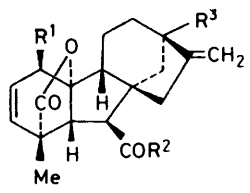
Allylic Chlorination of Gibberellins A_3 and A_7 Methyl Esters and of Gibberellin A_3: Preparation of Gibberellin A_5

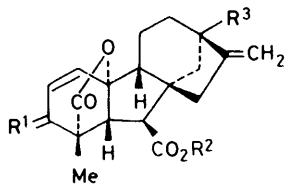
By **John R. Bearder, Paul S. Kirkwood,** and **Jake MacMillan,*** School of Chemistry, The University, Bristol BS8 1TS

A high-yield conversion of gibberellin A_3 to gibberellin A_5 is described. With thionyl chloride, gibberellin A_3 methyl ester gives mainly 1β-chlorogibberellin A_5 methyl ester; the isomeric 3α-chloro-1-ene was the main product from the reaction with toluene-*p*-sulphonyl chloride and lithium chloride. Each product is reduced by tri-n-butylstannane and acetylated to give the same mixture of the 13-acetates of gibberellin A_5 methyl ester and of the isomeric 1(10)-ene-19,2-lactone. Hydrolysis of gibberellin A_5 methyl ester 13-acetate gives gibberellin A_5 in 20% overall yield from gibberellin A_3. [1-$^2H_1$]Gibberellin A_5 is obtained in the same way by using tri-n-butyl-[$^2H_1$]stannane in the reduction step. Analogous chlorination products of gibberellin A_7 methyl ester and of gibberellin A_3 are described.

SEVERAL partial syntheses of gibberellin A_5 (1) from gibberellin A_3 (13) have been described. In the original method gibberellin A_3 methyl ester (14) was selectively hydrogenated [1] to gibberellin A_1 methyl ester (29) which was converted into gibberellin A_5 (1) *via* the 3,13-bis-toluene-*p*-sulphonate (30),[2] the 13-toluene-*p*-sulphonate (2),[3] and gibberellin A_5 methyl ester (3). This route was used by Musgrave and Kende [4] and by Durley *et al.*[5] to



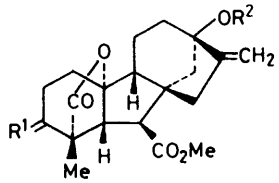
	R^1	R^2	R^3
(1)	H	OH	OH
(2)	H	OMe	OTs
(3)	H	OMe	OH
(4)	Cl	OMe	OH
(5)	Cl	OMe	H
(6)	Br	OMe	OH
(7)	Cl	OMe	OTs
(8)	H	OMe	OAc
(9)	Cl	OH	OH
(10)	Cl	Cl	OH
(11)	Cl	OEt	OH
(12)	F	OMe	OH



	R^1	R^2	R^3
(13)	H,β-OH	H	OH
(14)	H,β-OH	Me	OH
(15)	H,β-OAc	Me	OH
(16)	H,β-OAc	Me	OAc
(17)	H,β-OMs	Me	OH
(18)	O	Me	OAc
(19)	H,β-OH	Me	H
(20)	H,α-Cl	Me	OH
(21)	H,α-Cl	Me	OTs
(22)	H,α-Cl	Me	H
(23)	H,β-OTs	Me	OH
(24)	H,α-Br	Me	OH
(25)	H_2	Me	OH
(26)	H,α-Cl	H	OH
(27)	H,α-OH	Me	OH
(28)	H,β-F	Me	OH

prepare [^{3}H]gibberellin A_5. A second route, described by Murofushi *et al.*,[6] proceeded by catalytic reduction of gibberellin A_3 methyl ester 3-methanesulphonate (17) to give gibberellin A_5 methyl ester (3) and hence to the free acid (1); Murofushi *et al.*[6] prepared [1-$^3H_1$]gibberellin A_5 in this way. More recently gibberellin A_5, and [1β,3-$^2H_2$]- and [1β,3-$^3H_2$]-gibberellin A_5, have been prepared [7,8] by conjugate reduction of 3-didehydrogibberellin A_3 methyl ester 13-acetate (18), and dehydration of the products (31) or (32), followed by alkaline hydrolysis. By these methods the overall yields of gibberellin A_5 (1) from gibberellin A_3 (13) are <6%.

Continuing our investigations on the partial syntheses of less accessible gibberellins from accessible fungal gibberellins by methods which permit the introduction of stable and radioactive isotopes, we report a new,



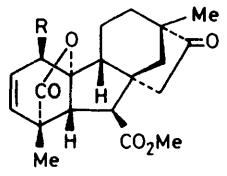
	R^1	R^2
(29)	H,β-OH	H
(30)	H,β-OTs	Ts
(31)	H,β-OH	Ac
(32)	H,α-OH	Ac

efficient route to gibberellin A_5 (1), and its derivatives, by chlorination of the allyl alcohol function in gibberellin A_3 (13) and its methyl ester (14). The analogous chlorination of gibberellin A_7 methyl ester (19) is also described.

RESULTS AND DISCUSSION

In the chlorination of gibberellin A_3 methyl ester (14), the products depended upon the reagents. With thionyl chloride in tetrahydrofuran and diethyl ether, 1β-chlorogibberellin A_5 methyl ester (4) was the main product (73%), accompanied by 9% of the ring C/D rearrangement product (33) and starting material (16%). An attempt to reduce the amount of acid-catalysed rearrangement to the ketone (33), using [9] thionyl chloride

and a catalytic amount of zinc chloride, gave a complex mixture of products. Chlorination of gibberellin A_7 methyl ester (19) with thionyl chloride in diethyl



(33) R = Cl
(34) R = H

ether gave 1β-chloro-2,3-didehydrogibberellin A_9 methyl ester (5). The 1β-chloro-compounds (4) and (5), and other new compounds described in this paper, were characterised principally by ^1H n.m.r. spectroscopy (Table) which is discussed later. The structures (4) and (5), assigned to these products, are consistent with their formation from the allylic alcohols (14) and (19) by an S_Ni' mechanism.[10]

With toluene-*p*-sulphonyl chloride and lithium chloride, chlorination of gibberellin A_3 methyl ester (14), afforded the 3α-chloro-compound (20) as the major product (63%) together with its 13-toluene-*p*-sulphonate (21) (7%) and the 1β-chloro-compound (4) (11%). These compounds were separated by p.l.c. and characterised mainly by ^1H n.m.r. spectroscopy (Table). Analogously gibberellin A_7 methyl ester (19) gave 3α-chloro-1,2-didehydrogibberellin A_9 methyl ester (22) and a small amount of the corresponding 1β-chloro-compound (5). The formation of the 1β-chloro-compounds in these

^1H N.m.r. data for some gibberellins and derivatives (measured at 100 MHz for chloroform solutions; multiplicity and *J* Hz, in parentheses)

Compound	1-H	2-H	3-H	5-H	6-H	17-H_2 [a]	18-Me [b]
(14) [c]	6.31 (dd, 9.1 and 0.85)	5.90 (dd, 3.8 and 9.1)	4.15 (d, 3.8)	3.2 (d, 11)	2.79 (d, 11)	4.96, 5.26	1.25
(15)	6.39 (d, 9)	5.86 (dd, 4 and 9)	5.32 (d, 4)	3.35 (d, 11)	2.79 (d, 11)	4.97, 5.28	1.16
(16)	6.43 (d, 9)	5.90 (dd, 4 and 9)	5.37 (d, 4)	3.38 (d, 11)	2.81 (d, 11)	5.05, 5.22	1.17
(27)	6.18 (dd, 1.5 and 10)	5.82 (dd, 2.5 and 10)	4.26 (m)	2.96 (d, 10)	2.76 (d, 10)	4.93, 5.24	1.29
(20)	6.29 (dd, 1.5 and 9)	5.92 (dd, 2.5 and 9)	4.67 (dd, 1.5 and 2.5)	3.06 (d, 11)	2.78 (d, 11)	4.97, 5.28	1.31
(24)	5.73 (dd, 1.2 and 9)	5.88 (dd, 2.5 and 9)	4.82 (m)	3.07 (d, 10)	2.71 (d, 10)	4.97, 5.28	1.22
(13) [d]	6.48 (d, 9)	6.18 (dd, 4 and 9)	4.54 (d, 4)	3.92 (d, 11)	3.28 (d, 11)	5.02, 5.60	1.76
(26) [d]	6.39 (dd, 2 and 9)	5.97 (dd, 3 and 9)	5.00 (dd, 2 and 3)	3.36 (d, 10)	3.10 (d, 10)	5.05, 5.57	1.57
(19)	6.29 (d, 9)	5.85 (dd, 4 and 9)	4.12 (d, 4)	3.18 (d, 11)	2.76 (d, 11)	4.83, 4.96	1.23
(22)	6.28 (dd, 1.5 and 9)	5.91 (dd, 3 and 9)	4.65 (dd, 1.5 and 3)	3.03 (d, 11)	2.78 (d, 11)	4.89, 5.02	.132
(25)	6.2 (m)	5.85 (m)		2.99 (d, 10)	2.76 (d, 10)	4.97, 5.28	1.20
(3)		5.77 (m)	5.77 (m)	2.83 (d, 10)	2.66 (d, 10)	4.97, 5.28	1.25
(8)		5.76 (m)	5.76 (m)	2.82 (d, 10)	2.65 (d, 10)	4.98, 5.13	1.24
(4)	4.52 (d, 2)	5.85 (m)	5.85 (m)	3.11 (d, 10)	2.65 (d, 10)	4.99, 5.25	1.25
(11)	4.54 (d, 3)	5.92 (m)	5.92 (m)	3.16 (d, 10)	2.66 (d, 10)	5.06, 5.33	1.26
(5)	4.55 (d, 3)	5.98 (dd, 3 and 9)	5.85 (d, 9)	3.18 (d, 11)	2.65 (d, 11)	4.94, 5.05	1.25
(6)	4.65 (d, 3.5)	5.98 (dd, 3.5 and 9)	5.70 (d, 9)	3.19 (d, 10)	2.53 (d, 10)	4.97, 5.23	1.24
(1) [d]		5.68 (m)	5.68 (m)	3.08 (d, 10)	2.96 (d, 10)	4.99, 5.52	1.42
(9) [d]	4.81 (d, 2)	5.87 (m)	5.87 (m)	3.43 (d, 9)	3.01 (d, 9)	5.03, 5.54	1.37
(35)	5.96 (dd, 2 and 4) [e] (t, 2) [f]	4.90 (m)		3.20 (d, 6) [g]	2.62 (d, 6)	4.94	1.25
(36)	5.80 (q, 2.5)	4.79 (t, 2.5)	4.27 (d, 5)	3.29 (dd, 2.5, 6)	2.57 (d, 6)	5.00, 5.14	1.20
(37)	5.74 (m)	5.02 (m)	5.02 (m)	3.31 (dd, 3, 6)	2.56 (d, 6)	4.99, 512	1.21
(38)	5.74 (q, 3)	5.00 (m)	5.00 (m)	3.30 (dd, 3, 6)	2.59 (d, 6)	4.98	1.21
(39)	5.76 (m, 2.5, 2.5 and 5)	4.73 (t, 5)	4.25 (d, 5)	3.28 (dd, 2.5 and 6)	2.51 (d, 6)	4.89	1.18

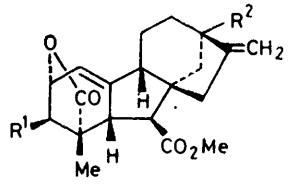
[a] Broad singlet. [b] Singlet. [c] Measured at 200 MHz. [d] In [$^2H_5$]pyridine. [e] After irradiation at δ 3.20. [f] After irradiation at δ 4.9. [g] After irradiation at δ 5.96.

reactions corresponds formally to a *syn*-S_N2' displacement.

In contrast, Bateson and Cross [11] obtained the 1β- and 3β-fluoro-compounds (12) and (28) from gibberellin A_3 methyl ester (14) and 2-chloro-*NN*-diethyl-1,1,2-trifluoroethylamine, and suggested an ionic mechanism.

Corey *et al.*[12] have reported that the reaction of 3β-toluene-*p*-sulphonyl gibberellin A_3 methyl ester (23) with sodium bromide in hexamethylphosphoramide gave a mixture of the 1α- and 1β-bromo-derivatives of gibberellin A_5 methyl ester. However, the products were not isolated or characterised. Bromination of the toluene-*p*-sulphonate (23), both under the conditions of Corey *et al.*[12] and our conditions, when lithium chloride was replaced by lithium bromide, gave the same pair of bromides. The olefinic region in the ^{1}H n.m.r. spectra of these bromides (Table and later discussion) was markedly different from the 1β- and 3-chloro-compounds (4) and (20). However, we suggest that the bromides are the 1β- and 3α-bromides (6) and (24).

Reduction, with tri-n-butylstannane, of the 1β- and 3α-chloro-compounds (4) and (20) from gibberellin A_3 methyl ester gave, in each case, the same mixture containing 70% of gibberellin A_5 methyl ester (3) and 30% of the 1,2-double-bond isomer (25). When the temperature of reduction was varied the product ratio was either unchanged or, at lower temperatures, no reduction occurred. The mixture could not be separated by p.l.c. but the components could be distinguished by ^{1}H n.m.r. (Table) and quantified by the high-field signal of the 1-H signal in the 1,2-double-bond isomer (25). Repeated crystallisation of the mixture gave gibberellin



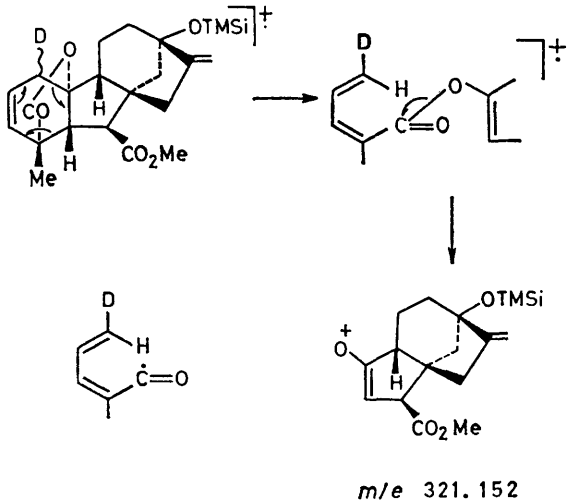
(35) R^1 = H, R^2 = OAc
(36) R^1 = R^2 = OH
(37) R^1 = OAc, R^2 = OH
(38) R^1 = R^2 = OAc
(39) R^1 = OH, R^2 = H
(40) R^1 = H, R^2 = OH

A_5 methyl ester (3) in 95% purity by n.m.r. and in 30% yield. A more satisfactory yield of gibberellin A_5 methyl ester (3) from the mixture was obtained as follows.

Acetylation of the mixture of double bond isomers (3) and (25), with acetic anhydride and toluene-*p*-sulphonic acid, gave a mixture of gibberellin A_5 methyl ester 13-acetate (8), and the product (35), derived by rearrangement of the 1,2-ene (25). The mixture was readily separable by p.l.c. and the gibberellin A_5 methyl ester 13-acetate (8) was hydrolysed to gibberellin A_5 (1) as previously described.[7] The rearrangement of the 1,2-ene-19,10-lactone (25) to the 1(10)-ene-19,2-lactone (35) did not occur with 2M-sodium hydroxide [13] and may be acid-catalysed. The structure of the rearrangement product was deduced from the ^{1}H n.m.r. spectrum (Table), aided by double-irradiation experiments.

Our preferred route from gibberellin A_3 (13) to gibberellin A_5 (1) proceeds by chlorination of gibberellin A_3 methyl ester (14) with thionyl chloride, reduction of the resultant 1β-chlorogibberellin A_5 methyl ester (4) to the mixture of 1,2- and 2,3-double-bond isomers (3) and (25), which is acetylated to the mixture of acetates (8) and (35), and the separated acetate (8) is hydrolysed by aqueous alkali to gibberellin A_5 (1). The overall yield is *ca.* 20%.

By using tri-n-butyl[^{2}H]stannane in the dechlorination step, [1ξ-$^2H_1$]gibberellin A_5 was obtained containing 0.96 atoms deuterium per molecule. G.l.c.–mass spectrometry of the TMSi-ether of [1ξ-$^2H_1$]gibberellin A_5 methyl ester showed, by comparison of the mass spectrum with that of the unlabelled compound, that most of the ions contained one deuterium atom. The ions at *m/e* 167, 193, 207, and 208 did not contain deuterium, supporting the assignment [14] of these ions to ring c/D fragmentation. An ion at *m/e* 321 did not contain deuterium and had the composition $C_{17}H_{25}O_4Si$ corresponding to the loss of $C_6H_6{}^2H_1O$ from the molecular ion; there was a corresponding ion at *m/e* 96. These data fit the retro-Diels–Alder cleavage shown in the Scheme.



SCHEME

1β-Chlorogibberellin A_5 (9) and the 3α-chloro-1,2-ene (26), required for biological testing, were prepared by direct chlorination of gibberellin A_3 (13). Reaction with carbon tetrachloride–triphenylphosphine, and a catalytic amount of pyridine (J. R. Hanson, personal communication) was complex. When work-up of the reaction was conducted below pH 7, 1β-chlorogibberellin A_5 (9), and the corresponding ethyl ester (11), were obtained in yields of 15 and 12%, respectively. When work-up was conducted above pH 7 only gibberellin A_3 (13) was

obtained although the 1β-chloro-compound (9) and its ethyl ester (11) were both found to be stable at pH 10. These observations indicate a base-sensitive intermediate. Castro and Selve [15] have shown that the ion pair $Ph_3P^+ORCl^-$, the suggested [16] intermediate, is stable in tetrahydrofuran at low temperature and that nucleophiles can compete with chloride ions in the decomposition of the ion pair. Although the reaction with giberellin A_3 (13) was conducted at ambient temperature in tetrahydrofuran, decomposition of the ion-pair intermediate by hydroxide ions may explain the results of work-up above pH 7; however it should be noted that 3-epi-GA_3 (27) and 1β-hydroxyGA_5, the products of allylic rearrangement, were not detected. The formation of the ethyl ester (11) indicates the intermediate formation of the acid chloride (10) and its reaction with ethanol, either present in the solvent or formed from the ethyl acetate during the acidic work-up. The white precipitate, formed in the reaction, gave a ^1H n.m.r. spectrum similar to that of $Ph_3P^+CH_2ClCl^-$, reported by Tömösközi *et al.*,[17] and supporting their conclusion that it is salts of this type which are formed, and not triphenylphosphine oxide or triphenylphosphine hydrochloride, as reported earlier.[18] The 3α-chloro-acid (26) was not detected from the reaction of gibberellin A_3 with carbon tetrachloride and triphenylphosphine although this method of chlorination has been reported [19] to convert allylic alcohols into allylic chlorides without rearrangement. Rearrangement was also observed in the case of gibberellin A_7 methyl ester (19) which gave the 1β-chloro-compound (5) and some of the 3α-chloro-1-ene (22).

The 3α-chloro-acid (26) was obtained by treatment of gibberellin A_3 (13) with toluene-*p*-sulphonyl chloride and lithium chloride as for the methyl ester (14). When the reaction mixture was worked up at pH 3 the 3α-chloro-compound (26) was obtained in 37% yield, with 21% of 1β-chlorogibberellin A_5 (9). These products were separated by repeated p.l.c. and identified by ^1H n.m.r. spectroscopy (Table). Work-up at pH values above 7.0 gave, in contrast, the 3α-chloro-acid (26) (12%) and gibberellin A_3 (13) (28%). No 1β-chlorogibberellin A_5 (9) was detected although it was stable at pH 10 and it is not converted into the 3α-chloro-acid by chloride ions. An alternative route to the 3α-chloro-acid (26) has recently been reported; this involved the reaction of gibberellin A_3 (13) with thionyl chloride in pyridine at reduced temperatures.[20]

The structure and stereochemistry of the chloro-compounds, described in this paper, were deduced from two features of the ^1H n.m.r. spectra (Table). Firstly the olefinic protons and the 3-protons of the 3α-chloro-compounds (20), (22), and (26) formed ABM systems, similar to those of gibberellin A_3 methyl ester (14), gibberellin A_7 methyl ester (19), and gibberellin A_3 (13). However, the $J_{1.3}$ values are larger (1.5 Hz) for the 3α-chloro-compounds than for that of the methyl esters of gibberellin A_3 ($J_{1.3}$ 0.85 Hz) and of gibberellin A_7 ($J_{1.3} < 1$ Hz) in accord with a ψ-axial *versus* a ψ-equatorial 3-proton. In the case of the 1β-chloro-compounds (4), (5), (9), and (11), the 2,3-olefinic protons occur as a narrow multiplet. These findings are in agreement with the n.m.r. data for the 1β- and 3β-fluoro-compounds (12) and (28).[11] Secondly, the stereochemistry of the chloro-substituent was deduced from the chemical shifts of the 5-proton, which is deshielded by 1β- and 3β-substituents in contrast to the 6-proton which, for $CDCl_3$ solutions, occurs in the range δ 2.78—2.64.[21] Thus, in accord with the assigned stereochemistry, the signal for the 5-proton is shifted to lower field in the spectra of the 1β-chloro-compounds (4), (5), (7), (9), and (11), compared to that in the unsubstituted compounds (1), (3), and (8). In contrast the 5-proton signals in the 3α-chloro-compounds (20), (22), and (26) occur at about the same chemical shift as in the 3-epimer (27) of gibberellin A_3 methyl ester.

The olefinic region of the brominated compounds (6) and (24) was significantly different from that of the chlorinated analogues (4) and (20). Instead of a complex multiplet for the 2- and 3-protons, observed for gibberellin A_5 methyl ester (3) and its 1β-chloro-derivative (4), the 1β-bromo-compound (6) revealed the 2-proton as a low-field doublet of doublets ($J_{1.2}$ 3.5, $J_{2.3}$ 9 Hz). Both 1β-halogeno-compounds show negligible allylic coupling between the 1- and 3-protons. Similarly for the 3α-bromo-compounds (24), the splitting pattern ($J_{1.2}$ 9, $J_{2.3}$ 2.5, $J_{1.3}$ 1.2 Hz) revealed that the 2-proton resonates at a lower field than the 1-proton, which is the converse of the order observed for the 3α-chloro-compound (20) or gibberellin A_3 methyl ester (14). These differences are ascribed to a greater deshielding by the bromine upon the proton on the adjacent carbon atom.

An interesting feature concerning the chemical shift of the 17-protons in gibberellin derivatives emerged from the present studies. In $CDCl_3$ solution, the signals of these hydrogens occur as two broad singlets at δ 5.30 — 4.80. The separation is *ca.* 0.15 p.p.m. in the absence of a 13-hydroxy-group, and increases to *ca.* 0.30 p.p.m. in the presence of a 13-hydroxy-group.[21] As shown in the Table, the separation is decreased to 0.15 p.p.m. by acetylation of the 13-hydroxy-group [compounds (8) and (16)] or by the presence of a 19,2-lactone bridge [compounds (36) and (37)]. When both these features are present, as in compounds (35) and (38), the 17-hydrogens have the same chemical shift; a 13-acetoxy-group is equivalent to a 13-hydrogen [compounds (19) and (39)]. A possible exception to this generalisation was the report [21] that the 2-, 3-, and 17-proton signals overlap in the 60-MHz spectrum of the 3-acetate (37) in $CDCl_3$ solution. However when the spectra of the mono-acetate (37) [22] and the di-acetate (38) [22] were re-determined at 100 MHz (Table), they were found to conform to the generalisation.

EXPERIMENTAL

For general experimental details see ref. 8. Unless otherwise stated mass spectra were obtained by g.l.c.–mass spectrometry.

ent-1α-*Chloro*-10,13-*dihydroxy*-7-*methoxycarbonyl*-20-*nor-gibberella*-2,16-*dien*-19-*oic Acid* 19,10-*Lactone* (4).—Gibberellin A_3 (13) (290 mg) in methanol was treated with ethereal diazomethane. After evaporation of the excess of diazomethane and the solvents, the methyl ester (14) was dissolved in dry tetrahydrofuran (500 μl) and diethyl ether (5 ml) at 0 °C. Redistilled thionyl chloride (1 ml) was added and the solution was allowed to warm to room temperature. After 20 h sodium hydrogencarbonate (200 mg) was added and the solvents were evaporated under a stream of nitrogen. Water was then added and the pH was adjusted to 7.0. The gum (352 mg), recovered in ethyl acetate, was fractionated by p.l.c. using ethyl acetate–light petroleum (1 : 1).

Material, recovered from the band at R_F 0.3—0.45, was crystallised from ethyl acetate–light petroleum to give 1β-*chlorogibberellin* A_5 *methyl ester* (4) (230 mg), m.p. 112—114 °C (Found: C, 63.5; H, 6.4; Cl, 8.9. $C_{20}H_{23}ClO_5$ requires C, 63.5; H, 6.1; Cl, 9.2%); $\nu_{max.}$ (CH_2Cl_2) 3 591, 1 787, 1 736, 1 658, 923, 900, and 876 cm^{-1}; *m/e* (for TMSi ether) 452 (M^+ + 2, 20%), 450 (M^+, 56), 437 (4), 435 (9), 415 (11), 389 (12), 370 (65), 355 (21), 208 (16), 207 (42), 75 (16), and 73 (100).

Elution of the band at R_F 0.55—0.65 gave the ketone (33) as a gum (28 mg) (Found: M^+, 378.123. $C_{20}H_{23}ClO_5$ requires *M*, 378.123); $\nu_{max.}$ ($CHCl_3$) 1 788, 1 738 and 1 643 cm^{-1}; δ 1.07 (s, 17-Me), 1.33 (s, 18-Me), 2.67 (d, *J* 6 Hz, 6-H), 3.19 (d, *J* 6 Hz, 5-H), 3.80 (s, CO_2Me), 4.60 (d, *J* 2 Hz, 1-H), and 5.94 (m, 2- and 3-H); *m/e* 378 (M^+, < 1%), 347 (2), 299 (8), 239 (95), 238 (100), 211 (56), 197 (27), 195 (18), and 155 (33).

Elution of the band at R_F 0.15—0.25 gave gibberellin A_3 methyl ester (54 mg) identified by ^1H n.m.r. and by g.l.c.–mass spectrometry.

ent-3β-*Chloro*-10,13-*dihydroxy*-7-*methoxycarbonyl*-20-*nor-gibberella*-1,16-*dien*-19-*oic Acid* 19,10-*Lactone* (20) (*with M. H. Beale*).—A solution of gibberellin A_3 methyl ester (14) (300 mg) and toluene-*p*-sulphonyl chloride (750 mg) in pyridine (2 ml) was left at room temperature in the dark. After 2 days lithium chloride (240 mg) was added and the solution was stirred for a further 24 h. After the addition of water, the solution was adjusted to pH 3.0 and extracted with ethyl acetate. Recovery from the ethyl acetate gave the crude product which was purified by p.l.c. using ethyl acetate–light petroleum (1 : 1). Elution of the band at R_F 0.2—0.3 gave the pure 3α-*chloro-compound* (20) as a gum (207 mg) which was crystallised from acetone–light petroleum as needles, m.p. 165—167 °C (Found: C, 63.2; H, 6.1; Cl, 9.55%; M^+, 378.123. $C_{20}H_{23}ClO_5$ requires C, 63.5; H, 6.1; Cl, 9.4%; *M*, 378.123): $\nu_{max.}$ 3 329, 1 771, 1 738, and 899 cm^{-1}; *m/e* (TMSi ether) 452 (M^+ + 2, 33%), 450 (M^+, 78), 437 (5), 435 (12), 415 (100), 371 (45), 370 (89), 355 (32), 311 (22), 75 (15), and 73 (76).

Elution of the band at R_F 0.3—0.4 gave the 1β-chlorogibberellin A_5 methyl ester (4) (36 mg), identical to the main product from chlorination with thionyl chloride.

Elution of the band at R_F 0.4—0.6 gave the 3α-*chloro*-13-*toluene*-p-*sulphonate* (21) as a gum (29 mg) (Found: M^+, 532.133. $C_{27}H_{29}ClO_7S$ requires *M*, 532.132); $\nu_{max.}$ ($CHCl_3$) 1 783, 1 733, 1 601, 1 170, 909, and 869 cm^{-1}; δ 1.33 (s, 18-Me), 2.49 (s, Ar-*Me*), 2.79 (d, *J* 11 Hz, 6-H), 3.06 (d, *J* 11 Hz, 5-H), 3.80 (s, CO_2Me), 4.68 (dd, *J* 1.5 and 2.5 Hz, 3-H), 5.17 and 5.41 (each br s, 17-H_2), 5.98 (dd, *J* 2.5 and 9.0 Hz, 2-H), 6.31 (dd, *J* 1.5 and 9.0 Hz, 1-H), 7.44 and 7.88 (each 2H doublets, *J* 8 Hz, 4 × Ar-*H*); *m/e* (probe) 534 (M^+ + 2, 1%), 532 (M^+, 2), 360 (32), and 91 (100).

Allylic Bromination of Gibberellin A_3 *Methyl Ester*.—Gibberellin A_3 methyl ester (14) (180 mg) and toluene-*p*-sulphonyl chloride (190 mg, 2 equiv.) were dissolved in pyridine (0.63 ml). After 25 h, water and concentrated hydrochloric acid were added to pH 3 and the products were extracted into ethyl acetate. The organic solvent was evaporated *in vacuo* to yield a 1 : 1 mixture (by n.m.r.) of the 3α-chloro-compound (20) and the 3β-toluene-*p*-sulphonate (23). Recrystallisation from dichloromethane–light petroleum (4 ×) yielded the pure 3β-toluene-*p*-sulphonate (23).[23]

(*a*) The 3β-toluene-*p*-sulphonate (23) (70 mg) and dry sodium bromide (60 mg) were dissolved in dry hexamethylphosphoramide (1 ml). After 5 h, water and concentrated hydrochloric acid were added to reach pH 3 and the products were extracted into ethyl acetate. After evaporation, the products were purified by p.l.c. using ethyl acetate–light petroleum (1 : 1). Elution of the band at R_F 0.35—0.45 yielded 1β-*bromogibberellin* A_5 *methyl ester* (6) as a gum (33 mg) (Found: M^+, 422.074. $C_{20}H_{23}{}^{79}BrO_5$ requires *M*, 422.074); $\nu_{max.}$ ($CHCl_3$) 3 585, 1 780, 1 731, 1 661, and 900 cm^{-1}; *m/e* (TMSi ether) 496 (M^+ + 2, 21%), 494 (M^+, 20), 481 (3), 479 (4), 437 (5), 435 (5), 415 (23), 370 (54), 355 (23), 311 (15), 221 (17), 207 (18), 75 (22), and 73 (100).

Elution of the band at R_F 0.25—0.35 yielded the suspected 3α-*bromo-compound* (24) as a gum (16 mg) (Found: M^+, 422.074. $C_{20}H_{23}{}^{79}BrO_5$ gives *M*, 422.074); $\nu_{max.}$ ($CHCl_3$) 3 595, 1 771, 1 723, and 900 cm^{-1}; *m/e* (TMSi ether) 496 (M^+ + 2, 14%), 494 (M^+, 13), 415 (49), 370 (62), 355 (23), 311 (15), 221 (14), 207 (17), 82 (12), 80 (13), 75 (25), and 73 (100).

(*b*) The 3β-toluene-*p*-sulphonate (23) (160 mg) and dry lithium bromide (150 mg) were dissolved in pyridine (1 ml). After 25 h, water and concentrated hydrochloric acid were added to pH 3 and the products extracted into ethyl acetate. Evaporation of the solvent followed by p.l.c. as in (*a*) above yielded 1β-bromogibberellin A_5 methyl ester (6) (75 mg) and the 3α-bromo-compound (24) (24 mg) (by n.m.r. and mass spectrometry).

ent-1α-*Chloro*-10,13-*dihydroxy*-20-*norgibberella*-2,16-*diene*-7,19-*dioic Acid* 19,10-*Lactone* (9).—(*a*) A solution of gibberellin A_3 (13) (500 mg) and triphenylphosphine (3 g) in carbon tetrachloride (3 ml), tetrahydrofuran (20 ml), and pyridine (0.5 ml) was stirred for 4 days at room temperature in the dark. The solution was evaporated, water was added, and the mixture was adjusted to pH 3.0. Extraction with ethyl acetate gave a gum which was fractionated by p.l.c. with ethyl acetate–light petroleum–acetic acid (80 : 20 : 1). Elution of the band at R_F 0.65—0.75 gave 1β-*chlorogibberellin* A_5 (9) (78 mg), m.p. 182—185 °C (from chloroform–light petroleum) (Found: M^+, 364.105. $C_{19}H_{21}O_5Cl$ requires *M*, 364.108); $\nu_{max.}$ ($CHCl_3$) 3 595, 3 200—2 400, 1 784, 1 722, 1 660, 889, and 862 cm^{-1}; *m/e* (probe) 366 (M^+ + 2, 17%), 364 (M^+, 56), 348 (20), 346 (63), 329 (13), 319 (25), 285 (47), 284 (81), 239 (100), 135 (67), and 84 (68).

The white precipitate, obtained from the reaction mixture, had δ 6.25 (d, *J* 6 Hz, $\overset{+}{P}$–CH_2–) and 7.25—8.15 (m, 15 × Ar-H).

(*b*) The above reaction was repeated with gibberellin A_3 (13) (200 mg), triphenylphosphine (600 mg), carbon tetrachloride (1 ml), tetrahydrofuran (5 ml), and pyridine (250

μl). After 4 days, the reaction mixture was divided into two portions. One half was worked up by evaporation then partitioning the product between an aqueous phase at pH 9.0 and ethyl acetate. The aqueous phase was adjusted to pH 3.0 and re-extracted with ethyl acetate which, on evaporation, yielded only gibberellin A_3 by n.m.r. The other half of the reaction mixture showed the presence of 1β-chlorogibberellin A_5 (9) by n.m.r. P.l.c. of the crude product, obtained by evaporation of the solvent, with ethyl acetate–light petroleum–acetic acid (80 : 20 : 1) and elution of the band at R_F 0.6—0.8 with ethyl acetate gave a mixture (29 mg, 1 : 1), shown by ^1H n.m.r. to contain 1β-chlorogibberellin A_5 (9) and its ethyl ester (11). This mixture was partitioned between an aqueous phase at pH 9.0 and ethyl acetate. Evaporation of the ethyl acetate gave 1β-*chlorogibberellin* A_5 *ethyl ester* (11) (14 mg) (Found: M^+, 392.140. $C_{21}H_{25}ClO_5$ requires M, 392.139); $\nu_{max.}$ ($CHCl_3$) 3 599, 1 788, 1 732, 1 664, 890, and 866 cm^{-1}; δ 1.30 (t, J 7 Hz, CO_2CH_2-*Me*) and 4.26 (q, J 7 Hz, CO_2CH_2Me) in addition to the signals in the Table; *m/e* (probe) 394 (M^+ + 2, 12%), 392 (M^+, 51), 319 (79), 310 (65), 239 (100), 238 (71), and 221 (41).

The aqueous fraction from the 1 : 1 mixture was adjusted to pH 3.0 and extracted with ethyl acetate to give 1β-chlorogibberellin A_5 (9) (15 mg).

Attempts to isolate the acid chloride of 1β-chlorogibberellin A_5 by p.l.c. of the reaction product in dichloromethane–acetic acid, followed by elution with dichloromethane and diethyl ether, gave only 1β-chlorogibberellin A_5.

ent-3β-*Chloro*-10,13-*dihydroxy*-20-*norgibberella*-1,16-*diene*-7,19-*dioic Acid* 19,10-*Lactone* (26).—Gibberellin A_3 (13) (200 mg) and toluene-*p*-sulphonyl chloride (250 mg) in pyridine (2 ml) were left for 2 days at room temperature. Anhydrous lithium chloride (200 mg) was added and the solution was stirred for 24 h. Extraction of the reaction mixture, adjusted to pH 3.0 by 2M-hydrochloric acid, with ethyl acetate gave 1β-chlorogibberellin A_5 (9) and the 3α-chloro-compound (26) as a mixture (210 mg, 1 : 1.8 by ^1H n.m.r.). P.l.c. of the mixture with ethyl acetate–light petroleum–acetic acid (80 : 20 : 1) gave, at R_F 0.75—0.95, a mixture (38 mg, 4 : 1 by ^1H n.m.r.) and, at R_F 0.55—0.75, a mixture (78 mg, 1 : 4) of 1β-chlorogibberellin A_5 (9) and the 3α-chloro-compound (26). Elution of the band at R_F 0.35—0.55 gave a mixture (20 mg, 3 : 7) of the 3α-chloro-compound and gibberellin A_3. Re-p.l.c. gave pure 3α-*chloro-compound* (26) as a gum (Found: M^+, 364.105. $C_{19}H_{21}ClO_5$ requires M, 364.108); $\nu_{max.}$ 3 599, 3 200—2 400, 1 782, 1 718, 1 663, 888, and 860 cm^{-1}; *m/e* (probe) 366 (M^+ + 2, 6%), 364 (M^+, 18), 329 (60), 284 (79), 283 (64), 239 (76), 136 (53), 135 (58), and 44 (100).

When the reaction was repeated and worked up by partitioning the product between aqueous buffer at pH 9.0 and ethyl acetate, the aqueous phase, after acidification and extraction with ethyl acetate, yielded the 3α-chloro-compound (26) only.

Tri-n-butylstannane Reductions.—(a) 1β-*Chlorogibberellin* A_5 *methyl ester* (4). To the chloro-compound (4) (204 mg) in benzene (4 ml) was added tri-n-butylstannane (280 μl) and 2,2′-azobis-(2-methylpropiononitrile) (*ca.* 3 mg) and the solution was refluxed for 1 h in a stream of nitrogen. Evaporation of the solvent and purification of the product by p.l.c. with acetone–light petroleum (3 : 7) gave, from R_F 0.2—0.3, a mixture (120 mg) containing (by ^1H n.m.r.) 70% of gibberellin A_5 methyl ester (3) and 30% of the Δ-1-*isomer* (25); *m/e* (for Δ-1-isomer TMSi-ether) 416 (M^+, 83%), 401 (9), 387 (12), 370 (31), 239 (18), 238 (69), 75 (13), and 73 (100); *m/e* [g.l.c.–mass spectrometry of the TMSi-ether of the 19,2-lactone (40)] 416 (M^+, 71%), 401 (9), 387 (23), 357 (31), 239 (30), 75 (15), and 73 (100).

Repeated recrystallisation of the 7 : 3 mixture from acetone–light petroleum gave gibberellin A_5 methyl ester (3), m.p. 187—189 °C (lit.,[2] 190—191 °C) of 95% purity (n.m.r.), identified by i.r., ^1H n.m.r., and mass spectometry.

(b) ent-3β-*Chloro*-10,13-*dihydroxy*-7-*methoxycarbonyl*-20-*norgibberella*-1,16-*dien*-19-*oic acid* 19,10-*lactone* (20). The 3-chloro-compound (20) (40 mg) in benzene (2 ml) was reduced as in (a) with tri-n-butylstannane (50 μl) and 2,2′-azobis-(2-methylpropiononitrile) to give, after p.l.c., a mixture (32 mg) of 70% gibberellin A_5 methyl ester (3) and 30% of the Δ-1-isomer (25).

(c) *The* 1β-*chloro-ketone* (33). The ketone (70 mg) in benzene (3 ml) was reduced as in (a) with tri-n-butylstannane (90 μl) and 2,2′-azobis-(2-methylpropiononitrile) (*ca.* 3 mg) to give, after p.l.c., a mixture (44 mg) of 70% ring-c/D rearranged gibberellin A_5 methyl ester (34) and 30% of its Δ-1-isomer; δ 1.31 (s, 18-Me) and 5.75 (m, 2- and 3-H) [assigned to the Δ-2-isomer (34)]; δ 1.28 (s, 18-Me), *ca.* 5.87 (m, 2-H), and 6.24 (m, 1-H) (assigned to the Δ-1 isomer); and δ 1.06 (s, 17-Me) and 3.74 (s, CO_2Me) (assigned to both isomers); *m/e* (for the Δ-2 isomer) 344 (M^+, < 1%), 313 (5), 300 (44), 241 (48), 240 (100), 197 (51), 167 (56), 105 (46), and 93 (45); *m/e* (g.l.c.–mass spectrometry, Δ-1 isomer) 344 (M^+, 18%), 312 (18), 300 (36), 241 (80), 240 (93), 211 (56), 197 (33), 155 (59), and 44 (100).

Recrystallisation of the mixture from acetone–light petroleum gave ring-c/D rearranged gibberellin A_5 methyl ester (34), m.p. 165—167 °C (lit.,[2] 160—164 °C).

(d) 1β-*Chlorogibberellin* A_5 (9). The chloro-acid (12 mg), in tetrahydrofuran (200 μl) and benzene (1.0 ml), was reduced as in (a) with tri-n-butylstannane (20 μl) and 2,2′-azobis-(2-methylpropiononitrile) (*ca.* 1 mg). Removal of the solvent and partitioning of the product between ethyl acetate and water at pH 9.0, then at pH 3.0, gave, from the ethyl acetate extract at pH 3.0, a mixture (10 mg) containing 70% gibberellin A_5 (1) and 30% of the Δ-1 isomer; δ ([$^2H_6$]acetone) 1.22 (s, 18-Me) and 5.83 (m, 2- and 3-H), assigned to gibberellin A_5 (1); δ 1.18 (s, 18-Me), 5.94 (dd, J 3 and 9 Hz, 2-H), and 6.32 (br, d, J 10 Hz, 1-H), assigned to the Δ-1-isomer; and δ 4.92 and 5.25 (each br s, 17-H_2), assigned to both isomers.

(e) 3α-*Chlorogibberellin* A_5 (26). The 3α-chloro-acid (17 mg), reduced as in (d), gave the same mixture (13 mg, 7 : 3) of gibberellin A_5 and its Δ-1-isomer.

(f) 3α-*Chlorogibberellin* A_5 *methyl ester with tri-n-butyl-*[^2H]*stannane*. The chloro-compound (20) (120 mg) in benzene was reduced with tri-n-butyl[^2H]stannane (180 μl) and 2,2′-azobis-(2-methylpropiononitrile) (4 mg) as in (b) to give a 7 : 3 mixture of [1ξ-$^2H_1$]*gibberellin* A_5 *methyl ester* (84 mg) and the [3ξ-$^2H_1$]-1-ene, each containing 96 atoms deuterium % by mass spectrometry; *m/e* (for [1ξ-$^2H_1$]-gibberellin A_5 methyl ester TMSi-ether) 417 (M^+, 100%), 402 (13), 358 (11), 351.152 ($C_{23}H_{30}O_5Si$ requires 321.152, 5%), 344 (7), 321 (5), 300 (17), 276 (5), 208 (28), 193 (15), 167 (11), 96 (6), and 73 (62).

ent-13-*Acetoxy*-10-*hydroxy*-7-*methoxycarbonyl*-20-*norgibberella*-2,16-*dien*-19-*oic Acid* 19,10-*Lactone* (8). A mixture (33 mg, 7 : 3) of gibberellin A_5 methyl ester (3) and its Δ-1-isomer (25) was dissolved in acetic anhydride (0.5 ml) and toluene-*p*-sulphonic acid (2 mg) was added. After 18 h at

room temperature, water was added and the usual work-up gave a mixture (36 mg) of acetates which were separated by p.l.c. using ethyl acetate–light petroleum (1 : 1). Elution of the band at R_F 0.55—0.65 gave methyl gibberellin A_5 13-acetate (8) (22 mg), m.p. 129—131 °C (from ethyl acetate–light petroleum) (lit.,[21] 125—127 °C) (Found: C, 68.7; H, 7.1. Calc. for $C_{22}H_{26}O_6$: C, 68.4; H, 6.7%), identical $\nu_{max.}$, δ, and *m/e* to the recorded [24] values.

Elution of the band at R_F 0.4—0.5 gave the rearranged *acetate* (35) (11 mg) as a gum (Found: M^+, 386.175. $C_{22}H_{26}O_6$ requires *M*, 386.173); $\nu_{max.}$ 1 771, 1 730, 1 671, 916, and 879 cm^{-1}; *m/e* 386 (M^+, 4%), 327 (34), 326 (100), 294 (41), 281 (38), 221 (79), and 43 (91); δ (see Table); from double irradiations at δ 5.96, 4.90, and 3.20, the following coupling constants were measured: $J_{1,2}$ 4, $J_{1.5}$ 2, and $J_{1,9}$ 2 Hz [*cf.* gibberellin A_3 methyl ester 19,2-lactone (36) with $J_{1.2}$ 5, $J_{1.5}$ *ca.* 2, and $J_{1.9}$ *ca.* 2 Hz].

Alkaline hydrolysis of gibberellin A_5 methyl ester 13-acetate (8), as previously described,[7] gave gibberellin A_5 in 70% yield (*ca.* 20% overall yield from gibberellin A_3).

Chlorination of ent-3α,10-*Dihydroxy*-7-*methoxcarbonyl*-20-*norgibberella*-1,16-*dien*-19-*oic Acid* 19,10-*Lactone* (19).—(a) *With toluene*-p-*sulphonyl chloride and lithium chloride.* The methyl ester (19) (120 mg) in pyridine (2.5 ml) was treated with toluene-*p*-sulphonyl chloride (680 mg). After stirring for 2 days, lithium chloride (370 mg) was added. After a further 2 days, the mixture was added to water, neutralised with 2M-hydrochloric acid, and extracted with ethyl acetate. The gum (113 mg), recovered from the ethyl acetate, was fractionated by p.l.c. with acetone–light petroleum (3 : 7). The band at R_F 0.5 gave 3α-*chloro*-1,2-*didehydrogibberellin* A_9 *methyl ester* (22) (73 mg), which crystallised from ethyl acetate with m.p. 134—143 °C (Found: C, 66.3; H, 6.3; Cl, 9.9. $C_{20}H_{23}ClO_4$ requires C, 66.2; H, 6.4; Cl, 9.8%); $\nu_{max.}$ 1 773, 1 733, and 660 cm^{-1}; *m/e* (probe) 364 ($M^+ + 2$ 0.5%), 362 (M^+ 0.7), 332 (6), 330 (10), 282 (14), 223 (100), 222 (87), and 155 (43).

Recovery from the band at R_F 0.55 gave 1β-*chloro*-2,3-*didehydrogibberellin* A_9 *methyl ester* (5) (38 mg) which crystallised from ethyl acetate–light petroleum, m.p. 92—93 °C (Found: C, 66.2; H, 6.4%; M^+, 362.128. $C_{20}H_{23}ClO_4$ requires C, 66.2; H, 6.4%; *M*, 362.128); $\nu_{max.}$ 1 785, 1 738, and 1 660 cm^{-1}; *m/e* (probe) 362 (M^+, 0.1%), 331 (2), 282 (8), 223 (100), 222 (79), and 155 (25).

(b) *With thionyl chloride.* The methyl ester (19) (70 mg) in dry ether (20 ml) was treated with thionyl chloride (1 ml). After standing at room temperature for 2 days, calcium carbonate (250 mg) was added and the solvent was evaporated. Water (30 ml) was added and the mixture was extracted with ethyl acetate. After filtration the ethyl acetate was evaporated to give a yellow oil (93 mg), which was purified by p.l.c. as in (a) to give 1β-chloro-2,3-didehydrogibberellin A_9 methyl ester (5) (62 mg) identified from its ^1H n.m.r. spectrum. Analytical t.l.c. (same solvent system) showed the absence of the 3α-chloro-isomer (22).

(c) *With triphenylphosphine–carbon tetrachloride.* The methyl ester (19) (37 mg) was dissolved in a mixture of dichloromethane (3 ml) and carbon tetrachloride (0.5 ml). A solution of triphenylphosphine in dichloromethane (0.5 ml) was added and the solution was stirred at room temperature for 16 h. The reaction mixture was then evaporated and the residue was purified by p.l.c. as in (a) giving 1β-chloro-2,3-didehydrogibberellin A_9 methyl ester (5) (21 mg) and 3α-chloro-1,2-didehydrogibberellin A_9 methyl ester (22) (11 mg), identified by their ^1H n.m.r. spectra.

In another experiment under the same conditions the two products were formed in 1 : 1 ratio (by n.m.r.).

We thank the S.R.C. for a Research Studentship (to P. S. K.), the A.R.C. for financial support, Dr. J. R. Hanson for the exchange of information and helpful discussions, and Miss K. Staples for technical assistance.

[0/712 *Received*, 13*th May*, 1980]

REFERENCES

[1] D. F. Jones and P. McCloskey, *J. Appl. Chem.*, 1963, 324.
[2] J. MacMillan, J. C. Seaton, and P. J. Suter, *Tetrahedron*, 1960, **11**, 60; B. E. Cross, J. R. Hanson, and R. S. Speake, *J. Chem. Soc.* (*C*), 1965, 3555.
[3] J. MacMillan and R. J. Pryce, *J. Chem. Soc.* (*C*), 1967, 550.
[4] A. Musgrave and H. Kende, *Plant Physiology*, 1970, **45**, 56.
[5] R. C. Durley, I. D. Railton, and R. P. Pharis, *Phytochemistry*, 1973, **12**, 1609.
[6] N. Murofushi, R. C. Durley, and R. P. Pharis, *Agric. Biol. Chem.*, 1974, **38**, 475; 1977, **41**, 1075.
[7] M. H. Beale, P. Gaskin, P. S. Kirkwood, and J. MacMillan, *J.C.S. Perkin I*, 1980, 885.
[8] M. H. Beale and J. MacMillan, *J.C.S. Perkin I*, 1980, 877.
[9] T. G. Squires, W. W. Schmidt, and C. S. McCandlish, *J. Org. Chem.*, 1975, **40**, 134.
[10] C. C. Lee, J. W. Clayton, D. G. Lee, and A. J. Finlayson, *Tetrahedron*, 1962, **18**, 1395, and refs. cited therein.
[11] J. H. Bateson and B. E. Cross, *J.C.S. Perkin I*, 1974, 2409.
[12] E. J. Corey, T. M. Brennan, and R. J. Carney, *J. Amer. Chem. Soc.*, 1971, **93**, 7316.
[13] P. S. Kirkwood, J. MacMillan, and M. L. Sinnott, *J.C.S. Perkin I*, 1980, 2117.
[14] R. Binks, J. MacMillan, and R. J. Pryce, *Phytochemistry*, 1969, **8**, 271; P. Gaskin, unpublished results.
[15] B. Castro and C. Selve, *Bull. Soc. chim. France*, 1971, 2296.
[16] J. I. G. Cadogan and R. K. Mackie, *Chem. Soc. Rev.*, 1974, **3**, 87; R. Aneja, A. P. Davies, and J. A. Knaggs, *Tetrahedron Letters*, 1974, 67.
[17] I. Tömösközi, L. Gruber, and L. Radics, *Tetrahedron Letters*, 1975, 2473.
[18] J. B. Lee and T. J. Nolan, *Tetrahedron*, 1967, **23**, 2789; N. S. Isaacs and D. Kirkpatrick, *J.C.S. Chem. Comm.*, 1972, 443; E. Yamato and S. Sugasawa, *Tetrahedron Letters*, 1970, 4383.
[19] E. I. Snyder, *J. Org. Chem.*, 1972, **37**, 1466.
[20] G. Adam and T. Van Sung, East Ger. P 134,643/1979 (*Chem. Abs.*, 1979, **91**, 141048n).
[21] J. R. Hanson, *J. Chem. Soc.*, 1965, 5036.
[22] B. E. Cross, J. F. Grove, and A. Morrison, *J. Chem. Soc.*, 1961, 2498.
[23] P. S. Kirkwood and J. MacMillan, in preparation.
[24] L. J. Beeley, Ph.D. Thesis, University of Bristol, 1975.