synthetic route for obtaining new transition-metal clusters. More detailed reports of this work, including the results of analogous reactions with related dimers (currently in progress), are forthcoming.

Acknowledgment. Financial support of this work was provided by the National Science Foundation (Grant CHE-77-24309). The financial support of J.-S.H. and Z.-H.Z. as visiting scholars at the UW—Madison by the People's Republic of China is gratefully acknowledged. We are also indebted to Mark A. Murphy for his advice and experimental help in performing the ^{1}H NMR measurements, to Dick A. Nagaki for carrying out the mass spectral measurements, and to Mark Englert for making the magnetic susceptibility measurements.

Supplementary Material Available: Tables listing the crystal data and atomic parameters for compounds **2**, **3**, **4**, and **5** (34 pages). Ordering information is given on any current masthead page.

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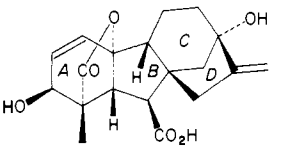
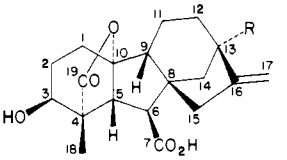
General Strategy for Gibberellin Synthesis: Total Syntheses of (±)-Gibberellin A_1[1] and Gibberellic Acid

Sir:

Extensive studies over 2 decades on the construction of the gibberellin phytohormones have provided a fund of innovative synthetic methodology,[2] and yet the completion of only two total syntheses—gibberellic acid (**1**) (~36 steps)[3] and gibberellin A_{15} (~40 steps)[4] —has been reported.[5] While the former achievement establishes a milestone in both gibberellin and synthetic chemistry, scope for more versatile and direct approaches still remains. Retrosynthetic analysis of the gibberellin molecule (Scheme I) suggests a strategy based on the construction of the C(3)–C(4) bond[6] by an aldol process,[7] C(4)–C(5) by a Michael reaction, and C(1)–C(10) through addition of an appropriate nucleophile to an enone such as **14**; reagent approach along the equatorial vector would be expected to establish the correct relative chirality of *pro*-C(10), and then geometric constraints can provide subsequent stereochemical control. We now describe the elaboration of these ideas into a very efficient strategy for gibberellin synthesis, the utility of which is demonstrated by the preparation of (±)-gibberellin A_1 (**2**)[8] in ~24 steps, and of gibberellic acid (**1**) in ~31 steps from 1,7-dimethoxynaphthalene.

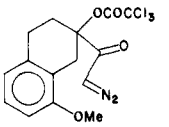


1

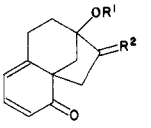


2 R = OH
3 R = H

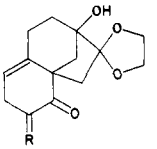
The synthesis of enone **14**, our first objective, was based on the development of earlier studies.[9] Thus, dienedione **5**, readily prepared from trifluoroacetic acid treatment of **4**,[10] was hydrolyzed



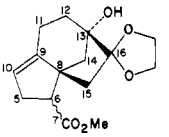
4



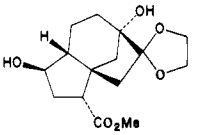
5 R' = $COCCl_3$, R² = O
6 R' = H, R² = O
7 R' = H, R² = OCH_2CH_2O



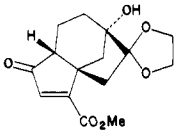
8 R = H_2
9 R = N_2



10 6β-CO_2Me
11 6α-CO_2Me



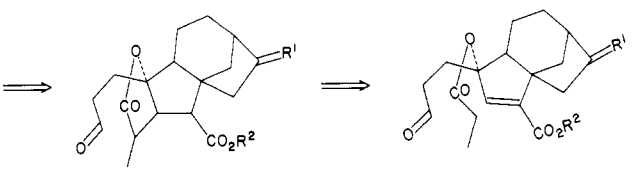
12
13 Δ^5



14

[10% aqueous Na_2CO_3/MeOH/THF (1:1.5:1.8), 5 min, 25 °C, 98.5% yield] to **6**, mp 113–114 °C,[11] the cyclopentanone function of which was selectively masked [$(CH_2OH)_2$, $(CH_2Cl)_2$, Dowex 50W × 8 (10% w/w), 4 A sieves, reflux 7 h, 59% yield] to give acetal **7**, mp 129–131 °C.[12] 1,4-Reduction [K-selectride[13] (1 equiv added over 30 min), EtOH (4 equiv),[14] THF, –65 °C, 97% yield] then furnished **8**, mp 103–104 °C, which was transformed directly[15] to diazo ketone **9**, mp 118–120 °C dec, in 82% yield. Irradiation of **9** [Pyrex, Hanovia 400-W medium-pressure mercury lamp, 13% aqueous $NaHCO_3$/THF (15:4), 0 °C, 4 h] furnished a mixture of ring-contracted acids, resolved by fractional crystallization to give the less soluble [chloroform/pentane (15:4)] 6β-epimer, mp 159–161 °C (17.5% yield), and then the desired 6α-epimer, indefinite mp 152–165 °C (63% yield), methyl ester

Scheme I



(1) This work was described at the Sixth International Symposium on Synthesis in Organic Chemistry, Cambridge, England, July 1979.
(2) For recent reviews, see: (a) Fujita, E.; Node, M. *Heterocycles* **1977**, *7*, 709–752. (b) Danheiser, R. L. Ph.D. Dissertation, Harvard University, 1978. (c) Urech, R. Ph.D. Dissertation, Australian National University, 1980.
(3) (a) Corey, E. J.; Danheiser, R. L.; Chandrasekaran, S.; Keck, G. E.; Gopalan, B.; Larsen, S. D.; Siret, P.; Gras, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 8034–8036. (b) Corey, E. J.; Danheiser, R. L.; Chandrasekaran, S.; Siret, P.; Keck, G. E.; Gras, J.-L. *Ibid.* **1978**, *100*, 8031–8034. (c) See also: Corey, E. J.; Gorzynski Smith, J. *Ibid.* **1979**, *101*, 1038–1039. Stork, G.; Boeckmann, R. K.; Taber, D. F.; Still, W. C.; Singh, J. *Ibid.* **1979**, *101*, 7107–7109.
(4) Nagata, W.; Wakabayashi, T.; Narisada, M.; Hayase, Y.; Kamate, S. *J. Am. Chem. Soc.* **1971**, *93*, 5740–5758.
(5) Totally synthetic routes via relays, but lacking optical resolutions, have been established for gibberellin A_4 (**3**), among others (~55 steps): Mori, K.; Shiozaki, M.; Itaya, N.; Matsui, M.; Sumiki, Y. *Tetrahedron* **1969**, *25*, 1293–1321. Gibberellins A_{15} and A_{37} (~40 steps): Fujita, E.; Node, M.; Hori, H. *J. Chem. Soc., Perkin Trans. 1* **1977**, 611–621.
(6) To avoid confusion, atoms are numbered throughout on the basis of the full gibberellin skeleton: Rowe, J. R., Ed. "The Common and Systematic Nomenclature of Cyclic Diterpenes", 3rd Rev.; Forest Product Labortory, U.S. Department of Agriculture: Wisconsin, 1968.
(7) (a) The feasibility of the aldol reaction was originally demonstrated by Dolby, L. J.; Milligan, R. J. *J. Am. Chem. Soc.* **1966**, *88*, 4536–4537. (b) Subsequent studies extended the scope of the method: Dolby, L. J.; Skold, C. N. *Ibid.* **1974**, *96*, 3276–3279. (c) The approach has been further refined concurrently with the present work: Stork, G.; Singh, J. *Ibid.* **1979**, *101*, 7109–7110.
(8) MacMillan, J.; Seaton, J. C.; Suter, P. J. *Tetrahedron* **1960**, *11*, 60–66.
(9) Cossey, A. L.; Mander, L. N. *Tetrahedron Lett.* **1979**, 969–972.
(10) Blair, I. A.; Ellis, A.; Johnson, D. W.; Mander, L. N. *Aust. J. Chem.* **1978**, *31*, 405–409.
(11) Structures **4–26** represent racemic compounds and are fully consistent with their NMR, IR, and mass spectral data. All crystalline compounds afforded satisfactory microanalytical data (± <0.3%) for carbon and hydrogen. All reactions were carried out under an atmosphere of purified nitrogen, where appropriate, and yields are reported for analytically pure products.
(12) The cyclopentanone function is only slightly more reactive than the dienone carbonyl group, so care must be taken to avoid formation of the bisacetal.
(13) Fortunato, J. M.; Ganem, B. *J. Org. Chem.* **1976**, *41*, 2194–2200.
(14) In the absence of a good proton donor, some of the initially formed enol boronate added 1,4 to the substrate. Ethanol was more effective than *tert*-butyl alcohol[13] in this case.
(15) Lombardo, L.; Mander, L. N. *Synthesis* **1980**, 368–369.

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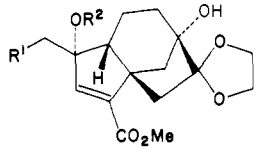
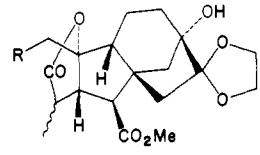
11 (diazomethane), mp 84–85 °C. The stereochemical assignments to the isomeric acids were made through analogy with the 13-deoxy analogues[9] and confirmed by ^{13}C NMR spectra of the derived methyl esters **10** and **11**,[16] which indicated shielding by the ester function of C(14) in the 6α-epimer and of C(15) in the 6β-epimer. The introduction of a C(10) oxygen function with concomitant elaboration of the thermodynamically less stable cis-B/C ring fusion[3b] was achieved through the addition of thexylborane[17] (ether, 0 °C, 3.5 h; Na_2HPO_4, H_2O_2, 35 °C, 2 h), giving diol **12**, mp 169–171 °C, in 90% yield (^{13}C NMR consistent with B/C cis fusion).[18] Finally, enone **14**, mp 126–130 °C, was obtained from **12** by α-selenenylation of the ester function [PhSeSePh, KH, THF/DMF (9:1), 20 °C, 0.4 h], selenoxide elimination (H_2O_2, CH_2Cl_2, 0 °C),[19] and manganese dioxide oxidation[20] of the resulting allylic alcohol **13** in 50–60% overall yield.

The addition of an operational equivalent of the O=$CHCH_2CH_2$: synthon[21] (or preferably the *cis*-propenal moiety)[7b,22] was crucial to the success of the strategy, but the C(10) carbonyl function was devoid of electrophilic reactivity toward most reagents.[23] However, the complex alane derived from 3-bromopropyne,[24] and also triallylalane[25] (THF, −78 °C, 5 min), furnished approximate quantitative yields of the carbinols **15** and **17**, respectively, with >95% stereoselectivity. Although propionate

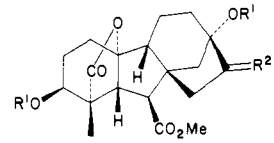


15 R¹ = C≡CH, R² = H
16 R¹ = C≡CH, R² = COEt
17 R¹ = CH=CH$_2$, R² = H
18 R¹ = CH=CH$_2$, R² = COEt

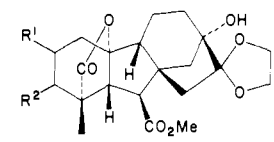


19 R = CH=CH$_2$, 4α-Me
20 R = CH=CH$_2$, 4β-Me
21 R = CH$_2$CH=O

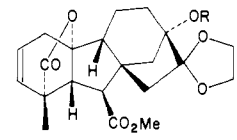
16, mp 128–129 °C, could not be induced to undergo an intramolecular Michael reaction,[26] propionate **18**, mp 90–91 °C [$(EtCO)_2O$, Et_3N, 4-(dimethylamino)pyridine,[27] 5 °C, 5.5 days, 78% yield; recovered **17** 7%, dipropionate 10%], was readily converted [KH (3 equiv), DMF, −20 °C, 20 min; $Et_3N^+H{\cdot}Ac^-$ quench at −40 °C][28] to a ~2:1 mixture of γ-lactones **19**, mp 161–163 °C, and **20**, mp 187–190 °C, respectively.[29] Oxidation to the aldehyde mixture **21** (disiamylborane,[17] ether, 0 °C, 1 h; Na_2HPO_4, H_2O_2, 35 °C, 3 h; $CrO_3{\cdot}2Py$,[30] CH_2Cl_2, 0 °C, 1 h, 89% overall yield) followed by the aldol reaction [10% aqueous K_2CO_3/MeOH (1:4), 25 °C, 3 h, careful deoxygenation] finally afforded a mixture[31] of unchanged aldehyde (10%) with the 3β-hydroxynorgibberellin **22** (29%), mp 225–228 °C, (−) enantiomer



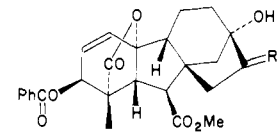
22 R¹ = H, R² = OCH$_2$CH$_2$O
23 R¹ = H, R² = O
24 R¹ = SiMe$_3$, R² = O



25 R¹ = H, R² = α-OH
26 R¹ = H, R² = α-OSO$_2$Ph
27 R¹ = β-OH, R² = β-OH
28 R¹ = α-Br, R² = β-OCOPh



29 R = H
30 R = CONHCH(Me)Ph



31 R = OCH$_2$CH$_2$O
32 R = O
33 R = CH$_2$

mp 254–256 °C,[32] and the 3α-epimer **25** (29%), mp 275–277 °C, (−) enantiomer mp 203–206 °C.[33] In each case, TLC mobility and IR, NMR, and mass spectral data were indistinguishable from those of the (−) enantiomer. Completion of the A_1 structure from **22** was effected simply by hydrolysis [3 M HCl/THF (1:1), 25 °C, 6 h] to ketol **23**,[34] mp 229–232 °C, silylation (Me_3SiCl, *i*-Pr_2NEt) to **24**, mp 166–169 °C, and then Wittig methylenation ($Ph_3P^+Me{\cdot}Br^-$, KO-*t*-Bu, *t*-BuOH, THF, 20 °C, 20 min).[36,37]

(16) **10**: ^{13}C NMR δ 22.2 (C-11), 32.5 (12), 34.7 (5), 44.7 (15), 49.5 (6), 51.4 (OMe), 51.7 (14), 53.2 (8), 64.9, 65.8 (OCH_2CH_2O), 79.2 (13), 113.6 (16), 117.8 (10), 145.8 (9), 174.7 (7). **11**: ^{13}C NMR δ 22.5 (C-11), 32.6 (12), 33.6 (5), 46.5 (14), 47.8 (15), 49.3 (6), 51.6 (OMe), 52.7 (8), 64.9, 65.8 (OCH_2CH_2O), 80.0 (13), 113.2 (16), 117.5 (10), 146 (9), 173.9 (7). Ester **11** could be obtained directly as a 3:1 mixture with **10** by photolysis of **9** in methanol, but separation of the acids was achieved more readily. Ester **10** was converted to a 3:1 mixture of **11**/**10** by NaOMe/MeOH.

(17) Zweifel, G.; Brown, H. C. *Org. React. (N.Y.)* **1963**, *13*, 1–54.

(18) **12**: ^{13}C NMR δ 19.2 (C-11), 30.1 (12), 35.1 (5), 41.7 (14), 46.1 (15), 47.6 (6, 8), 51.6 (OMe), 54.5 (9), 64.8, 65.8 (OCH_2CH_2O), 73.0 (10), 79.0 (13), 113.6 (16), 173.2 (7). Higher frequencies would be expected for C-(11)–C(14) in the B/C trans-fused derivative.

(19) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434–5447. The use of KH is a crucial modification; lithium diisopropylamide and alkoxide bases were ineffectual in the removal of the very hindered 6β-proton.

(20) Goldman, I. M. *J. Org. Chem.* **1969**, *34*, 1979–1981.

(21) Evans, D. A.; Andrews, G. C.; Buckwalter, B. *J. Am. Chem. Soc.* **1974**, *96*, 5560–5561. Still, W. C.; Macdonald, T. L. *Ibid.* **1974**, *96*, 5561–5563.

(22) Kluge, A. F.; Untch, K. G.; Fried, J. H. *J. Am. Chem. Soc.* **1972**, *94*, 9256–9258.

(23) An extensive range of alkyne, alkene, and alkane-derived organometallic reagents, in the presence or absence of amines and Lewis acids, was added to **14** and dihydro-**14**, but either enolization or no reaction was observed. Cf.: Martin, J. L.; Tou, J. S.; Reusch, W. *J. Org. Chem.* **1979**, *44*, 3666–3671.

(24) Eiter, v. K. *Justus Liebigs Ann. Chem.* **1962**, *658*, 91–95.

(25) Zakharkin, L. I.; Savina, L. A. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1964**, 1133–1135. This reagent and the propyne-derived alane were chosen in the expectation that they would not react readily with the ester function and that their Lewis acid properties would enhance the electrophilic properties of the ketone group. Cf.: Mole, T.; Jeffery, E. A. "Organoaluminum Compounds", Elsevier: New York, 1972; pp 302, 337. The S_E2' mode of reaction may be essential for success, cf.: Benkeser, R. A. *Synthesis* **1971**, 347–358.

(26) Attempts to convert alkyne **15** to the aldehyde prior to the planned Michael reaction were unsuccessful: Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 3834–3840.

(27) Hassner, A.; Krepski, L. R.; Alexanian, V. *Tetrahedron*, **1978**, *34*, 2069–2076.

(28) Protonation by this reagent gave a stereochemically more discreet mixture and a higher proportion of the 4α-methyl derivative **19**. This is the preferred isomer for the subsequent aldol reaction, since the 4β-proton is more accessible, leading to a faster rate.

(29) Stereochemical assignments were made from ^{13}C NMR spectra. In both compounds, C(14) gives a resonance at δ 46.3, indicating that the ester group has the 6β configuration. Cf.: δ 41.7 for C(14) in the 6α-ester **12**. Resonances for C(18) occur at δ 12.0 in the 4α-isomer **19** and at δ 17.5 in the 4β-epimer **20**.

(30) Collins, J. C.; Hess, W. W.; Frank, F. J. *Tetrahedron Lett.* **1968**, 3363–3366.

(31) The 13-deoxy analogue of **21** gave a 3:1 mixture of 3β/3α epimers, respectively, under comparable conditions. Cf.: ref 7c.

(32) Prepared from (+)-**23**[35] as for acetal **7**.

(33) Prepared[32] from the ketone [mp 187–189 °C, $[\alpha]^{30}_D$ +30° (*c* 0.5, $CHCl_3$)], which was obtained from methyl 3β,13-diacetylgibberellate by selective hydrolysis (K_2CO_3) to the 13-monoacetate, Jones oxidation to the Δ^1-3-one, K-selectride reduction, ozonolysis, and then further hydrolysis. Full details of this and other improved gibberellin degradation sequences will be reported elsewhere.

(34) Acid-catalyzed ketol rearrangement in similar compounds[3b] is very facile, but $J_{5,6}$ of 10.5 Hz is consistent with structure **23**, cf.: (a) Mander, L. N.; Pyne, S. G. *J. Am. Chem. Soc.* **1979**, *101*, 3373–3375. (b) Hanson, J. R. *J. Chem. Soc.* **1965**, 5036–5040. Spectroscopic identity (^1H NMR, IR, and mass spectrum) was also established with (+)-**23**.[35]

(35) Bourn, P. M.; Grove, J. F.; Mulholland, T. P. C.; Tidd, B. K.; Klyne, W. *J. Chem. Soc.* **1963**, 154–162.

(36) Under basic conditions, epimerization at C(3) (Cross, B. E.; Grove, J. F.; Morrison, A. *J. Chem. Soc.* **1961**, 2498–2515) and ketol rearrangement at C(13) (Mosettig, E.; Beglinger, U.; Dolder, F.; Lichti, H.; Quitt, P.; Waters, J. A. *J. Am. Chem. Soc.* **1963**, *85*, 2305–2309) occur rapidly.

(37) *tert*-Butyl alcohol ensures reprotonation of the enolate anion which forms very readily from the C(16) carbonyl function. Epimerization at C(3) begins to occur at temperatures above 20 °C [H(5) in **24**: δ 3.21 (J = 10.5 Hz). H(5) in 3-epi-**24**: δ 2.52 (J = 10.5 Hz)].[34b] The precise nature of the isomerization is under investigation.

Demethylation (*n*-PrSLi, DMF, 20 °C, 2 h)[38] and desilylation (acidic workup) finally furnished (±)-gibberellin A_1, mp 251–254 °C, then 271–274 °C (>80% overall yield from **23**), with IR, ^1H NMR, and mass spectra indistinguishable from those of the (+) enantiomer (**2**).[8]

The elaboration of the gibberellic acid (A_3) structure (**1**), however, poses a rather more formidable challenge. The allylic lactone moiety is labile toward weak bases[39] and acids (even autocatalysis),[40] while Wagner–Meerwein rearrangement of the C/D-ring system is readily initiated by electrophiles.[41] Consequently, assembly of the complete A_3 structure requires delicate timing, as well as a judicious selection of reagents and conditions.

It appeared that Δ^1-3β-ol functionality of A_3 could most readily be introduced from a Δ^2-olefin,[42] so **25** was converted into phenylsulfonate **26**, mp 212–214 °C ($PhSO_2Cl$, C_5H_5N, 25 °C, 4 h, 95%), and thence (±)-**29**, mp 244–248 °C, by treatment with a mixture of tetra-*n*-butylammonium bromide (5 equiv) and 1,5-diazabicyclo[4.3.0]non-5-ene (DBN)(5 equiv) in dimethylformamide (DMF) at 90 °C for 21 h (82% yield).[43] An optical resolution of (±)-**29** was effected through chromatographic separation of the derived diastereomeric urethanes **30** [phosgene, pyridine, DMAP, 25 °C, 6 h; (−)-α-phenylethylamine].[44,45] Reaction of the more polar urethane with tetrachlorosilane (10 equiv) and triethylamine (20 equiv) in dichloromethane (25 °C, 48 h)[46] afforded (−)-**29**, identical in all respects (mp, TLC ^1H NMR, IR and mass spectra) with an authentic sample [mp 263–264 °C, $[\alpha]^{27}_D$ −88° (*c* 0.56, $CHCl_3$)] prepared from the 3α-phenylsulfonate, mp 186–188 °C, of (−)-ketal **25**, which had been obtained from natural A_3.[33]

Hydroxylation[47] [OsO_4, *N*-methylmorpholine *N*-oxide, acetone/H_2O (3:1), 5 °C, 90 h] of **29** furnished triol **27** [mp 256–258 °C, $[\alpha]^{27}_D$ + 17° (*c* 0.54, EtOH)] in 98% yield, and the derived benzylidene acetal (diastereomeric mixture) [PhCHO, $(CH_2Cl)_2$, *p*-toluenesulfonic acid, 4 A sieves, reflux 16 h] was treated with *N*-bromosuccinimide [CCl_4, reflux 1 min; 250-W tungsten lamp, 0.9 m, 35 °C, 1.25 h]. Stereoelectronically controlled fission of the 1,3-dioxolan-2-ylium cation[48] generated in this way ensured specific formation of the 2α-bromide **28**, mp 186–189 °C (95% yield), which was converted [DBN (5 equiv), THF/DMF (1:1), 65 °C, 1 h, 90% yield] into allylic benzoate **31** [mp 243–246 °C, $[\alpha]^{28}_D$ + 190° (*c* 0.79, $CHCl_3$)] and then ketol **32** [mp 231–234 °C, $[\alpha]^{30}_D$ +197° (*c* 0.8, $CHCl_3$)] by treatment with dilute acid [3 M HCl/THF (1:2), 30 °C, 6 h, ~100% yield]. The A_3 structure was then completed in ~75% overall yield in essentially the same manner as in the A_1 synthesis, i.e., silylation, Wittig methylenation,[49] and desilylation to give **33**; mp 169–170 °C, $[\alpha]^{25}_D$ +214° (*c* 1.0, $CHCl_3$). Finally, hydrolysis at pH 10 [$K_2CO_3/KHCO_3$, MeOH/THF/H_2O (4:1:1), 25 °C, 1 h] furnished methyl gibberellate, which was demethylated, as reported,[50] to gibberellic acid **1**. Spectra (^1H NMR, IR, mass spectra), mp, and TLC mobility of **1** and its methyl ester were indistinguishable from those of authentic samples.[51]

While the focus of this work has been the preparation of A_3 (**1**), it is clear that all the most common C_{19} gibberellins are accessible through applications of the present strategy.[52] Moreover, many of the procedures are highly suited to the manipulation of natural gibberellins and the preparation of analogues for biological investigations.

(38) Bartlett, P. A.; Johnson, W. S. *Tetrahedron Lett.* **1970**, 4459–4462. The rate of the present reaction is similar to that in the carcinogenic solvent hexamethylphosphoric triamide.

(39) Cross, B. E.; Grove, J. F.; Morrison, A. *J. Chem. Soc.* **1961**, 2498–2515.

(40) (a) Cross, J. *J. Chem. Soc.* **1954**, 4670–4676. (b) Pryce, R. J. *Phytochemistry* **1973**, *12*, 507–514, and references cited therein.

(41) Hanson, J. R. "The Tetracyclic Diterpenes", Pergamon Press: Oxford, 1968; pp 41–59.

(42) Approaches based on a 3-oxo derivative are unattractive since hydride reduction at C(3) favors the formation of 3α-alcohols: Voigt, B.; Adam, G.; Kobrina, N. S.; Serebrayakov, E. P. *Z. Chem.* **1977**, *17*, 372–374. Gurvich, I. A.; Kobrina, N. S.; Kucherov, V. F. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1969**, 1668–1671.

(43) Lower concentrations of bromide ion or DBN resulted in an accumulation of the 3α-bromide (double inversion), which does not undergo elimination at this temperature. The excess of bromide ion increases the rate of formation of 3β-bromide, which is then eliminated by the nitrogen base. The 3β-epimer of **26** afforded olefin **29** in 90% yield after only 4.5 h under equivalent conditions.

(44) Pirkle, W. H.; Hauske, J. R. *J. Org. Chem.* **1977**, *42*, 1839–1844. Cf. ref 3b.

(45) Three 15-min developments in ether/pentane (3:2) on Merck DC-Alufolien Kieselgel 60 (0.2 mm) cleanly separated the two diastereomers (R_f 0.53 and 0.58). The more polar isomer, $[\alpha]^{25}_D$ −48° (*c* 0.22, $CHCl_3$), was spectroscopically (^1H NMR, IR) and chromatographically identical with an authentic sample, $[\alpha]^{25}_D$ −48.7° (derived from natural A_3). The less polar isomer was chromatographically and spectroscopically (^1H NMR, IR) indistinguishable from the enantiomeric urethane derived from (−)-**29** and (+)-α-phenylethylamine.

(46) Cf.: Pirkle, W. H.; Hauske, J. R. *J. Org. Chem.* **1977**, *42*, 2781–2782.

(47) Van Rheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973–1976.

(48) Pittman, C. U.; McManus, S. P.; Larson, J. W. *Chem. Rev.* **1972**, 357–438.

(49) Greater care was required than in the A_1 preparation. The KO-*t*-Bu was prepared from potassium metal; traces of moisture or the use of commercially obtained KO-*t*-Bu, even after resublimation, led to cleavage of the benzoate group with a consequent retroaldol reaction and methylenation of the seco aldehyde.

(50) Corey, E. J.; Brennan, T. M.; Carney, R. L. *J. Am. Chem. Soc.* **1971**, *93*, 7316–7317.

(51) We are indebted to A. Cossey for technical assistance and to G. W. Elson, I.C.I. Plant Protection, for gifts of gibberellins.

(52) The obvious conversions of **27** and **29** into gibberellins A_8 and A_5, respectively, have been completed. The adoption of the general strategy to the preparation of 13-deoxy C_{19} gibberellins, culminating in the synthesis of (±)-A_4 (**3**), mp 220–222 °C, has also been carried out. Applications to further gibberellins, including C_{20} derivatives, are well advanced.

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Total Synthesis of Gibberellic Acid. The Hydrofluorene Route

Sir:

A recurring theme in a broad spectrum of proposals[1] for the synthesis of the C_{19} gibberellin phytohormones[2] has been the utilization of a benzenoid synthon as a precursor to the A-ring/lactone moiety in these compounds. The pioneering studies undertaken by Loewenthal,[3] in particular, appeared to hold considerable promise for this strategy,[4] which dovetails efficiently with the construction of the remainder of the molecule through the application of our diazo ketone based methodology.[5] We now report the application of these concepts to the transformation of fluorenone **1**[6] into the tetracyclic lactone **2**, an advanced intermediate in our recently completed total synthesis of gibberellic acid.[7]

Our first objective was the development of an efficient preparation of tetracyclic ketone **8**. This was achieved through the use of reported procedures,[5c] but with several important refine-

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(3) (a) Bachi, M. D.; Epstein, J. W.; Herzberg-Minzly, Y.; Loewenthal, H. J. E. *J. Org. Chem.* **1969**, *34*, 126–135. (b) Loewenthal, H. J. E.; Schatzmiller, S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 944–950.

(4) See also: (a) House, H. O.; Strickland, R. C.; Zaiko, E. J. *J. Org. Chem.* **1976**, *41*, 2401–2408. (b) House, H. O.; Zaiko, E. J. *Ibid.* **1977**, *42*, 3780–3783. (c) Baker, A. J.; Goudie, A. C. *J. Chem. Soc., Chem. Commun.* **1972**, 951.

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(6) Hook, J. M.; Mander, L. N. *J. Org. Chem.* **1980**, *45*, 1722–1724.

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