Base-Promoted Reactions of α-Azido Ketones with Aldehydes and Ketones: A Novel Entry to α-Azido-β-hydroxy Ketones and 2,5-Dihydro-5-hydroxyoxazoles

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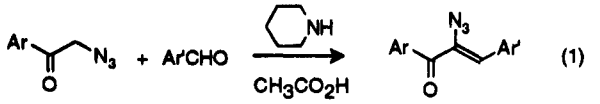
The base-promoted reaction of α-azido ketones with aldehydes and ketones provides a new and simple route to either α-azido-β-hydroxy ketones, which are valuable 1,2,3-trifunctionalized synthons, or 2,5-dihydro-5-hydroxyoxazoles, which are a little known type of oxazoline. These two products are formed by the electrophilic trapping of two different anions that are produced sequentially during the reaction. The α-azido-β-hydroxy ketones are formed by an aldol reaction between an enolate of the α-azidoketone and an aldehyde. The 2,5-dihydro-5-hydroxyoxazoles are formed by electrophilic trapping of an imino anion which is produced by nitrogen loss from the α-azido ketone enolate.

Introduction

α-Azido ketones **1** which also have α-hydrogens are highly base-sensitive and undergo base-promoted loss of nitrogen to form α-imino ketones **2** (or 1,2-diketones by hydrolysis) (Scheme 1).[2,3] This reaction has limited synthetic value unless the α-imino ketone **2** has β-hydrogens and is thus able to tautomerize to an α-amino enone **3**. This sequence has been utilized for the synthesis of α-amino cyclic enones, heterocyclic enones,[4] and acyclic enamines which have a functional group in the β-position capable of conjugation with the enone.[5] It was suggested that deprotonation of **1** affords carbanion **A** which extrudes nitrogen to yield imino anion **B** and hence the observed products (Scheme 1). A key feature of this scenario is the assumption that two discrete anionic intermediates **A** and **B** are produced sequentially. To the best of our knowledge only two reports have appeared which have used either of these intermediates as nucleophiles. It was found that the condensation of phenacyl azides and aromatic aldehydes could be catalyzed by piperidinium acetate (eq 1).[6] While the products could be formed by dehydration of an initial aldol product, the authors suggested that the reaction actually occurs between an enol of the azido ketone and an iminium ion of the aldehyde, hence the β-hydroxy-α-azido ketone is not formed nor is it an intermediate.

More recently lithium enolates of phenacyl azides were generated from azido ketones at −78 °C and trapped with



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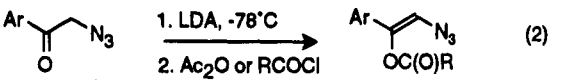
acetic anhydride or acid chlorides to produce the O-acylated vinyl azides (eq 2).[7] Only α-azidoacetophenone derivatives gave satisfactory results, however.



(2)

Recently we reported a general and efficient synthesis of α-azido ketones **1** which allows the high yield preparation of azides **1** of widely varying structure.[8] This easy access to **1** makes possible for the first time a broad survey of the reactivity and synthetic utility of α-azido ketones **1**. Our first goal was to study the possibility of generating anions **A** and/or **B** and trapping them with carbonyl electrophiles. This process could provide interesting and useful multifunctionalized structures of general formulae **C** and **D** (Scheme 1).

In this contribution we wish to describe the base-promoted transformations of α-azido ketones **1** in the presence of aldehydes and ketones as electrophiles. Either α-azido-β-hydroxy ketones from the trapping of enolate **A** or 2,5-dihydro-5-hydroxyoxazoles from the trapping of imino anion **B** can be prepared by controlling the structures of the substrate and electrophile and the reaction conditions.

Results and Discussion

2-Azido-3-hydroxy Ketones via Aldol Reactions. We first examined the reaction of 2-azido-1-phenyl-1-ethanone (phenacyl azide) **5** with aldehydes **4a–c** in the presence of amine bases and were delighted to find that α-azido-β-hydroxy ketones **14a–c** were obtained in moderate-to-good yields (eq 3, Table 1, entries 1–3). A catalytic amount of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was found to be the best way to promote the

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Scheme 1

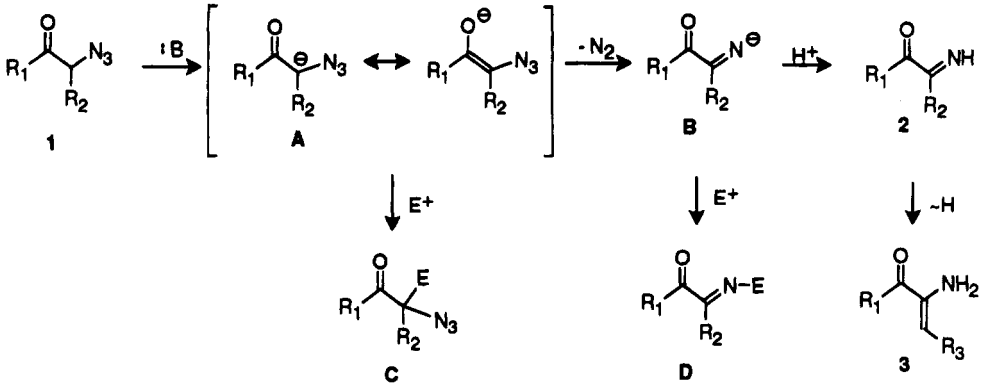


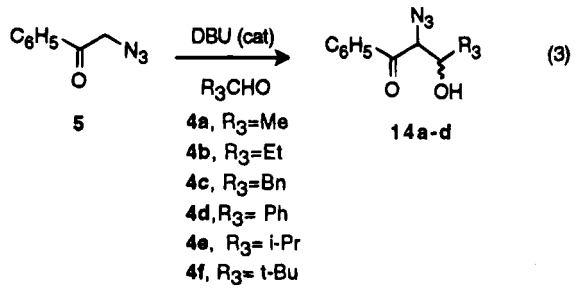
Table 1. Synthesis of α-Azido-β-hydroxy Ketones

entry	reactants	proced[a]	T (°C)	t (h)	product	yield (%)	*syn/anti*	remarks
1	**5** + MeCHO (**4a**)	A[b]	0	24	**14a**	70	55:45	–
2	**5** + EtCHO (**4b**)	A[b]	rt	3	**14b**	33	65:35	–
3	**5** + BnCHO (**4c**)	A[b]	rt	2.33	**14c**	49	76:24	–
4	**5** + PhCHO (**4d**)	A[b]	−25	28	**14f**	~9[c]	–	+61% **5**
5		A[b]	rt	27	**14f**	~8[c]	~1:1	+22% **5**
6	**6** + **4a**	B[b]	0	2.5	**15a**	30	52:48	+11% **16**
7	**7** + **4a**	C[d]	0	95	**17a**	13	–	dec
8		B[d]	0	5	**17a**	85	54:46	–
9	**8** + **4a**	B[d]	0	6.5	**18a**	95	45:55	–
10	**8** + **4b**	B[d]	0	24	**18b**	75	65:35	–
11	**9** + **4a**	C[b]	0	4.75	**21**	29[c]	38:62	–
12	**10** + **4b**	B[b]	0	1.5	**22**	0	–	15% **24**
13	**11** + **4b**	C[b]	−25	92	**23**	0	–	35% **25**
14	**12** + **4a**	B[d]	0	168	–	–	–	dec
15		C[b]	0	1.5	**26**	34	–	–

[a] Procedure A: 0.1 equiv of base and 3−4 equiv of carbonyl component in absolute THF solution. Procedure B: 1 equiv of base, carbonyl component as solvent. Procedure C: 1 equiv of base and 3−4 equiv of carbonyl component in absolute THF solution. [b] With DBU as base. [c] Unstable product. [d] With TEA as base.

reaction. The use of 1 equiv of DBU resulted in vigorous evolution of nitrogen and a dramatic decrease in the yield of the aldol product. The use of triethylamine (TEA) gave no aldol products but instead resulted in slow decomposition of the starting azide **5**.

In terms of the reaction scenario shown in Scheme 1, these observations suggest that the reaction of enolate **A** with aldehydes to give aldol products is competitive with nitrogen extrusion from enolate **A** to give imino anion **B**. Catalytic amounts of the base produces low concentrations of **A** in an excess of the electrophile and maximizes the condensation of the enolate **A** with the



(3)

aldehyde, whereas the generation of anion **A** in higher concentrations using stoichiometric amounts of base appears to favor the competitive decomposition processes.

Because of the delicate kinetic balance between aldol condensation and other base-promoted decompositions of enolate **A**, any steric or electronic factor which slows the rate of the condensation process should have a drastic effect on the yield of the aldol product. For example, α-branched aldehydes fail to give aldol-type products in effective yields. The reaction of **5** and benzaldehyde (**4d**) gave azido alcohol **14d** which could only be isolated in low yield (Table 1, entries 4, 5), and the product was very unstable. The ^{1}H-NMR spectrum of the crude product, which was obtained by rapid chromatography on a short column in 80−85% purity, was in good accordance with the expected structure. All attempts at further chromatographic purification failed. The reaction of **5** and isobutyraldehyde (**4e**) or trimethylacetaldehyde (**4f**) failed to give aldol products under any conditions. Azide **5** also failed to react with ketones such as methyl ethyl ketone or 2-cyclopentenone.

The assignment of *syn* and *anti* stereochemistry in **14a−d** was made from the coupling constants of the methine protons at C-2 and C-3.[9] The diastereoselectivity in the formation of **14** is low; the weak *syn* preference appears to increase slightly with increasing steric bulk of the aldehyde (Table 1). This low diastereoselection seems characteristic of condensations of α-substituted ketones with substitutents other than alkyl groups at the α-position. A very similar low diastereoselection was recently reported for the samarium hexamethyldisilazide-catalyzed aldol reaction of α-chloro ketones.[10]

As a next step, we extended the study to include secondary α-azidoalkyl aryl ketones such as **6−8** as the enolate precursors. Attachment of an alkyl group to the nucleophilic center at the α-position is expected to sterically impede carbonyl addition. It was found for these substrates that the reaction with aldehydes re-

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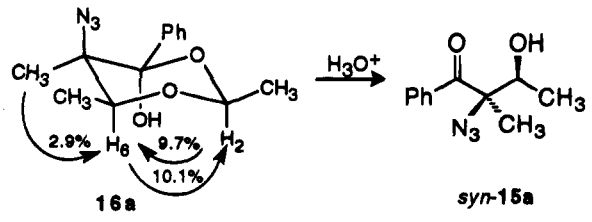
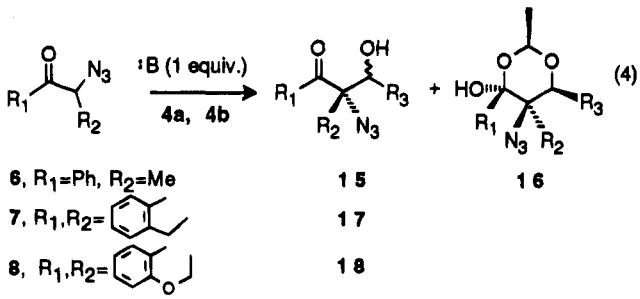


Figure 1.

quires at least 1 equiv of base and a larger excess of the aldehyde component.

Reaction of 2-azido-1-phenyl-1-propanone (**6**) in the presence of 1 equiv of DBU using acetaldehyde (**4a**) itself



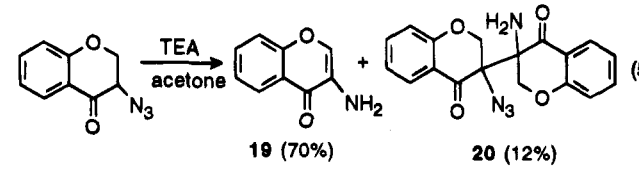
as solvent (Table 1, entry 6) resulted in the isolation of aldol product **15a** in 30% yield as a diastereomeric mixture and 1,3-dioxane derivative **16a** in 11% yield which appeared to be a single diastereomer. Most likely **16a** originates from the addition of the initially formed alkoxide to a second molecule of **4a** followed by a ring closure at the carbonyl carbon. This picture was verified by a control experiment. When **15a** was allowed to react with 3 equiv of acetaldehyde in THF for 7 days in the presence of 1 equiv of DBU, a mixture of **16a** (in this case a 73:27 diastereomeric mixture) and the starting material **15a** was obtained. As no evidence of azido ketone **6** or other products could be detected in the product mixture, this experiment also excludes the possibility of a *retro*-aldol reaction under basic conditions.

The relative stereochemistry of hemiketal **16a** was determined by NOE difference measurements (Figure 1) and appears to be the most stable isomer since the largest groups all occupy equatorial positions. Hydrolysis of **16a** by treatment with 1 N hydrochloric acid–EtOAc (10:1) gave **15a** which must have *syn* stereochemistry as dictated by the stereochemistry determined for **16a** (Figure 1). With the NMR signals for *syn*-**15a** known, the signals for *anti*-**15a** could be obtained from the diasteromeric mixture of **15a** obtained in the aldol reaction between **5** and **4a**.

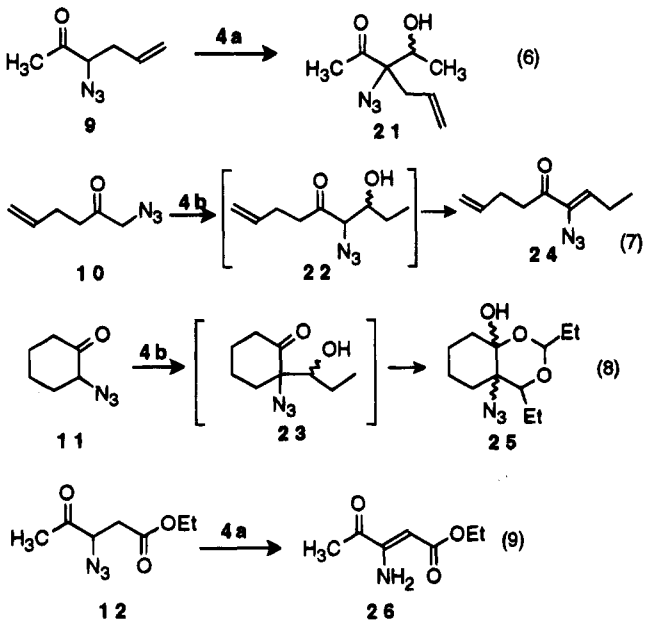
The correlations of the chemical shift data for the *syn-anti* diastereomers of **14a–c** and **15a** showed that (a) the methine proton on the carbinol carbon is found at lower field in the *syn* isomer than in the *anti* isomer, and (b) the ^{13}C chemical shift of the methyl group on the azido carbon in **15a** is at lower field in the *syn* isomer. This latter observation parallels previous ^{13}C chemical shift correlations for aldol products with methyl groups at C-2.[9] These two correlations were then used as guidelines to assign the *syn-anti* isomers of diastereomeric α-azido-β-hydroxy ketones **17a** and **18a,b** which have carbon groups other than methyl attached at C-2 (vide infra). These product assignments must only be regarded as tentative because some discrepancies in the chemical shifts were observed.

Reaction of 2-azido-1-indanone (**7**) with **4a** gave aldol product **17a** (Table 1, entries 7, 8), while reaction of 3-azido-4-chromanone (**8**) with **4a** and **4b** gave and **18a** and **18b**, respectively (Table 1, entries 9, 10). Because of the increased acidity of the α-hydrogen in these substrates, triethylamine was sufficient to initiate the reaction. The best results were obtained if the aldehyde was used as the reaction solvent. The success of these aldol reactions is noteworthy because it is known that azides **7** and **8** show a marked tendency toward loss of nitrogen and the formation of imino anion **B** in the presence of base. Subsequent tautomerization leads to stabilized enamines **3** (Scheme 1).[4c,g] However, using a large excess of aldehyde in order to trap the enolate prior to nitrogen loss gave α-azido-α-(1-hydroxyalkyl)benzocyclanones **17a** and **18a,b** as *syn*/*anti*-mixtures in excellent yield, but with very low diastereoselectivity (Table 1, entries 7–10). Comparison of Entries 7 and 8 demonstrates clearly that competitive reactions of the enolate **A** determine the product partitioning. In the presence of lower concentrations of the aldehyde **4a** (entry 7), nitrogen loss from the enolate of **7** and subsequent reactions of the imino anion **B** dominate the chemistry, and the yield of aldol product **17a** is very poor. Using much higher aldehyde concentrations (entry 8) efficiently traps the enolate **A** and gives a high yield of the aldol product.

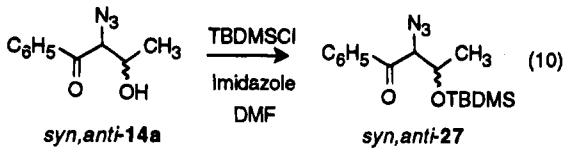
Similar consequences were found for the reactions of 3-azido-4-chromanone (**8**). Simple aldehydes **4a** and **4b** gave high yields of the aldol products **18a** and **18b** when used as the reaction solvent (entries 9, 10). Chain branching in the aldehyde as in isobutyraldehyde **4e** completely suppressed the aldol-type reaction. Similarly, no aldol product could be detected when azide **8** was treated with TEA in acetone solution (eq 5). Acetone trapping of the enolate **A** is unable to compete with nitrogen loss to **B** (Scheme 1). The major product of the reaction was 3-aminochromone (**19**) (70%), the tautomerized form of the primary product 3-iminochromanone. In addition to **19**, a unique dimeric byproduct **20** was also obtained in 12% yield. The 3,3′-bonding pattern of the chromanone subunits of **20** was assigned on the basis of its $^1H-^{13}C$ coupled ^{13}C-NMR spectrum. Formation of **20** may be rationalized by an attack of the enolate of **8** on an α-imino ketone **2** (Scheme 1).



Next a group of aliphatic α-azido ketones **9–12** (eqs 6–9 and Table 1, entries 11–15) were examined as aldol substrates. Although it appears that an aldol reaction does occur for **9–11** which gives α-azido-β-hydroxy ketone products **21–23** in low yields, the reaction mixtures are much more complex, and aldol products **22** and **23** are apparently transformed under the reaction conditions into secondary products **24** and **25**, respectively. Keto azide **12** failed to undergo the aldol reaction but did produce enamine **26** by loss of nitrogen followed by tautomerization. It is not clear why the aliphatic series of azido ketones gives such divergent results, but it may be that lowered acidity of the α-proton and/or the presence of α′-protons could be influencing the chemistry.

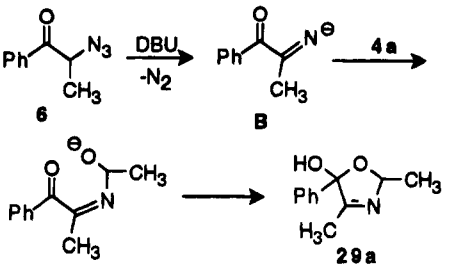


α-Azido-β-hydroxy ketones available by the reaction of α-azido ketones and aldehydes represent valuable new trifunctionalized molecules which could find wide utility in synthesis.[11] Their different functionalities allow selective manipulations. Reduction of the azido group in the presence of a carbonyl function is well documented.[4b,12] The hydroxyl group of these azido alcohols can be selectively silylated. Treatment of model compound **14a** with *tert*-butyldimethylsilyl chloride in the presence of imidazole and DMF[13] yielded the silyl ether **27** (eq 10). Steric hindrance about the secondary hydroxyl group resulted in relatively slow silylation.[14]

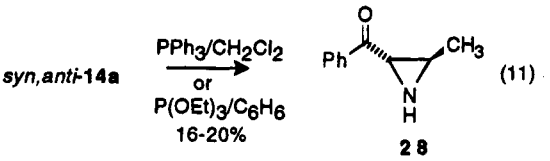


Treatment of **14a** with trivalent phosphorus compounds such as triphenylphosphine or triethyl phosphite furnished *trans*-2-benzoyl-3-methylaziridine **28** (eq 11). The formation of aziridines from 1,2-azido alcohols *via* the intramolecular attack of hydroxyl group on the initially formed phosphinimine has been reported,[15,16] but this is the first example of such a ring closure in the presence of an adjacent carbonyl group. In spite of the relatively low yield, this transformation yields 2-acyl-3-alkylaziridines which, in contrast to the easily available

Scheme 2



and widely-investigated 2-aroyl-3-arylaziridines (chalcone aziridines),[17,18] have not been described.



These studies have revealed that both phenacyl azide and substituted α-azidophenones can be used successfully in the aldol reaction with unhindered aldehydes to produce α-azido-β-hydroxy phenones in moderate to good yields (Table 1). While the reaction is very sensitive to steric effects in the aldehyde electrophile, appropriate adjustment of the aldehyde and base can often produce synthetically useful yields. In general, best results are obtained when the enolate of the azido ketone is generated in low concentrations in the presence of an excess of the aldehyde electrophile. For phenacyl azide 3–4 equiv of the aldehyde and a catalytic amount of base fulfill these requirements, while for α-azidophenones, using the aldehyde as the reaction solvent in the presence of 1 equiv of the base produces the best conditions for the aldol reaction. Unfortunately diastereoselectivity in the process is low. Aliphatic azido ketones appear to undergo the aldol reaction as well, but these reactions cannot be considered synthetically viable due to secondary reactions of the aldol products and complex reaction mixtures which result.

2,5-Dihydro-5-hydroxyoxazoles. Careful TLC analysis of the reaction mixture of 2-azido-1-phenyl-1-propanone (**6**) and excess of acetaldehyde (Table 1, Entry 6) indicated that, in addition to the aldol-derived products **15a** and **16**, a highly polar product was produced in low yield which had a low R_f value and was unstable during chromatography on silica gel. This compound was found to be 2,5-dihydro-2,4-dimethyl-5-hydroxy-5-phenyloxazole (**29a**). This product results from nucleophilic addition of an imino anion **B** to the aldehyde carbonyl group followed by intramolecular cyclization (Scheme 2).

Since **29a** is a rather unique product, conditions were sought to maximize its production. According to the chemistry outlined in Scheme 1, enolate **A** can undergo either the aldol reaction or nitrogen loss to imino anion **B**. Since **29a** results from a nucleophilic reaction of imino anion **B**, its formation could be increased by minimizing the competing aldol reaction. As seen earlier this can be done by lowering the concentration of the trapping aldehyde and/or by increasing the steric bulk of the aldehyde by chain branching at the α-carbon. Thus by

(11) In contrast with α-azido-β-hydroxy ketones, α-azido-β-hydroxy esters are well-known compounds easily available by nucleophilic displacement of α-sulfonyloxy-β-hydroxy esters. Fleming, P. R.; Sharpless, K. B. *J. Org. Chem.* **1991**, *56*, 2869. Hoffman, R. V.; Kim, H.-O. *J. Org. Chem.* **1991**, *56*, 6759 and references cited therein.

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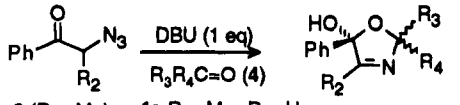
Table 2. Synthesis of 2,5-Dihydro-5-hydroxyoxazoles

entry	reagents	proced[a]	T (°C)	t (h)	product	yield (%)[b]	syn/anti[f]
1	**6** + **4a**	C[c]	0	27	**29a**	55	42:58
2	**6** + **4b**	C[c]	0	25	**29b**	62	42:58
3	**6** + **4g**	C[c]	−25	46	**29g**	39(64)[d]	31:69 (47:53)[d]
4	**6** + **4h**	C[c]	0	22	**29h**	73	90:10
5	**13** + **4d**	C[e]	rt	24	**30d**	78	57:43
6	**13** + **4e**	C[e]	rt	20	**30e**	72	85:15
7	**13** + **4f**	C[e]	rt	42	**30f**	64	47:53
8	**13** + **4i**	B[e]	rt	19.5	**30i**	65	–
9	**13** + **4j**	B[e]	rt	18	**30j**	74	–

[a] Procedure B: 1 equiv of base, oxo component as solvent. Procedure C: 1 equiv of base and 3−4 equiv of oxo component in absolute THF solution. [b] Yields refer to pure crystalline products. [c] With DBU as base. [d] Data for the pure but oily mixture of diastereomers obtained by chromatography. [e] With TEA as base. [f] *Syn* refers to the C-2 substituent being *syn* to the hydroxyl group at C-5 and *anti* refers to the C-2 substituent being *anti* to the C-5 hydroxyl group.

reacting **6** with 1 equiv of DBU and only 3−4 equiv of **4a** in dry THF, **29a** was obtained as the major product in 55% yield. (Table 2, Entry 1).

Using these conditions α-azidopropiophenone (**6**) and α-azidodeoxybenzoin (**13**) were reacted with a range of aldehydes to give the corresponding oxazolines **29** and **30**, respectively, in good yield (eq 12). As the data in Table 2 indicate, there is no marked steric influence of the aldehyde component (entries 6, 7), and electrophiles such as (hetero)aromatic aldehydes also give good results (entries 4, 5). Moreover, oxazolines **30i,j** were obtained in the reaction of **13** with ketones, as well, although the use of the ketones as solvent was necessary in these cases (Table 2, entries 8, 9).



(12)

6 (R_2 = Me) **13** (R_2 = Ph)

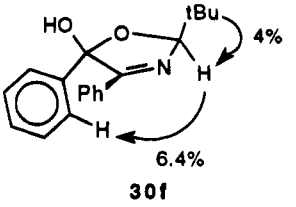
4a R_3=Me, R_4=H
4b R_3=Et, R_4=H
4d R_3=Ph, R_4=H
4e R_3=iPr, R_4=H
4f R_3=tBu, R_4=H
4g R_3=$PhCH_2CH_2$, R_4=H
4h R_3=2-pyridyl, R_4=H
4i R_3=R_4=Me
4j R_3R_4=$(CH_2)_4$

29 (R_2 = Me) **30** (R_2 = Ph)

Because the nucleophilic center of imino anion **B** is less sterically hindered, a much wider range of carbonyl reactants can be employed for producing oxazolines than can be used in the aldol-type reaction of enolate **A**. However oxazoline formation is limited to azido ketones whose imino anions do not undergo rapid tautomerism, such as **6**, which does not appear to tautomerize readily, and **13**, which is incapable of tautomerism because it lacks β-hydrogens. Azido ketones with β-hydrogens such as **7**, **8**, and **12** all lose nitrogen rapidly under the reaction conditions but fail to give oxazoline products. Apparently tautomerism is more rapid than nucleophilic addition to the carbonyl group.

2,5-Dihydro-5-hydroxyoxazoles **29**, **30** are stable under neutral or basic conditions but show only moderate stability in the presence of acids. A slow decomposition was observed on silica gel, although rapid chromatography may be used for partial purification in most cases.

Using aldehydes as electrophiles results in the formation of mixtures of diastereomers. The stereochemical



30f

Figure 2.

assignments for the series are based on NOE difference measurements performed on the major diastereomer of 2,5-dihydro-2-*tert*-butyl-4,*t*-5-diphenyl-*c*-5-hydroxyoxazole (**30f**) (Figure 2). It was found that the bulky *tert*-butyl substituent at C-2 is *syn* to the C-5 hydroxyl group and is designated C-2-*syn*-OH (*syn*). The diastereomer is designated C-2-*anti*-OH (*anti*). The C-2 proton appears at lower field in the C-2-*syn*-OH isomer than in the C-2-*anti*-OH diastereomer since it is opposite the C-5 phenyl group in the *syn* isomer. Thus the stereoselectivity for diasteromeric mixtures was determined by assigning the downfield C-2 methine signal to the C-2-*syn*-OH diastereomer and the upfield C-2 signal to the C-2-*anti*-OH diastereomer. As shown in Table 2, the diastereoselectivity of oxazoline formation is generally low unless a bulky substituent (Table 2, entry 6), or a group capable of hydrogen bonding (Table 2, entry 4) is present at C-2 of the oxazoline. These substituents are usually *cis* to the 5-hydroxyl group.

The base-promoted reaction of α-azido ketones with aldehydes and ketones offers a new and easy access to 2,5-dihydrooxazoles. Contrary to the well-known 4,5-dihydro isomers,[19] 2,5-dihydrooxazoles are a rare class of of compounds and only few methods have been elaborated for their preparation. The most common method for producing the 2,5-dihydrooxazole ring system is the 1,3-dipolar cycloaddition of nitrile ylides, usually generated photochemically from 1-azirines, to carbonyl compounds.[20,21] Other approaches, such as intramolecular azide−olefin cycloaddition[22] or copper(II) complex-catalyzed coupling of diarylmethanimines with aromatic α-diazo ketones,[23] have also been reported but these methods have significant structural limitations. 2,5-Dihydrooxazoles with oxygen substituents at C-5 are even more rare. 5-Alkoxy-2,5-dihydrooxazoles are available by the photoreaction of 1-azirines and carboxylic acid esters that are activated by electron-withdrawing groups.[20] The only previously reported route to 2,5-dihydro-5-hydroxyoxazoles involves the cyclization of 3-(N-*tert*-butyl-N-methylhydrazono)-1,1,1-trifluoroalkan-2-ones using wet silica gel, but this method is limited to the synthesis of 5-hydroxy-5-trifluoromethyl derivatives.[24] The present method allows access to a much wider range

(19) For reviews see: (a) Maryanoff, B. E. Oxazoles and Oxazolines in Organic Synthesis. In: *Oxazoles*; Turchi, I. J., Ed., Interscience: New York, 1986; p 963. (b) Gant, T. G.; Meyers, A. I. *Tetrahedron* **1994**, *50*, 2297.

(20) For a review see: Nair, V. Azirines. In: *The Chemistry of Heterocyclic Compounds, Vol. 42., Small Ring Heterocycles, Pt. 1.*; Hassner, A., Ed.; Interscience: New York, 1983; p 217.

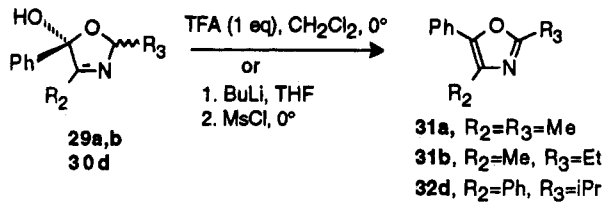
(21) (a) Kitamura, T.; Kobayashi, S.; Taniguchi, H. *J. Org. Chem.* **1984**, *49*, 4755. (b) Padwa, A.; Gasdaska, J. R.; Tomas, M.; Turro, N. J.; Cha, Y.; Gould, I. R. *J. Am. Chem. Soc.* **1986**, *108*, 6739.

(22) Hassner, A.; Amarasekara, A. S.; Andisik, D. *J. Org. Chem.* **1988**, *53*, 27.

(23) Singh, G. S. *Indian J. Chem.* **1987**, *26B*, 270.

(24) (a) Kamitori, Y.; Hojo, M.; Masuda, R.; Wada, M.; Takahashi, T. *Heterocycles* **1994**, *37*, 153. (b) Kamitori, Y.; Hojo, M.; Masuda, R.; Takahashi, T.; Wada, M.; Hiyama, T.; Mimura, Y. *Heterocycles* **1994**, *38*, 803.

Scheme 3



of potential structures, the major constraint being that the starting azidoketone should lack β-protons or its imine derivative **2** should show limited tendency for tautomerization.

No detailed studies were performed on the chemistry of 2,5-dihydro-5-hydroxyoxazoles but their obvious utilization for the synthesis of oxazoles was demonstrated (Scheme 3). Oxazolines **29a,b**, and **30d** were converted into the corresponding oxazoles **31a,b**, and **32d** either by treatment with 1 equiv of trifluoroacetic acid (TFA) or by initial conversion to the corresponding mesylate. In the latter case some unreacted starting material was recovered since the alkoxide ion generated in the reaction promotes the elimination of methanesulfonic acid and gives back the starting material.

In summary, we have found that the base-promoted reaction of α-azido ketones with aldehydes and ketones provides a new and simple route to either α-azido-β-hydroxy ketones, which are valuable 1,2,3-trifunctionalized synthons, or 2,5-dihydro-5-hydroxyoxazoles, which are a little known type of oxazoline. These two products are formed by the electrophilic trapping of two different anions that are produced sequentially during the reaction. The α-azido-β-hydroxy ketones are formed by an aldol reaction between an enolate of the α-azido ketone and an aldehyde. The 2,5-dihydro-5-hydroxyoxazoles are formed by electrophilic trapping of an imino anion which is produced by nitrogen loss from the α-azido ketone enolate. Investigations of the reactions of these anions with various dicarbonyl compounds and other C-electrophiles are in progress.

Experimental Section

General. All chemicals were of reagent grade and used as received. THF was freshly distilled from sodium benzophenone ketyl. Melting points are uncorrected. ^{1}H-NMR (200 and 400 MHz) and ^{13}C-NMR (50 and 100 MHz) spectra were recorded in $CDCl_3$ solution, using TMS as internal standard. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ. Column chromatography utilized Silica gel 60 (Aldrich), 70–230 mesh particle size for gravity and 230–400 mesh for flash chromatography. TLC was carried out on Kieselgel 60 F_{254} plastic sheets (Merck). Starting α-azido ketones were synthesized according to the procedure reported previously.[8]

Caution: While the azides prepared and used in this study have never exhibited any tendency toward violent decomposition, they should be handled with precautions appropriate for materials capable of such behavior.

General Procedures. Procedure A. A mixture of the α-azido ketone (1.50 mmol), aldehyde (5.00 mmol), and DBU (22 μL, 0.15 mmol) in THF (15 mL) was stirred until the reaction was complete as indicated by TLC. Temperature and time data are given in Table 1. The mixture was poured into water and extracted with CH_2Cl_2 (3 × 50 mL), and the organic fraction was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography.

Procedure B. A mixture of the α-azido ketone (1.50 mmol), aldehyde (8 mL), and base (1.50 mmol) stirred until the reaction was complete as indicated by TLC. Temperature and time data are given in Tables 1 and 3. The reaction was worked up the same as procedure A.

Procedure C. The base (1.51 mmol) was added to stirred solution of the α-azido ketone (1.50 mmol) and the aldehyde (4.50 mmol) in THF (15 mL) and stirred until the reaction was complete as indicated by TLC. Temperature and time data are given in Tables 1 and 2. The reaction was worked up the same as procedure A.

2-Azido-3-hydroxy-1-phenyl-1-butanone (14a). From the reaction of 2-azido-1-phenylethanone, **5** (1.62 g, 10.03 mmol), and acetaldehyde (**4a**) (1.95 mL, 34.88 mmol) using procedure A and short-column chromatography (3.5 × 12 cm, eluant: hexane–EtOAc = 3:1), was obtained azido alcohol **14a** (1.43 g, 70%) as a colorless oil which was a 55:45 mixture of the *syn* and *anti* diastereomers (based on ^{1}H-NMR). When this oil was allowed to stand with hexane (6 mL) in the refrigerator, 70 mg pure and crystalline *anti*-**14a** diastereomer could be isolated. Mp: 69–73 °C. IR (KBr): 3460, 2132, 1683 cm^{-1}. ^{1}H-NMR: 7.98 (d, J = 7.6 Hz, 2H), 7.65 (m, 1H), 7.52 (m, 2H), 4.59 (d, J = 6.4 Hz, 1H), 4.36 (m, 1H), 2.48 (deuterable d, J = 6.0 Hz, 1H), 1.34 (d, J = 6.4 Hz, 3H). ^{13}C-NMR: 196.0, 135.4, 134.3, 129.0, 128.8, 68.1, 67.1, 19.46. Anal. Calcd for $C_{10}H_{11}N_3O_2$ (205.22): C, 58.53; H, 5.40; N, 20.48. Found: C, 58.72; H, 5.41; N, 20.50.

***syn*-14a.** ^{1}H-NMR: 4.44 (d, J = 3.7 Hz, 1H), 4.38 (m, 1H), 2.65 (deuterable d, J = 4.0 Hz, 1H), 1.36 (d, J = 6.4 Hz, 3H). ^{13}C-NMR: 196.4, 134.9, 68.5, 67.3, 20.0. NMR data were taken from the spectrum of the diastereomeric mixture.

2-Azido-3-hydroxy-1-phenyl-1-pentanone (14b). The reaction of **5** (293 mg, 1.82 mmol) and propionaldehyde (**4b**) (317 mg, 5.46 mmol) using procedure A and short-column chromatography (3.5 × 12 cm, eluant: hexane–EtOAc = 4:1) gave azido alcohol **14b** (133 mg, 33%) as a yellow oil, which was a 65:35 mixture of the *syn* and *anti* diastereomers (based on ^{1}H-NMR). IR (neat): 3441br , 2104, 1685 cm^{-1}.

***syn*-14b.** ^{1}H-NMR: 7.95 (d, J = 7.7 Hz, 2H), 4.54 (d, J = 3.3 Hz, 1H), 2.55 (deuterable d, J = 4.4 Hz, 1H). ^{13}C-NMR: 196.4, 134.2, 129.0, 128.7, 73.9, 66.0, 27.2, 10.2.

***anti*-14b.** ^{1}H-NMR: 7.99 (dd, J = 7.7, 1.1 Hz, 2H), 4.56 (d, J = 6.6 Hz, 1H), 2.43 (deuterable d, J = 6.6 Hz, 1H). ^{13}C-NMR: 196.5, 134.2, 128.9, 128.8, 73.2, 65.5, 26.4, 9.8.

Nonseparable signals: ^{1}H-NMR: 7.65 (m, 1H), 7.52 (m, 2H), 4.10 (m, 1H), 1.54–1.78 (m, 2H), 1.01–1.06 (m, 3H). ^{13}C-NMR: 134.9. NMR data were taken from the spectra of the diastereomeric mixture. Elemental analysis could not be obtained for **14b** due to the slow decomposition of the oily diastereomeric mixture upon storage.

1-Azido-1,4-diphenyl-3-hydroxy-1-butanone (14c). The reaction of **5** (265 mg, 1.64 mmol) and phenylacetaldehyde (**4c**) (592 mg, 4.93 mmol) using procedure A and short-column chromatography (3.5 × 13 cm, eluant: PhMe–EtOAc = 5:1) gave azido alcohol **14c** (225 mg, 49%) as a yellow oil which was a 76:24 mixture of the *syn* and *anti* diastereomers (based on ^{1}H-NMR). IR (neat): 3446 br, 2923, 2105, 1696 cm^{-1}.

***syn*-14c.** ^{1}H-NMR : 7.74 (d, J = 7.2 Hz, 2H), 4.47 (d, J = 2.2 Hz, 1H), 2.97 (dd, J = 13.6, 7.7 Hz, 1H), 2.61 (deuterable d, J = 5.1 Hz, 1H). ^{13}C-NMR: 196.0, 134.1, 73.7, 64.5, 40.5.

***anti*-14c.** ^{1}H-NMR: 7.94 (d, J = 7.2 Hz, 2H), 4.57 (d, J = 6.6 Hz, 1H), 2.88 (dd, J = 13.7, 8.8 Hz, 1H), 2.45 (deuterable d, J = 5.9 Hz, 1H). ^{13}C-NMR: 196.2, 134.2, 72.8, 64.6, 39.9. Nonseparable signals: ^{1}H-NMR: 7.19–7.64 (m, 8H), 4.38–4.44 (m, 1H), 3.06 (overlapping dd's, 1H). ^{13}C-NMR: 136.9, 134.5, 129.5, 129.4, 128.9, 128.8, 128.8, 128.6, 127.0, 126.8. NMR data were taken from the spectrum of the diastereomeric mixture.

Elemental analysis could not be obtained for **14c** due to the slow decomposition of the oily diastereomeric mixture upon storage.

2-Azido-3-hydroxy-2-methyl-1-phenyl-1-butanone (15a) and *(2R*,4S*,5S*, 6R*)*-5-Azido-4-hydroxy-4-phenyl-2,5,6-trimethyl-1,3-dioxane (16). The reaction of 2-azido-1-phenyl-1-propanone (**6**) (417 mg, 2.38 mmol) and **4a** (10 mL, 0.179 mol) using procedure B and column chromatography (2.5 × 35 cm, eluant: PhMe–EtOAc = 3:1) gave two fractions. Trituration of the first fraction gave dioxane *(2R*,4S*,5S*,6R*)*-**16** as colorless crystals (67 mg, 11%). Mp: 123–126 °C dec.

IR (KBr): 3375, 2113, 1115 cm^{-1}. ^{1}H-NMR: 7.69 (m, 2H), 7.41 (m, 3H), 5.62 (q, J = 5.2 Hz, 1H), 4.41 (q, J = 6.4 Hz, 1H), 2.67 (deuterable s, 1H), 1.44 (d, J = 5.2 Hz, 3H), 1.33 (d, J = 6.4 Hz, 3H), 1.02 (s, 3H). ^{13}C-NMR: 140.2, 129.0, 127.9, 126.9, 99.8, 91.8, 76.0, 64.3, 20.3, 16.6, 15.6. Anal. Calcd for $C_{13}H_{17}N_3O_3$ (263.30): C, 59.30; H, 6.51; N, 15.96. Found: C, 59.43; H, 6.59; N, 16.18.

Results of 1D NOE Measurements for 16

Irradiated nucleus	Observed nuclei (difference%)
2-H	6-H (9.7); 2-Me (3.5)
6-H	2-H (10.1)
2-Me	2-H (3.8); 2',6'-H (1.7)
5-Me	6-H (2.9); 2',6'-H (4.4)
6-Me	6-H (3.5)
4-OH	2-H (3.5); 2',6'-H (7.5)

The second fraction was a mixture which was combined with the mother liquor from the crystallization of **16** and rechromatographed (3.5 × 12 cm, eluant: hexane–EtOAc = 3:1). Elution afforded first 1-phenyl-1,2-propanedione (**33**) (13.5 mg, 3.8%) followed by azido alcohol **15a** (155 mg, 30%) as a nearly colorless oil which was a 52:48 mixture of the *syn* and *anti* diastereomers (based on ^{1}H-NMR). IR (neat): 3468 br, 2108, 1676 cm^{-1}.

***syn*-15a.** ^{1}H-NMR: 8.08 (d, J = 7.6 Hz, 2H), 7.58 (m, 1H), 7.59 (m, 2H), 4.39 (q, J = 6.2 Hz, 1H), 2.65 (br deuterable s, 1H), 1.52 (s, 3H), 1.25 (d, J = 6.2 Hz, 3H). ^{13}C-NMR: 201.0, 135.4, 133.0, 129.4, 128.5, 74.5, 72.3, 18.8, 16.9. This isomer was obtained from hydrolysis of **16**.

***anti*-15a.** ^{1}H-NMR: 8.03 (d, J = 7.4 Hz, 2H), 7.58 (m, 1H), 7.47 (m, 2H), 4.31 (q, J = 6.2 Hz, 1H), 2.55 (br deuterable s, 1H), 1.65 (s, 3H), 1.28 (d, J = 6.2 Hz, 3H). ^{13}C-NMR: 201.2, 135.5, 132.9, 129.3, 128.4, 73.0, 71.4, 17.8, 17.7. Anal. Calcd for $C_{11}H_{13}N_3O_2$ (219.25): C, 60.26; H, 5.98; N, 19.17. Found: C, 60.40; H, 6.16; N, 19.17. Analysis was obtained for the diastereomeric mixture.

Acid Hydrolysis of *(2R*,4S*,5S*,6R*)*-5-Azido-4-hydroxy-4-phenyl-2,5,6-trimethyl-1,3-dioxane (16). A solution of *(2R*,4S*,5S*,6R*)*-**16** (46 mg, 0.175 mmol) in ethyl acetate (5 mL) was treated with 1 N HCl (0.5 mL). The mixture was stirred for 6 h at room temperature, poured into saturated $NaHCO_3$ solution, extracted with CH_2Cl_2, and dried. Evaporation afforded an oil (35 mg) that was a 95:5 mixture of *syn*-**15a** (86% yield) and unreacted **16** (based on ^{1}H-NMR).

5-Azido-4-hydroxy-4-phenyl-2,5,6-trimethyl-1,3-dioxane (16) from 15a. A mixture of 2-azido-3-hydroxy-2-methyl-1-phenyl-1-butanone (**15a**) (133 mg, 0.607 mmol, *syn*/*anti* = 52:48), **4a** (0.11 mL, 1.97 mmol), and DBU (0.1 mL, 0.669 mmol) in anhydrous THF (10 mL) was stirred at 0 °C for 7 days and then worked up as in procedure A. Evaporation afforded a colorless oil (133 mg) which was a 73:27 mixture of **16** diastereomers and the unreacted **15a** (based on ^{1}H-NMR). (Diastereomeric ratios: *(2R*,4S*,5S*,6R*)*-**16**/*(2R*,4S*,5R*, 6R*)*-**16** = 59:41, *syn*-**15a**/*anti*-**15a** = 46:54). Recrystallization of the residue from hexane yielded 44 mg (28%) crystalline *(2R*,4S*,5S*,6R*)*-**16.**

***(2R*,4S*,5R*,6R*)*-16.** ^{1}H-NMR: 5.56 (q, J = 5.2 Hz, 1H), 4.47 (q, J = 6.4 Hz, 1H), 1.41 (d, J = 5.1 Hz, 3H), 0.94 (s, 3H). NMR data were taken from the spectra of the diastereomeric mixture.

2-Azido-2-(1-hydroxyethyl)-1-indanone (17a). The reaction of 2-azido-1-indanone (**7**) (260 mg, 1.50 mmol) and **4a** (8 mL, 0.143 mol) using procedure B and column chromatography (2.5 × 40 cm, eluant: hexane–EtOAc = 3:1) gave pure samples of both *syn*-**17a** (96 mg) and *anti*-**17a** (84 mg). In addition a diastereomeric mixture of *syn*-**17a** and *anti*-**17a** in a ratio of 46:54 was isolated from the intermediate fractions. Total yield of **17a** was 278 mg (85%), overall *syn*/*anti* ratio was 54:46.

***syn*-17a.** Mp: 38–40.5 °C (hexane); R_f = 0.46 (hexane–EtOAc = 3:1). IR (KBr): 3385, 2106, 1705, 1607 cm^{-1}. ^{1}H-NMR: 7.78 (d, J = 7.7 Hz, 1H), 7.65 (dd, J = 7.7, 7.9 Hz, 1H), 7.47 (d, J = 7.7 Hz, 1H), 7.40 (dd, J = 7.7, 7.9 Hz), 4.39 (q, J = 6.6 Hz, 1H), 3.44, 2.91 (AB q, J = 17.6 Hz, 2H), 2.24 (br deuterable s, 1H), 1.35 (d, J = 6.6 Hz, 3H). ^{13}C-NMR: 203.2, 152.7, 136.2, 134.6, 127.9, 126.5, 124.7, 70.8, 68.5, 33.9, 18.1.

***anti*-17a.** Oil; R_f = 0.42 (hexane–EtOAc = 3:1); IR (neat): 3441 br, 2103, 1713, 1607 cm^{-1}. ^{1}H-NMR: 7.82 (d, J = 7.7 Hz, 1H), 7.68 (dd, 1H, J = 7.8, 7.7 Hz, 1H), 7.43–7.48 (m, 2H), 4.23 (q, J = 6.2 Hz, 1H), 3.25, 2.96 (ABq, J = 17.9 Hz, 2H), ~3.2 (br deuterable s, 1H), 1.20 (d, J = 6.2 Hz, 3H). ^{13}C-NMR: 202.9, 152.1, 136.5, 134.4, 128.3, 126.5, 125.0, 71.3, 70.8, 35.2, 17.3. Anal. Calcd for $C_{11}H_{11}N_3O_2$ (217.23): C, 60.82; H, 5.10; N, 19.34. Found: C, 60.85, H, 5.08, N, 19.33. Analysis was obtained for the diasteromeric mixture.

3-Azido-3-(1-hydroxyethyl)-4-chromanone (18a). The reaction of 3-azido-4-chromanone (**8**) (192 mg, 1.02 mmol) and **4a** (5 mL, 89.44 mmol) using procedure B and short-column chromatography (3.5 × 12 cm, eluant: hexane–EtOAc = 3:1) gave azide **18a** (224 mg, 95%) as a pale yellow oil which was a 45:55 mixture of the *syn* and *anti* diastereomers (based on ^{1}H-NMR). IR (neat): 3467, 2111, 1694, 1607 cm^{-1}.

***syn*-18a.** ^{1}H-NMR: 4.68, 4.36 (AB q, J = 11.6 Hz, 2H), 2.28 (deuterable s, 1H), 1.30 (d, J = 6.6 Hz, 3H). ^{13} C-NMR: 189.2, 161.0, 137.0, 127.9, 122.2, 119.2, 118.0, 68.0, 17.12.

***anti*-18a.** ^{1}H-NMR: 4.29 (s, 2H), 2.98 (br deuterable s, 1H), 1.34 (d, J = 6.2 Hz, 3H). ^{13}C-NMR: 190.5, 161.1, 137.1, 128.0, 122.4, 119.6, 117.9, 67.0, 17.11.

Nonseparable signals: ^{1}H-NMR: 7.94 (m, 1H), 7.55 (m, 1H), 7.09, 7.00 (2 × m, 2 × 1H), 4.38 (m, 1H). ^{13}C-NMR: 70.0, 69.2, 68.9, 66.7. NMR data were taken from the spectra of the diastereomeric mixture.

The assignment of *syn*- and *anti*-stereochemistry in **18a** is quite tenuous because of overlapping signals. The assignments given are based on the ^{13}C chemical shift of the methylene carbon attached to the azido carbon being at lower field in the *syn*-isomer. In the present case the *syn*-isomer has an absorption at δ 68.0 for this carbon while the anti isomer has this carbon at δ 67.0.

Anal. Calcd for $C_{11}H_{11}N_3O_3$ (233.23): C, 56.65; H, 4.75; N, 18.02. Found: C, 56.26; H, 5.00; N, 17.81. Analysis was obtained for the diasteromeric mixture.

3-Azido-3-(1-hydroxypropyl)-4-chromanone (18b). The reaction of 3-azido-4-chromanone (**8**) (166 mg, 0.88 mmol) and **4b** (5 mL, 89.44 mmol) using procedure B and column chromatography (2.5 × 45 cm, eluant: PhMe–EtOAc = 9:1) gave pure samples of *syn*-**18b** (36 mg) and *anti*-**18b** (34 mg). In addition a mixture of *syn*-**18b** and *anti*-**18b** (92 mg) in a ratio of 3:1 was isolated from the intermediate fractions. The total yield of **18b** was 162 mg (75%), overall *syn*/*anti* ratio was 65:35.

***syn*-18b.** Oil; R_f = 0.37 (toluene–EtOAc = 9:1). IR (neat): 3459, 2110, 1685, 1608 cm^{-1}. ^{1}H-NMR: 7.94 (dd, J = 8.1, 1.5 Hz, 1H), 7.55 (ddd, J = 8.4, 7.3, 1.5 Hz, 1H), 7.09 (dd, J = 8.4, 8.1 Hz, 1H), 7.01 (d, J = 8.4 Hz, 1H), 4.69, 4.35 (AB q, J = 11.7 Hz, 2H), 4.11 (m, 1H), 2.11 (br deuterable s, 1H), 1.67, 1.49 (2 × m, 2 × 1H), 1.05 (t, J = 7.1 Hz, 3H). ^{13}C-NMR ($CDCl_3$): 189.1, 161.1, 137.0, 127.9, 122.2, 119.6, 118.1, 72.1, 69.3, 67.9, 23.7, 10.8.

***anti*-18b.** Oil; R_f = 0.42 (toluene–EtOAc = 9:1). IR (neat): 3490, 2111, 1686, 1608 cm^{-1}. ^{1}H-NMR: 7.96 (dd, J = 7.7, 1.5 Hz, 1H), 7.55 (ddd, J = 8.1, 7.7, 1.5 Hz, 1H), 7.11 (dd, J = 7.7, 7.7 Hz, 1H), 7.00 (d, J = 8.1 Hz, 1H), 4.36, 4.32 (AB q, J = 12.3 Hz, 2H), 4.09 (m, 1H), 2.70 (br deuterable s, 1H), 1.54–1.66 (m, 2H), 1.07 (t, J = 7.2 Hz, 3H). ^{13}C-NMR: 190.2, 161.0, 137.0, 128.1, 122.4, 119.3, 117.9, 74.1, 69.8, 67.4, 24.1, 10.6.

The assignment of *syn*- and *anti*-stereochemistry in **18b** is tenuous because of conflicting chemical shift data. The assignments given are based on the chemical shift of the methine -*H*COH- proton being at lower field in the *syn*-isomer. Anal. Calcd for $C_{12}H_{13}N_3O_3$ (247.26): C, 58.29; H, 5.30; N, 16.99. Found: C, 58.39; H, 5.39; N, 16.79. Analysis was obtained for the diasteromeric mixture.

3-Azido-3-(1-hydroxyethyl)-5-hexen-2-one (21a). The reaction of 3-azido-5-hexen-2-one (**9**) (212 mg, 1.52 mmol) and **4a** (0.3 mL. 5.34 mmol) using procedure C and short-column

chromatography (3.5 × 11 cm, eluant: hexane–EtOAc = 3:1) gave azide **21a** (81 mg, 29%) as an unstable yellow oil which was a 38:62 mixture of the *syn* and *anti* diastereomers (based on ^{1}H-NMR). IR (neat): 3480, 3370, 2110, 1715, 1669, 1623 cm^{-1}.

***syn*-21a.** ^{1}H-NMR: 6.05 (d, J = 11.4 Hz, 1H), 5.73 (m, 1H), 4.14 (q, J = 6.6 Hz, 1H), 2.22 (s, 3H), 1.30 (d, J = 6.6 Hz, 3H).

***anti*-21a.** ^{1}H-NMR: 6.54 (dt, J = 16.8, 10.6 Hz), 5.42 (d, J = 16.8 Hz, 1H), 4.08 (q, J = 6.2 Hz, 1H), 2.38 (s, 3H), 1.20 (d, J = 6.2 H, 3H).

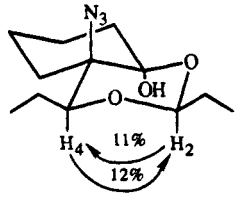
Nonseparable signals: 5.17–5.26 (m, 1H), ~4.00 (br deuterable s, 1H), 2.68–2.86, 2.40–2.58 (2 × m, 2H). NMR data were taken from the spectra of the diastereomeric mixture; *syn*, *anti*-**21a**. ^{13}C-NMR: 208.52, 131.1, 130.6, 120.1, 119.0, 112.4, 72.2, 72.1, 38.3, 38.0, 29.7, 29.2, 18.8, 17.9. Formation of an insoluble white precipitate was observed in the NMR tube during measurements. The stereochemical assignment given is based on the chemical shift of the methine -*H*COH- proton being at lower field in the *syn*-isomer. Elemental analysis could not be obtained for **21a** due to its instability.

6-Azido-1,6-nonadien-5-one (24). The reaction of 1-azido-5-hexen-2-one (**10**) (171 mg, 1.23 mmol) and **4b** (5 mL, 69.30 mmol) using procedure B followed by flash chromatography (2.5 × 45 cm, eluant: hexane–EtOAc = 4:1) of the viscous residue afforded azide **24** (24 mg, 15%) as a pale yellow oil. IR (neat): 2971, 2924, 2119, 1682, 1623 cm^{-1}. ^{1}H-NMR: 6.05 (t, J = 7.3 Hz, 1H), 5.83 (dddd, J = 16.2, 10.2, 3.7 and 1.3 Hz, 1H), 5.07, 4.99 (2 × m, 2 × 1H), 2.78 (t, J = 7.2 Hz, 2H), 2.40 (qd, J = 7.2, 1.3 Hz, 2H), 2.30 (m, 2H), 1.06 (t, J = 7.6 Hz, 3H). ^{13}C-NMR: 195.4, 136.8, 135.7, 133.5, 115.6, 36.6, 28.3, 21.2, 12.9.

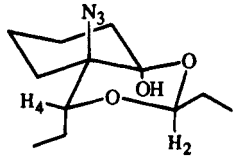
Elemental analysis could not be obtained for **24** due to the slow decomposition of the oily diastereomeric mixture on storage.

4a-Azido-2,4-diethyl-8a-hydroxy-1,3-dioxadecalin (25). The reaction of 2-azidocyclohexanone (**11**) (292 mg, 2.10 mmol) and **4b** (0.75 mL, 10.40 mmol) using procedure C and short-column chromatography (3.5 × 12 cm, eluant: hexane–EtOAc = 3:1) gave dioxane *(2R*,4R*,4aS*,8aS*)*-**25** (38 mg, 7.1%). Mp: 84–86 °C (hexane). IR (KBr): 3416, 2974, 2110 cm^{-1}. ^{1}H-NMR: 5.15 (t, J = 5.0 Hz, 1H), 4.03 (dd, J = 9.7, 2.8 Hz, 1H), 2.40 (deuterable s, 1H), 1.35–2.10 (m, 12H), 1.03, 0.94 (2 × t, J = 7.1 and 7.5 Hz, 2 × 3H). ^{13}C-NMR: 97.0, 95.7, 77.5, 63.2, 36.4, 27.4, 25.4, 21.9, 21.6, 20.7, 10.7, 8.1.

The stereochemistry of this, the major isomer was assigned by an NOE experiment which showed a syn relationship between the C-2 and C-4 protons.



(2R,4R*,4aS*,8aS*)*-**25** (major)



(2R,4R*,4aR*,8aS*)*-**25** (minor)

The fraction eluted next (152 mg, 28%, mp: 63–81 °C) was a 59:41 mixture of the *(2R*,4R*,4aS*,8aS*)*-**25** and a second diastereomer which is presumed to be *(2R*,4R*,4aR*,8aS*)*-**25** based on the similarity of its ^{1}H NMR spectrum to the major isomer. The total yield of **25** was 190 mg (35%) and the *(2R*,4R*,4aS*,8aS*)*/*(2R*,4R*,4aR*,8aS*)* ratio was 67:33.

***(2R*,4R*,4aR*,8aS*)*-25.** ^{1}H-NMR: 5.30 (t, J = 5.1 Hz, 1H), 4.03 (m, 1H), 2.00 (deuterable s, 1H), 1.01, ~0.95 (2 × t, J = 7.6 and ~7.5 Hz, 2 × 3H); ^{13}C-NMR: 97.2, 96.5, 80.2, 65.4, 34.0, 27.5, 27.1, 21.7, 21.7, 20.4, 10.3, 8.7. NMR data were taken from the spectra of the diastereomeric mixture. In a ^{1}H–^{13}C coupled ^{13}C-NMR spectrum signals at δ 97.1, 97.2, 65.4, 63.2 appear as singlets and signals at δ 96.5, 96.7, 80.2, amd 77.4 appear as doublets. Elemental analysis was carried out on the diastereomeric mixture. Anal. Calcd for $C_{12}H_{21}N_3O_3$ (255.32): C, 56.45; H, 8.29; N, 16.46. Found: C, 56.33; H, 7.97; N, 16.40.

Continued elution afforded 26 mg (8.9%) of unreacted starting material.

Ethyl 3-Amino-4-oxo-2-pentenoate (26). The reaction of ethyl 3-azido-4-oxopentanoate (**12**) (222 mg, 1.20 mmol) and **4a** (0.24 mL, 4.29 mmol) using procedure C and column chromatography (2 × 35 cm, eluant: hexane–EtOAc = 3:1) gave enamine **26** (64 mg, 34%) as a colorless liquid. IR (neat): 3477, 3353, 1701, 1677, 1617 cm^{-1}. ^{1}H-NMR: 5.38 (s, 1H), 4.20 (q, J = 7.0 Hz, 2H), 2.41 (s, 3H), 1.31 (t, J = 7.0 Hz, 3H). ^{13}C-NMR: 195.2, 170.1, 150.6, 90.2, 59.7, 24.8, 14.4.

This compound was reported in reference 5 without any physical or spectral data.

3-Aminochromone (19) and 3-Amino-3′-azido-3,3′-bichromanone (20). A solution of 3-azido-4-chromanone (**8**) (200 mg, 1.06 mmol) and triethylamine (0.15 mL, 1.08 mmol) in acetone (10 mL) was allowed to stand at 0 °C for 15 days, and then was poured into water, extracted with CH_2Cl_2, dried, and evaporated. The residue was separated by short-column chromatography (3.5 × 12 cm, eluant: hexane–EtOAc = 1:1) to give dimer **20** (23 mg, 12%). Mp 119–121 °C (hexane). IR (KBr): 3368, 3316, 2117, 1673, 1605 cm^{-1}. ^{1}H-NMR: 7.81 (overlapping doublets, 2H), 7.50 (m, 2H), 7.02 (m, 4H), 5.43, 4.96 (AB q, J = 12.5 Hz, 2H), 5.20, 4.53 (AB q, J = 11.9 Hz, 2H), 1.91 (br, deuterable s, 2H). ^{13}C-NMR: 191.7, 187.1, 160.7, 160.4, 136.7, 136.3, 128.2, 128.1, 122.1, 119.6, 119.1, 117.7, 117.6, 73.0, 70.6, 67.8, 61.5. In a ^{1}H-^{13}C coupled ^{13}C-NMR spectrum the signals at δ 73.0 and 70.6 appear as triplets corresponding to the C-4 and C-4′ methylene groups. Thus the dimeric components must be joined at the C-3 and C-3′ carbons.

From the fractions eluting next, enamine **19** (119 mg, 70%) was isolated. Mp 118–121 °C (hexane–EtOAc) (lit.[25] mp: 126–128 °C). IR (KBr): 3392, 3305, 1643, 1623, 1618 cm^{-1}. ^{1}H-NMR: 8.26 (dd, J = 8.1, 1.1 Hz, 1H), 7.78 (s, 1H), 7.61 (ddd, J = 8.4, 7.9, 1.1 Hz, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.35 (dd, J = 8.1, 7.9 Hz, 1H), 3.64 (br s, 2H). ^{13}C-NMR: 173.4, 156.0, 137.7, 132.7, 131.5, 125.6, 124.1, 122.0, 118.2.

2-Azido-3-[(*tert*-butyldimethylsilyl)oxy]-1-phenyl-1-butanone (27). A mixture of **14a** (202 mg, 0.984 mmol, *syn*/*anti* = 57:43), *tert*-butyldimethylsilyl chloride (180 mg, 1.19 mmol), and imidazole (170 mg, 2.50 mmol) in DMF (5 mL) was stirred at room temperature. After 44 h a second portion of *tert*-butyldimethylsilyl chloride (190 mg, 1.26 mmol) was added. After 112 h the mixture was poured into water, extracted with CH_2Cl_2, dried, and evaporated. Column chromatography (2.5 × 35 cm; eluant: hexane–EtOAc = 4:1) afforded *anti*-**27** (42 mg, 13%) as a colorless oil and *syn*-**27** (136 mg, 43%) as white crystals. The *syn*:*anti* ratio was 76:24. The stereochemistry was assigned by the coupling constant of the azido methine carbon ($J_{syn} < J_{anti}$).[9]

***anti*-27**: R_f = 0.56 (hexane–EtOAc = 4:1). IR (neat): 2962, 2930, 2857, 2106, 1686 cm^{-1}. ^{1}H-NMR: 7.97 (d, J = 7.3 Hz, 2H), 7.60 (m, 1H), 7.49 (m, 2H), 4.51 (d, J = 7.3 Hz, 1H), 4.32 (m, 1H), 1.36 (d, J = 5.9 Hz, 3H), 0.70 (s, 9H), 0.03, −0.14 (2 × s, 2 × 3H). ^{13}C-NMR: 196.8, 136.2, 133.8, 128.9, 128.7, 69.7, 67.1, 25.5, 20.9, 17.7, −4.5, −5.2. Anal. Calcd for $C_{16}H_{25}N_3O_2Si$ (319.48): C, 60.15; H, 7.89; N, 13.15. Found: C, 59.91; H, 7.77; N, 12.77.

***syn*-27.** R_f = 0.44 (hexane–EtOAc = 4:1). Mp: 58–59 °C. IR (KBr): 2926, 2886, 2857 (CH_3), 2099 (N_3), 1691 (C=O), 1596, 1472, 1248 (N_3), 1212 (C–O), 1128, 1103, 837 (Si–O), 776, 697 cm^{-1}. ^{1}H-NMR: 7.89 (dd, J = 6.8, 1.6 Hz, 2H), 7.62 (m, 1H), 7.50 (m, 2H), 4.44 (qd, J = 6.2, 3.7 Hz, 1H), 4.30 (d, J = 3.7 Hz, 1H), 1.35 (d, J = 6.2 Hz, 3H), 0.84 (s, 9H), −0.02, −0.18 (2 × s, 2 × 3H). ^{13}C-NMR: 195.79, 135.01, 133.76, 128.88, 128.58, 70.41, 68.75, 25.57, 21.67, 17.86, −4.49, −5.39. Anal. Calcd for $C_{16}H_{25}N_3O_2Si$ (319.48): C, 60.15; H, 7.89; N, 13.15. Found: C, 60.21; H, 7.77; N, 13.43.

Continued elution afforded 85 mg (42%) unreacted **14a**.

***trans*-2-Benzoyl-3-methylaziridine (28).** (a) A mixture of **14a** (213 mg, 1.04 mmol, *syn*/*anti* = 57:43) and triphenylphosphine (272 mg, 1.04 mmol) in dry CH_2Cl_2 (10 mL) was stirred at room temperature for 20 h. After addition of 0.3 N

(25) Becket, G. J. P.; Ellis, G. P. *Tetrahedron Lett.* **1976**, 719.

HCl (10 mL), the mixture was stirred vigorously for 5 h. The layers were separated, the aqueous phase was neutralized with saturated $NaHCO_3$ solution and extracted with Et_2O, and the combined organic layers were dried and evaporated. The residue was passed through a short pad of silica gel and washed with EtOAc to give 27 mg (16%) pure **28** as a pale yellow oil. IR (neat): 3267, 1766, 1669 cm^{-1}. ^{1}H-NMR: 8.01 (dd, J = 6.8, 1.5 Hz, 2H), 7.47–7.63 (m, 3H), 3.22 (d, J = 2.5 Hz), 2.23 (m, 1H), ~2.22 (br deuterable s, 1H), 1.36 (d, J = 5.4 Hz, 3H). ^{13}C-NMR: 197.2, 136.1, 133.7, 128.8, 128.1, 40.6, 38.2, 18.5.

(b) A solution of **14a** (466 mg, 2.27 mmol, *syn*/*anti* = 57:43) and triethyl phosphite (388 mg, 2.34 mmol) in benzene (22 mL) was stirred at room temperature for 31 h, poured into saturated $NaHCO_3$ solution, and extracted with CH_2Cl_2, and the organic extracts were dried and evaporated. Short-column chromatography (3.5 × 12 cm, eluant: hexane–EtOAc = 1:1) of the residue afforded 72 mg (20%) of aziridine **28** as a yellow oil.

2,5-Dihydro-2,4-dimethyl-5-hydroxy-5-phenyloxazole (29a). The reaction of 2-azido-1-phenylpropanone (**6**) (565 mg, 3.23 mmol) and **4a** (0.62 mL, 11.09 mmol) using procedure C gave a crystalline residue upon evaporation which was triturated with hexane (10 mL) to give oxazoline **29a** (341 mg, 55%) as a mixture of the C-2-*anti*-OH:C-2-*syn*-OH diastereomers (58:42 based on ^{1}H-NMR). Mp 117–120 °C dec. IR (KBr): 3119, 1670 cm^{-1}.

(C-2-*anti*-OH)-29a. ^{1}H-NMR: 7.52 (dd, 2H), 5.78 (m, 1H), 4.13 (deuterable s, 1H), 1.87 (d, J = 1.6 Hz, 3H), 1.54 (d, J = 6.0 Hz, 3H). ^{13}C-NMR: 170.1, 139.4, 128.8, 128.3, 126.3, 108.5, 99.2, 21.2, 13.9.

(C-2-*syn*-OH)-29a. ^{1}H-NMR: 7.46 (dd, 2H), 5.86 (m, 1H), ~4.00 (br deuterable s, 1H), 1.91 (d, J = 2.0 Hz, 3H), 1.52 (d, J = 6.4 Hz, 3H). ^{13}C-NMR: 169.7, 139.9, 128.9, 128.4, 125.9, 108.8, 100.9, 22.9, 13.7.

Nonseparable signals: ^{1}H-NMR: 7.37 (m, 3H). NMR data were taken from the spectra of the diastereomeric mixture. Anal. Calcd for $C_{11}H_{13}NO_2$ (191.23): C, 69.09; H, 6.85; N, 7.32. Found: C, 69.15; H, 6.76; N, 7.31. Analysis was obtained for the diasteromeric mixture.

2,5-Dihydro-2-ethyl-5-hydroxy-4-methyl-5-phenyloxazole (29b). The reaction of **6** (644 mg, 3.68 mmol) and **4b** (0.8 mL, 11.09 mmol) using procedure C afforded a yellowish oily residue which was treated with hexane (5 mL) to give white crystals of oxazoline **29b** (467 mg, 62%) as a mixture of the C-2-*anti*-OH:C-2-*syn*-OH diastereomers (58:42 based on ^{1}H-NMR). Mp 80–84 °C. IR (KBr): 3120, 1673 cm^{-1}.

(C-2-*anti*-OH)-29b. ^{1}H-NMR: 7.53 (dd, J = 8.0, 2.0 Hz, 2H), 5.60 (m, 1H), 3.69 (deuterable s, 1H), 1.90 (d, J = 1.8 Hz, 3H), 1.13 (t, J = 7.7 Hz, 3H). ^{13}C-NMR: 170.0, 128.8, 128.4, 126.4, 108.2, 103.8, 28.7, 14.0, 9.4.

(C-2-*syn*-OH)-29b. ^{1}H-NMR: 7.47 (dd, J = 7.2, 1.6 Hz, 2H), 5.73 (m, 1H), 3.45 (deuterable s, 1H), 1.93 (d, J = 1.5 Hz, 3H), 1.04 (t, J = 7.7 Hz, 3H). ^{13}C-NMR: 169.7, 128.9, 128.5, 125.9, 108.7, 105.6, 29.6, 13.7, 8.8.

Nonseparable signals: ^{1}H-NMR: 7.35–7.41 (m, 3H). ^{13}C-NMR: 139.5. NMR data were taken from the spectra of the diastereomeric mixture. Anal. Calcd for $C_{12}H_{15}NO_2$ (205.26); C, 70.22; H, 7.37; N, 6.82. Found: C, 69.96; H, 7.23; N, 6.77. Analysis was obtained for the diasteromeric mixture.

2,5-Dihydro-5-hydroxy-4-methyl-5-phenyl-2-(2-phenylethyl)oxazole (29g). Reaction of **6** (274 mg, 1.56 mmol) and **4g** (0.62 mL, 4.71 mmol) by procedure C gave an oily residue which was filtered onto a short pad of silica gel 60 (4 × 3 cm) and washed successively with six 20 mL portions of hexane:EtOAc (3:1) and then four 25 mL portions of hexane:EtOAc (2:1). Evaporation of fractions 4–9 afforded crude **29g** (313 mg, ca. 90% purity, C-2-*anti*-OH:C-2-*syn*-OH = 53:47). Crystallization of the crude product from hexane gave 171 mg (39%) of pure, crystalline oxazoline **29g** as a mixture of the C-2-*anti*-OH:C-2-*syn*-OH diastereomers (69:31 based on ^{1}H-NMR). Mp 84–88 °C. IR (KBr): 3085, 1671 cm^{-1}.

(C-2-*anti*-OH)-29g. ^{1}H-NMR: 5.70 (m, 1H), 3.33 (br deuterable s), 1.92 (d, J = 2.2 Hz, 3H). ^{13}C-NMR: 170.1, 141.3, 139.3, 108.2, 101.9, 37.1, 31.2, 14.0.

(C-2-*syn*-OH)-29g. ^{1}H-NMR: 5.80 (m, 1H), 3.19 (br deuterable s), 1.95 (d, J = 1.8 Hz, 3H). ^{13}C-NMR: 169.9, 141.4, 139.9, 108.6, 103.7, 38.1, 30.8, 13.8.

Nonseparable signals: ^{1}H-NMR: 7.20–7.56 (m, 10H), 2.92, 2.86 (overlapping multiplets, 2H), 2.20, 2.11 (overlapping multiplets, 2H). ^{13}C-NMR: 128.9, 128.9, 128.5, 128.4, 128.4, 128.4, 126.3, 126.0, 125.9. NMR data were taken from the spectra of the diastereomeric mixture. Anal. Calcd for $C_{18}H_{19}NO_2$ (281.36): C, 76.85; H, 6.81; N, 4.98. Found: C, 76.72; H, 6.88; N, 4.83. Analysis was obtained for the diasteromeric mixture.

2,5-Dihydro-5-hydroxy-4-methyl-5-phenyl-2-(2-pyridyl)oxazole (29h). Reaction of **6** (351 mg, 2.00 mmol) and 2-pyridinecarboxaldehyde (**4h**) (0.60 mL, 6.31 mmol) using procedure C and the purification method given for **29g** yielded **29h** (373 mg, 73%) as a colorless syrup which was a mixture of the C-2-*anti*-OH:C-2-*syn*-OH diastereomers (1:9 based on ^{1}H-NMR). Crystallization from hexane afforded 289 mg of the pure C-2-*syn*-OH diastereomer.

(C-2-*syn*-OH)-29h. Mp 93–97 °C dec. IR (KBr): 3078, 1657, 1597 cm^{-1}. ^{1}H-NMR: 8.59 (d, J = 4.4 Hz, 1H), 7.79 (m, 1H), 7.64–7.29 (m, 7H), 7.59 (deuterable s, 1H), 6.74 (s, 1H), 1.97 (s, 3H). ^{13}C-NMR: 172.6, 155.7, 149.5, 137.9, 128.7, 128.3, 126.4, 123.9, 122.6, 108.9, 103.2, 14.0; Anal. Calcd for $C_{15}H_{14}N_2O_2$ (254.29): C, 70.85; H, 5.55; N, 11.02. Found: C, 70.98; H, 5.61; N, 11.00.

(C-2-*anti*-OH)-29h. ^{1}H-NMR (taken from the spectra of the diastereomeric mixture): 8.70 (d, 1H), 6.52 (s, 1H), 2.01 (s, 3H).

2,5-Dihydro-5-hydroxy-2,4,5-triphenyloxazole (30d). Reaction of **13** (187 mg, 0.79 mmol) and **4d** (251 mg, 2.37 mmol) using procedure C gave an oily residue which was crystallized from hexane–EtOAc to afford oxazoline **30d** (158 mg, 64%) as a mixture of the C-2-*anti*-OH:C-2-*syn*-OH diastereomers (53:47 based on ^{1}H-NMR). Mp 107–109 °C. IR (KBr): 3240, 1621 cm^{-1}.

(C-2-*anti*-OH)-30d. ^{1}H-NMR: 7.85 (dd, J = 7.6, 1.2 Hz, 2H), 6.87 (s, 1H), 3.48 (deuterable s, 1H). ^{13}C-NMR: 168.2, 139.7, 139.0, 131.1, 108.7, 102.5.

(C-2-*syn*-OH)-30d. ^{1}H-NMR: 7.95 (d, J = 7.2 Hz, 2H), 6.91 (s, 1H), 3.87 (deuterable s, 1H). ^{13}C-NMR: 167.9, 139.9, 131.2, 138.2, 109.1, 103.7.

Nonseparable signals: ^{1}H-NMR: 7.27–7.58 (m, 11H). ^{13}C-NMR: 129.2, 129.1, 128.9, 128.7, 128.7, 128.6, 128.6, 128.5, 128.3, 128.3, 126.7, 126.5, 126.5, 125.8. NMR data were taken from the spectra of the diastereomeric mixture. Anal. Calcd for $C_{21}H_{17}NO_2$ (315.38): C, 79.98; H, 5.43; N, 4.44. Found: C, 79.91; H, 5.51; N, 4.38. Analysis was obtained for the diasteromeric mixture.

2,5-Dihydro-4,5-diphenyl-5-hydroxy-2-isopropyloxazole (30e). Reaction of 2-azido-1,2-diphenylethanone (**13**) (356 mg, 1.50 mmol) and **4e** (0.41 mL, 4.51 mmol) using procedure C produced an oily residue which was crystallized from hexane to afford oxazoline **30e** (329 mg, 78%) as white crystals which was a mixture of the C-2-*anti*-OH:C-2-*syn*-OH diastereomers (43:57, based on ^{1}H-NMR). mp 97–100 °C. IR (KBr): 3228, 1614 cm^{-1}.

(C-2-*syn*-OH)-30e. ^{1}H-NMR: 7.89 (d, J = 7.7 Hz, 2H), 5.74 (d, J = 4.8 Hz, 1H), 1.07, 1.06 (overlapping doublets, J = 7.2 and 6.8 Hz, 6H). ^{13}C-NMR: 167.7, 140.3, 130.9, 129.8, 107.7, 106.8, 33.7, 18.0, 17.1.

(C-2-*anti*-OH)-30e. ^{1}H-NMR: 7.79 (d, J = 7.7 Hz, 2H), 5.59 (d, J = 5.9 Hz, 1H), 1.31, 1.11 (overlapping doublets, J = 6.8 and 6.8 Hz, 6H). ^{13}C-NMR: 167.2, 140.0, 130.8, 130.0, 108.3, 108.0, 33.8, 18.3, 17.8.

Nonseparable signals: 7.47–7.53 (m, 2H), 7.24–7.38 (m, 6H), 3.22 (br, deuterable s, 1H), 2.13, 2.06 (overlapping multiplets, 1H). ^{13}C-NMR: 129.0, 128.9, 128.7, 128.6, 128.5, 128.3, 128.3, 128.2, 126.4, 125.6. NMR data were taken from the spectra of the diastereomeric mixture. Anal. Calcd for $C_{18}H_{19}NO_2$ (281.36): C, 76.84; H, 6.81, N, 4.98. Found: C, 76.86; H, 6.92; N, 5.10. Analysis was obtained for the diasteromeric mixture.

2,5-Dihydro-2-*tert*-butyl-4,5-diphenyl-5-hydroxyoxazole (30f). Reaction of **13** (356 mg, 1.50 mmol) and **4f** (0.5 mL, 4.60 mmol) using procedure C gave a crystalline

residue. Trituration with hexane gave **30f** (319 mg, 72%) as white crystals which was a mixture of the C-2-*anti*-OH:C-2-*syn*-OH diastereomers (15:85 based on ^{1}H-NMR). Mp 139–142 °C (hexane–EtOAc). IR (KBr): 3257, 1625 cm^{-1}.

(C-2-*syn*-OH)-30f. ^{1}H-NMR: 7.99 (d, J = 7.3 Hz, 2H), 7.49 (d, J = 6.8 Hz, 2H), 5.61 (s, 1H), 3.08 (br, deuterable s, 1H), 1.09 (s, 9H). ^{13}C-NMR: 167.2, 140.4, 130.9, 129.8, 110.8, 108.4, 35.6, 25.3.

(C-2-*anti*-OH)-30f. ^{1}H-NMR: 7.77 (d, J = 7.3 Hz, 2H), 5.56 (s, 1H), 1.07 (s, 9H). ^{13}C-NMR: 168.0, 139.7, 130.7, 130.2, 108.9, 107.5, 35.6, 25.4.

Nonseparable signals: ^{1}H-NMR: 7.27–7.37 (m, 6H). ^{13}C-NMR: 128.9, 128.9, 128.7, 128.6, 128.5, 128.3, 128.1, 126.4, 125.5. NMR data were taken from the spectra of the diastereomeric mixture. Anal. Calcd for $C_{19}H_{21}NO_2$ (295.39): C, 77.26; H, 7.17; N, 4.74. Found: C, 77.12; H, 7.10; N, 4.70. Analysis was obtained for the diasteromeric mixture.

2,5-Dihydro-2,2-dimethyl-4,5-diphenyl-5-hydroxyoxazole (30i). (a) Reaction of **13** (237 mg, 1.00 mmol) and acetone (**4i**) (10 mL, 0.136 mol) using procedure B gave a solid residue which was triturated with hexane and filtered to give oxazoline **30i** (174 mg, 65%). Mp 142–144 °C (hexane–EtOAc). IR (KBr): 3057, 1637 cm^{-1}. ^{1}H-NMR: 7.81 (dd, J = 7.6, 1.6 Hz, 2H), 7.70 (d, J = 6.4 Hz, 2H), 7.24–7.36 (m, 6H), 3.32 (deuterable s, 1H), 1.70, 1.69 (2 × s, 2 × 3H). ^{13}C-NMR: 165.4, 140.4, 130.7, 128.6, 128.9, 128.3, 128.2, 126.1, 108.5, 107.3, 29.3, 27.7. Anal. Calcd for $C_{17}H_{17}NO_2$ (267.33): C, 76.38; H, 6.41; N, 5.24. Found: C, 76.38; H, 6.18; N, 5.11.

(b) A mixture of 2-[(4-nitrobenzenesulfonyl)oxy]-1,2-diphenylethanone,[26] (1.191 g, 3.00 mmol) and sodium azide (390 mg, 6.00 mmol) in acetone (45 mL) was stirred at room temperature for 32 h and then poured into water and extracted with CH_2Cl_2 (4 × 40 mL). The organic layer was dried and evaporated. The solid residue was crystallized from hexane–EtOAc to give oxazoline **30i** (581 mg, 73%).

2-Hydroxy-2,3-diphenyl-1-oxa-4-azaspiro[4.4]non-3-ene (30j). Reaction of **13** (356 mg, 1.50 mmol) and cyclopentanone (**4j**) (10 mL, 0.113 mol) using procedure B gave an oily residue which was triturated with hexane to give oxazoline **30j** (324 mg, 74%) as a white solid. Mp 129–131 °C (hexane–EtOAc). IR (KBr): 3242 2975, 2935, 2869, 1622 cm^{-1}. ^{1}H-NMR: 7.82 (d, J = 7.6 Hz, 2H), 7.51 (d, J = 7.6 Hz, 2H), 7.25–7.35 (complex m, 6H), 3.13 (deuterable s, 1H), 2.25, 2.05 (2 × m, 2 × 2H), 1.92 (m, 4H). ^{13}C-NMR: 165.3, 140.4, 130.7, 129.9, 128.6, 128.9, 128.3, 128.2, 126.0, 116.7, 108.0, 40.0, 38.4, 24.7, 24.5. Anal. Calcd for $C_{19}H_{19}NO_2$ (293.37): C, 77.79; H, 6.53; N, 4.77. Found: C, 78.14; H, 6.58; N, 4.58.

2,4-Dimethyl-5-phenyloxazole (31a). Procedure D. 2,5-Dihydro-2,4-dimethyl-5-hydroxy-5-phenyloxazole (**29a**) (153 mg, 0.80 mmol, diastereomeric mixture) and TFA (60 μL, 0.78 mmol) in CH_2Cl_2 (20 mL) was allowed to react at 0 °C for 18 h. The mixture was diluted with CH_2Cl_2 (30 mL) and washed successively with water, saturated $NaHCO_3$, and water. The dried organic extracts were evaporated *in vacuo*, and the residue was separated by short-column chromatography (3.5 × 10 cm, eluant: hexane–EtOAc = 3:1). The first component was 1-phenyl-1,2-propanedione (**33**) (23 mg, 19%), yellow liquid.[27] IR (neat): 1713, 1674 cm^{-1}. ^{1}H-NMR: 8.01 (d, J = 7.6 Hz, 2H), 7.64 (m, 1H), 7.49 (m, 2H), 2.52 (s, 3H). ^{13}C-NMR: 200.5, 191.3, 134.5, 131.7, 130.3, 128.8, 26.3.

The second component was oxazole **31a** (49 mg, 35%), a colorless oil which was crystallized on standing. Mp 44–45.5 °C (hexane). lit[28] mp: 45–46 °C, lit.[7] mp: 49–51 °C. IR (KBr): 2930, 1576, 1569 cm^{-1}. ^{1}H-NMR: 7.57 (d, J = 7.6 Hz, 2H), 7.42 (m, 2H), 7.29 (m, 1H), 2.48 (s, 3H), 2.38 (s, 3H). ^{13}C-NMR: 159.4, 145.1, 131.5, 129.3, 128.7, 127.3, 125.1, 13.9, 13.2.

Procedure E. Butyllithium (2.5 M solution in hexane, 0.45 mL, ca. 1.12 mmol) was added dropwise to a stirred and cooled (0 °C) solution of **29a** (207 mg, 1.08 mmol) in absolute THF (10 mL). The mixture was stirred for 5 min then methanesulfonyl chloride (125 mg, 1.09 mmol) in absolute THF (3 mL) was added over 2 min. After 2 h stirring the mixture was poured into water and extracted with CH_2Cl_2 (3 × 30 mL), and the organic extracts were dried and evaporated. Short-column chromatography (3.5 × 7 cm; eluant: hexane–EtOAc = 3:1) afforded 70 mg (37%) pure oxazole **31a**.

2-Ethyl-4-methyl-5-phenyloxazole (31b). 2,5-Dihydro-2-ethyl-4-methyl-5-hydroxy-5-phenyloxazole (**29b**) (212 mg, 1.03 mmol) and TFA (80 μL, 1.04 mmol) were reacted by procedure D to yield **31b** (126 mg, 65%) as colorless oil. IR (neat): 2930, 1568 cm^{-1}. ^{1}H-NMR: 7.57 (d, J = 7.6 Hz, 2H), 7.42 (m, 2H), 7.29 (m, 1H), 2.81 (q, J = 7.7 Hz, 2H), 2.40 (s, 3H), 1.37 (t, J = 7.7 Hz, 3H). ^{13}C-NMR: 163.2, 144.8, 131.4, 129.4, 128.7, 127.2, 125.1, 21.6, 13.2, 11.2. Anal. Calcd for $C_{12}H_{13}NO$ (187.24): C, 76.98; H, 7.00; N, 7.48. Found: C, 77.06; H, 7.22; N, 7.25.

4,5-Diphenyl-2-isopropyloxazole (32d). 2,5-Dihydro-4,5-diphenyl-5-hydroxy-2-isopropyloxazole (**30d**) (266 mg, 0.945 mmol) was treated with butyllithium (2.5 M solution in hexane, 0.4 mL, ca. 1.00 mmol)) and then methanesulfonyl chloride (115 mg, 1.00 mmol) according to procedure E. Short-column chromatography (3.5 × 10 cm, eluant: hexane–EtOAc = 4:1) gave **32d** (126 mg, 51%) as a colorless oil. IR (neat): 2973, 1605, 1569 cm^{-1}. ^{1}H-NMR: 7.64, 7.58 (2 × d, J = 7.2, 7.2 Hz, 2 × 2H), 7.29–7.38 (m, 6H), 3.18 (septet, J = 7.1 Hz, 1H), 1.44 (d, J = 7.1 Hz, 6H). ^{13}C-NMR: 167.6, 144.8, 134.9, 132.7, 129.2, 128.6, 128.5, 128.2, 128.0, 127.9, 126.3, 28.5, 20.5. Anal. Calcd for $C_{18}H_{17}NO$ (263.34): C, 82.10; H, 6.51; N, 5.32. Found: C, 81.97; H, 6.46; N, 5.16. Unreacted **30d** (105 mg, 40%) was recovered from the following fractions.

1-Phenyl-1,2-propanedione (33). To a stirred and cooled (0 °C) mixture of **29a** (287 mg, 1.50 mmol) and 2,6-lutidine (0.20 mL, 1.72 mmol) in CH_2Cl_2 (25 mL) was added trifluoromethanesulfonic anhydride (0.28 mL, 1.66 mmol). After 15 min the mixture was poured into dilute $NaHCO_3$ solution, extracted with CH_2Cl_2 (3 × 20 mL), and dried. Short-column chromatography (3.5 × 8 cm, eluant: hexane–EtOAc = 3:1) afforded 158 mg (71%) **33** dione as a yellow liquid.

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Supplementary Material Available: Copies of the ^{13}C NMR spectra of **14b,c**, **21a**, **24**, and **28** and the ^{1}H NMR spectrum of **21a** (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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