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PHOTOSENSITIVE PROTECTION OF CARBOXYL GROUP AND THE SYNTHESIS OF THREE O-METHYL DERIVATIVES OF GIBBERELLIN A_3

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Abstract—The methylation of *p*-methoxyphenacyl ester of gibberellin A_3 (**5**) and its isomeric monoacetates (**6**, **7**) followed by the removal of *p*-methoxyphenacyl group gives rise to 3,13-O-dimethylgibberellin A_3 (**14**) and to the isomeric O-acetyl-O-methyl-derivatives (**15** and **16**); the latter afford 3-O-methylgibberellin A_3(**17**) and 13-O-methylgibberellin A_3 (**18**) upon Zemplén deacetylation. The removal of *p*-methoxyphenacyl group can be achieved either upon photolysis in abs ethanol or with zinc-acetic acid. This protective group survives the conditions of Koenigs–Knorr synthesis as well as oxidation with manganese dioxide. The limitations of this way of protecting the carboxyl group can be seen on the example of the enone ester **20**.

The protection of carboxyl group is of special interest for the preparation of physiologically active gibberellin analogs. The sensitivity of gibberellins of types A_3–A_7 and A_1–A_7 both to acid-catalysed and base-catalysed hydrolysis was till recently an obstacle to their recovery from the much less active alkyl esters.[1] Two procedures for a clean regeneration of gibberellins from their esters are now known: the cleavage of alkyl esters with lithium mercaptides[2] and the reduction of phenacyl esters with zinc in acetic acid.[3] The present communication describes yet another way of protecting the carboxyl group of gibberellins. It consists in their transformation in *p*-methoxyphenacyl esters from which the modified free acids can be recovered either upon photolysis in abs ethanol according to Sheehan and Umezawa[4] or reductively according to reported data.[3] This protection was applied by us to the synthesis of three O-methyl ethers of gibberellin A_3 (see[5,6] for preliminary communications).

Starting from gibberellin A_3 (**1**), its 3-monoacetate (**2**) and 13-monoacetate (**3**) were obtained (the latter via the diacetate **4**) as described earlier.[7,8] The reaction of **1**, **2** and **3** with equimolar amounts of triethylamine and *p*-methoxyphenacyl bromide in abs DMF at 0–5° afforded the corresponding *p*-methoxyphenacyl esters **5**, **6** and **7** in 46–83% yields; this procedure[4] gave better results than the phenacylation in ethanol.[3] Acetylation of *p*-methoxyphenacyl ester of gibberellin A_3 (**5**) according to data[7] gives the 3-monoacetate (**6**) in equally good yield together with small amount of the diacetyl derivative (**8**).

p-Methoxyphenacyl esters **5**, **6** and **7** were treated with excess of methyl iodide and dry silver oxide in polar solvents to give the methyl ethers **9**, **12** and **13**; among solvents tried (acetone, DMF, THF) the most convenient was abs THF where the methylation proceeded in 48–79% yields. Upon methylation of the dihydroxy ester **5** in addition to the main product **9** a mixture of monomethyl ethers **10** and **11** was also obtained; the 13-O-methyl isomer **11**, which slightly predominates in this mixture, could be isolated by fractional crystallization.

The photolysis of *p*-methoxyphenacyl esters **9**, **12** and **13** was carried out in abs ethanol (1% solutions) with $\lambda \geqslant 300$ nm to afford 3,13-O-dimethylgibberellin A_3 (**14**), 3-O-acetyl-13-O-methyl- (**15**) and 3-O-methyl-13-O-acetylgibberellin A_3 (**16**) respectively, in 36–62% yields. Besides these acids and the starting esters (recovery from 60 to 30%) the photolysates contained only small amounts of more polar products whose structure was not investigated. Although a free-radical mechanism had been postulated for the photolysis of *p*-methoxyphenacyl esters in ethanol,[4] no decarboxylation products derived from the fragmentation of radical **A** could be detected in any of photolysis studied. On the other hand, the yield of acids **14**, **15** and **16** decreases sharply if the solvent contains the traces of moisture. Alternatively, these acids were obtained in 50–70% yields when the esters **9**, **12** and **13** were reduced with zinc powder in glacial acetic acid.

The isomeric acids **15** and **16** in analogy to data[2,8] were deacetylated with NaOMe in abs methanol and thus gave 3-O-methylgibberellin A_3 (**17**) and 13-O-methylgibberellin A_3 (**18**) in good yields. The latter was also obtained photolytically from the ester **11**. All three O-methylated analogs of gibberellin A_3 were additionally characterised by their methyl esters, **14a**, **17a** and **18a**. The mass spectra of **17** and **17a**, in analogy to those of **1** and its methyl ester (**1a**) display very intense peaks at *m/e* 136 (ion **B**) while in the mass spectra of **14**, **14a**, **18** and **18a** the analogous peaks (ion **C**) are shifted to *m/e* 150; this corroborates the origin of ion **B** as postulated earlier.[9] The methylation of OH groups at C-3 and C-13 is accompanied by positive shifts in the molecular rotation (about 140° for 3-OH and 60° for 13-OH), the additivity of which can be seen from the following values of $[M]_D$:

$$\begin{array}{ccc} \mathbf{1}\,(+292°) & \longrightarrow & \mathbf{17}\,(+435°) \\ \downarrow & & \downarrow \\ \mathbf{18}\,(+354°) & \longrightarrow & \mathbf{14}\,(+494°) \end{array}.$$

The advantage of *p*-methoxyphenacyl protective group is connected with the very mild conditions of its photolytical removal. However, two points should be noted: (1) Non-aqueous conditions are required for the photolysis to give satisfactory yields; (2) *p*-Methoxyphenacyl esters are sensitive to bases. Thus, when dihydroxy ester **5** was methylated in DMF containing traces of dimethylamine or when silver oxide was not sufficiently dry the alkaline splitting of the phenacyl

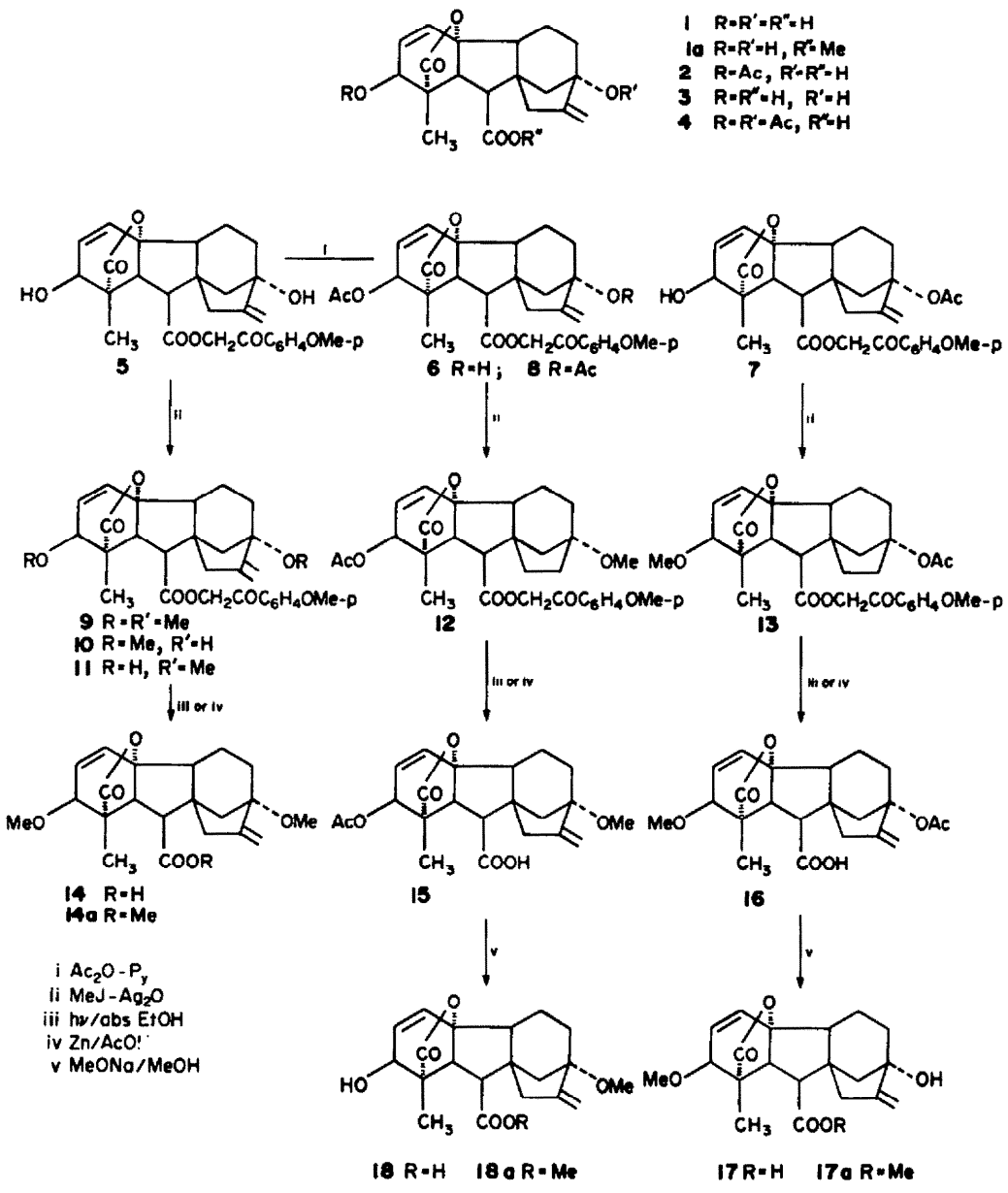

Fig. 1.

group took place and the methylation product (**9**) was contaminated by the methyl ester **14a**; besides, small amounts of yellow tars were also formed.

Dihydroxy ester **5** reacts with α-acetobromoglucose and silver oxide in abs DMF to give a mixture of 3-O- and 13-O-tetraacetyl glucosides (**19a** and **19b**, respectively, the glycoside linkage is assumed to be β) in about 9% yield, i.e. the Koenigs–Knorr synthesis proceeds analogously with the previously described[2] glycosylation of gibberellin A_3 methyl ester **1a**. The protective group proved to be stable upon the oxidation of the ester **5** with neutral manganes dioxide in dry acetone; the yield of 3-dehydrogibberellin A_3 *p*-methoxyphenacyl ester **20** amounted to 40% and the recovery of the starting ester **5** was 55%. The same ester **20** was obtained in 30% yield when 3-dehydrogibberellin A_3 (**21**) was treated with *p*-methoxyphenacyl bromide and triethylamine in abs DMF. When the enone ester **20** is photolysed in abs ethanol the removal of the protective group is accompanied by the previously observed delactonization-aromatization;[10] a mixture of two phenolic acids is formed, **22** and **23**, in which the tetracyclic compound predominates. The reductive cleavage of **20** with zinc dust in acetic acid is again accompanied by reductive delactonization which now gives the acid **24**. The structures of acids **22**, **23** and **24** were proved by their transformation in the corresponding methyl esters which had been described earlier;[10,11] moreover, the acid **22** was directly identified with the previously obtained specimen.[12] Thus, the clean removal of the *p*-methoxyphenacyl group is not possible when a system similar to that of 3-dehydrogibberellin A_3 is present in the molecule.

The spectral data of serial compounds obtained in this

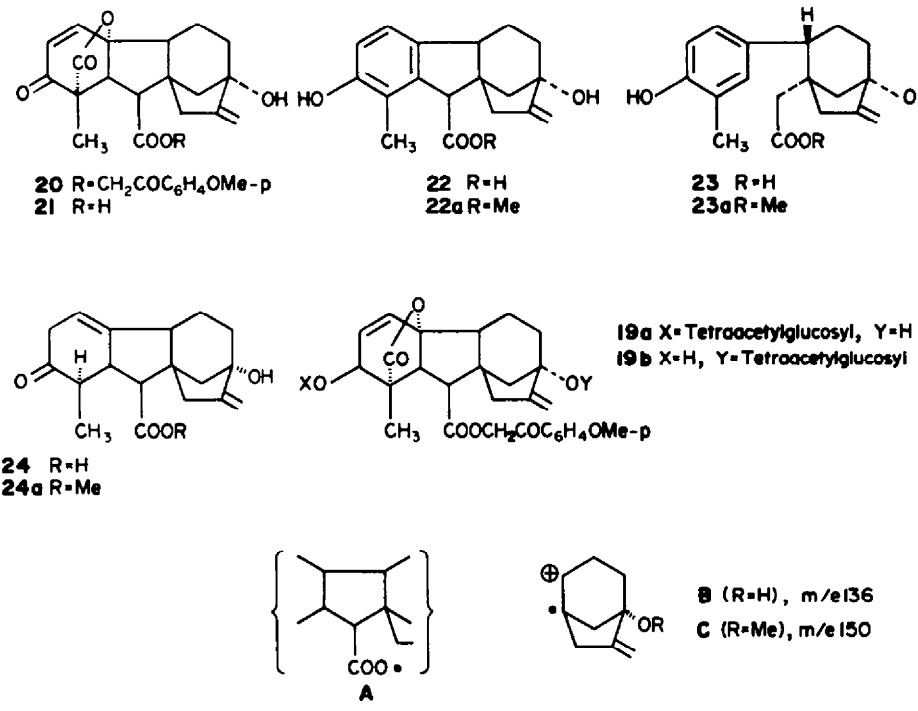

Fig. 2.

work are presented in Tables 1–3. The data concerning the physiological activity of acids 14, 17 and 18 will be published elsewhere (see[6] for preliminary).

EXPERIMENTAL

The starting acids 1, 2, 3 and 21 were obtained according to the known procedures[7,8,13] and their constants coincided with those given in the literature, although 13-monoacetate 3 was obtained in two crystalline modifications: m.p. 140–142° (from MeOH aq) and m.p. 216–218° (from AcOEt–hexane). All m.p. are corrected. All specific rotations—in abs EtOH at $c = 0.1$ M. IR spectra: in KBr-pellets, with Karl Zeiss UR-10 instrument. NMR spectra: Varian DA-60-IL instrument. Mass spectra (70 eV): Varian MAT CH-6 instrument with all-glass inlet system. Silica-gel L (Chemapol) was used for both column and TLC chromatography.

p-Methoxyphenacyl esters (general procedure). To a 10% soln of 1 or its derivatives 2, 3 and 21 in abs DMF a precisely equimolar amount of abs triethylamine was added followed by equimolar amount of *p*-methoxyphenacylbromide (prepared

Table 1(a). PMR-data (δ in ppm) for O-methyl analogs of gibberellin A_3. solvent—$CDCl_3$

Protons	Signal patterns and J	3,13-O-Dimethyl-		3-O-Monomethyl-			13-O-Monomethyl-		
		14	14a	16	17*	17a	15	18	18a
$C_{(4)}$-CH_3	s, 3H	1.26	1.20	1.26	1.20	1.21	1.20	1.19	1.19
$C_{(5)}$-H	d, J_{AB}=10–11 c/s	2.77	2.69	2.75	2.65	2.70	2.80	2.83	2.79
$C_{(6)}$-H	d, J_{AB} =10–11 C/s	(a)	(a)	3.18	3.14	3.12	(a)	(a)	(a)
$C_{(17)}$-OCH_3	s, 3H	3.17	3.13	-	-	-	3.17	3.18	3.16
$C_{(7)}$-COOCH_3	s, 3H	-	3.67	-	-	3.68	-	-	3.66
$C_{(3)}$-H	d, J = 3.5–4 c/s	3.61	3.61	3.62	3.62	3.61	5.31	4.30	4.21
$C_{(17)}$-H	broad s, 1H	5.03	5.03	4.96	4.94	4.97	5.02	5.06	5.00
$C_{(17)}$-H	broad s, 1H	5.11	5.12	5.11	5.16	5.12	5.12	5.15	5.10
$C_{(1)}$-H	d, J_{AB} = 9 c/s	6.24	6.20	6.20	6.32	6.26	6.30	6.23	6.21
$C_{(2)}$-H	dd, J_{AB}= 9, J 4c/s	6.00	5.86	5.95	6.05	6.00	5.85	5.86	5.90
$C_{(13)}$-COOCH_3	s, 3H	-	-	1.98	-	-	-	-	-
$C_{(3)}$-COOCH_3	s, 3H	-	-	-	-	-	2.07	-	-

* in CD_3OD ; (a) The signal is partially masked by the signal of the $C_{(13)}$ - OCH_3 group.

Table 1(b). PMR-data for *p*-methoxyphenacyl esters

Protons	Signal patterns and J	δ, ppm (in d_6 – acetone, if not stated otherwise)								
		5[a]	6	7[b]	8[c]	9[c]	11[c]	12	13	20[c]
$C_{(4)}-CH_3$	s, 3H	1.54	1.19	1.22	1.30	1.35	1.33	1.18	1.27	1.25
$C_{(5)}-H$	d, J_{AB} =10–11 c/s	3.10	2.90	2.87	2.98	2.94	2.96	2.89	2.83	2.97
$C_{(6)}-H$	d, J_{AB}=10–11 c/s	3.50(m)	3.24	3.17	3.34	3.23(m)	3.26	3.19	3.18	3.38
$C_{(13)}-OCH_3$	s, 3H	–	–	–	–	3.20(m)	3.20	3.13	–	–
$C_{(3)}-OCH_3$	s, 3H	–	–	–	–	3.48	–	–	3.42	–
$C_{(3)}-H$	d, J = 4 c/s	4.25	5.20	3.94	5.29	3.65	4.13	5.30	3.58	–
$C_{(12)}$ H	broad s, 1H	4.86	4.92	4.89	4.97	5.08(m)	5.07(m)	5.02(m)	4.93	4.86
$C_{(12)}$ H	broad s, 1H	5.35(m)	5.20(m)	5.03	5.16	5.13(m)	5.12(m)	5.07(m)	5.02	5.17(m)
$COOCH_2COAr$	s, 2H	5.35(m)	5.20(m)	5.32	5.34	5.35	5.33	5.50	5.43	5.17(m)
$C_{(1)}-H$	d, J_{AB}= 9 c/s	6.20	6.30	6.20	6.36	6.34	6.27	6.39	6.37	7.06
$C_{(2)}-H$	dd, J_{AB}=9, J=4 c/s	6.00	5.80	5.78	5.87	6.03	5.97	6.01	6.11	5.90(t)
$C_{(13)}-OCOCH_3$	s, 3H	–	–	1.94	1.94	–	–	–	1.95	–
$C_{(3)}-OCOCH_3$	s, 3H	–	2.02	–	2.02	–	–	2.02	–	–
$Ar-OCH_3$	s, 3H	3.55(m)	3.80	3.78	3.83	3.87	3.85	3.87	3.85	3.72
Aromatic	A_2B_2(2H+2H)	6.85	6.94	7.10	6.93	6.98	6.98	6.92	6.90	6.76
	J_{ortho} 9 c/s	7.81	7.78	7.95	7.81	7.82	7.85	7.79	7.82	7.67

(m) Partial or total overlap with adjacent signals; (t) AB-doublet.
(a) In d_5 -pyridine; (b) in CD_4OD; (c) in $CDCl_3$.

Table 2. IR-data for O-methyl analogs (a) and *p*-methoxyphenacyl esters (b)

Compounds	ν (cm^{-1}, in KBr – pellets)
(a) 14	3320, 3090, 3050, 1767, 1735, 1660, 1190, 1100, 1090, 897.
14a	3095, 1778, 1735, 1665, 1205, 1095, 890.
16	3280, 3090, 3060, 1775, 1750, 1710(sh), 1670, 1250, 1165, 1095, 900.
17	3410, 3085, 1770, 1740, 1710(sh), 1665, 1195, 1100, 900.
17a	3550–3490, 3100, 3050, 1780 (sh), 1760, 1735, 1665, 1110, 895.
15	3300–3100, 3040, 1775, 1740, 1708, 1670, 1255, 1100, 900.
18	3450, 3085, 3055, 1780–1735 (broad), 1715 (sh), 1665, 1165, 1110, 895.
18a	3490, 3095, 3055, 1765, 1740, 1670, 1195, 1165, 1095, 897.
(b) 5	3420, 1770, 1742, 1690, 1600, 1515, 900.
6	3525, 1785, 1750, 1695, 1600, 1525, 1250, 900.
7	3450, 1775, 1750, 1690, 1600, 1520, 1270, 1250, 900.
8	1780, 1745, 1695, 1600, 1518, 1275–1240 (broad), 895
9	1780, 1750, 1700, 1610, 1520, 1175, 1090, 900.
11	3400, 1770, 1742, 1695, 1600, 1515, 1165, 1110, 895.
12	3450, 1760, 1740, 1690, 1610, 1515, 1250, 1230, 1170, 1110, 900.
13	3500, 1780, 1750, 1700, 1610, 1520, 1270, 1250, 1175, 1090, 900.
20	3500, 1778, 1740, 1690, 1660, 1605, 1515, 1170, 1110, 9000.

Table 3. Mass spectrometry data for methyl (a) and *p*-methoxyphenacyl esters (b)

Compound		Ions (Rel.abundance)[m]	
		M^+	m/e
(a)	14a	388(1.00)	357(0.12), 344(0.06), 329(0.17), 313 (0.14), 312 (0.20), 298 (0.11), 253 (0.25), 150 (0.97).
	17a	374(0.27)	343(0.25), 342(0.43), 328(0.12), 315 (0.23), 314(0.26), 298(0.55), 238(1.00), 136 (0.78).
	18a	374(0.24)	343(0.05), 342(0.14), 315(0.17), 301 (0.09), 253(0.06), 239 (0.06), 150(0.36), 31 (1.00).
(b)	5	494(0.04)	492(0.02), 476(0.01), 300(0.15), 299 (0.08), 238(0.12), 237(0.27), 136(0.11), 135 (1.00).
	6	536(0.05)	135 (1.00)
	7	536(0.02)	135 (1.00)
	8	578 (0.09)	135 (1.00)
	9	522(0.11)	490(0.05), 445(0.12), 374 (0.20), 298 (0.11), 297 (0.16), 253 (0.09), 150 (0.38), 135 (1.00)
	11	508(0.61)	490(0.06), 445(0.17), 374(0.20), 359 (0.56), 297 (0.28), 253 (0.13), 150(0.50), 135 (1.00).
	12	550(0.16)	491(0.14), 476(0.26), 384 (0.08), 324 (0.09), 297 (0.73), 253 (0.27), 150 (0.60), 135 (1.00).
	13	550(0.01)	491(0.09), 362(0.13), 299 (0.07), 239 (0.41), 149 (0.29), 135 (1.00).
	20	492(0.14)	448(0.02), 326 (0.06), 299(0.30), 254 (0.24) 253 (0.18), 239(0.05), 149(0.38), 135 (1.00).

[m] Varian MAT CH-6 instrument with all-glass inlet system, heating 70–80°C for methyl esters and 150–210° for p-methoxyphenacyl esters (at 70 eV).

according to[14]) in minimal amount of abs DMF. The mixture was stored for 5 days at 0–5°. The ppt of triethylammonium bromide was separated and the soln concentrated in vacuum to about one half and then poured onto 100–800 g of crushed ice. The crystalline ppt was filtered off, dried in dessicator, washed with small amounts of benzene and recrystallized. The following *p*-methoxyphenacyl esters were thus obtained:

3,13-Dihydroxy ester (**5**), $C_{28}H_{30}O_8$, m.p. 208–210° (from AcOEt) or 232–237° (from acetone); UV spectrum (in EtOH): λ_{sh} 226 (ϵ 9500) and λ_{max} 280 nm (ϵ 12300). (Found: C, 68.26; H, 6.25. $C_{28}H_{30}O_8$ requires: C, 68.00; H, 6.12%) yield 83%.

3-Acetoxy-13-hydroxy ester (**6**), $C_{30}H_{32}O_9$, m.p. 108–110° (from MeOH). (Found: C, 67.51; H, 6.09. $C_{30}H_{32}O_9$ requires: C, 67.15; H, 6.01%). yield 46%. This compound was also obtained in 76% yield when ester **5** was acetylated with Ac_2O and pyridine;[7] in addition, 3,13-diacetoxy ester (**8**), $C_{32}H_{34}O_{10}$ was isolated in 15% yield as white solid foam, m.p. 85–95°. (Found: C, 66.89; H, 6.17. $C_{32}H_{34}O_{10}$ requires: C, 66.42; H, 5.92%). Upon column chromatography **8** was eluted with benzene–AcOEt 8:2 and **6** was eluted with benzene–AcOEt 7:3.

3-hydroxy-13-acetoxy ester (**7**), $C_{30}H_{32}O_9$, m.p. 142–144° (from AcOEt–hexane). (Found: C, 66.94; H, 6.07. $C_{30}H_{32}O_9$ requires: C, 67.15; H, 6.01%) yield 69%.

3-oxo-13-hydroxy ester (**20**), $C_{28}H_{28}O_8$, m.p. 179–184° (from AcOEt–hexane); UV spectrum (in EtOH): λ_{sh} 225 (ϵ 14.800) and λ_{max} 280 nm (ϵ 14.100). (Found: 68.69; H, 5.86. $C_{28}H_{28}O_8$ requires: C, 68.28; H, 5.73%) yield 30%.

Methylation of p-*methoxyphenacyl esters*

Silver oxide was carefully washed with water (by manifold decantation) to remove the traces of alkali and then with MeOH, ether and benzene; it was azeotropically dried in vacuum at 60–65°. Abs acetone, abs DMF abs THF were used as solvents with nearly equal success; however, in the latter solvent the yields of the methylation products were more stable.

3,13-*Dimethoxy ester* (**9**) *and* 3-*hydroxy*-13-*methoxy ester* (**11**)

A mixture of **5** (2.452 g, 5 mmole), Ag_2O (15 g) and MeI (40 g) in 50 ml THF was refluxed for 2 hr, filtered from the ppt and evaporated. The residue (2.6 g) was column chromatographed on 130 g silicagel. Elution with benzene–AcOEt 8:2 gave **9**, $C_{30}H_{34}O_8$, m.p. 156–158° (from ether–hexane with a few drops of AcOEt); UV spectrum (in EtOH): λ_{sh} 225 (ϵ 9.500) and λ_{max} 280 nm (ϵ 12.000). Found: C, 69.29; H, 6.70. $C_{30}H_{34}O_8$ requires: C, 68.95; H, 6.56%), yield 1.270 g (48%). Elution with benzene–AcOEt 7:3 gave 770 mg of crystals with m.p. 148–154°, which represented a mixture of isomeric **10** and **11** in a ratio ~4:6 (from the ratio of Me singlets at δ 3.37 and 3.20 in the NMR spectrum). Fractional crystallization of this mixture afforded pure **11**, $C_{29}H_{32}O_8$, m.p. 172–174° (from ether with small amount of

AcOEt). Further elution of the column with benzene–AcOEt 5:5 gave 240 mg of the starting ester **5**.

3-*Methoxy*-13-*acetoxy ester* **13**. A mixture of **7** (1.072 g, 2 mmole), Ag_2O (7.2 g) and MeI (14 g) in 25 ml THF was refluxed for 2.5 hr and then worked up as above. Column chromatography on 60 g silica gel upon elution with benzene–AcOEt 8:2 afforded **13**, $C_{31}H_{34}O_9$, m.p. 57–59° (pptd from benzene–hexane). (Found: C, 67.41; H, 6.39. $C_{31}H_{34}O_9$ requires: C, 67.62; H, 6.22%), yield 630 mg (60%).

3-*Acetoxy*-13-*methoxy ester* **12**. A mixture of **6** (1.072 g, 2 mmole), Ag_2O (7.3 g) and MeI (14 g) in 30 ml THF was refluxed for 2.5 hr and worked up as above. Column chromatography on 60 g silicagel upon elution with benzene–AcOEt 8:2 afforded **12**, $C_{31}H_{34}O_9$, m.p. 191–194° (from AcOEt–hexane). (Found: C, 67.21; H, 6.14. $C_{31}H_{34}O_9$ requires: C, 67.62, H, 6.22%), yield 810 mg (79%).

Photolytical removal of the protective group

All photolysis were carried out at 15–18° under slow stream of dry argon in the flat-bottomed Pyrex vessels provided with a barboter, a reflux with $CaCl_2$-tube and a water-jacket. Two medium-pressure PRK-2M lamps (375 W each) arranged horizontally in a half-cylindrical reflector were used as light source, the distance to the vessels bottom being kept at 25 cm. Abs EtOH distilled over Mg shavings just before photolysis was used as solvent.

3,13-O-*Dimethylgibberellin* A_3 (**24**). A soln of **9** (1.044 g, 2 mmole) in 100 ml EtOH was irradiated for 24 hr and then evaporated. The residue was dissolved in 50 ml AcOEt and the soln was extracted with 5% Na_2CO_3 (4 × 30 ml). The aqueous layer was acidified to pH 2, extracted with AcOEt (4 × 40 ml), the extract was washed with NaCl-brine, dried over $MgSO_4$ and evaporated to give a residue (660 mg) which was column chromatographed on 35 g of silica gel. Elution with benzene–AcOEt 7:3 and 6:4 afforded **14**, $C_{21}H_{26}O_6$, m.p. 181–184° (from ether–hexane with a few drops of AcOEt), $[\alpha]_D^{22}$ + 132.0°; mass spectrum: M^+ 374 (1.00), *m/e* 150 (0.64). (Found: C, 67.14; H, 7.06. $C_{21}H_{26}O_6$ requires: C, 67.36; H, 7.00%), yield 435 mg (58%). Treatment with diazomethane gave **14a**, $C_{22}H_{28}O_6$, m.p. 143–145° (from ether–hexane). (Found: C, 67.89; H, 7.36. $C_{22}H_{28}O_6$ requires: C, 68.02; H, 7.27%). From the neutral fraction of the photolysate 415 mg of the starting **9** were regenerated (39% recovery).

3-*Methoxy*-13-*acetoxy acid* (**16**). A soln of **13** (510 mg, 1 mmole) in 60 ml EtOH was irradiated for 24 hr, worked up as above and the acidic fraction was chromatographed on 20 g silicagel. Elution with benzene–AcOEt 6:4 afforded **16**, $C_{22}H_{28}O_7$, m.p. 177–181° (from ether–hexane–AcOEt); mass spectrum: M^+ 402, yield 225 mg (62%). The recovery of the starting **13** from the neutral fraction was 30%.

3-*Acetoxy*-13-*methoxy acid* (**15**). A soln of **12** (800 mg) in a mixture of EtOH (80 ml) and abs THF (20 ml), which was added to increase the solubility of **12**, after 24 hr irradiation was evaporated and worked up as above. The acidic fraction was chromatographed on 30 g silicagel to give **15** (elution with benzene–AcOEt 7:3), $C_{22}H_{28}O_7$, m.p. 168–173° (from ether–hexane–AcOEt); mass spectrum: M^+ 402 (0.77), *m/e* 150 (1.00), yield 204 mg (36%). The recovery of the starting **12** from the neutral fraction was 60%.

Photofragmentation of the ester **20**. A soln of the enone **20** (250 mg, ~0.5 mmole) in 30 ml EtOH was irradiated for 24 hr and worked up as above. The acidic products were column chromotographed on 12 g silicagel. Elution with chloroform–AcOEt 7:3 and 6:4 gave 48 mg (about 30% yield) of a chromatographically inseparable mixture of the phenolic acids **22** and **23** in the form of a solid foam with m.p. 135–148°. Fractional crystallization from AcOEt afforded 6 mg of pure **22**, m.p. 242–246°, which was identical with the previously obtained specimen[12] by its R_f and IR, UV and mass spectra. The rest was treated with etheral diazomethane (for 2–3 min), the soln was quickly evaporated and the residue was analysed by combined GLC-MS (LKB instrument with 1% QF-1 on Chromosorb W at 190–210°). Two main components of the mixture displayed fragmentation patterns identical with those observed earlier[10] for the phenolic esters **22a** and **23a**: the ratio of peaks giving ions M^+ 314 and M^+ 316 (i.e. **22a** and **23a**) was close to 7:3.

Reductive removal of the protective group

All reactions were carried out at 20–23° in 3-necked flasks with a strong mechanical stirrer. Zn dust was activated with 0.5% HNO_3 and then washed with water and AcOH. To a suspension of 0.5–2.0 g of Zn dust in glacial AcOH a soln of 0.5–2.0 mmole of a *p*-methoxyphenacyl ester in a minimal amount of glacial AcOH was added and the mixture was vigorously stirred for 4–6 hr. The solid cake was thoroughly washed with AcOEt, the combined organic soln evaporated in vacuum and the gummy residue re-dissolved in 40–150 ml of AcOEt. This soln was washed several times with water and then extracted 5 times with sat. $NaHCO_3$ aq. Bicarbonate layer was acidified to pH 2 and thoroughly extracted with AcOEt, the extract washed with NaCl-brine, dried over $MgSO_4$ and evaporated. The recrystallization of the residue afforded the following acids:

14, m.p. 181–184°, yield 70% from **9**;
15, m.p. 169–172°, yield 64% from **12**;
16, m.p. 178–181°, yield 50% from **13**.

19,20 - *Bisnor* - 13 - *hydroxy* - 3 - *oxo* - *ent* - *gibberelldien* - 1(10),16 - *oic* - 7 *acid* (**24**). To a suspension of Zn dust (0.2 g) in 10 ml of AcOH, **20** (50 mg, ~0.1, mmole) was added and the mixture was stirred for 5 hr. The mixture was worked up as above to give a gum (19 mg) which after preparative TLC on silicagel afforded **24**, $C_{18}H_{22}O_4$ (yield 8 mg), as a solid foam with m.p. 107–115°; IR spectrum: 3430–3280, 3060, 1720 (broad), 1660, 1095 cm^{-1}; mass spectrum: M^+ 302 (0.11). The corresponding methyl ester (**24a**), obtained by diazomethane treatment, was identical with the specimen described earlier[11] by its R_f value and IR and mass spectra.

3-O-*Methylgibberellin* A_3 (**17**). To a chilled soln of **16** (105 mg, 0.25 mmole) in abs MeOH (10 ml) a 0.02 N soln of MeONa in abs MeOH (100 ml) was added and the mixture was stirred for 15 min at 0–2°. Thereupon a few drops of AcOH were added, the solvent was evaporated in vacuum and the residue suspended in 20 ml water. The suspension was acidified to pH 2 and extracted with AcOEt (5 × 20 ml), the extract washed with water, dried over $MgSO_4$ and evaporated to dryness. Recrystallization from AcOEt–hexane afforded pure **17**, $C_{20}H_{24}O_6$, m.p. 228–233°, $[\alpha]_D^{20}$ + 121.4°; mass spectrum: M^+360 (0.39), *m/e* 136. (Found: C, 66.49; H, 6.82. $C_{20}H_{24}O_6$ requires: C, 66.65; H, 6.71%), yield 54 mg (57%). The corresponding methyl ester (**17a**), $C_{21}H_{26}O_6$, obtained with diazomethane, had m.p. 203–207° (from ether–AcOEt). (Found: C, 67.46; H, 7.08. $C_{21}H_{26}O_6$ requires: C, 67.36, H; 7.0%).

13-O-*Methylgibberellin* A_3 (**18**). To a chilled soln of **15** (105 mg, 0.25 mmole) in 15 ml of abs MeOH a 0.02 N soln of MeONa in abs MeOH (25 ml) was added and the mixture was stirred at 0–2° for 10 min. Thereupon the working up was carried out as above to give pure **18**, $C_{20}H_{24}O_6$, m.p. 168–171° (from AcOEt–hexane), $[\alpha]_D^{20}$ + 98.3°; mass spectrum: M^+ 360 (1.00), *m/e* 150 (0.80). (Found: C, 67.01; H, 6.73. $C_{20}H_{24}O_6$ requires: C, 66.65; H, 6.71%), yield 51 mg (54%). The corresponding methyl ester (**18a**), $C_{21}H_{26}O_6$, obtained with diazomethane, had m.p. 153–155° (from ether–AcOEt). (Found: C, 67.56; H, 7.21. $C_{21}H_{26}O_6$ requires: C, 67.36; H, 7.00%).

The same acid **18** was obtained in 37% yield upon photolysis of **11** in abs EtOH according to the procedure described above.

Acetylglycosylation of the ester **5**. A mixture of **5** (810 mg), freshly prepared tetraacetyl-α-bromo-D-glucose (920 mg) and Ag_2O (1.0 g) in 15 ml abs DMF (molar ratio 1:1.36:5.3) was shaken in a dark-glass jar at 20–22° for 72 hr. Then 600 mg of acetobromoglucose and 1.0 g Ag_2O were added and the shaking was continued for further 36 hr. Thereupon the soln was evaporated (45–50°/3 mm), the residue extracted with acetone (3 × 20 ml) and the extract filtered from the dark ppt and evaporated. The gum thus obtained (2.3 g) was column chromatographed on 100 g silicagel. Elution with benzene–AcOEt 7:3 afforded a mixture of **19a** and **19b** as a colourless solid foam with m.p. 86–104°; mass spectrum: *m/e* 331 (the splitting of the

clucosyl fragment); IR spectrum: 3480, 3080, 1770(sh), 1750, 1735(sh), 1690, 1600, 1515, 1240–1230, 1175, 1045, 900 cm^{-1}. PMR spectrum (δ in $CDCl_3$): 1.17 (3H, s), 1.87–1.94 (12H, three peaks), 2.88 and 3.23 (2H, AB-system, J_{AB} 10.5 c/s), 3.80 (3H, s), 4.07 (1H, d), 4.70 (2H), 4.86–4.93 (2H), 5.25 (5H), 5.76 and 6.30 (2H, AB-system, J_{AB} 9 c/s), 6.86 and 7.70 (2H + 2H, J_{ortho} 8 c/s), yield 119 mg (8.8%). The recovery of the starting **5**, eluted with benzene–AcOEt 5:5, was 68%.

The pilot-scale photolysis of the **19a + 19b** mixture (10 mg) in abs EtOH for 24 hr followed by the working up the photolysate as described above afforded an acidic substance with chromatographic and mass spectrometric (*m/e* 331) properties compatible with those of gibberellin A_3 tetraacetyl glucosides.

Allylic oxidation of the ester **5**. To a soln of **5** (495 mg, 1 mmole) in 200 ml of freshly distilled acetone neutral MnO_2 (10 mg) was added and the suspension was shaken for 140 hr at 20–23° in a dark-glass jar. After filtration the ppt was thoroughly washed with acetone and the combined acetone soln was passed through a small column of silicagel (~10 g) and evaporated. The colourless residue (0.47 g) was column chromatographed on 25 g of silicagel. Elution with benzene–AcOEt 7:3 and 6:4 afforded pure **20**, m.p. 178–183°, identical with the sample, described above, yield 196 mg (40%). Further elution with benzene–AcOEt 5:5 afforded 270 mg of the starting material.

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