at 34.5 and 23.5, and at 23.5 °C were 1.41×10^{-3}, 7.36×10^{-4}, 1.46×10^{-4} s^{-1}, respectively ($E^{\ddagger}$ = 24.0 ± 2.7 kcal/mol).

Reaction of 7 with DMAD. DMAD (284 mg, 2 mmol) was added to a 10-mL solution of 378 mg (2 mmol) of **7** in $CHCl_3$, acetone, or acetaldehyde at 16 °C and was allowed to react over 10 h. The solvent was evaporated, and the residue was chromatographed over Al_2O_3 to give 496, 402, and 331 mg of **8** (75%, 61%, and 50% yield) respectively: mp 72 °C; IR (KBr) 2980, 1740, 1700, 1605 cm^{-1}; UV (hexane) λ_{max} 289 (ϵ 19500); ^1H NMR (CCl_4) δ 0.97 (t, J = 7 Hz, 3 H), 3.3 (q, J = 7 Hz, 2 H), 3.57 (s, 3 H), 3.93 (s, 3 H), AB q at 4.10 and 4.39 (J = 14 Hz, 2 H), ABX system with δ(A) 5.36, δ(B) 5.50, and δ(X) 5.99 (J_{AB} = 1.5 Hz, J_{AX} = 16 Hz, J_{BX} = 10 Hz), 7.43 (br s, 5 H); ^{13}C NMR 16.1 (q), 43.3 (t), 50.1 (q), 52.8 (q), 59.6 (t, C-6), 90.9 (s, C-5), 97.7 (s, C-2), 119.6 (t), 128.0 (d), 128.5 (d), 128.9 (d), 136.3 (d), 138.6 (s), 147.4 (s, C-4), 164.9 (s), 165.4 (s) ppm; ^{13}C NMR assignments are tentative and are based on chemical shifts and off-resonance decoupled spectra; mass spectrum, m/e (relative intensity) 331 (M^+, 10). Anal. Calcd for $C_{18}H_{21}NO_5$: C, 65.26; H, 6.34; N, 4.23. Found: C, 65.55; H, 6.37; N, 4.07.

Crystal Structure Analysis of 8. Suitable single crystals of the compound were obtained by slow evaporation from a hexane solution. Accurate cell constants were obtained by a least-squares procedure applied to 25 reflections with $12° < \theta \leq 18°$ automatically centered on an Enraf-Nonius CAD4 diffractometer at the beginning of data collection. Crystal data: $C_{18}H_{21}NO_5$, M_r = 331.4, monoclinic, a = 7.834 (1) Å, b = 13.334 (2) Å, c = 16.595 (2) Å, β = 95.06 (1)°, V = 1726.7 Å^3, Z = 4, d_c = 1.275 g cm^{-3}, $F(000)$ = 704; Mo Kα radiation, λ_{mean} = 0.71069 Å, μ(MoKα) = 1.1 cm^{-1}; space group $P2_1/n$.

The intensities of all reflections within $1° < \theta < 27°$ were measured by using graphite-monochromatized Mo Kα radiation and an ω–2θ scan technique with a scan width of 1.2 + 0.35 tan θ. The scan rate varied according to the detected intensity between 1.0 and 4.0° min^{-1}. Three intensity-control reflections, monitored frequently, showed no decay of the crystal. The intensities were corrected for Lorentz and polarization effects and variable measuring time but not for absorption or secondary extinction. A total of 3127 unique reflections were collected, of which 2074 reflections had intensities above a threshold of three standard deviations of the intensity and were used in the final refinement.

The structure was solved by direct methods using the MULTAN system of computer programs. Refinement was carried out by full-matrix least-squares methods, including the atomic coordinates of all atoms, anisotropic thermal parameters of the nonhydrogen atoms, and isotropic thermal parameters of the hydrogens. All hydrogen atom positions could be found from difference maps. Refinement of the structural model converged to R = 0.039; the quantity minimized was $\sum w(\Delta F)^2$ with $w = 1/\sigma^2(F_0)$. There were no significant features in the difference map after the refinement was complete; the highest peak and deepest trough were 0.26 and −0.17 e Å^{-3}, respectively. Positional and thermal atomic parameters and lists of observed and calculated structure factors are available as supplementary material.

Reaction of 8 with HCl. A solution of 331 mg (1 mmol) of **8** in 5 mL of $CHCl_3$ was stirred with 0.5 mL of concentrated HCl for 15 min. The acid was neutralized with solid K_2CO_3, and the aqueous solution extracted with $CHCl_3$ (3 × 30 mL). The combined organic layers were dried (K_2CO_3) and filtered, and the solvents were removed in vacuum to give 330 mg of crude **12**. Recrystallization (hexane) gave the product: 298 mg (81%); mp 89 °C; IR (KBr) 2920, 1740, 1700, 1605 cm^{-1}; UV (hexane) λ_{max} 287.4 (ϵ 11000); ^1H NMR (CCl_4) δ 1.13 (t, J = 7 Hz, 3 H), 2.6 (t, J = 7.5 Hz, 2 H), 3.13 (q, J = 7 Hz, 2 H), 3.48 (s, 3 H), 3.77 (s, 3 H), 3.5 (m, 2 H), AB q at 3.81 and 4.21 (J = 14.k Hz, 2 H), 7.27 (s, 5 H); ^{13}C NMR δ 16.2 (q), 39.0 (t), 40.2 (t), 42.9 (t), 51.1 (q), 52.9 (q), 59.1 (t, C-6), 90.5 (s, C-5), 97.9 (s, C-2), 127.1 (d), 128.6 (d), 128.9 (d), 138.4 (s), 147.3 (s, C-4), 164.9 (s), 165.3 (s) ppm; mass spectrum, m/e (relative intensity) 368 (M^+, 12). Anal. Calcd for $C_{18}H_{22}NO_5Cl$: C, 58.78; H, 6.03; N, 3.81; Cl, 9.64. Found: C, 58.43; H, 6.24; N, 3.67; Cl, 9.83.

Hydrogenation of 8. Compound **8** (331 mg, 1 mmol) in 25 mL of methanol reacted in the presence of 10 mg of 10% Pd/C with 24 mL of H_2. The catalyst was filtered off (Celite), and the solvents were removed under vacuum. The product was crystallized (hexane) to give **9**: 310 mg (93%); mp 75 °C; IR (KBr) 2920, 1735, 1705, 1605 cm^{-1}; UV λ_{max} 289.5 (ϵ 30000); ^1H NMR δ 0.82 (t, J = 7.5 Hz, 3 H), 1.01 (t, J = 6 Hz, 3 H), 2.1 (q, J = 7.5 Hz, 2 H), 3.15 (q, J = 6 Hz, 2 H), 3.48 (s, 3 H), 3.75 (s, 3 H), AB q at 3.87 and 4.18 (J = 15 Hz, 2 H); ^{13}C NMR 7.9 (q), 16.4 (q), 29.1 (t), 42.6 (t), 51.0 (q), 52.8 (q), 59.3 (t, C-6), 91.6 (s, C-5), 98.1 (s, C-2), 127.5 (d), 128.5 (d), 128.8 (d), 139.4 (s), 147.7 (s, C-4), 165.4 (s) 165.9 (s) ppm; mass spectrum, m/e (relative intensity) 333 (M^+, 33). Anal. Calcd for $C_{18}H_{23}NO_5$: C, 64.85; H, 6.95; N, 4.20. Found: C, 64.63; H, 6.73; N, 4.29.

Hydrolysis of 12. A solution of 100 mg (0.27 mmol) of **12** in 5 mL of $CHCl_3$ was stirred with 5 mL of concentrated HCl for 4 h. The acid was neutralized with solid K_2CO_3, the $EtNH_2$ evolved was trapped in CCl_4, the aqueous layer was extracted with $CHCl_3$ (3 × 50 mL), the combined $CHCl_3$ solutions were dried (K_2CO_3) and filtered, and the solvent was removed under vacuum. The crude product was separated on preparative TLC (silica gel, TLC 7731 Merck), eluting with 3:7 $CHCl_3$/hexane. The less polar fraction (R_f 8–9) was identified as 3-chloro-1-phenyl-1-propanone (57 mg). The second fraction (R_f 5–7) was unreacted **12**, and the lower layer (R_f 2–3) consists of a mixture of alcohols which was not separated. When **10** was treated similarly the same products mixture was obtained.

Hydrolysis of 9. Compound **9** (100 mg, 0.3 mmol) was hydrolyzed analogously to **12** and gave the following: Ethylamine (trapped in CCl_4), a crude oil, was separated on preparative TLC (silica gel acc to stahl for TLC 7731 Merck), eluting with 3:7 $CHCl_3$/hexane. The less polar fraction (R_f 8.1–9.7) was identified as 1-phenyl-1-propanone. The second fraction (R_f 4–7.8) was unreacted **11**, and the lower layer (R_f 2–3.5) consists of a mixture of alcohols which were not separated.

Registry No. **4**, 3308-98-3; **5**, 75343-42-9; **6**, 81096-81-3; **7**, 81096-82-4; **8**, 81096-83-5; **9**, 81096-84-6; **12**, 81096-85-7; DMAD, 762-42-5.

Supplementary Material Available: Tables of bond distances, bond angles, atomic coordinates, and isotropic and anisotropic thermal parameters for **8** (4 pages). Ordering information is given on any current masthead page.

Highly Stereoselective Synthesis of Allenic Halides by means of Halocuprate-Induced Substitution in Propargylic Methanesulfonates

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For the preparation of racemic allenic halides several methods are available, but the number of routes to optically active allenic halides is rather restricted.[1] Hitherto optically active allenes have been synthesized mainly via S_N2'-like reactions in propargylic substrates (cf. ref 1). Of special interest in this connection is the difference in stereochemistry observed for halocuprate-induced formation of allenic halides from propargylic alcohols and chlorides. Thus the conversion of a propargylic alcohol by a halocuprate species prepared from HX and CuX into the allene preferentially follows the syn 1,3-substitution mode,[2] while that of 3-chloro-3-phenyl-1-propyne by tet-

(1) See for a comprehensive review: Patai, S., Ed. "The Chemistry of Ketenes, Allenes, and Related Compounds"; Wiley: Chichester, 1980.
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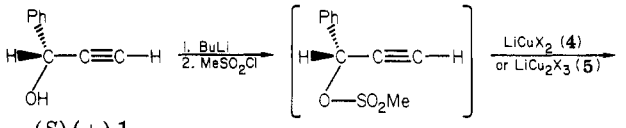
0022-3263/82/1947-2194$01.25/0

Table I. Specific Optical Rotations for (*S*)-(+)-Allenic Halides 3a-c Prepared by Reaction of (*S*)-2 with $LiCuX_2$ (4) or $LiCu_2X_3$ (5)

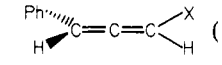
cuprate	molar equiv of cuprate	$[\alpha]^{20}_D$,[a] deg 3a (X = Cl)	3b (X = Br)	3c (X = I)
$LiCuX_2$	1.2	530[b]	920[d]	1210[e]
$LiCu_2X_3$	0.6	600[b]	1040[d]	1350[e]
$LiCu_2X_3$	1.2	610[c]	1235	1550[e]

[a] Measured in EtOH (c = 2) for undistilled compounds and corrected for small amounts of 3-halo-3-phenyl-1-propynes. The recorded rotations refer to conversion of optically pure (*S*)-1 and were obtained by extrapolating the rotations measured on starting from a mixture of 75% (*S*)- and 25% (*R*)-1. [b] Contained 5% of 3-chloro-3-phenyl-1-propyne. [c] Compound 3a was contaminated with 7% of 3-chloro-3-phenyl-1-propyne and a trace of an unknown compound. [d] 2% of 3-bromo-3-phenyl-1-propyne was present. [e] The optical rotation decreased considerably upon standing at room temperature.

rabutylammonium dichlorocuprate is mainly an anti 1,3-substitution.[3] The latter reaction proceeds under mild conditions and would be an attractive method to prepare optically active allenic halides, were it not that the synthesis of the required optically enriched propargylic chlorides may be a serious problem. For instance, optically active 3-chloro-3-phenyl-1-propyne could be prepared in only moderate optical yield by reaction of the corresponding alcohol and thionyl chloride.[3] Obviously, a better strategy should be one in which the propargylic alcohol is converted into a derivative without disrupture of the original C–O bond. We were very pleased to find that such an approach is indeed very efficient for the synthesis of optically active allenic halides. Our route is delineated in eq 1 and involves an in situ conversion of the alcohol via



(*S*)-(+)-1 (*S*)-2



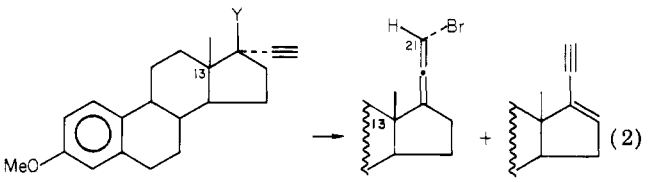
(1)

(*S*)-(+)-3a, X = Cl
b, X = Br
c, X = I

its methanesulfonate into the desired allene by reaction with a suited halocuprate.[4] Starting from (*S*)-(+)-1[5] we obtained dextrorotatory allenes 3 (chemical yield 90–95%).

As the suggested relevant parameters (λ(Cl) and λ(Br)) are only tentative values, the chirality-functions approach[6a] is not reliable for the deductions of the absolute configurations of haloallenes. By use of the Lowe–Brewster rules,[6b,c] the *S* configurations would be assigned to dextrorotatory 3. For **3a,b** the (*S*)-(+) configurations have been confirmed independently by measuring their CD spectra[7] which exhibit intense positive bands for the B_{1u}–(L_a) transitions near 250 nm (cf. ref 6a). Rotations for optically pure allenes 3 are not known yet. From the literature[3] a minimum specific rotation of **3a**, $[\alpha]_D$ +522° ($CHCl_3$), may be deduced from chemical correlation. Our $[\alpha]_D$ values given in Table I show that pure **3a** has a specific rotation of at least 610°.[8]

The tetrabutylammonium dichlorocuprate induced 1,3-substitution in 3-chloro-3-phenyl-1-propyne thus proceeds with less stereoselectivity than was believed (cf. ref 3). Note in Table I that the reaction of ester 2 with the halocuprate species 5 took place with higher stereoselectivity than that with cuprates 4. At the moment we explain this by assuming that ester 2 reacts in two ways with cuprates 4, viz., via a real anti 1,3-substitution (see eq 1) and via an S_N2 reaction with formation of (*R*)-3-halo-3-phenyl-1-propynes[9] which in turn undergo anti 1,3-displacement of halide to give (*R*)-(−)-3. The second way is net a "syn 1,3-substitution". The latter reaction route must then be less important if cuprates 5 are used, especially if these species are applied in equimolar amounts (see Table I). Experimentally we do not have evidence for this, but the alternative involving the simultaneous occurrence of a real syn and anti S_N2' reaction in 2 seems to be less likely in view of the *stereospecific* lithium dibromocuprate induced allene formation from the sulfonate ester 7 derived from mestranol (6). The allene is formed in 90% yield together with 10% of the elimination product 9 (eq 2) from which it can be purified by washing with pentane.



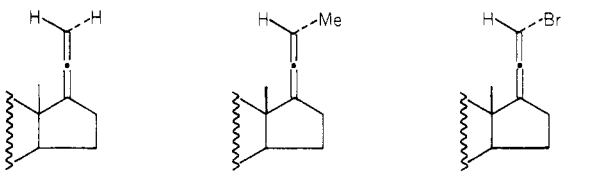
(2)

6, Y = OH
7, Y = OSO_2Me

8 9

The pure allene shows a negative rotation ($[\alpha]^{22}_D$ −173°) and melts sharply at 117.0 °C. In the ^1H NMR spectrum of 8 only one, sharp 13-Me signal is found, viz., at 0.90 ppm. This indicates that the 21-epimer of 8 is absent (cf. ref 10). To the produced levorotatory allene (8 in eq 2) we tentatively assign the 21α-Br configuration on the basis of the following arguments.

Relative to the unsubstituted compound 10[11] it is assumed that the substituent effect of bromine (at the 21-carbon atom) acts in the same direction as that of methyl (as is the case in the chirality-functions approach to optical rotations of open-chain allenes[6a] and the Lowe–Brewster approach[6b,c]). Therefore, levorotatory 8 should have the



10 ($[\alpha]_D$ +41.2°) 11 ($[\alpha]_D$ −15.5°) 8 ($[\alpha]_D$ −173°)

(3) Muscio, O. J.; Jun, Y. M.; Philip, J. B. *Tetrahedron Lett.* **1978**, 2379.

(4) The halocuprates were obtained by mixing copper(I) halide with an appropriate amount of lithium halide with THF as the solvent. During the course of our investigation the preparation of some racemic bromoallenes was reported by a similar method: Montury, M.; Goré, J. *Synth. Commun.* **1980**, *10*, 873.

(5) Enantiomeric excess of 50%.

(6) (a) Runge, W., in ref 1, Chapter 3. (b) Lowe, G. *Chem. Commun.* **1965**, 411. (c) Brewster, J. H. *Top. Stereochem.* **1967**, *2*, 33–39.

(7) The CD investigations will be published separately.

(8) Recent experiments concerning the transitions of liquid crystals from nematic into cholesteric phases induced through chiral phenylallenes indicate that the rotations of optically pure **3a,b** should be $[\alpha]_D$(**3a**) +633 ± 84° ($CHCl_3$) and $[\alpha]_D$(**3b**) + 1092 ± 125° ($CHCl_3$).

(9) For comparison: the reaction of lithium diphenylcuprate with (*S*)-(+)-2-butyl mesylate has been found to proceed with 100% inversion.

(10) Van Dijck, L. A.; Lankwerden, B. J.; Vermeer, J. G. C. M. *Recl. Trav. Chim. Pays-Bas* **1979**, *98*, 553 and references cited therein.

(11) Van Dijck, L. A.; Lankwerden, B. J.; Vermeer, J. G. C. M.; Weber, A. J. M. *ibid, Recl. Trav. Chim. Pays-Bas* **1971**, *90*, 801.

same configuration as the levorotatory 21-Me analogue 11.[11] A recent X-ray study[12] has revealed that levorotatory 11 has the 21α-configuration, contrary to an assignment based on ^{1}H NMR data and the Lowe-Brewster rules.[11]

An unambiguous determination of 8 has yet to be performed. On the basis of our configurational assignment to 8, the reaction depicted in eq 2 proceeds with the same stereochemistry as that in eq 1, viz, anti.

Experimental Section

General Procedures. Infrared spectra were recorded on a Perkin-Elmer 457 IR spectrometer. ^{1}H NMR spectra were determined on a Varian EM-390 spectrometer by using CCl_4 or $CDCl_3$ as the solvent and Me_4Si as the internal standard. ^{13}C NMR spectra were measured on a Bruker WP-200 spectrometer by using $CDCl_3$ as the solvent and Me_4Si as the internal standard. All reactions were carried out in an atmosphere of dry nitrogen.

Materials. THF was distilled from $LiAlH_4$. *n*-Butyllithium was obtained as a 1.50 M solution in *n*-hexane from Metallgesellschaft A.G., Frankfurt am Main; its molarity was determined by using Watson's titration method.[13] Optically enriched 1-phenyl-2-propyn-1-ol was obtained according to the literature;[14] in the presented study the *S* compound (ee 50%) was used. Mestranol was obtained as generous gift from Organon, Oss, The Netherlands; it was converted into the methanesulfonate according to our procedure.[15]

General Procedure for the Preparation of Optically Active Halides 3a–c. To a well-stirred solution of 0.66 g of **1** (5.0 mmol) in 15 mL of dry THF were successively added, at −70 °C, 3.4 mL of *n*-butyllithium (1.50 M) in hexane and, at once, 0.63 g of methanesulfonyl chloride (5.5 mmol). After 2 min[16] a solution of cuprate **4** (6.0 mmol) or a suspension of cuprate **5** (3.0 or 6.0 mmol; see Table I) in 5 mL of dry THF was added at once.[17] The mixture was then allowed to warm to 20 °C in 15–20 min. Allenes **3a–c** were isolated by pouring the respective reaction mixtures into 100 mL of a saturated aqueous NH_4Cl solution containing 1 g of NaCN and 0.5 mL of a THF solution of Ionox (c = 1 g/L) in order to prevent decomposition via free radicals, extracting the aqueous layer with pentane (2 × 25 mL), washing the combined extracts with water (5 × 50 mL), and drying the extract with K_2CO_3. The solvent was evaporated in vacuo to give **3a-c** in 90–95% yield. The specific rotations of **3a–c** were determined in ethanol; extrapolation of the obtained values to optically pure **1** gave the data as compiled in Table I. For determination of the physical constants of **3a–c**, racemic **1** was converted on a 30.0-mmol scale into **3a–c** by following the procedure described above.

1-Chloro-3-phenylpropadiene (3a): bp 50 °C (0.01 mm Hg); n^{20}_D 1.6147; IR 1945 cm^{-1}; ^{1}H NMR (CCl_4) δ 6.38 (d, 1 H), 6.50 (d, 1 H), ^4J(HC=C=CH) = 6.0 Hz; ^{13}C NMR ($CDCl_3$) δ 203.3 (=C=).

1-Bromo-3-phenylpropadiene (3b): bp 65 °C (0.001 mm Hg); n^{20}_D 1.6435; IR 1943 cm^{-1}; ^{1}H NMR (CCl_4) δ 6.21 (d, 1 H), 6.27 (d, 1 H), ^4J(HC=C=CH) = 5.9 Hz; ^{13}C NMR ($CDCl_3$) δ 202.8 (=C=).

1-Iodo-3-phenylpropadiene (3c): bp 70 °C (0.001 mm Hg);[18] n^{20}_D 1.6855; IR 1930 cm^{-1}; ^{1}H NMR (CCl_4) δ 5.92 (d, 1 H), 6.05 (d, 1 H), ^4J(HC=C=CH) = 5.9 Hz; ^{13}C NMR ($CDCl_3$) δ 205.5 (=C=).

Preparation of 8. To a stirred solution of cuprate **4** (X = Br; 10.0 mmol) in 10 mL of dry THF was added, at 25 °C, 1.95 g of steroid **7** (5.0 mmol). The resulting mixture was stirred for 90 min at 25 °C. The product was isolated as described for **3** by using a mixture of Et_2O/hexane (1:1 v/v) for the extraction. The crude product **8** was obtained in 90% yield together with 10% of enyne **9**. It was purified from **9** by washing twice with 5 mL of boiling pentane. According to ^{1}H NMR spectroscopy the remaining crystalline allene **8** was pure (yield after purification 0.90 g; the pentane fraction contained the rest of **8** together with enyne **9**). The following characteristic data were found for **8**: $[\alpha]^{22}_D$ −173° (c 1.2, CH_2Cl_2); mp 117 °C; IR 1956 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (s, 13-Me), 5.95 (t, C-21, β-H), ^5J(HC=C=C—CH_2) = 3.0 Hz; ^{13}C NMR ($CDCl_3$) δ 193.7 (=C=).

Acknowledgment. The investigations were supported in part by the Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Organization for the Advancement of Pure Research (ZWO).

Registry No. (*S*)-(+)-1, 64599-56-0; (*S*)-(+)-**3a**, 81158-17-0; (*S*)-(+)-**3b**, 81158-18-1; (*S*)-(+)-**3c**, 81158-19-2; **7**, 76685-96-6; (−)-**8**, 81158-20-5; **9**, 23640-47-3.

(12) Elsevier, C. J.; Meijer, J.; Westmijze, H.; Vermeer, P.; van Dijck, L. A. *J. Chem. Soc., Chem. Commun.* **1982**, 84.
(13) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.
(14) Tadema, G.; Everhardus, R. H.; Westmijze, H.; Vermeer, P. *Tetrahedron Lett.* **1978**, 3935.
(15) Westmijze, H.; Kleijn, H.; Vermeer, P.; van Dijck, L. A. *Tetrahedron Lett.* **1980**, 2665.
(16) Longer reaction times caused a decrease of the optical rotation value of **3** which is most likely due to an interference of lithium chloride liberated during the formation of the ester. Separate experiments showed that ester **2** may undergo a S_N2 reaction by lithium chloride.
(17) For the preparation of **5**, 2 molar equiv of CuX was added to a solution of LiX in THF; after a short time a homogeneous solution was obtained which then turned into a suspension.
(18) If distilled at higher pressure, the compound may explode violently.

Synthesis of Some Dihydroxyphenyl 4,5-Dichloroimidazol-2-yl Ketones: Compounds Related to Pyoluteorin[1]

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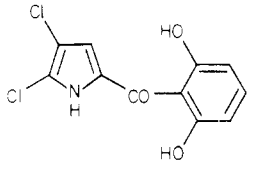
Pyoluteorin (1), a pyrrole antibiotic isolated by Takeda[2]



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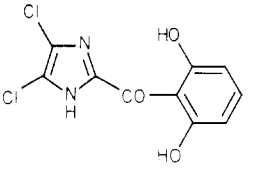

2

from certain strains of *Pseudomonas aeruginosa*, and a wide variety of analogues obtained by total synthesis have been the subject of numerous publications.[3] However, in the analogues reported to date, the pyrrole moiety has always been present. We therefore sought to prepare some compounds similar to pyoluteorin in which the pyrrole ring is replaced with an imidazole ring [e.g., azapyoluteorin (**2**)]. Although 4,5-dibromo and 4,5-diiodo derivatives of imidazoles can be prepared easily and in good yield by halogenation,[4] the corresponding chlorine derivatives are relatively unknown.[5] It was therefore necessary during the

(1) This paper has been presented in part. See "Abstracts of Papers", 178th National Meeting of the American Chemical Society, Washington, DC, Sept 1979; American Chemical Society: Washington, DC, 1979; Abstr Medi 71.
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