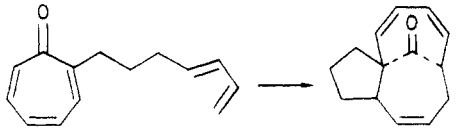
with Me_3SiCl/NaI[8] followed by PDC oxidation gave dione 8[5] (mp 159–160 °C) in 56% yield for the two steps. The structure of this compound was unambiguously established by X-ray analysis (Figure 1). This intermediate appears to be most attractive as a potential precursor to ingenol in view of the well-positioned functional groups suitable for selective elaboration of the remaining structural features common to the ingenane system.

An equally fascinating entry into the ring system of ingenol can be envisioned to arise from an *intra*molecular [6 + 4] cycloaddition process as seen in Scheme III.[9] This possibility was particularly intriguing to us in view of the recalcitrant behavior of substituted tropones toward *inter*molecular [6 + 4] cycloaddition. Heating the readily accessible 2-substituted tropone **9**[5,10] in xylene at reflux for 6 h provided tricyclic ketone **10**[5] in 81% yield, as a single product uncontaminated with materials derived from the [4 + 2] cycloaddition mode. Again the assigned



9 **10**

stereochemistry of the adduct was based on the well-established propensity for tropone–diene [6 + 4] cycloadditions to proceed through an exo transition state.[2] Thus the ingenane skeleton can be assembled in only two steps from readily available 2-chlorotropone.

The viability of both intra- and intermolecular [6 + 4] cycloadditions in the tropone series for application to natural product synthesis has been clearly established, and work is currently under way to elaborate these intermediates into the ingenane diterpenes.

Acknowledgment. We thank the National Institutes of Health (CA-36543) for support of this research. We would also like to thank Dr. Mary Jane Heeg for obtaining the X-ray structure of compound 8.

(9) While this manuscript was in preparation, another example of an intramolecular [6 + 4] tropone cycloaddition surfaced: Funk, R. L., personal communication.

(10) 2-Substituted tropones are relatively difficult to prepare. Compound **9** is available in 61% from the reaction of 2-chlorotropone[11] and the Grignard reagent derived from 1-bromohept-4,6-diene. Details of this procedure will be reported in a separate paper: Rigby, J. H., Kierkus, P.; Moore, T. L.; Rege, S., manuscript in preparation.

(11) TerBorg, A. P.; Van Helden, R.; Bickel, A. F. *Recl. Trav. Chim. Pays-Bas* **1962**, *81*, 177.

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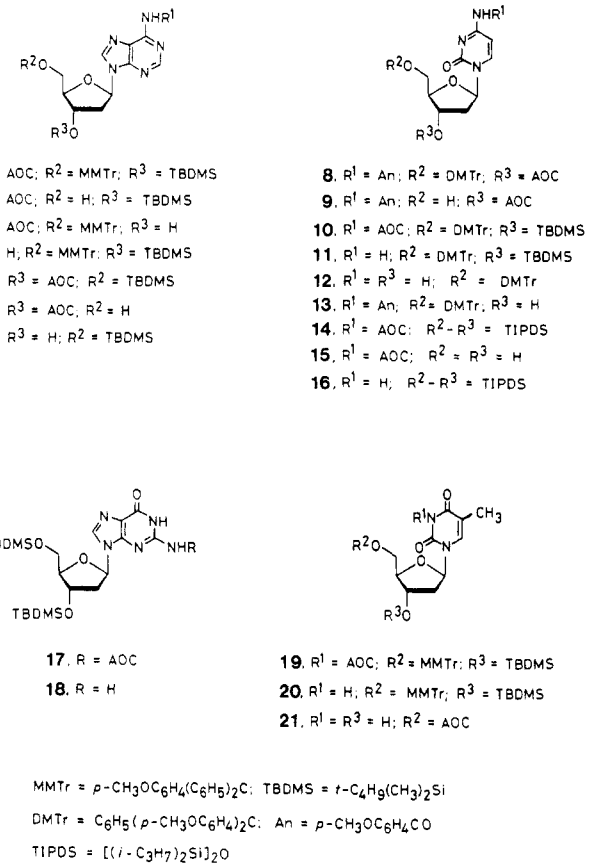
Allyloxycarbonyl Group: A Versatile Blocking Group for Nucleotide Synthesis

Summary: Allyloxycarbonyl (AOC) is excellent for the protection of sugar hydroxyls and amino and imide moieties of nucleoside bases. The deblocking is easily performed by brief treatment with a palladium catalyst and a variety of nucleophiles at room temperature.

Sir: Efficient functional group protection is one of the most fundamental and crucial problems in nucleotide synthesis.[1] Protectors requiring harsh deblocking conditions are not appropriate for the highly functionalized synthetic intermediates. Acyl groups, for instance, are the most widely employed for the amino group protection, but removal of such groups is frequently accompanied by undesired side reactions including cleavage of the internucleotide linkage, resulting in serious loss of the products. We disclose here that the allyloxycarbonyl (AOC) group serves as an extremely useful protecting group in nucleoside and nucleotide synthesis. AOC can block amino and imide moieties of nucleoside bases and sugar hydroxyls and is removable by brief treatment with a palladium catalyst.[2]

Chart I



First, the sensitivity of AOC-protected nucleoside bases was examined. Conditions for deblocking of the MMTr or DMTr and TBDMS protecting groups do not affect the AOC protection. For example, when the adenosine nucleoside **1** (Chart I), having three kinds of protecting groups, was treated with dichloroacetic acid in dichloromethane at room temperature, only MMTr group was removed to give the 5′-O-unprotected derivative **2** in 84% yield. Exposure of **1** to tetrabutylammonium fluoride (TBAF) in THF furnished selectively the 3′-O-free nucleoside **3** in 97% yield. Similarly, the 5′-O-*tert*-butyldimethylsilylated adenosine nucleoside **5** underwent the selective deblocking of TBDMS protection by treatment with TBAF to give quantitatively the 5′-O-free derivative **6**. TBAF treatment of N^4-allyloxycarbonylated deoxycytidine **14** removed selectively the 3′,5′-cyclic silyl pro-

(1) Comprehensive reviews: Reese, C. B. *Tetrahedron* **1978**, *34*, 3143. Ikehara, M.; Ohtsuka, E.; Markham, A. F. *Adv. Carbohydr. Chem. Biochem.* **1979**, *36*, 135. Crockett, G. C. *Aldrichimica Acta* **1983**, *16* (3), 47. Hata, T. *J. Synth. Org. Chem. Jpn.* **1984**, *42*, 429. Zhdanov, R. I.; Zhenodarova, S. M. *Synthesis* **1975**, 222. Amarnath, V.; Broom, A. D. *Chem. Rev.* **1977**, *77*, 183. Ishido, Y.; Hata, T. *Kagaku Sosetsu* **1978**, *19*, 207. Ohtsuka, E. *Ibid.* **1985**, *46*, 209.

(2) For a comprehensive review: Trost, B. M.; Verhoeven, T. R. *Comprehensive Organometallic Chemistry*; Pergamon: Oxford, 1983; Vol. 8, pp 799–938.

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Table I. Deprotection of Allyloxycarbonylated Nucleosides[a]

protected nucleoside	Pd catalyst	nucleophile	time, min	product	% yield[b]
1	$Pd[P(C_6H_5)_3]_4$	dimedone	5	4	96[c]
1	$Pd[P(C_6H_5)_3]_4$	n-$C_4H_9NH_2$	90	4	79[c,d]
1	$Pd[P(C_6H_5)_3]_4$	$(C_2H_5)_2NH$	15	4	80[c,d]
1	$Pd[P(C_6H_5)_3]_4$	$(C_2H_5)_3N$	30	4	38[c,d]
1	$Pd[P(C_6H_5)_3]_4$	C_5H_5N	30	4	34[c,d]
1	$Pd[P(C_6H_5)_3]_4$	CH_3OH	20	4	40[c,d]
1	$Pd[P(C_6H_5)_3]_4$	HCOOH	30	4	100[c]
1	$Pd[P(C_6H_5)_3]_4$	HCOOH/n-$C_4H_9NH_2$	5	4	94
1	$Pd[P(C_6H_5)_3]_4$	CH_3COOH	10	4	96[c]
1	$Pd[P(C_6H_5)_3]_4$	CH_3COOK	120	4	42[c,d]
1	$Pd[P(C_6H_5)_3]_4$	$(n$-$C_4H_9)_3SnH$	15	4	45[c,d]
1	$Pd_2(dba)_3$·$CHCl_3$[e]	HCOOH/n-$C_4H_9NH_2$	5	4	100[c]
1	$PdCl_2$	HCOOH/n-$C_4H_9NH_2$	240	4	99
1	$PdCl_2(C_6H_5CN)_2$	HCOOH/n-$C_4H_9NH_2$	240	4	100[c]
1	$Pd(OCOCH_3)_2$	HCOOH/n-$C_4H_9NH_2$	45	4	96
10	$Pd[P(C_6H_5)_3]_4$	$(C_2H_5)_2NH$	180	11	68[f]
10	$Pd[P(C_6H_5)_3]_4$	HCOOH	20	11	90
10	$Pd[P(C_6H_5)_3]_4$	$HCOONH_4$	160	11	75[f]
10	$Pd[P(C_6H_5)_3]_4$	HCOOH/n-$C_4H_9NH_2$	5	11	96
10	$Pd[P(C_6H_5)_3]_4$	HCOOH/$(C_2H_5)_2NH$	35	11	96
10	$Pd[P(C_6H_5)_3]_4$	HCOOH/$(C_2H_5)_3N$	100	11	93
10	$Pd[P(C_6H_5)_3]_4$	HCOOH/C_5H_5N	50	11	81
10	$Pd(OCOCH_3)_2$	HCOOH/n-$C_4H_9NH_2$	40	11	93
10	$Pd(OCOCH_3)_2$[g]	HCOOH/n-$C_4H_9NH_2$	960	11	94
10	$Pd(OCOCH_3)_2$[h]	HCOOH/n-$C_4H_9NH_2$	45	11	92
14	$Pd[P(C_6H_5)_3]_4$	HCOOH/n-$C_4H_9NH_2$	5	16	94
17	$Pd[P(C_6H_5)_3]_4$	HCOOH/n-$C_4H_9NH_2$	5	18	80[i,j]
19	$Pd[P(C_6H_5)_3]_4$	$NaCH(COOC_2H_5)_2$[k]	15	20	93
19	$Pd[P(C_6H_5)_3]_4$	n-$C_4H_9NH_2$	5	20	97

[a] The reaction was carried out in THF containing the protected nucleoside (1 equiv), the Pd catalyst (5 mol %), $P(C_6H_5)_3$ (20–30 mol %), and the nucleophile (2 equiv) at 20–25 °C. [b] Unless otherwise stated, isolated yield is listed. [c] The yield was estimated by HPLC (ODS Develosil, a 1:15:2 mixture of CH_3CN, CH_3OH, and H_2O, 50 °C). [d] N^6-Allylated adenosine was formed in 10–55% yield as the byproduct. [e] Tris(dibenzylideneacetone)dipalladium(0) chloroform. [f] Byproducts consisting mainly of N^4-allylated cytodine nucleoside were obtained in 15–30% yield. [g] In place of $P(C_6H_5)_3$, $P(n$-$C_4H_9)_3$ was used as the additive. [h] In place of $P(C_6H_5)_3$, $P(OCH_3)_3$ was added. [i] The reaction was achieved in a 5:1 mixture of THF and hexamethylphosphoric triamide. [j] The TLC analysis indicated that the clean reaction took place, but low solubility of the deblocked product in ordinary organic solvents caused some loss of the product during extractive workup. [k] An 8.5 equiv of the nucleophile was used.

Table II. Allyloxycarbonylation of Nucleosides[a]

nucleoside	AOC agent (equiv)	base (equiv)	temp, °C	time	product	% yield[b]
4	**23** (1.5)	t-C_4H_9Li (2)	−78	5 min	1	95
11	**23** (1.2)	$(C_2H_5)_3N$ (1.5)	20	1.5 h	10	87
16	**23** (1.2)	$(C_2H_5)_3N$ (2)	20	3 h	14	93
18	**22** (3.3)	t-C_4H_9MgCl (3)[c]	20	10 min	17	70
20	**22** (3)	t-C_4H_9MgCl (1)	20	4 h	19[d]	94

[a] The reaction was conducted in THF, unless otherwise noted. [b] Isolated yield. [c] A 5:1 mixture of THF and hexamethylphosphoric triamide was used as the solvent. [d] The structure was assigned tentatively. The alternative possibility of the O^4-allyloxycarbonylated derivative could not be excluded.

tection[3] to give the *N*-AOC-protected derivative **15** in 92% yield. Further, exposure of the 5′-O-(*p,p*′-dimethoxytrityl)-3′-O-(allyloxycarbonyl)cytidine derivative **8** to dichloroacetic acid afforded exclusively the detritylated product **9**. By contrast, AOC is extremely sensitive to palladium complexes. Thus the AOC group was removed readily from the nucleoside bases by brief treatment with 5 mol % of $Pd[P(C_6H_5)_3]_4$ and 20–30 mol % of $P(C_6H_5)_3$ in the presence of various nucleophiles shown in Table I. In place of $Pd[P(C_6H_5)_3]_4$, various palladium compounds such as $Pd_2(dba)_3$·$CHCl_3$, $Pd(OCOCH_3)_2$, $PdCl_2$, $PdCl_2(C_6H_5CN)_2$, etc. were also usable. As the nucleophilic agent, ammonium formates gave satisfactory results in all cases. Use of primary and secondary amines is also recommended except for the deprotection of adenosine or cytidine derivative which affords a considerable amount of the N^6- or N^4-allylated byproduct, respectively. These unique, mild deblocking conditions tolerate other hydroxyl protecting groups such as MMTr, DMTr, and TBDMS as well as methyl or *o*-chlorophenyl internucleotide-linkage protector. The *N*-AOC group was stable in pyridine but readily hydrolyzed by stronger bases in methanol. For example, exposure of **10** to a 1:1 mixture of concentrated ammonia and methanol or 2 N aqueous sodium hydroxide and methanol (10 °C, 20 h) afforded **11** or **12**, respectively.

The AOC protection of *aliphatic* amines in conjunction with transition-metal catalysis is known in chemistry of penicillins,[4] amino acids,[5] etc.[6] However, introduction of AOC to heteroaromatics is not straightforward; the reaction conditions are highly dependent on the structure. We

(3) Markiewicz, W. T. *J. Chem. Res., Synop.* **1979**, 24; *J. Chem. Res., Miniprint* **1979**, 0181.

(4) Jeffery, P. D.; McCombie, S. W. *J. Org. Chem.* **1982**, *47*, 587.

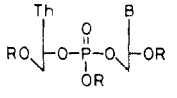
(5) Kunz, H.; Unverzagt, C. *Angew. Chem.* **1984**, *96*, 426. Minami, I.; Ohashi, Y.; Shimizu, I.; Tsuji, J. *Tetrahedron Lett.* **1985**, *26*, 2449. See also: Kinoshita, H.; Inomata, K.; Kameda, T.; Kotake, H. *Chem. Lett.* **1985**, 515.

(6) For AOC deprotection by reagents other than the palladium complex, see: Stevens, C. M.; Watanabe, R. *J. Chem. Soc.* **1950**, *72*, 725. Boissonnas, R. A.; Preitner, G. *Helv. Chim. Acta* **1953**, *36*, 875. Corey, E. J.; Suggs, J. W. *J. Org. Chem.* **1973**, *38*, 3223.

recommend the procedures of Table II using allyloxycarbonyl chloride (AOCCl) (**22**)[7] or allyl 1-benzotriazoylcarbonate (AOCOBT) (**23**),[8] where choice of the base and solvent is important for obtaining satisfactory yields.

The AOC group is also employable for the sugar-hydroxyl protection.[4,9] The *O*-allyloxycarbonylated nucleoside **8** was prepared in 95% yield by *tert*-butylmagnesium chloride (2 equiv) aided reaction of cytidine nucleoside **13** (1 equiv) and the AOC agent **22** (1.2 equiv). When this *O*-AOC nucleoside was treated with a catalytic amount of $Pd[P(C_6H_5)_3]_4$ in the presence of HCOOH/n-$C_4H_9NH_2$ (2 equiv each) for 1 h, **13** was brought back. Conveniently, the Pd(0)-catalyzed reaction of the N,O-bis(allyloxycarbonylated) derivative **5** removed contemporaneously both protections to afford the nucleoside **7** in quantitative yield.

Internucleotide linkage is protectable by allyl group.[10] The above described characteristic properties of AOC, coupled with the phosphite method using allyl phosphorodichloridite, enabled us to open an extremely convenient way to dinucleoside phosphates. The key operation here is complete deprotection of fully-protected dinucleoside phosphotriester intermediates by single treatment with Pd(0) catalyst. Thus, collidine-assisted (4.6 equiv) condensation of the 3′-O-unprotected thymidine nucleoside **21** (2 equiv), $CH_2{=}CHCH_2OPCl_2$ (2 equiv), and the 5′-O-free adenosine **6** (1 equiv) followed by NO_2 oxidation (THF, −78 °C) afforded the protected TpA **24** in 80% yield. When **24** was treated with a mixture of $Pd[P(C_6H_5)_3]_4$ and $P(C_6H_5)_3$ (5 and 20 mol %/allyl), formic acid (10 equiv), and butylamine (10 equiv) in THF at room temperature for 30 min, the four allylic protecting groups were removed all at once from the nucleoside base, sugar hydroxyl, and internucleotide bond to give TpA (**25**) in 97% yield.



24, B = Ad^{AOC}; R = AOC

25, B = Ad; R = H

In summary, the AOC group acts as both specific and general protectors. This method is useful in view of mildness of the deprotection conditions and simplicity of the workup, providing a powerful tool in nucleotide synthesis.

Supplementary Material Available: Experimental details (16 pages). Ordering information is given on any current masthead page.

(7) We are grateful to Hodogaya Chemicals, Co., for the generous gift of allyloxycarbonyl chloride.

(8) AOCOBT (**23**), mp 107–111 °C, was prepared by the triethylamine-promoted (1 equiv) reaction of AOCCl (**22**) (1 equiv) and 1-hydroxybenzotriazole (1 equiv) in THF at room temperature for 10 min.

(9) Guibe, F.; M'Leux, Y. S. *Tetrahedron Lett.* **1981**, *22*, 3591.

(10) Hayakawa, Y.; Uchiyama, M.; Kato, H.; Noyori, R. *Tetrahedron Lett.* **1985**, *26*, 6505.

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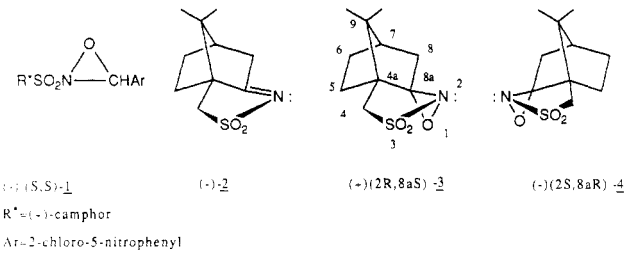
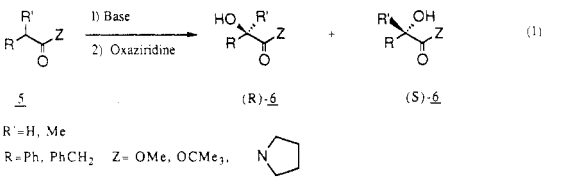
Asymmetric Oxidation of Ester and Amide Enolates Using New (Camphorylsulfonyl)oxaziridines

Summary: The first asymmetric oxidation of ester and amide lithium enolates **5** to optically active α-hydroxy carbonyl compounds **6** is reported using new, easily prepared, stable (camphorylsulfonyl)oxaziridines (+)-(2*R*,8a*S*)-**3** and (−)-(2*S*,8a*R*)-**4**. Either enantiomer of **6** can be readily obtained because the configuration of the oxaziridine three-membered ring determines the product stereochemistry.

Sir: Optically active α-hydroxy carbonyl compounds are versatile chiral building blocks for asymmetric synthesis and are important structural subunits of natural products.[1] Recently we[2] and Evans[3] independently reported that oxidation of chiral enolates, using 2-(phenylsulfonyl)-3-phenyloxaziridine (**1**, R* = Ar = Ph), is an attractive route to these valuable compounds in high optical purity (80–98% de).[4] However, a disadvantage of any chiral auxiliary based asymmetric synthesis is the necessity of preparing and eventually removing the chiral auxiliary reagent.

We now report the first examples of a simple procedure for the synthesis of *both* enantiomers of α-hydroxy compounds **6** in good optical purity. This procedure involves the asymmetric oxidation of enolates using new, readily available camphorsulfonic acid derived sulfonyloxaziridines (+)-**3** and (−)-**4** (eq 1).





Our previous studies have demonstrated that chiral 2-sulfonyloxaziridines, such as (−)-(*S*,*S*)-**1**, are useful asymmetric oxidizing reagents which give high enantioselectivities for the oxidation of certain unfunctionalized sulfides and alkenes.[5-8] However, in the synthesis of

(1) For leading references on chiral α-hydroxy carbonyl compounds, see: (a) Brown, H. C.; Pai, G. G.; Jadhav, P. K. *J. Am. Chem. Soc.* **1984**, *106*, 1531. (b) Gamboni, R.; Mohr, P.; Waespe-Sarcebvic, N; Tamm, C. *Tetrahedron Lett.* **1985**, 203. (c) Oppolzer, W.; Dudfield, P. *Helv. Chim. Acta* **1985**, *68*, 216.

(2) Davis, F. A.; Vishwakarma, L. C. *Tetrahedron Lett.* **1985**, 3539.

(3) Evans, D. A.; Morrissey, M. M.; Dorow, R. L. *J. Am. Chem. Soc.* **1985**, *107*, 4346.

(4) The MoOPH oxidation of ester enolates using a camphor-based chiral auxiliary has been reported (14–93% de).[1b]

(5) For a review of the asymmetric oxidations using chiral 2-sulfonyloxaziridines, see: Davis, F. A.; Jenkins, R. H., Jr. In *Asymmetric Synthesis*; Morrison, J. D.; Ed.; Academic: New York, 1984, Vol. 4, Chapter 4, pp 313–353.

(6) Asymmetric oxidation of sulfides: (a) Davis, F. A.; Lamendola, J. F., Jr.; Nadir, U.; Kluger, E. W.; Sedergran, T. C.; Panunto, T. W.; Billmers, R.; Jenkins, R., Jr.; Turchi, I. J.; Watson, W. H.; Chen, J. S.; Kimura, M. *J. Am. Chem. Soc.* **1980**, *102*, 2000. (b) Davis, F. A.; McCauley, J. P., Jr.; Harakal, M. E. *J. Org. Chem.* **1984**, *49*, 1466.

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