sients. In addition, the role of donor or acceptor molecules is being surveyed.[19]

Acknowledgment. The authors wish to acknowledge Messrs. B. Lapier and R. Kovach for their skilled technical assistance.

(19) NOTE ADDED IN PROOF. We have now extended these measurements to whole chloroplasts and can report that the same kinetic correspondence of esr response and bleaching at 703 nm is found for the intact system. In addition, preliminary results on a quantitative comparison show that the ratio of P700 molecules bleached to signal I radicals formed is very close to unity for several types of preparations. Details will be reported later.

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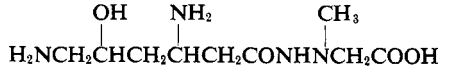
The Total Syntheses of Negamycin and the Antipode

Sir:

The structure of negamycin (**1**) and its partial synthesis have bteen reported.[1] The mechanism of action of negamycin is similar to that of most aminoglycosidic antibiotics including streptomycin and kanamycin; that is, negamycin causes inhibition of protein synthesis and misreading of the genetic code.[2]

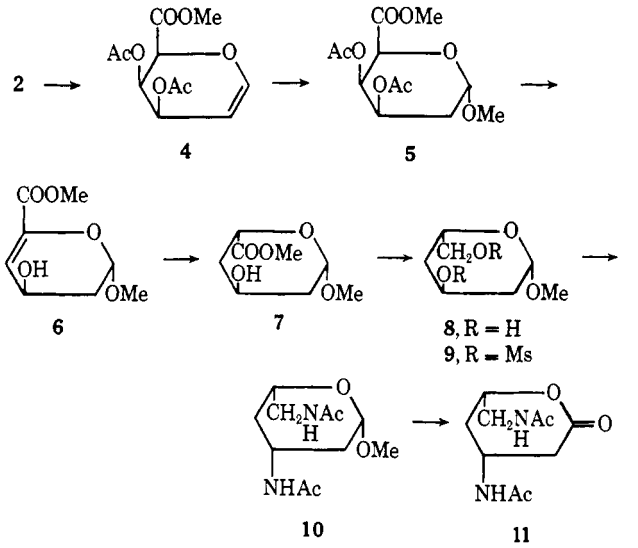


1

Therefore, it is important to investigate the possibility of a close relationship between hydroxy amino acid and aminoglycosidic antibiotics. We report herein the stereoselective conversions of D-galacturonic acid[3] (**2**) and 3-amino-3-deoxy-D-glucose[4] (**3**) to δ-hydroxy-β-lysine, the amino acid moiety of **1**, which have led to the total syntheses of **1** and the antipode, respectively. In addition, it has been shown that a difference in the absolute configuration of δ-hydroxy-β-lysine causes a marked difference in biological activity.

D-Galacturonic acid commercially available has the 3*S* and 5*S* configurations. A transformation to the amino acid moiety of **1** has been realized in the following way (Scheme I). A glycal compound **4** was obtained in a good yield from **2**[5] by the usual methods. 2-Deoxy derivative **5** was obtained by treatment of **4** with iodine in methanol in the presence of silver acetate followed by catalytic hydrogenation over Pd/C. The method of Schmidt and Neukom[6] was applied to **5** to afford **6**, $[\alpha]^{21}D$ +234° (*c* 0.85, MeOH). Catalytic

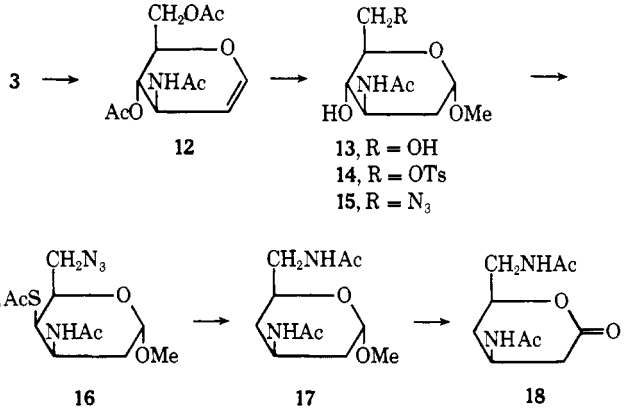
Scheme I



hydrogenation of **6** gave methyl (methyl 2,4-dideoxy-β-L-*erythro*-hexosid)uronate (**7**) as a major product[7] (60% yield): mp 60–62°; $[\alpha]^{21}D$ +113° (*c* 0.8, $CHCl_3$); M^+ = 190; δ 4.55 (H-5, quartet at −30° with $J_{4,5}$ = 7.5 and $J_{4',5}$ = 2.5 Hz). The reduction of the carboxyl group with $LiAlH_4$ afforded methyl 2,4-dideoxy-β-L-*erythro*-hexopyranoside (**8**), and then two hydroxyl groups were mesylated to afford **9**. The treatment of **9** with sodium azide followed by hydrogenation with Pd/C afforded a diamino compound which was acetylated with Ac_2O to afford methyl 3,6-diacetamido-2,3,4,6-tetradeoxy-β-L-*threo*-hexopyranoside (**10**). After hydrolysis and oxidation with aqueous bromine, a crystalline lactone of (3*R*,5*R*)-3,6-diacetamido-5-hydroxyhexanoic acid (**11**), mp 183–185°, $[\alpha]^{21}D$ −5.8° (*c* 1.0, H_2O), was obtained. It was identical in all respects with the compound derived from natural negamycin.

3-Amino-3-deoxy-D-glucose (**3**) has the 3*S*,5*R* configuration. Therefore, the antipode of δ-hydroxy-β-lysine of **1** can be synthesized by replacing two hydroxyl groups at C-2 and C-4 with hydrogen and converting the primary alcohol at C-6 to the primary amino group without disturbing the stereochemistry at C-3 and C-5. Such a transformation has been realized in the following way (Scheme II). 3-Acetamido-4,6-di-*O*-acetyl-1,2,3-

Scheme II



(1) S. Kondo, S. Shibahara, S. Takahashi, K. Maeda, H. Umezawa, and M. Ohno, *J. Amer. Chem. Soc.*, **93**, 6305 (1971).

(2) S. Mizuno, K. Nitta, and H. Umezawa, *J. Antibiot.*, **23**, 581, 589 (1970).

(3) J. Staněk, M. Cerny, J. Kocourek, and J. Pacák, "The Monosaccharides," Academic Press, New York and London, 1963, p 703.

(4) This amino sugar is now easily available by fermentation of *Bacillus aminoglycosidicus*, and the absolute structure is already known: S. Umezawa, K. Umino, S. Shibahara, M. Hamada, and S. Omoto, *J. Antibiot., Ser. A*, **20**, 355 (1967).

(5) T. Kondo and T. Goto, *Agr. Biol. Chem.*, **35**, 912 (1971).

(6) H. W. H. Schmidt and H. Neukom, *Carbohyd. Res.*, **10**, 361 (1969).

(7) The diastereomer at C-5 was obtained as a minor product and the purification of **7** was easily carried out on silica gel chromatography.

Table I. The Antimicrobial Spectra of Negamycin and Its Antipode on 0.5% Peptone Agar

Test organisms	Minimum inhibitory concentration, μg/ml: Negamycin	Antipode of negamycin
Staphylococcus aureus FDA 209P	12.5	50
Escherichia coli K-12	3.1	100
Escherichia coli K-12 ML1629	1.6	100
Shigella sonnei 191-66	6.3	200
Salmonella typhi T-63	3.1	100
Klebsiella pneumoniae PCI 602	3.1	100
Pseudomonas aeruginosa A3	6.3	100
Pseudomonas aeruginosa No. 12	6.3	100

trideoxy-D-*arabino*-hex-1-enopyranose (**12**) was obtained in excellent yields from **3** by the usual methods. Methanol was added to **12** in the presence of HCl to afford **13**. The primary alcohol was tosylated and replaced by azide with NaN_3 in DMF to give **15**. The secondary alcohol at C-4 was subjected to mesylation and then treated with potassium thiolacetate, affording **16**: mp 160–163°; $[\alpha]^{20}D$ +167° (*c* 0.9, $CHCl_3$); $J_{3,4} = 4$ and $J_{4,5} = 2.5$ Hz, in a fair yield. The azide and *S*-acetyl groups were reduced with Raney Ni in methanol at the same time. After acetylation of the primary amino group, methyl 3,6-diacetamido-2,3,4,6-tetradeoxy-α-D-*threo*-hexopyranoside (**17**), mp 192–193°, $[\alpha]^{20}D$ +137° (*c* 0.8, H_2O), was obtained in a good yield. Hydrolysis of **17** followed by oxidation with bromine–water afforded a crystalline lactone of (3*S*,5*S*)-3,6-diacetamido-5-hydroxyhexanoic acid (**18**), mp 183–185°, $[\alpha]^{25}D$ +8.7° (*c* 2.3, H_2O).

The total syntheses of negamycin and the antipode have been completed using the δ-hydroxy-β-lysines[8] obtained from **11** and **18**, respectively.[1,9]

The antimicrobial spectra of negamycin and its antipode are shown in Table I, showing that the latter has generally far weaker activity against a variety of organisms than that of the former, but it is noteworthy that the antipode still has a definite biological activity.

Acknowledgment. We wish to express our deep gratitude to Professor S. Umezawa, Keio University, for his encouragement through the course of this work.

(8) These hydroxy amino acids were obtained by acid hydrolysis of the lactones **11** and **18** followed by purification with resin chromatography of Amberlite CG-50, respectively.

(9) Satisfactory elemental analyses were obtained for all the compounds for which melting point or [α]D values were given. All the compounds cited showed reasonable spectral data.

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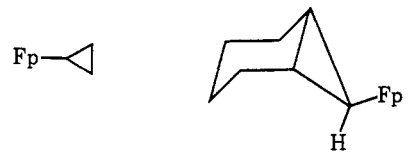
Cationic Metal–Carbene Complexes in Cycloaddition Reactions. Synthesis and Reactions of Iron–Cyclopropyl Complexes

Sir:

Although numerous cyclopropyl derivatives of the main group elements are known,[1] no transition metal complexes having a σ-bonded cyclopropane ring have been reported.[2] Our interest in the nucleophilic properties of transition metal–allyl complexes[4] in metal-assisted cycloaddition reactions prompted us to reexamine the synthesis of the isomeric cyclopropyl derivatives with a view toward comparing their chemistry.

We wish now to report the preparation of two such complexes (**1** and **2**) and their reactions with electro-



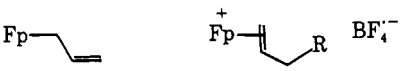
1 **2**

Fp ≡ $(h^5\text{-}C_5H_5)Fe(CO)_2$

philic reagents. Each may be prepared in moderate yield by treatment of the requisite cyclopropyl bromide[5] with $(h^5\text{-}C_5H_5)Fe(CO)_2Na$, while the first may also be obtained by alkylation of $(h^5\text{-}C_5H_5)Fe(CO)_2Br$ with cyclopropyllithium.[6]

The parent complex **1** is an air-stable amber oil, which may be distilled at room temperature under high vacuum without decomposition.[7] The comparative electronegativity of the cyclopropyl group is manifest in the carbonyl stretching frequencies of **1** (2014 and 1961 cm^{-1}) and of a typical secondary alkyl derivative $(h^5\text{-}C_5H_5)Fe(CO)_2(i\text{-}C_3H_7)$ (2006, 1952 cm^{-1}). Its nmr spectrum, taken in CS_2, exhibits two high-field multiplet absorptions at τ 9.48 (three protons) and 10.12 (two protons) assignable to protons trans and cis, respectively, to the carbon–metal bond.

Gaseous hydrogen chloride reacts with **1** to give $(h^5\text{-}C_5H_5)Fe(CO)_2Cl$ and a mixture of cyclopropane and propene. The compound reacts rapidly with fluoroboric acid and with trityl fluoroborate, as does the isomeric h^1-allyl complex **3**, to give the propene complexes **4**[8] and **5**,[7] respectively.



3 **4**, R = H; **5**, R = CPh_3

The formation of **4** with fluoroboric acid does not proceed as might be anticipated, through cleavage of C_2–C_3 with metal migration. Thus, treatment of the 1-deuterio derivative **1**-*d* with fluoroboric acid gave the

(1) For a list of references to these, see A. H. Cowley, J. L. Mills, T. H. Loehr, and T. V. Long, *J. Amer. Chem. Soc.*, **93**, 2151 (1971).

(2) Several attempts to prepare such derivatives of manganese, rhenium, iron, and iridium by decarbonylation of the related acyl–metal complexes were unsuccessful.[3]

(3) M. I. Bruce, M. Z. Igbal, and F. G. A. Stone, *J. Organometal. Chem.*, **20**, 161 (1969).

(4) W. P. Giering and M. Rosenblum, *J. Amer. Chem. Soc.*, **93**, 5299 (1971).

(5) D. Seyferth, *et al.*, *ibid.*, **87**, 4259 (1965); D. Seyferth, H. Yamazaki, and D. L. Alleston, *J. Org. Chem.*, **28**, 703 (1963). The norcarane complex **2** was obtained from the mixture of stereoisomeric halides formed in the reduction of the corresponding dibromide. The Fp group is assigned as exo since models show that the alternative endo form would be prohibitively crowded.

(6) In view of the low reactivity of cyclopropyl halides in SN2 reactions, it seems likely that the former synthesis involves an initial metal–halogen exchange reaction.

(7) An acceptable C and H analysis was obtained for this compound.

(8) M. L. H. Green and P. L. I. Nagy, *J. Chem. Soc.*, 189 (1963).