available.[20] Alternatively, they were analyzed as their HCl salts.

Preparation of the Oximes (*E*)- and (*Z*)-6a–d.—The *E* oximes were prepared by standard procedures[19] and isomerized to their *Z* counterparts by the method of Crawford and Woo.[21] The melting point data are given in Table I.

Reaction of *E* and *Z* Oximes 4a and 4b with Chlorosulfonyl Isocyanate.—Each of the oximes (0.01 mol) was dissolved in anhydrous benzene and treated with chlorosulfonyl isocyanate (0.01 mol) at room temperature. The precipitate that formed was collected by filtration and washed with hexane. The adducts were permitted to stand in aqueous solution (20 ml) overnight and filtered and the solids obtained were examined by pmr (acetone-d_6) spectroscopy. *E* oxime and *O*-carbamoyloxime (2:1, respectively, by comparison to known mixtures) were found in each case.

Reaction of Aldehydes with Hydroxyurea.—*p*-Bromobenzaldehyde (1.0 g, 5.4 mmol) and *N*-hydroxyurea (814 mg, 10.7 mmol) were mixed, at room temperature, in ethanol–water (2:1) (25 ml), and acid (1.9 ml, 1 *N* HCl) was added. The solution was heated to reflux for 1 hr and poured over ice. The solid so generated (67%) was identified as (*E*)-*p*-bromobenzaldehyde oxime by comparison with a known sample (*vide supra*). In a similar fashion, but without heating, *m*-nitrobenzaldehyde yielded crystalline (*E*)-*m*-nitrobenzaldehyde oxime (83%). It should be pointed out for this latter material that tlc (2:1 benzene–ether) always demonstrates a small amount of *Z* contaminant. The *Z* isomer cannot be detected by pmr.

Acknowledgment.—One of us (H. G. F.) gratefully acknowledges financial assistance from the Fund for Scientific Education, Inc., Philadelphia, Pa.

Registry No.—**4a**, 41514-42-5; **4b**, 41514-43-6; **4c**, 41514-44-7.

(20) "The Sadtler Standard Spectra," Sadtler Research Laboratories, Philadelphia, Pa., 1972.

(21) R. J. Crawford and C. Woo, *Can. J. Chem.*, **43**, 3178 (1965).

Conversion of 1,2-Diols *via* Cyclic Ortho Acetates to Acetates of Chlorohydrins by Treatment with Trimethylsilyl Chloride[1]

MELVIN S. NEWMAN* AND DANIEL R. OLSON[2]

Evans Chemistry Laboratory, The Ohio State University, Columbus, Ohio 43210

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In earlier papers, the conversion of 1,2-diols, **1**, into esters of the corresponding chlorohydrins, **2**, was accomplished by two methods: A, reaction with an α-keto acid to produce a ketal acid, **3**, followed by treatment of the latter with phosphorus pentachloride or thionyl chloride,[3] and B, reaction with trimethyl orthoacetate to form a cyclic ortho ester, **4**, followed by treatment with triphenylmethyl (trityl) chloride.[4] In both cases the reactions were shown to be highly regio- and stereospecific. Since the chlorohydrin esters are readily converted into epoxides by suitable treatment with bases, the synthesis of optically active epoxides is readily accomplished.

A disadvantage of method A is that the yields of **3** based on **1** lie in the 50–70% range. The yields of **4** in method B are excellent but the removal of methyl trityl ether can be troublesome. In this paper we describe method C, in which the disadvantages of methods A and B are overcome. The new method consists of heating the ortho esters, **4**, in methylene chloride with excess trimethylsilyl chloide[5] (much less expensive than trityl chloride). The conversions of **4** to **2** are of the same excellence as the corresponding steps in methods A and B. The removal of excess trimethylsilyl chloride and methyl trimethylsilyl ether is easily accomplished by distillation. The stereochemical results are the same as those reported.[3,4]

(1) This work was supported by Grant CA-07394 from the National Institutes of Health.

(2) Postdoctoral research associate.

(3) (a) M. S. Newman and C. H. Chen, *J. Amer. Chem. Soc.*, **94**, 2149 (1972); (b) *J. Org. Chem.*, **38**, 1173 (1973).

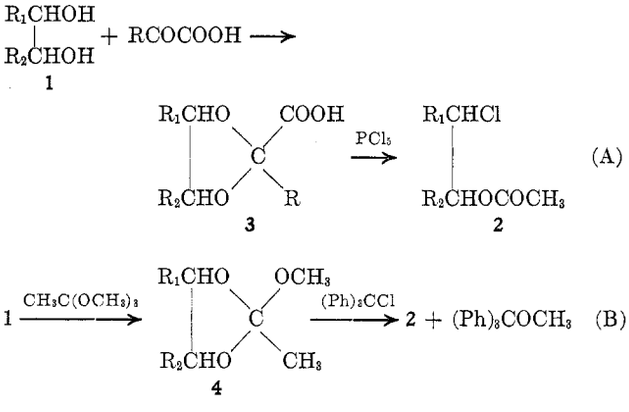
(4) M. S. Newman and C. H. Chen, *J. Amer. Chem. Soc.*, **95**, 278 (1973).

TABLE I

REACTIONS OF CYCLIC ORTHO ESTERS WITH $(CH_3)_3SiCl$

Cyclic ortho ester **4**	Time, hr	Ortho ester, mmol	$(CH_3)_3$-SiCl, mmol	Yield, % **2**
4a, $R_1 = CH_3$; $R_2 = H$	2	20.3	33	86[a]
4b, $R_1 = Ph$; $R_2 = H$	1.5	17.8	28	91[b]
4b, $R_1 = Ph$; $R_2 = H$	2	11.3	12	92[c]
4c, $R_1 = R_2 = CH_3$	1.7	11.8	19	97[d]
4c, $R_1 = R_2 = CH_3$	5	35	37	73[e]
$(CH_3)_2CO$ $>C<$ OCH_3 / H_2CO CH_3	0.5	20.6	26	89[g]

[a] Bp 48–49° (25 mm). This compound was 1-chloro-2-propyl acetate as shown by nmr. However, no europium shift reagent was used as was the case when the same compound was obtained previously and shown to contain about 6% of 2-chloro-1-propyl acetate (see footnote 7 in ref 4). [b] Bp 83–85° (0.2 mm), inactive, mixture of about 95% 2-chloro-2-phenyl acetate and 5% 2-chloro-1-phenyl acetate. [c] $[\alpha]^{25}D$ 86 ± 1° (*c* 3.550, $CHCl_3$). Treatment with sodium hydroxide gave (*R*)-(−)styrene oxide, $\alpha^{25}D$ 34.1° neat, 1 dm, of 97% optical purity [the highest rotation for styrene oxide, 35.2° neat, 1 dm, is reported by C. R. Johnson and C. W. Schroeck, *J. Amer. Chem. Soc.*, **93**, 5303 (1971)], $[\alpha]^{25}D$ −22.5 ± 0.2° (*c* 2.39, $CHCl_3$). [d] Bp 83–84° (52 mm), inactive. [e] The center cut only, bp 75.5–76.0° (34 mm), was taken for measurement of optical activity, $\alpha^{25}D$ 13.32°, neat, 1 dm. Treatment with sodium hydroxide gave D-(+)-2,3-epoxybutane, $\alpha^{25}D$ 45.6°, neat, 1 dm [P. J. Leroux and H. J. Lucas, *J. Amer. Chem. Soc.*, **73**, 41 (1951), report $\alpha^{25}D$ 46.75°]. [f] Bp 82.0–82.5° (85 mm); nmr [CCl_4, $(CH_3)_4Si$] δ 3.75 (s, 2, CH_2), 3.22 (s, 3, OCH_3), 1.45, 1.35 [2 singlets, 6, $(CH_3)_2C$], 1.27 [s, 3, $OC(CH_3)O$]; molecular ion, 146. *Anal.* Calcd for $C_7H_{14}O_3$: C, 57.5; H, 9.7. Found (analysis by Galbraith Laboratories, Knoxville, Tenn.): C, 57.5; H, 9.6. This new compound was prepared by the method described.[4] [g] Bp 63.5–64.5° (23 mm) [A. Bruylants, M. Tits, C. Dieu, and R. Gauthier, *Bull. Soc. Chim. Belg.*, **61**, 366 (1952), give bp 90–91°]. No isomer detected (see footnote 7 in ref 4). Nmr [CCl_4, $(CH_3)_4Si$] δ 4.09 (s, 2, CH_2), 2.40 (s, 3, CH_3CO), 1.77 [s, 6, $(CH_3)_2C$].



(5) The use of $(CH_3)_3SiCl$ was first demonstrated by Dr. Paul Tornstrom in our laboratory.

$$4 + (CH_3)_3SiCl \longrightarrow 2 + (CH_3)_3SiOCH_3 \qquad (C)$$

In a typical reaction a solution of 3.46 g (17.8 mmol) of inactive 2-methoxy-2-methyl-4-phenyl-1,3-dioxolane[4]

(**4b**, R_1 = H; R_2 = Ph) and 3 g (28 mmol) of trimethylsilyl chloride in 8 ml of methylene chloride was held at reflux for 1.5 hr. On distillation there was obtained 3.22 g (91%) of a 95:5 mixture of 2-chloro-2-2-phenylethyl acetate, **2** (R_1 = C_6H_5; R_2 = H), and 2-chloro-1-phenylethyl acetate, **2** (R_1 = H; R_2 = C_6H_5), respectively. This and other compounds prepared by the new procedure are listed in Table I.

It should be pointed out that, while the yields of 1,2-chlorohydrin acetates obtained from 1,3-dioxolanes by method C are comparable to those by method B, the reaction of trimethylsilyl chloride with 2-methoxy-2,5,5-trimethyl-1,3,-dioxane (compound **4** in ref 4) and with 2-methoxy-2-methyl-1,3-dioxepane (compound **5** in ref 4) did not take place to give the expected chloro esters in good yield.

Registry No.—**2a**, 627-68-9; **2b**, 6509-95-1; **2c**, 760-86-1; **2** [R_1 = $(CH_3)_2$; R_2 = H], 6509-93-9; **4a**, 39834-09-8; **4b**, 39904-21-7; **4c**, 42077-65-6; **4** [R_1 = $(CH_3)_2$; R_2 = H], 42077-66-7; trimethylsilyl chloride, 75-77-4.

Structure of the Metabolite LL-S490β from an Unidentified *Aspergillus* Species

GEORGE A. ELLESTAD,* PATRICK MIRANDO, AND MARTIN P. KUNSTMANN

Lederle Laboratories, A Division of American Cyanamid Company, Pearl River, New York 10965

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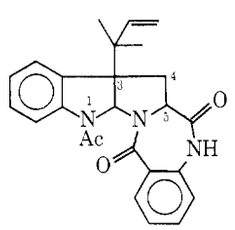
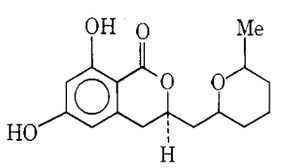
In relation to a screening program seeking useful biologically active mold metabolites, we examined fermentations of an unidentified *Aspergillus* species. We describe here the structure of a novel benzodiazepinedione (I) designated LL-S490β. In addition to I, we isolated cladosporin[1] (asperentin,[2] II), an antifungal



I



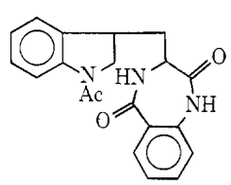
II

metabolite recently obtained from *Cladosporium cladosporiodes*[1] and *Aspergillus flavus*.[2]

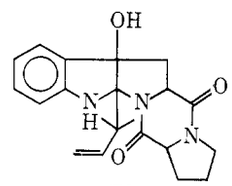
LL-S490β, $C_{25}H_{25}N_3O_3$, mp 238–240°, $[\alpha]_D$ +425° (MeOH), exhibits a mass spectrum characterized by a strong molecular ion at *m/e* 415 in addition to significant peaks at *m/e* 373 (M − 42), 346 (M − 69), and the base peak at 304 [M − (42 + 69)]. A high-intensity peak at *m/e* 130 is assigned to the indoline-3-methylene ion.[3] The general appearance of the uv spectrum [λ_{max} 210 (ε 61,000), 245 (22,000), and 284 nm (sh, 3940)] is very reminiscent of the *N*-acylindoline chromophore,[4] although the high extinction values indicate the presence of an additional chromophoric unit.

The nmr spectrum of I discloses the presence of eight aromatic proton signals between δ 6.83 and 8.17. A sharp 3-H singlet at δ 2.60 is assigned to the methyl of an *N*-acetyl group. Two tertiary *C*-methyl signals resonate at δ 1.02 and 1.21 and, in conjunction with the loss of 69 mass units in the mass spectrum, are assigned to the inverted γ,γ-dimethylallyl group. Consistent with this is the appearance of the very characteristic ABX pattern of the three vinyl protons of the C_5 moiety between δ 5.16 and 5.92.[5]

The ir spectrum of I shows absorption at 3300, 1689, and 1647 cm^{-1} assigned to NH and amide functionalities, respectively. In fact the latter two absorptions strongly suggest the presence of a dipeptide system.[6] Consideration of the molecular formula and the functionality described above suggests the combination of a tryptophane portion with anthranilic acid to give the partial structure III below. The uv of 3,4-dihydro-



III



IV

4-methyl-1*H*-1,4-benzodiazepine-2,5-dione [λ_{max} 215 nm (ε 32,100) and 291 (2180)][7] superimposed with that of the *N*-acylindoline system accounts for the observed uv spectrum of I.

The final molecular assembly was arrived at by examination of an ABX pattern in the nmr spectrum between δ 2.46 and 3.90 assigned to the geminal protons at C-4 and the methine hydrogen at C-5. The geminal pair resonate as four-line patterns at δ 2.46 and 3.42 with J_{AB} = 14, J_{AX} = 8.5, and J_{BX} = 8.0 Hz. The H-5 signal appears at δ 3.90 as an apparent triplet (J = 8 Hz). The similar J values of the corresponding nmr system in brevianamide E[5] (IV) provide a good analogy.

Placement of the inverted terpene unit at C-3 is dictated by the fact that the aforementioned geminal hydrogens are spin coupled only to the C-5 methine hydrogen. A sharp 1-H singlet at δ 6.00 is assigned to the C-2 methine hydrogen on comparison with the spectrum of a model compound.[4b] The singlet nature of this signal supports the absence of a proton at C-3.

An exchangeable 1-H singlet (br d) at δ 8.5 is attributable to the NH of the benzodiazepinedione ring.

The occurrence of I with the inverted C_5 unit at C-3 is unusual and raises the question as to the mode of incorporation of the terpene moiety into the indolyl system. A chemical precedent comes from the work of Bycroft and Landon,[8] who incorporated the inverted C_5 grouping at C-3 by a thio-Claisen rearrange-

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(8) B. W. Bycroft and W. Landon, *Chem. Commun.*, 967 (1970).