 H, 2-H), 5.45 (s, 1 H, 1′-H), 6.85 (d, J = 8.5 Hz, 1 H, 8-H), 7.30 (d, J = 8.5 Hz, 1 H, 7-H), 7.78 (d, J = 8.0 Hz, 2 H, 2′′,6′′-H) ppm. ***anti*-13e:** δ = 2.33 (s, 3 H, 6-Me), 4.20, 4.71 (AB q, J = 11.8 Hz, 2 H, 2-H), 5.54 (s, 1 H, 1′-H), 6.94 (d, J = 8.5 Hz, 1 H, 8-H), 7.69 (d, J = 7.9 Hz, 2 H, 2′′,6′′-H) ppm. Inseparable signals: δ = 7.37−7.41 [m, 3 H, 3′′,5′′-H, 7-H (*anti*)], 7.52 (br. s, 1 H, 5-H) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. ^{13}C NMR: ***syn*-13e:** δ = 67.8 (C-3), 69.2 (C-2), 73.2 (C-1′), 117.5 (C-8), 133.3 (C-1′′), 137.9 (C-7), 140.6 (C-4′′), 158.6 (C-8a), 188.1 (C-4) 196.9 (C-2′) ppm. ***anti*-13e:** δ = 67.1 (C-3), 69.5 (C-2), 71.3 (C-1′), 117.8 (C-8), 133.5 (C-1′′), 138.4 (C-7), 140.9 (C-4′′), 158.9 (C-8a), 187.5 (C-4) 197.7 (C-2′) ppm. Inseparable signals: δ = 20.2 (6-Me), 119.2 (C-4a), 127.4, 128.9, 130.0, 130.2 (C-5,2′′,3′′,5′′,6′′), 132.3 (C-6) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. $C_{18}H_{14}ClN_3O_4$ (371.8): C 58.15, H 3.80, N 11.30; found C 58.09, H 3.79, N 11.33.

3-Azido-3-(1-hydroxy-3,3-dimethyl-2-oxobutyl)-6-methyl-4-chromanone (14e): A solution of 3-azido-6-methyl-4-chromanone (**10e**) (100 mg, 0.49 mmol) in dry THF (6 mL) was cooled to 0 °C. *tert*-Butylglyoxal (**5**) (130 mg, 0.98 mmol)[10] and DBU (8.0 µL, 8.2 mg, 0.05 mmol) were added, and the mixture was allowed to stand at 0 °C. When the reaction was complete (2.5 h), the reaction mixture was concentrated in vacuo and the residue was purified by column chromatography (toluene/ethyl acetate, 9:1, v/v) to give **14e** (146 mg, 94%) as a yellow oil made up of a 46:54 mixture of the *syn* and *anti* diastereomers (by ^{1}H NMR). IR (neat): $\tilde{\nu}$ = 3472 (OH), 2114 (N_3), 1682 (C=O), 1620, 1494, 1296, 1222 cm^{-1}. ^{1}H NMR: ***syn*-14e:** δ = 1.21 (s, 9 H, *t*Bu), 2.34 (s, 3 H, 6-Me), 3.65 (d, J = 9.8 Hz, 1 H, 1′-OH), 4.34, 4.48 (AB q, J = 12.0 Hz, 2 H, 2-H), 4.99 (d, J = 9.8 Hz, 1 H, 1′-H), 6.91 (d, J = 8.5 Hz, 1 H, 8-H) ppm. ***anti*-14e:** δ = 1.26 (s, 9 H, *t*Bu), 2.33 (s, 3 H, 6-Me), 3.02 (d, J = 6.1 Hz, 1 H, 1′-OH), 4.48, 4.77 (AB q, J = 12.5 Hz, 2 H, 2-H), 5.16 (d, J = 6.1 Hz, 1 H, 1′-H), 6.92 (d, J = 8.4 Hz, 1 H, 8-H) ppm. Inseparable signals: δ = 7.35−7.37 (m, 1 H, 7-H), 7.75 (overlapping doublets, 1 H, 5-H) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. ^{13}C NMR: ***syn*-14e:** δ = 22.8 (6-Me), 26.4 (C*Me*$_3$), 65.6 (C-3), 69.9 (C-2), 72.1 (C-1′), 119.4 (C-4a), 132.1 (C-6), 138.4 (C-7), 188.8 (C-4), 213.2 (C-2′) ppm. ***anti*-14e:** δ = 20.4 (6-Me), 26.1 (C*Me*$_3$), 67.6 (C-3), 69.7 (C-2), 74.8 (C-1′), 119.1 (C-4a), 131.9 (C-6), 138.0 (C-7), 187.3 (C-4), 211.9 (C-2′) ppm. Inseparable signals: δ = 44.5 (C-3′), 117.8 (C-8), 127.4 (C-5), 159.1 (C-8a) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. $C_{16}H_{19}N_3O_4$ (317.3): C 60.56, H 6.03, N 13.24; found C 60.45, H 6.04, N 13.22.

2-Azidobenzosuberone (15): A mixture of 2-bromobenzosuberone (1.139 g, 4.76 mmol),[11] sodium azide (619 mg, 9.52 mmol), 18-crown-6 (126 mg, 0.47 mmol), and acetone (50 mL) was stirred at room temperature for 25 h. It was then poured into water and extracted with dichloromethane (3 × 50 mL). The dried ($MgSO_4$) solution was concentrated and subjected to column chromatography (hexane/ethyl acetate, 11:1, v/v) to give pure **15** (609 mg, 64%) as a colorless oil that spontaneously crystallized on standing in a refrigerator. M.p. 24−26 °C. IR (neat): $\tilde{\nu}$ = 3064, 2940, 2866, 2098 (N_3), 1692 (C=O), 1596, 1276, 1258, 1216, 768 cm^{-1}. ^{1}H NMR: δ = 1.79, 1.95 (2 × m, 2 × 1 H, 4-H), 2.07−2.28 (m, 2 H, 3-H), 3.00 (m, 2 H, 5-H), 4.28 (dd, J = 10.6, 4.9 Hz, 1 H, 2-H), 7.23 (d, J = 7.5 Hz, 1 H, 6-H), 7.33 (dd, J = 7.7, 7.4 Hz, 1 H, 8-H), 7.45 (dd, J = 7.5, 7.4 Hz, 1 H, 7-H), 7.78 (d, J = 7.7 Hz, 1 H, 9-H) ppm. ^{13}C NMR: δ = 23.6 (C-4), 29.0, 33.4 (C-3,5), 66.1 (C-2), 126.7 (C-8), 129.0, 130.0 (C-6,9), 132.4 (C-7), 136.6 (C-9a), 141.7 (C-5a), 200.6 (C-1) ppm. $C_{11}H_{11}N_3O$ (201.2): C 65.66, H 5.51, N 20.88; found C 65.89, H 5.44, N 21.02.

2-Azido-2-(1-hydroxy-2-oxo-2-phenylethyl)benzosuberone (16): A solution of 2-azidobenzosuberone (**15**) (250 mg, 1.24 mmol) in dry THF (10 mL) was cooled to 0 °C. Phenylglyoxal (**2**) (333 mg, 2.19 mmol)[10] and DBU (20.5 µL, 20.9 mg, 0.14 mmol) were added, and the mixture was allowed to stand at 0 °C for 24 h. Another batch of DBU (20.5 µL) was then added to the reaction mixture. After 4 d, the reaction mixture was concentrated in vacuo and subjected to column chromatography (hexane/ethyl acetate, 3:1, v/v) to give **16** (193 mg, conversion: 54%, yield: 86%, normalized to 100% conversion) as a yellow oil made up of a 75:25 mixture of the **16** and **16′**

diastereomers (by ^{1}H NMR). IR (neat): $\tilde{\nu}$ = 3444 (OH), 2110 (N_3), 1676 (C=O), 1596, 1448, 1252 cm^{-1}. ^{1}H NMR: **16:** δ = 5.60 (s, 1 H, 1′-H), 6.92 (d, *J* = 7.2 Hz, 1 H, 6-H), 7.82 (d, *J* = 7.2 Hz, 1 H, 2′′,6"-H) ppm. **16′:** δ = 5.59 (s, 1 H, 1′-H), 7.93 (d, *J* = 7.2 Hz, 1 H, 2′′,6"-H) ppm. Inseparable signals: 1.58−1.98 (m, 4 H, 3,4-H), 2.74−3.01 (m, 2 H, 5-H), 7.06−7.64 (m, 6 H, 7,8,9,3′′,4′′,5"-H) ppm. NMR spectroscopic data were taken from the spectrum of the diastereomeric mixture. ^{13}C NMR: **16:** δ = 77.1 (C-1′). **16′:** δ = 78.4 (C-1′) ppm. Inseparable signals: 22.3 (C-4), 29.0, 32.2 (C-3,5), 73.8 (C-2), 126.5, 128.1, 128.6, 128.7, 129.1, 131.7, 133.7 (C-6,7,8,9,2′′,3′′,4′′,5′′,6"), 135.6, 138.3, 138.6 (C-5a,9a,1"), 199.5 (C-2′), 204.1 (C-1) ppm. $C_{19}H_{17}N_3O_3$ (335.4): C 68.05, H 5.11, N 12.53; found C 67.90, H 5.33, N 12.36.

Ethyl 3-Azido-2-hydroxy-4-(4-methoxyphenyl)-2-methyl-4-oxobutanoate (18): A solution of 2-azido-1-(4-methoxyphenyl)ethanone (**1d**) (1.00 g, 5.25 mmol) in dry THF (50 mL) was cooled to 0 °C, ethyl 1-oxopropionate (**17**, 1.73 mL, 1.83 g, 15.75 mmol) and DBU (84 μL, 86 mg, 0.56 mmol) were added to the solution, 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 (toluene/ethyl acetate, 9:1, v/v) to give pure **18** (982 mg, conversion: 88%, yield: 69%, normalized to 100% conversion) as a colorless oil made up of a 67:33 mixture of the **18** and **18′** diastereomers (by ^{1}H NMR). Repeated column chromatography (toluene/ethyl acetate, 9:1, v/v) afforded pure diastereomers.

Diastereomer 18: Colorless 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: δ = 1.13 (t, *J* = 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, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 4.55 (s, 1 H, 3-H), 6.95 (d, *J* = 9.1 Hz, 2 H, 3′,5′-H), 7.97 (d, *J* = 9.1 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR: 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): C 54.72, H 5.58, N 13.67; found C 54.59, H 5.52, N 13.75.

Diastereomer 18′: 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: δ =1.35 (t, *J* = 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, *J* = 7.2, 2.2 Hz, 2 H, OCH_2CH_3), 4.67 (s, 1 H, 3-H), 6.96 (dd, *J* = 9.2, 2.1 Hz, 2 H, 3′,5′-H), 7.99 (dd, *J* = 9.2, 2.1 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR: 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): C 54.72, H 5.58, N 13.67; found C 54.51, H 5.54, N 13.62.

3-Benzoyl-5-phenylisoxazole (19a): (a) Mesyl chloride (0.06 mL, 0.77 mmol) and TEA (0.23 mL, 1.63 mmol) were added to a cooled (−15 °C) solution of azido alcohol **6a** (200 mg, 0.68 mmol) (*syn*/*anti* = 77:23) in dry CH_2Cl_2 (5 mL) and the mixture was stirred at room temperature for 1.5 h. The reaction mixture was poured into water and extracted with dichloromethane (3 × 20 mL), and the organic layer was dried (Na_2SO_4), concentrated in vacuo, and purified by column chromatography (hexane/ethyl acetate, 3:1, v/v) to give pure **19a** (66 mg, 39%). White needles, m.p. 81−83 °C (hexane) (ref.[7f] 86−87 °C, ref.[9a] 80−82 °C). IR: $\tilde{\nu}$ = 1656 (C=O), 1449 (isoxazole ring), 1243, 894, 726, 682 cm^{-1}. ^{1}H NMR: δ = 7.05 (s, 1 H, 4-H), 7.46−7.57 (m, 5 H, 3′,5′,3′′,4′′,5"-H), 7.66 (m, 1 H, 4′-H), 7.85 (m, 2 H, 2′′,6"-H), 8.34 (m, 2 H, 2′,6′-H) ppm. ^{13}C NMR: δ = 100.2 (C-4), 126.0 (C-2′′,6"), 126.7 (C-1′′), 128.6 (C-3′,5′), 129.1 (C-3′′,5"), 130.7 (C-2′,6′,4′′), 134.0 (C-4′), 135.7 (C-1′), 162.4 (C-3), 170.7 (C-5), 185.8 (C=O) ppm. $C_{16}H_{11}NO_2$ (249.2): C 77.10, H 4.45 N, 5.62; found C 77.12, H 4.43 N, 5.61. **(b)** Sodium azide (172 mg, 2.65 mmol) was added at room temperature to a stirred solution of *trans*-1,2-dibenzoylethylene dibromide (**26**) (477 mg, 1.20 mmol) [12] in dry DMF (6 mL). The stirring was maintained for 5 h and the mixture was then poured into water and extracted with diethyl ether (2 × 60 mL). The dried (Na_2SO_4) solution was concentrated in vacuo and the crude product was crystallized from methanol to give isoxazole **19a** (90 mg, 30%). M.p. 82−84 °C (ref.[7f] 86−87 °C).

3-(4-Chlorobenzoyl)-5-phenylisoxazole (19b): Mesyl chloride (0.04 mL, 0.51 mmol) and TEA (0.14 mL, 1.02 mmol) were added to a cooled (−15 °C) solution of azido alcohol **6b** (140 mg, 0.42 mmol, *syn*/*anti* = 76:24) in dry CH_2Cl_2 (3 mL), and the mixture was stirred at room temperature for 4 h. The reaction mixture was poured into water and extracted with dichloromethane (3 × 20 mL), and the organic layer was dried ($MgSO_4$), concentrated in vacuo, and purified by column chromatography (hexane/ethyl acetate, 3:1, v/v) to give pure **19b** (55 mg, 46%). Pale yellow needles, m.p. 134−136 °C (hexane). IR: $\tilde{\nu}$ = 1651 (C=O), 1587, 1442 (isoxazole ring), 1252, 897, 851, 765 cm^{-1}. ^{1}H NMR: δ = 7.04 (s, 1 H, 4-H), 7.40−7.54 (m, 5 H, 3′,5′,3′′,4′′,5′′-H), 7.83 (m, 2 H, 2′′,6′′-H), 8.33 (d, *J* = 9.2 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR: δ = 100.2 (C-4), 126.0 (C-2′′,6′′), 126.6 (C-1"), 128.9, 129.1 (C-3′,5′,3′′,5′′), 130.8 (C-4′′), 132.1 (C-2′,6′), 133.9 (C-1′), 140.7 (C-4′), 162.2 (C-3), 170.9 (C-5), 184.3 (C=O) ppm. $C_{16}H_{10}ClNO_2$ (283.7): C 67.74, H 3.55, N 4.94; found C 67.78, H 3.53, N 4.95.

3-(4-Fluorobenzoyl)-5-phenylisoxazole (19c): Mesyl chloride (0.06 mL, 0.77 mmol) and TEA (0.21 mL, 1.51 mmol) were added to a cooled (−15 °C) solution of azido alcohol **6c** (200 mg, 0.64 mmol, *syn*/*anti* = 76:24) in dry CH_2Cl_2 (5 mL), and the mixture was stirred at room temperature for 4 h. The reaction mixture was poured into water and extracted with dichloromethane (3 × 20 mL), and the organic layer was dried ($MgSO_4$), concentrated in vacuo, and purified by column chromatography (hexane/ethyl acetate, 3:1, v/v) to give pure **19c** (83 mg, 48%). Pale yellow needles, m.p. 98−101 °C (hexane). IR: $\tilde{\nu}$ = 1653 (C=O), 1599, 1442 (isoxazole ring), 1253, 1230, 901, 771 cm^{-1}. ^{1}H NMR: δ = 7.05 (s, 1 H, 4-H), 7.21 (dd, J_{ortho} = 9.1, $J_{H,F}$ = 9.0 Hz, 2 H, 3′,5′-H), 7.46−7.55 (m, 3 H, 3′′,4′′,5′′-H), 7.81−7.88 (m, 2 H, 2′′,6′′-H), 8.43 (dd, J_{ortho} = 9.1, $J_{H,F}$ = 5.5 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR: δ = 100.2 (C-4), 115.8 (d, $J_{C,F}$ = 21.8 Hz, C-3′,5′), 126.0 (C-2′′,6′′), 126.6 (C-1"), 129.1 (C-3′′,5′′), 130.8 (C-4′′), 132.0 (C-1′), 133.5 (d, $J_{C,F}$ = 9.6 Hz, C-2′,6′), 162.3 (C-3), 166.4 (d, $J_{C,F}$ = 255 Hz, C-4′), 170.8 (C-5), 183.9 (C=O) ppm. $C_{16}H_{10}FNO_2$ (267.2): C 71.91, H 3.77, N 5.24; found C 71.96, H 3.75, N 5.25.

3-(4-Methoxybenzoyl)-5-phenylisoxazole (19d): Mesyl chloride (0.06 mL, 0.77 mmol) and TEA (0.21 mL, 1.51 mmol) were added to a cooled (−15 °C) solution of azido alcohol **6d** (200 mg, 0.61 mmol, *syn*/*anti* = 87:13) in dry CH_2Cl_2 (5 mL), and the mixture was stirred at room temperature for 5 h. It was then poured into water and extracted with dichloromethane (3 × 15 mL), and the organic layer was dried ($MgSO_4$), concentrated in vacuo, and purified by column chromatography (hexane/ethyl acetate, 3:1, v/v) to give pure **19d** (73 mg, 42%). White needles, m.p. 111−114 °C (hexane). IR: $\tilde{\nu}$ = 1646 (C=O), 1602, 1443 (isoxazole ring), 1252, 1178, 897 cm^{-1}. ^{1}H NMR: δ = 3.88 (s, 3 H, 4′-OMe), 7.00 (d, *J* = 8.8 Hz, 2 H, 3′,5′-H), 7.01 (s, 1 H, 4-H), 7.48 (m, 3 H, 3′′,4′′,5′′-H), 7.83 (dd, *J* = 7.9, 2.5 Hz, 2 H, 2′′,6′′-H), 8.38 (d, *J* = 8.8 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR: δ = 55.5 (4′-OMe), 100.3 (C-4), 113.8 (C-3′,5′), 125.9 (C-2′′,6′′), 126.7 (C-1′′), 128.6 (C-1′), 129.0 (C-3′′,5′′), 130.5 (C-4′′), 133.1 (C-2′,6′), 162.6 (C-3), 164.4 (C-4′), 170.4 (C-5), 183.8 (C=O) ppm. $C_{17}H_{13}NO_3$ (279.3): C 73.11, H 4.69, N 5.02; found C 73.09, H 4.65, N 5.08. When the reaction was repeated starting from pure *syn*-**6d** (80 mg,

0.246 mmol), isoxazole **19d** (26 mg, 38%) was obtained, m.p. 108−110 °C.

3-(4-Methoxybenzoyl)-5-(4-methoxyphenyl)isoxazole (20d): Mesyl chloride (0.03 mL, 0.39 mmol) and TEA (0.11 mL, 0.79 mmol) were added to a cooled (−15 °C) solution of azido alcohol **7d** (117 mg, 0.33 mmol, *syn*/*anti* = 72:28) in dry CH_2Cl_2 (3 mL), and the mixture was stirred at room temperature for 3.5 h. It was then poured into water and extracted with dichloromethane (3 × 15 mL), and the organic layer was dried ($MgSO_4$), concentrated in vacuo, and purified by column chromatography (hexane/ethyl acetate, 3:1, v/v) to give pure **20d** (65 mg, 63%). Pale yellow needles, m.p. 118−121 °C (hexane). IR: $\tilde{\nu}$ = 1652 (C=O), 1592, 1506, 1436 (isoxazole ring), 1252, 1174 cm^{-1}. ^1H NMR: δ = 3.88, 3.91 (2 × s, 2 × 3 H, 4′,4′′-OMe), 6.90 (s, 1 H, 3-H), 7.01 (overlapping doublets, 4 H, 3′,5′,3′′,5′′-H), 7.79 (d, *J* = 8.7 Hz, 2 H, 2′′,6"-H), 8.38 (d, *J* = 9.2 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR: δ = 55.4, 55.5 (4′,4′′-OMe), 99.0 (C-4), 114.0, 114.6 (C-3′,5′,3′′,5′′), 119.7 (C-1"), 127.8 (C-2′′,6′′), 129.0 (C-1′), 133.4 (C-2′,6′), 161.7, 162.9 (C-3,4"), 164.7 (C-4′), 170.8 (C-5), 184.5 (C=O) ppm. $C_{18}H_{15}NO_4$ (309.3): C 69.89, H 4.89, N 4.53; found C 69.91, H 4.69, N 4.55.

5-(4-Chlorophenyl)-3-(4-methoxybenzoyl)isoxazole (21d): Mesyl chloride (0.02 mL, 0.25 mmol) and TEA (0.07 mL, 0.49 mmol) were added to a cooled (−15 °C) solution of azido alcohol **8d** (74 mg, 0.20 mmol, *syn*/*anti* = 74:26) in dry CH_2Cl_2 (2 mL) and the mixture was stirred at room temperature for 4 h. It was then poured into water and extracted with dichloromethane (3 × 10 mL), and the organic layer was dried ($MgSO_4$), concentrated in vacuo, and purified by column chromatography (toluene/ethyl acetate, 6:1, v/v) to give pure **21d** (30 mg, 48%). Pale yellow needles, m.p. 185−188 °C (hexane/ethyl acetate). IR: $\tilde{\nu}$ = 1646 (C=O), 1602, 1438 (isoxazole ring), 1252, 896 cm^{-1}. ^1H NMR: δ = 3.90 (s, 3 H, 4′-OMe), 7.00 (d, *J* = 8.9 Hz, 2 H, 3′,5′-H), 7.01 (s, 1 H, 4-H), 7.48 (d, *J* = 8.8 Hz, 2 H, 3′′,5′′-H), 7.78 (d, *J* = 8.8 Hz, 2 H, 2′′,6"-H), 8.37 (d, *J* = 8.9 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR: δ = 55.5 (4′-OMe), 100.7 (C-4), 113.9 (C-3′,5′), 125.2 (C-1"), 127.2 (C-2′′,6"), 128.5 (C-1′), 129.5 (C-3′′,5′′), 133.2 (C-2′,6′), 136.7 (C-4′′), 162.7 (C-3), 164.5 (C-4′), 169.3 (C-5), 183.7 (C=O) ppm. $C_{17}H_{12}ClNO_3$ (313.7): 65.08, H 3.86, N 4.46; found C 65.12, H 3.79 N 4.47.

5-*tert*-Butyl-3-(4-methoxybenzoyl)isoxazole (22d): Mesyl chloride (0.04 mL, 0.51 mmol) and TEA (0.14 mL, 1.02 mmol) were added to a cooled (−15 °C) solution of azido alcohol **9d** (130 mg, 0.43 mmol) (**9d**/**9d′** = 89:11) in dry CH_2Cl_2 (2.5 mL) and the mixture was stirred at room temperature for 3.5 h. It was then poured into water and extracted with dichloromethane (3 × 15 mL), and the organic layer was dried ($MgSO_4$), concentrated in vacuo, and purified by column chromatography (hexane/ethyl acetate, 6:1, v/v) to give pure **22d** (26 mg, 23%) as a colorless oil. IR (neat): $\tilde{\nu}$ = 1652 (C=O), 1600, 1574, 1448 (isoxazole ring), 1252, 1178, 896 cm^{-1}. ^1H NMR: δ = 1.40 (s, 9 H, (*t*Bu), 3.89 (s, 3 H, 4′-OMe), 6.45 (s, 1 H, 4-H), 6.98 (d, *J* = 8.8 Hz, 2 H, 3′,5′-H), 8.34 (d, *J* = 8.8 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR: δ = 28.8 (C**Me**$_3$), 32.8 (**C**Me$_3$), 55.5 (4′-OMe), 99.4 (C-4), 113.8 (C-3′,5′), 128.8 (C-1′), 133.2 (C-2′,6′), 161.9 (C-3), 162.9 (C-4′), 181.9 (C-5), 184.5 (C=O) ppm. $C_{15}H_{17}NO_3$ (259.3): C 69.48, H 6.61, N 5.40; found C 69.52, H 6.58, N 5.43.

Ethyl 3-Azido-4-(4-methoxyphenyl)-2-methyl-4-oxo-2-butenoate (28): Mesyl chloride (0.1 mL, 1.32 mmol) was added to a cooled (−15 °C) solution of azido alcohol **18** (203 mg, 0.66 mmol, **18**/**18′** = 67:33) in dry pyridine (5 mL) and the mixture was stirred at room temperature for 25 h. It was then poured into water and extracted with dichloromethane (3 × 30 mL), and the organic layer was extracted with saturated $NaHCO_3$ solution (25 mL) and water, dried ($MgSO_4$), concentrated in vacuo, and purified by column chromatography (hexane/ethyl acetate, 3:1, v/v) to give pure **28** (66 mg, conversion: 69%, yield: 50%, normalized to 100% conversion) as a yellow oil. IR (neat): $\tilde{\nu}$ = 2108 (N_3), 1712, 1662 (C=O), 1598, 1290, 1264, 1244, 1172, 844 cm^{-1}. ^1H NMR: δ = 0.98 (t, *J* = 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, *J* = 7.0 Hz, 2 H, OCH_2CH_3), 6.98 (d, *J* = 9.4 Hz, 2 H, 3′,5′-H), 7.92 (d, *J* = 9.4 Hz, 2 H, 2′,6′-H) ppm. ^{13}C NMR: δ = 12.6 (2-Me), 13.5 (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): C 58.13, H 5.23, N 14.53; found C 57.91, H 5.20, N 14.49.

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