reaction of $AcImMe^+$ with methoxyamine ($pK = 4.7$) is also catalyzed by methylimidazole (0.002 M methoxyamine, other conditions as in Figure 1) and the observed catalytic constant ($k = 46{,}400\ M^{-2}\ min^{-1}$) is sufficient to account for most or all of the imidazole-catalyzed methoxyaminolysis of $AcImH^+$ ($k = 59{,}000\ M^{-2}\ min^{-1}$) according to mechanism 1.

These results suggest that the breakdown of the symmetrical transition state or intermediate, with two amines bonded to the acyl carbon atom, involves proton donation by a general acid catalyst to the more weakly basic amine. Mechanisms involving proton transfer to or from the carbonyl oxygen atom are less likely in view of the symmetry of the reaction and its catalysis as well as the fact that $AcImMe^+$ is a satisfactory model for the general base catalyzed reactions of weakly basic amines and for the uncatalyzed reactions of a number of other nucleophiles with acetylimidazole near neutrality;[3,6] *i.e.*, protonation of the leaving imidazole by either specific or general acid catalysis is the preferred pathway for reactions of acetylimidazole. These reactions may be interpreted in the following way, according to the expected structure–reactivity relationships and the notion that catalysis occurs where it is most needed. Attack of a weakly basic amine is significantly aided by proton removal ($\beta > 0$), whereas the reaction of a strongly basic amine does not require such assistance ($\beta \sim 0$). Conversely, the expulsion of imidazole by the relatively small driving force provided by a weakly basic nucleophile requires complete protonation ($\alpha \sim 1.0$), whereas expulsion driven by a stronger base can occur with only partial proton donation ($\alpha < 1.0$).

(6) D. Oakenfull, K. Salvesen, and W. P. Jencks, unpublished experiments.

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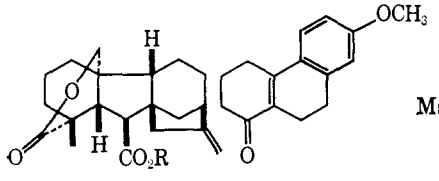
The Stereocontrolled Total Synthesis of *dl*-Gibberellin A_{15}

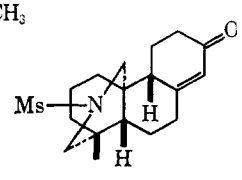
Sir:

Considerable efforts have long been devoted by many research groups to construct gibberellin molecules and very recently Mori, *et al.*,[1] have succeeded, although in a formal sense, in a total synthesis of some C_{19} gibberellins. In the present communication, we wish to report a stereocontrolled total synthesis of gibberellin A_{15}[2] (**1**) in the racemic form.



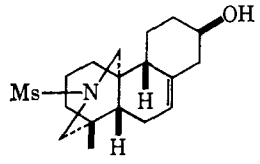
1, R = H
2, R = CH_3

3



4

The conjugated ketone **4**, a key intermediate in our previous total synthesis of diterpene alkaloids,[3] prepared from the tricyclic conjugated ketone **3** (24% yield through nine steps), was transformed into a mixture (mp 177–179°) of the enols **5** and **6** (*ca.* 4:1) by dienol acetylation and subsequent $NaBH_4$ reduction.[4] Ozonization, reduction, and successive alkaline treatment of the mixture gave the dihydroxy aldehyde **7**, mp 234–235.5°[5] (34% from **4**) and some amounts of unchanged



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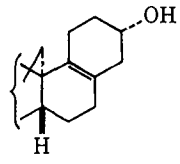

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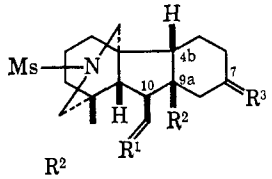
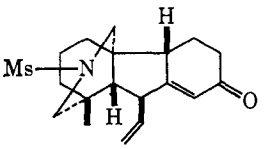


	R^1	R^2	R^3
7,	O	OH	
8,	O	OH	
9,	CH_2	OH	
10,	CH_2	OH	O
12,	CH_2	CN	O
13,	CH_2	CN	
14,	CH_2	CN	
15,	CH_2	CHO	
16,	CH_2	*t*-CH=CH—CHO	
17,	CH_2	*t*-CH=CH—CHO	
18,	CH_2	*t*-CH=CHCH(OAc)$_2$	
19,	O	*t*-CH=CHCH(OAc)$_2$	



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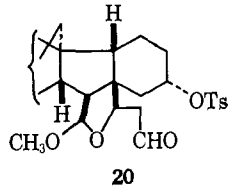


20

(1) (a) K. Mori, M. Shinozaki, N. Itaya, T. Ogawa, M. Matsui, and Y. Sumiki, *Tetrahedron Lett.*, 2183 (1968); (b) K. Mori, M. Shinozaki, N. Itaya, M. Matsui, and Y. Sumiki, *Tetrahedron*, **25**, 1293 (1969).

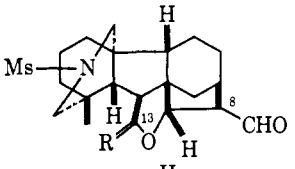
(2) (a) B. E. Cross, R. H. B. Galt, and J. R. Hanson, "Regulations Naturels de la Croissance Vegetale," Centre National de la Recherche Scientifique, Paris, 1964, p 265; (b) J. R. Hanson, *Tetrahedron*, **23**, 733 (1967).

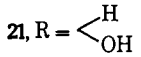
(3) (a) W. Nagata, T. Sugasawa, M. Narisada, T. Wakabayashi, and Y. Hayase, *J. Amer. Chem. Soc.*, **85**, 2342 (1963); **89**, 1483 (1967); (b) W. Nagata, M. Narisada, T. Wakabayashi, and T. Sugasawa, *ibid.*, **86**, 929 (1964); **89**, 1499 (1967).

(4) *Cf.* B. Belleau and T. F. Gallagher, *ibid.*, **73**, 4458 (1951).

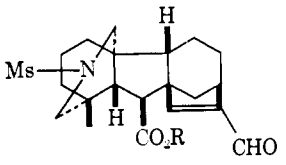
(5) (a) All the intermediates show reasonable spectral data and those for which melting points are recorded give satisfactory compositional analyses. (b) The 9aβ and 10β configurations of the newly formed substituents were assigned on the following bases: (i) the ir spectra

6, mp 236–238°. The Wittig reaction of the acetate **8** followed by alkaline hydrolysis gave the olefin **9**, mp 198–199.5° (60% yield), which on oxidation (CrO_3–H_2SO_4 in acetone), followed by dehydration ($SOCl_2$ in methylene chloride and pyridine, −73°, 2 min) was converted to the conjugated enone **11**, mp 212–213° (83% from **9**), *via* the ketol **10**, mp 208–210°. Hydrocyanation of **11** with diethylaluminum cyanide[6] in methylene chloride–benzene (5:1) gave exclusively the *cis*-cyano ketone **12**, mp 214–215°, in 87% yield. The dipole moment of **12** supports the assigned 4bβ,9aβ configuration with ring C chair conformation (**12**; calcd, 4.24 D; found, 3.8 D). Reduction of **12** with aluminum isopropoxide gave a 5:1 mixture of the epimeric alcohols **13** and **14**. Acid treatment (TsOH in benzene) converted the *cis*-hydroxy nitrile **14** into a basic iminolactone, mp 188–190°, the major *trans* isomer **13**, mp 161–162° (71%), remaining unchanged and thus being readily separated. Compound **13** was transformed into the angular formyl derivative **15**, mp 150–154° (81%), by the sequence of reactions: reduction (*i*-Bu_2AlH), hydrolysis (NaOAc–HOAc in aqueous THF), and tetrahydropyranylation of the 7-hydroxyl. Formylolefination[7] of **15** with sodium diethyl β-(cyclohexylamino)vinylphosphonate followed by acid hydrolysis gave the *trans*-α,β-unsaturated aldehyde **16** (87%), mp 191–194°. For selective ozonization, compound **16**, after tosylation (**17**), was converted (Ac_2O and $ZnCl_2$) into the diacetoxy tosylate **18** (79%), mp 118–126°. This compound was now ozonized and reduced (Zn–HOAc) to give the desired aldehyde **19**, which without purification was subjected to a unique cyclization method devised particularly for construction of the B–C–D ring system of gibbane with requisite functionalities. Thus, the crude **19** was treated with 3 equiv of potassium hydroxide (in dry MeOH–THF, −8°, 5 min) giving the intermediate **20**, which on treatment with 2 equiv of pyrrolidine in methanol–N-methylpyrrolidone followed by hydrolysis with 50% acetic acid gave a mixture of hexacyclic hemiacetals **21** (epi-



21, R = 

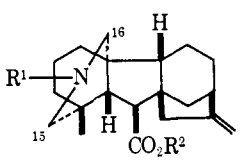
22, R = O

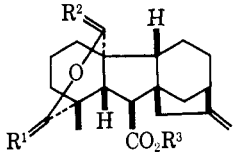


23, R = H

24, R = CH_3

meric both at C_8 and C_{13}). This mixture was oxidized selectively with the Collins reagent[8] to a mixture of the formyl lactones **22** (epimeric at C_8). Ring opening of **22** with base (aqueous K_2CO_3) eliminates C_8 asymmetry giving the crystalline pentacyclic carboxylic acid **23** [the methyl ester **24**, mp 184–186°, λ_{max}^{EtOH} 253.5 mμ (ε 13,050)]. The Wolff–Kishner reduction of **23** yielded the *exo*-methylene carboxylic acid **25** (30% overall





25, R^1 = Ms; R^2 = H

26, R^1 = R^2 = H(HCl salt)

27, R^1 = $COCF_3$; R^2 = H

28, R^1 = $COCF_3$; R^2 = CH_3

29, R^1 = H; R^2 = CH_3

30, R^1 =  ; R^2 = H_2; R^3 = CH_3

31, R^1 = H_2; R^2 =  ; R^3 = CH_3

32, R^1 = H_2; R^2 = O; R^3 = CH_3

33, R^1 = H_2; R^2 = O; R^3 = H

yield from **16** through nine steps), mp 163–164°, construction of the A–B–C–D ring parts thus being completed. Reduction (Li in liquid NH_3) of **25** gave the amino acid isolated as its hydrochloride **26** (56%), mp >300°. Attempted selective methylation of the carboxylic function in **26** with diazomethane failed and, therefore, the secondary amino group had to be first reprotected by treating **26** with trifluoroacetic anhydride giving **27**, which was then methylated (**28**) and hydrolyzed selectively to the ester **29** (reflux with 3 *N* K_2CO_3 in methanol, 1.5 hr). Dehydrogenation of the secondary amine **29** with lead tetraacetate yielded a mixture of azomethine isomers [$\Delta^{15(N)}$ and $\Delta^{(N)16}$ in **29**], which was converted into the hemiacetals **30** and **31** according to the method developed by ApSimon, *et al.*[9] The crude mixture of the hemiacetals was oxidized with the Collins reagent[8] to a mixture of lactones, which was separated by preparative tlc affording *dl*-gibberellin A_{15} methyl ester **2**, mp 168–170°, *m/e* 344, and the less polar isomeric lactone **32**, mp 114–116°, *m/e* 344, each in *ca.* 5% overall yield from **27** (through five steps). Demethylation of **2** and **32** was effected without double bond migration by treatment with lithium iodide in refluxing collidine[10] in the presence of triphenylphosphine[11] giving *dl*-gibberellin A_{15}, **1** (over 40% yield), mp 236–237°, *m/e* 330, and its lactone isomer **33** (over 32% yield), mp 197–198°, *m/e* 330. The synthetic materials **1** and **2** have been rigorously proved to be the racemic forms of gibberellin A_{15} and its methyl ester, respectively, by identity of their ir (in $CHCl_3$) and mass spectra, and also by their chromatographic behavior (tlc and glc) relative to that of authentic specimens.[12]

Acknowledgments. We wish to thank the late Mr. M. Sahori, Mr. M. Yamaguchi, and Mr. Y. Haga for their participation in this work.

show that the 9aβ-hydroxyl is hydrogen bonded with the 7β-acetyl in **8** and with the vinyl in **10**; (ii) facile β-lactone formation between the 9aβ-hydroxyl and the 10β-formyl group was observed on oxidation of **7** with the Collins reagent (J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968)).

(6) (a) W. Nagata, M. Yoshioka, and S. Hirai, *Tetrahedron Lett.*, 461 (1962); (b) W. Nagata and M. Yoshioka, *ibid.*, 1913 (1966).

(7) W. Nagata and Y. Hayase, *ibid.*, 4359 (1968); *J. Chem. Soc.*, 1400 (1969).

(8) See Collins, *et al.*, ref 5b.

(9) J. W. ApSimon, O. E. Edwards, and R. Howe, *Can. J. Chem.*, 40, 630 (1962).

(10) F. Elsinger, J. Schreiber, and A. Eschenmoser, *Helv. Chim. Acta*, 43, 113 (1960).

(11) Undesirable migration of the double bond from *exo* to *endo* can be prevented effectively by addition of triphenylphosphine.

(12) The authors are very grateful to Professor J. R. Hanson for kindly providing us with the authentic sample of gibberellin A_{15}.

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Free-Radical Rearrangement of Enol Sulfonates

Sir:

Enol esters of sulfonic acids, which are readily available by a recently published synthesis,[1] are com-