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# COMPUTER-ASSISTED SITE-SPECIFIC FUNCTIONALIZATION IN THE GIBBERELLIN SERIES; NORRISH TYPE II PHOTOCYCLIZATION VIA A 9-MEMBERED TRANSITION STATE[1]

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Abstract - The site-specific Norrish II type reaction of the gibberellin oxo ester 4, prepared in two steps from tetraacetyl-GA$_3$ anhydride 1, to the photolactone 5 is reported. By potential energy calculations based on the X-ray analysis of 4, it is shown that the regio- and stereoselectivity of the photocyclization can be predicted involving a 9-membered cyclic transition state in the H-abstraction step. The structure of the photolactone was determined by spectroscopic data, especially NOE measurements.

The concept of remote oxidation was shown to be a valuable tool for selective functionalization in rigid systems. Especially in the steroid field e. g. with benzophenone acetic acid esters interesting synthetic applications have been reported leading upon excitation via internal photoreduction-photooxidation to site-specific introduction of a double bond[3]. In search for similar strategies for a remote functionalization of diterpenoid gibberellins we have investigated the photochemical behaviour of gibberellin oxo esters bearing a saturated carbonyl chromophore in the 6β-located side chain moiety. In this paper we describe the intramolecular photocyclization of the oxo ester 4 to the 7-membered gibberellin lactone 5 predictable in its regio- and stereospecific course by potential energy calculations based on the X-ray analysis of starting 4[4].

For synthesis of the oxo ester 4 tetraacetyl-GA$_3$ anhydride (1), readily available in 2 steps from gibberellin A$_3$ (GA$_3$)[5], was treated with 1,2-propanediol to give upon SiO$_2$ column chromatography 70 % of 3,13-diacetyl-GA$_3$-(2'-hydroxy) propyl ester (2). As indicated by $^1$H NMR data, 2 consisted of a mixture of 2'-diastereomers in a 2:1 ratio. As a minor product the primary alcohol 3 was also isolated in 9 % yield. Oxidation of hydroxy ester 2 with pyridinium chlorochromate (PCC)[6] afforded smoothly the desired oxo propyl ester whose spectral data were in good agreement with structure 4. Especially the $^1$H and $^{13}$C NMR data (Tables 1 and 2) as well as the UV spectrum indicated the introduced oxo functionality and the fragmentation pattern in the mass spectra reflected the presence of the oxo propyl ester side chain moiety.

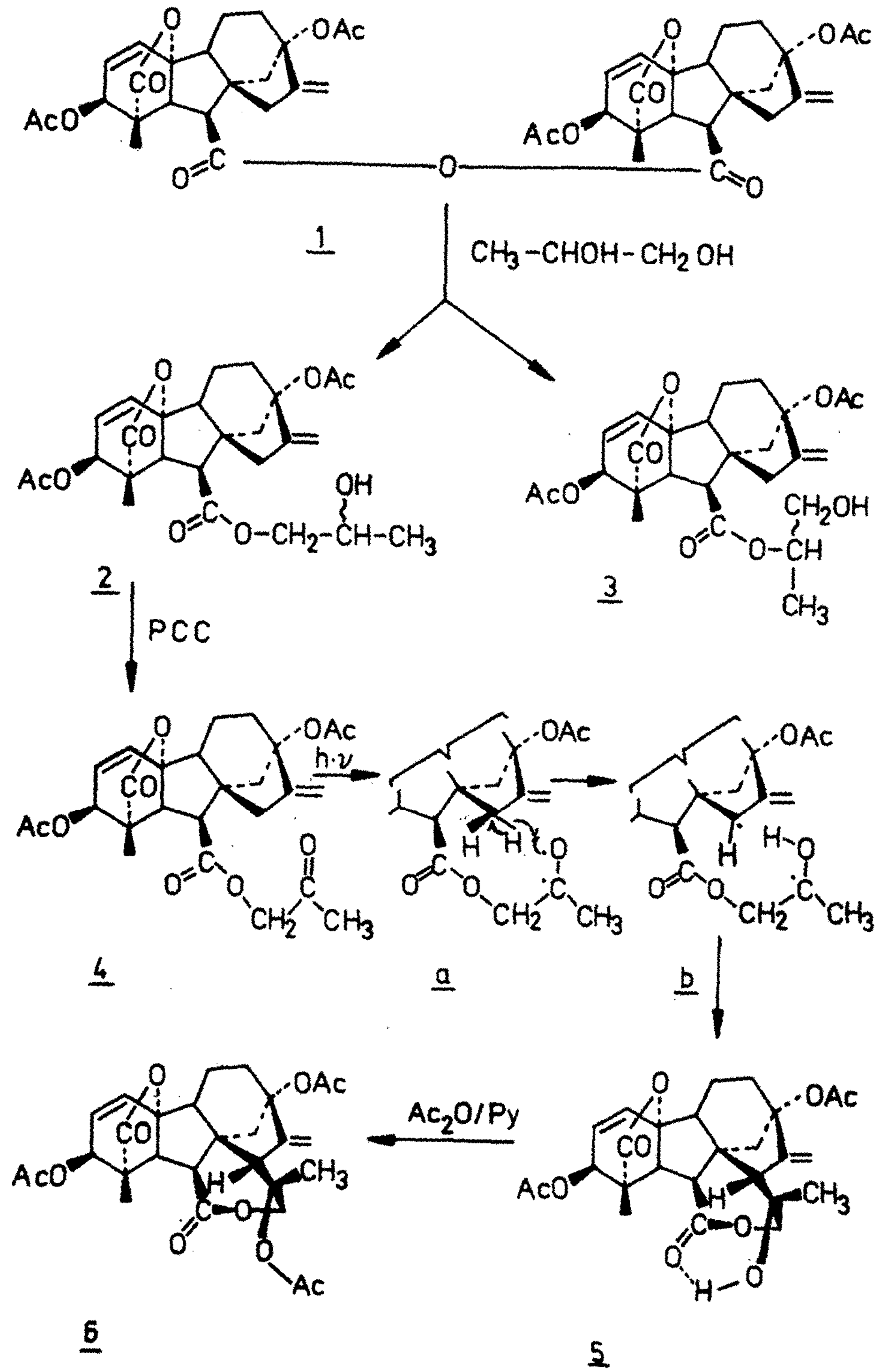

1
CH3-CHOH-CH2 OH
2
3
PCC
h·ν
4
a
b
Ac2O/Py
6
5
OAc
AcO
CO
CH3

Table 1. $^1$H NMR data of 4 and 5 in pyridine-$d_5$/TMS at 200.13 MHz[a].

| | 4 | 5 |
|---|---|---|
| H(1) | 6.49<br>($J_{1,2}$ = 9.3) | 6.51<br>($J_{1,2}$ = 9.3) |
| H(2) | 5.91<br>($J_{1,2}$ = 9.3; $J_{2,3}$ = 3.8) | 5.93<br>($J_{1,2}$ = 9.3; $J_{2,3}$ = 3.7) |
| H(3) | 5.67<br>($J_{2,3}$ = 3.8) | 5.75<br>($J_{2,3}$ = 3.7) |
| H(5) | 3.62<br>($J_{5,6}$ = 11.0) | 3.37[d]<br>($J_{5,6}$ = 8.3) |
| H(6) | 3.29<br>($J_{5,6}$ = 11.0) | 3.50[d]<br>($J_{5,6}$ = 8.3) |
| H(14α) | 2.53<br>($J_{14\alpha,14\beta}$ = -10.8) | 2.92<br>($J_{14\alpha,14\beta}$ = -11.3) |
| H(14β) | 2.47<br>($J_{14\alpha,14\beta}$ = -10.8) | 3.15<br>($J_{14\alpha,14\beta}$ = -11.3) |
| H(15α) | 2.73<br>($J_{15\alpha,15\beta}$ = -15.3; $J_{15\alpha,17}$ = $J_{15\alpha,17'}$ = 2.9) | - |
| H(15β) | 2.28<br>($J_{15\alpha,15\beta}$ = -15.3) | 2.83<br>e |
| H(17) | 5.07<br>b | 5.31<br>($J_{15\beta,17}$ = 1.5) |
| H(17') | 5.32<br>b | 5.51<br>($J_{15\beta,17'}$ = 2.0) |
| $H_3$(18) | 1.53 | 1.71 |
| $H_3$(3-OAc) | 2.00[c] | 2.01 |
| $H_3$(13-OAc) | 1.97[c] | 2.01 |
| $H_2$(1') | 4.90; 4.96<br>($J_{AB}$ = -16.8) | 4.22; 3.77[f]<br>($J_{AB}$ = -12.0) |
| $H_3$(3') | 2.05 | 1.59 |

[a] Chemical shifts (δ) with coupling constants (Hz) in parentheses.

[b] Allylic couplings to 15α-H were unresolved, probably due to further long range couplings[15].

[c] Assignment was confirmed by NOE difference spectra.

[d] The assignment of these two protons is reversal in comparison to 4 or 3,13-diacetyl-$GA_3$ and was performed on the basis of the relative NOE enhancements after irradiation of the 18-methyl group.

[e] Allylic couplings to 17-H and 17'-H were unresolved, probably due to further long range couplings.

[f] H(1'α) δ 4.22; H(1'β) δ 3.77.

**Table 2.** $^{13}C$ chemical shifts of 4 and 5 in $CDCl_3$/TMS at 62.5 MHz.

| Carbon | 4 | | 5 | | Carbon | 4 | | 5 | |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 134.3 | d | 133.0 | d | 13 | 84.1 | s | 84.9 | s |
| 2 | 129.3 | d | 129.9 | d | 14 | 39.8 | t | 38.6 | t |
| 3 | 70.3 | d | 71.1 | d | 15 | 42.6 | t | a | |
| 4 | 52.3 | s | 52.5 | s | 16 | 153.5 | s | 150.7 | s |
| 5 | 53.7 | d | a | | 17 | 108.2 | t | 110.6 | t |
| 6 | 50.3 | d | a | | 18 | 14.3 | q | 15.3 | q |
| 7 | 171.2 | s | b | s | 19 | 177.0 | s | 177.0 | s |
| 8 | 51.2 | s | 50.1 | s | 1' | 68.7 | t | 64.7 | t |
| 9 | 51.1 | d | a | | 2' | 200.0 | s | 86.3 | s |
| 10 | 90.0 | s | 89.8 | s | 3' | 26.0 | q | 26.7 | q |
| 11 | 16.9 | t | 15.7 | t | $O\underline{C}OCH_3$ | 169.9<br>170.1 | s<br>s | 169.9<br>170.0 | s<br>s |
| 12 | 36.4 | t | 37.4 | t | $OCO\underline{CH}_3$ | 20.9<br>22.1 | q<br>q | 20.7<br>22.0 | q<br>q |

[a] The signals of the methine carbons appear at δ 45.0, 52.7, 55.4 and 57.1 but could not be assigned unambiguously only on the basis of chemical shift arguments.

[b] Probably overlapped with one of the acetate carbonyls.

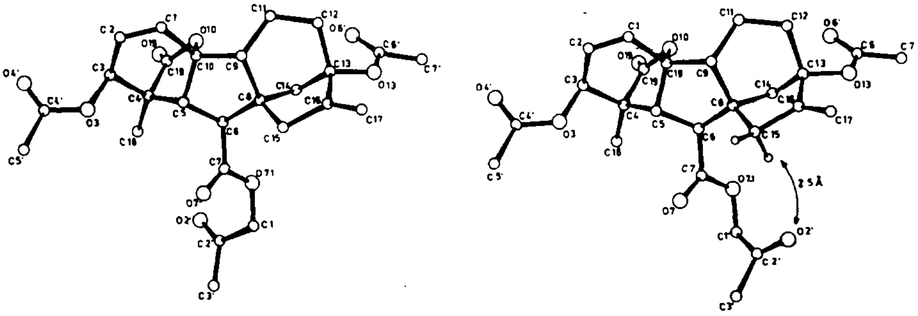


**Figure 1.** Molecular structure of oxo ester 4: a, with side chain conformation obtained by X-ray analysis; b, with computer-calculated side chain conformation preferred for 15α H-abstraction.

Table 3. Final fractional coordinates and equivalent isotropic thermal parameters for non-hydrogen atoms. Estimated standard deviations are in parentheses.

$$B_{eq} = 4/3(B_{11}a^2+B_{22}b^2+B_{33}c^2)$$

| | x/a | y/b | z/c | $B_{eq}$(Å$^2$) |
|---|---|---|---|---|
| O(3) | 0.5157(3) | 0.5050(2) | 0.6087(2) | 5.6(1) |
| O(7) | 0.5974(2) | 0.2656(2) | 0.4572(2) | 5.0(1) |
| O(7.1) | 0.7958(3) | 0.1904(2) | 0.4373(1) | 4.7(1) |
| O(10) | 0.8540(2) | 0.3201(2) | 0.6815(2) | 4.6(1) |
| O(13) | 0.8913(4) | -0.0993(2) | 0.6211(2) | 6.5(1) |
| O(19) | 0.9672(3) | 0.4520(2) | 0.6438(2) | 6.5(1) |
| O(2') | 0.8388(4) | 0.3451(3) | 0.3518(2) | 7.8(1) |
| O(4') | 0.4998(5) | 0.6524(3) | 0.6538(3) | 9.2(1) |
| O(6') | 1.0895(4) | -0.0290(3) | 0.6611(3) | 10.1(1) |
| C(1) | 0.6261(4) | 0.3385(4) | 0.7279(2) | 5.2(1) |
| C(2) | 0.5980(4) | 0.4316(3) | 0.7156(3) | 5.5(1) |
| C(3) | 0.6404(4) | 0.4832(3) | 0.6499(2) | 5.2(1) |
| C(4) | 0.7337(4) | 0.4212(3) | 0.6005(2) | 4.4(1) |
| C(5) | 0.6776(3) | 0.3177(3) | 0.5983(2) | 3.6(1) |
| C(6) | 0.7539(3) | 0.2431(3) | 0.5537(2) | 3.4(1) |
| C(7) | 0.7051(3) | 0.2371(3) | 0.4794(2) | 3.6(1) |
| C(8) | 0.7400(3) | 0.1444(3) | 0.5946(2) | 3.5(1) |
| C(9) | 0.7055(4) | 0.1743(3) | 0.6725(2) | 4.0(1) |
| C(10) | 0.7084(4) | 0.2845(3) | 0.6737(2) | 4.1(1) |
| C(11) | 0.7967(5) | 0.1214(3) | 0.7269(2) | 5.2(1) |
| C(12) | 0.8048(4) | 0.0121(4) | 0.7129(2) | 5.2(1) |
| C(13) | 0.8153(4) | -0.0092(3) | 0.6334(2) | 4.5(1) |
| C(14) | 0.8690(3) | 0.0805(3) | 0.5933(2) | 3.9(1) |
| C(15) | 0.6306(4) | 0.0722(3) | 0.5675(2) | 4.2(1) |
| C(16) | 0.6713(4) | -0.0237(3) | 0.6005(2) | 4.8(1) |
| C(17) | 0.6032(6) | -0.1038(4) | 0.6024(4) | 7.8(1) |
| C(18) | 0.7627(5) | 0.4710(3) | 0.5309(3) | 5.5(1) |
| C(19) | 0.8656(4) | 0.4037(3) | 0.6445(2) | 4.9(1) |
| C(1') | 0.7583(4) | 0.1842(3) | 0.3648(2) | 4.5(1) |
| C(2') | 0.7718(4) | 0.2799(3) | 0.3280(2) | 4.9(1) |
| C(3') | 0.7014(6) | 0.2875(4) | 0.2566(3) | 7.1(1) |
| C(4') | 0.4590(5) | 0.5910(3) | 0.6144(3) | 5.6(1) |
| C(5') | 0.3331(6) | 0.6031(4) | 0.5713(3) | 7.9(1) |
| C(6') | 1.0308(5) | -0.0987(4) | 0.6353(3) | 7.8(1) |
| C(7') | 1.0892(8) | -0.1935(5) | 0.6170(4) | 12.4(2) |

Table 4. Bond distances (Å) with their e.s.d.'s in parentheses.

| | | | | | |
|---|---|---|---|---|---|
| O(3)-C(3) | 1.476(4) | C(1)-C(2) | 1.320(5) | C(8)-C(15) | 1.541(4) |
| O(3)-C(4') | 1.302(4) | C(1)-C(10) | 1.495(4) | C(9)-C(10) | 1.503(4) |
| O(7)-C(7) | 1.198(3) | C(2)-C(3) | 1.484(5) | C(9)-C(11) | 1.538(4) |
| O(7.1)-C(7) | 1.350(3) | C(3)-C(4) | 1.555(4) | C(11)-C(12) | 1.517(5) |
| O(7.1)-C(1') | 1.419(4) | C(4)-C(5) | 1.515(4) | C(12)-C(13) | 1.532(5) |
| O(10)-C(10) | 1.509(3) | C(4)-C(18) | 1.505(5) | C(13)-C(14) | 1.532(4) |
| O(10)-C(19) | 1.342(4) | C(4)-C(19) | 1.552(4) | C(13)-C(16) | 1.550(4) |
| O(13)-C(13) | 1.454(4) | C(5)-C(6) | 1.515(4) | C(15)-C(16) | 1.503(5) |
| O(13)-C(6') | 1.389(6) | C(5)-C(10) | 1.524(4) | C(16)-C(17) | 1.280(5) |
| O(19)-C(19) | 1.192(4) | C(6)-C(7) | 1.483(4) | C(1')-C(2') | 1.486(5) |
| O(2')-C(2') | 1.192(4) | C(6)-C(8) | 1.558(4) | C(2')-C(3') | 1.516(5) |
| O(4')-C(4') | 1.189(4) | C(8)-C(9) | 1.563(4) | C(4')-C(5') | 1.484(6) |
| O(6')-C(6') | 1.213(6) | C(8)-C(14) | 1.534(3) | C(6')-C(7') | 1.455(7) |

Table 5. Bond angles (°) with their e.s.d.'s in parentheses.

| | | | |
|---|---|---|---|
| C(3)-O(3)-C(4') | 119.2(3) | O(10)-C(10)-C(1) | 106.4(2) |
| C(7)-O(7.1)-C(1') | 115.2(2) | O(10)-C(10)-C(5) | 100.5(2) |
| C(10)-O(10)-C(19) | 107.6(2) | O(10)-C(10)-C(9) | 109.9(2) |
| C(13)-O(13)-C(6') | 117.8(3) | C(1)-C(10)-C(5) | 112.7(3) |
| C(2)-C(1)-C(10) | 117.7(3) | C(1)-C(10)-C(9) | 119.5(3) |
| C(1)-C(2)-C(3) | 123.1(3) | C(5)-C(10)-C(9) | 106.2(2) |
| O(3)-C(3)-C(2) | 107.8(3) | C(9)-C(11)-C(12) | 112.1(3) |
| O(3)-C(3)-C(4) | 106.0(3) | C(11)-C(12)-C(13) | 111.1(3) |
| C(2)-C(3)-C(4) | 114.0(3) | O(13)-C(13)-C(12) | 110.5(3) |
| C(3)-C(4)-C(5) | 108.2(3) | O(13)-C(13)-C(14) | 114.9(2) |
| C(3)-C(4)-C(18) | 112.9(3) | O(13)-C(13)-C(16) | 107.0(3) |
| C(3)-C(4)-C(19) | 104.4(3) | C(12)-C(13)-C(14) | 110.8(3) |
| C(5)-C(4)-C(18) | 117.7(3) | C(12)-C(13)-C(16) | 110.9(2) |
| C(5)-C(4)-C(19) | 99.9(2) | C(14)-C(13)-C(16) | 102.4(2) |
| C(18)-C(4)-C(19) | 112.3(3) | C(8)-C(14)-C(13) | 99.5(2) |
| C(4)-C(5)-C(6) | 117.6(2) | C(8)-C(15)-C(16) | 103.6(2) |
| C(4)-C(5)-C(10) | 100.3(2) | C(13)-C(16)-C(15) | 107.2(3) |
| C(6)-C(5)-C(10) | 102.9(2) | C(13)-C(16)-C(17) | 124.7(3) |
| C(5)-C(6)-C(7) | 113.8(2) | C(15)-C(16)-C(17) | 128.1(3) |
| C(5)-C(6)-C(8) | 105.2(2) | O(10)-C(19)-O(19) | 123.1(3) |
| C(7)-C(6)-C(8) | 113.1(2) | O(10)-C(19)-C(4) | 109.8(3) |
| O(7)-C(7)-O(7.1) | 121.6(3) | O(19)-C(19)-C(4) | 126.9(3) |
| O(7)-C(7)-C(6) | 126.6(3) | O(7.1)-C(1')-C(2') | 112.0(3) |
| O(7.1)-C(7)-C(6) | 111.8(2) | O(2')-C(2')-C(1') | 121.9(3) |
| C(6)-C(8)-C(9) | 105.0(2) | O(2')-C(2')-C(3') | 122.2(3) |
| C(6)-C(8)-C(14) | 114.3(2) | C(1')-C(2')-C(3') | 115.8(3) |
| C(6)-C(8)-C(15) | 116.6(2) | O(3)-C(4')-O(4') | 123.0(3) |
| C(9)-C(8)-C(14) | 109.9(2) | O(3)-C(4')-C(5') | 114.0(3) |
| C(9)-C(8)-C(15) | 109.3(2) | O(4')-C(4')-C(5') | 122.8(3) |
| C(14)-C(8)-C(15) | 101.6(2) | O(13)-C(6')-O(6') | 123.1(4) |
| C(8)-C(9)-C(10) | 105.7(2) | O(13)-C(6')-C(7') | 109.5(5) |
| C(8)-C(9)-C(11) | 112.4(2) | O(6')-C(6')-C(7') | 127.3(5) |
| C(10)-C(9)-C(11) | 116.6(3) | | |

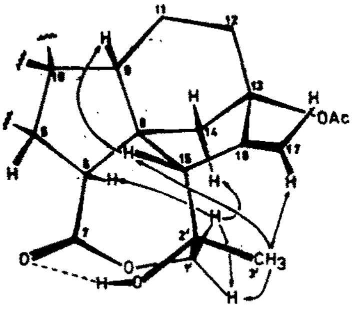
Table 6. Relevant torsion angles (°) with their e.s.d.'s in parentheses.

| | | | |
|---|---|---|---|
| C(4')-O(3)-C(3)-C(2) | 96.2(4) | C(10)-C(5)-C(6)-C(8) | 36.1(3) |
| C(3)-O(3)-C(4')-O(4') | -3.1(4) | C(5)-C(6)-C(7)-O(7) | -18.8(3) |
| C(1')-O(7.1)-C(7)-C(6) | -178.3(4) | C(5)-C(6)-C(8)-C(9) | -20.8(3) |
| C(7)-O(7.1)-C(1')-C(2') | 73.3(4) | C(6)-C(8)-C(9)-C(10) | -2.8(4) |
| C(19)-O(10)-C(10)-C(5) | 34.1(3) | C(14)-C(8)-C(9)-C(11) | -7.6(3) |
| C(10)-O(10)-C(19)-C(4) | -8.3(3) | C(9)-C(8)-C(14)-C(13) | 65.4(3) |
| C(6')-O(13)-C(13)-C(12) | -69.6(4) | C(14)-C(8)-C(15)-C(16) | 37.7(4) |
| C(13)-O(13)-C(6')-O(6') | 4.3(4) | C(8)-C(9)-C(10)-C(5) | 25.4(3) |
| C(10)-C(1)-C(2)-C(3) | 2.1(3) | C(11)-C(9)-C(10)-C(1) | -80.1(3) |
| C(2)-C(1)-C(10)-C(5) | -34.8(3) | C(8)-C(9)-C(11)-C(12) | -47.9(3) |
| C(1)-C(2)-C(3)-C(4) | -6.0(3) | C(9)-C(11)-C(12)-C(13) | 40.1(4) |
| C(2)-C(3)-C(4)-C(5) | 41.8(3) | C(11)-C(12)-C(13)-C(14) | 21.8(4) |
| C(3)-C(4)-C(5)-C(10) | -68.7(4) | C(12)-C(13)-C(14)-C(8) | -75.1(4) |
| C(19)-C(4)-C(5)-C(10) | 40.2(3) | C(16)-C(13)-C(14)-C(8) | 43.1(3) |
| C(5)-C(4)-C(19)-O(10) | -20.8(3) | C(14)-C(13)-C(16)-C(15) | -20.6(4) |
| C(4)-C(5)-C(6)-C(7) | -90.5(3) | O(7.1)-C(1')-C(2')-O(2') | 18.0(5) |

Our synthetic concept involved the use of the $n \rightarrow \pi^*$-excited oxo function of compound 4 for a Norrish type II intramolecular hydrogen abstraction from the gibberellin skeleton via an "in plane" n-orbital-initiated mechanism[7] followed by C-C bond formation of the intermediate diradical species. In order to provide detailed information about the intramolecular contact geometry between the carbonyl chromophore and nearest neighbour hydrogens suitable for abstraction, an X-ray analysis of oxo ester 4 was performed. The structure has been solved by direct methods and refined by full-matrix least-squares using the Enraf-Nonius structure determination package[8]. The final anisotropic refinement of the non-hydrogen atoms (Table 1) with H atoms in calculated positions gave a R-value of 0.049. Figure 1a shows a perspective view of the obtained structure in the crystal together with the numbering scheme. The final relative coordinates are listed with their e.s.d.'s in Table 3. The bond lengths, valency angles and relevant torsion angles are listed in Tables 4, 5 and 6, respectively.

The obtained geometry of the skeleton corresponds nearly to that as found earlier for $GA_3$[9]. In regard to the 6β-located side chain moiety the ester carbonyl group exhibits a synperiplanar conformation with the torsion angle C(5)-C(6)-C(7)-O(7) = -18.8° which is the preferred conformation[10] also in most other gibberellins[11]. The shortening of the bond C(7)-O(7.1) to 1.350(3) Å indicates its partial double bond character with a torsion angle C(6)-C(7)-C(7.1)-C(1') = -178.3°. However, the more outside part of the side chain moiety can be expected as flexible. Therefore, its favoured conformations were analyzed by calculating the potential energy with the program EENY[12] under systematical variation of the torsion angles around O(7.1)-C(1') and C(1')-C(2'). The two-dimensional energy map indicated in addition to the minimum corresponding to the conformation observed in the crystal structure (Figure 1a, C(7)-O(7.1)-C(1')-C(2') = 73.3° and O(7.1)-C(1')-C(2')-O(2') = 18°) three further nearly equivalent minima. One of them corresponds to a side chain conformation (Figure 1b) in which the atoms C(15), H(15α) and O(2') lie in good approximation on a straight line. The distance between O(2') and H(15α) amounts only 2.5 Å which is nearly the sum of the van der Waals radii of both atoms. In the three other conformations the distance between O(2') and the nearest neighbour hydrogen atoms of the gibberellin skeleton amounts more than 3.6 Å. Therefore, the 15α-hydrogen was assumed to be preferred for an intramolecular abstraction followed by C-C bond formation at this position. This expectation was in agreement with the obtained experimental results. Thus, upon $n \rightarrow \pi^*$-excitation of the oxo ester 4 in absolute benzene (254 nm, argon) regio- and stereospecific ring closure took place leading under functionalization at 15α-position in 56 % yield to compound 5. In hydrogen donating solvents, e. g. methanol or ethanol, no 5 but other photoproducts were formed among them 3,13-diacetyl-$GA_3$[13].

From compound 5 no suitable single crystal for X-ray analysis could be obtained. Therefore, its structure was determined by spectroscopic data. Whereas the electron impact mass spectrum of 5 showed no molecular ion, with the softer field desorption and electron attachment[14] techniques peaks at m/z 509 $[M+Na]^+$ 487 $[M+H]^+$ and 486($M^+$) as well as 545($M^-$-1-AcOH), 486($M^-$) and 485($M^-$-1), respectively, indicated the same molecular weight as that of starting ketone 4. The lack of UV-absorption for saturated carbonyl and a new IR-absorption at 3430 $cm^{-1}$ (nujol) suggested the expected ring closure under formation of a hydroxyl. This was indicated also in the $^{13}C$ NMR spectrum (Table 2) in which the signal for the side chain carbonyl ($\delta$ 200.0 in 4) has disappeared. Instead of this a new signal for an O-substituted quaternary carbon at $\delta$ 86.3 was observed.



2'S

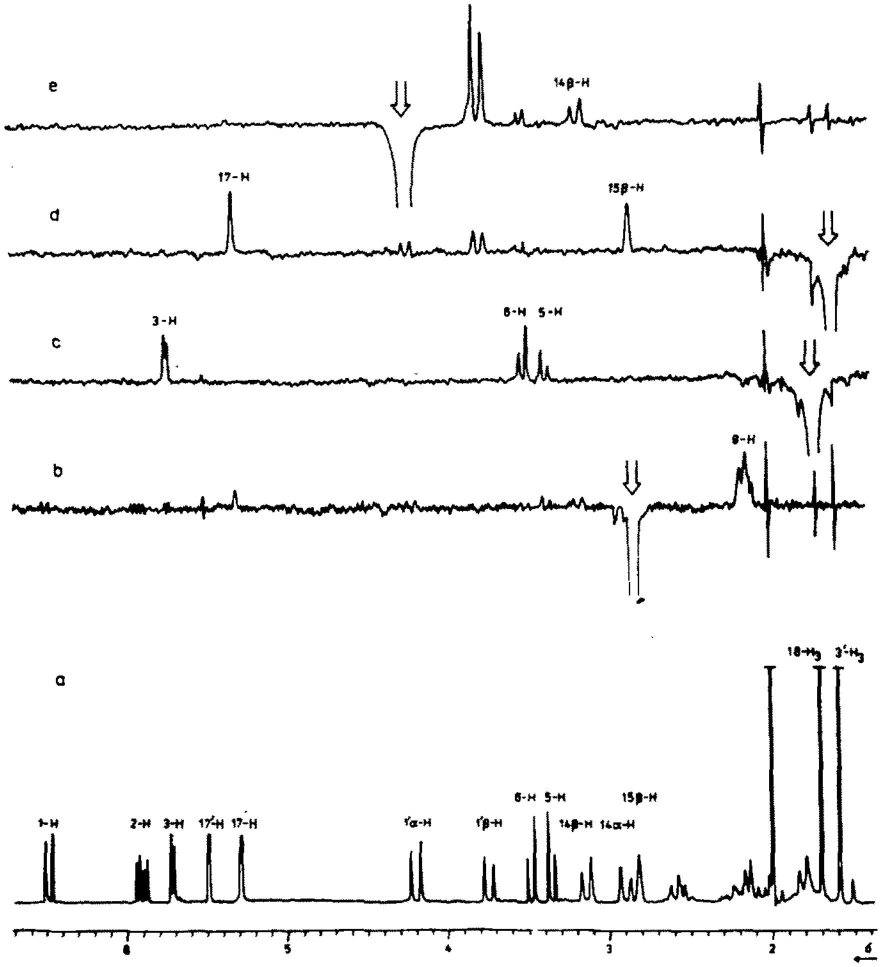


Figure 2. $^1$H (200.13 MHz) spectra of 5 in pyridine-d$_5$: a, control spectrum; b-e, NOE difference spectra arising from irradiation of the $^1$H resonances marked by arrows.

Full evidence for the occurred 15α-ring closure as well as (S)-configuration at the newly created asymmetric centre C(2') was given by detailed $^1H$ investigations on the basis of our recent 2D NMR studies on $GA_3$ and its 3,13-diacetyl derivative[15]. In the $^1H$ shift range between δ 2.2 and 3.1 where in starting 4 the two AB-quartets of the methylene protons at C(14) and C(15) appear, in 5 only one AB quartet centered at δ 3.03 and additionally a new one-proton singlet at δ 2.83 were observed. The comparison of the coupling constants of this remained AB quartet with the corresponding values of 4 and 3,13-diacetyl-$GA_3$ indicated the ring closure at C(15). On the other hand the observed downfield shift of the singlet at δ 2.83 compared to the shifts of the 15α- and 15β-protons in 4 suggested the α-connection, which was clearly confirmed by NOE measurements (Figure 2). Thus, irradiation of the singlet at δ 2.83 produced in the difference spectrum a large response of the 9-proton signal at δ 2.12, which can accept such a positive NOE only from the 15β-proton. The conformation of the newly formed lactone ring and the configuration at C(2') were likewise clarified by NOE-experiments. In 5 the 7-membered lactone ring is fixed via three carbon atoms to the rigid gibberellin skeleton and therefore its conformational flexibility[16] is strongly restricted. From the remaining three conformers (Dreiding models) only in the twisted boat form (Figure 2) the H(1'α)- and H(14β) are in a close spatial proximity. The observed NOE at H(14β) (and also at H(6)) upon irradiation of the 1'α-H signal confirmed that this conformation must be favoured. On the other hand the strong NOE's at H(17) and H(15β) after irradiation of the methyl singlet at δ 1.59 proved the quasi-equatorial position of the methyl group and therefore (2'S)-configuration. The observed intramolecular hydrogen bond of the type OH---COOR[17] in the IR spectrum of 5 ($\Delta \nu_{OH}$ = 145 $cm^{-1}$) is also in agreement with this stereochemical assignment. Acetylation of photolactone 5 with acetic anhydride-pyridine for 24 hours afforded the triacetyl derivative 6 with m/z 528($M^+$).

Intramolecular hydrogen abstraction via a carbonyl type II process normally require a cyclic 6-membered transition state[18]. With the Yang-type photocyclization of gibberellin-7-aldehydes to 7,15α-cyclobutanols such a process was described earlier[19,20] also in the gibberellin series. The herewith reported photocyclization of the oxo ester 4 to compound 5 can be explained by abstraction of the 15α-hydrogen via a 9-membered transition state a to the intermediate 1,7-diradical b followed by C-C-bond formation. The reaction allows a direct functionalization of the gibberellin molecule using an oxo ester function as "reagent" capable of H-abstracting and is predictable in its steric course by computer-assisted conformational analysis. Further results with other gibberellin oxo esters of variable length of the side chain moiety will be given in a forthcoming paper.

## EXPERIMENTAL

Melting points were determined on a Boetius hot-stage microscope and are corrected. Specific rotations were determined in chloroform. IR spectra were recorded on a ZEISS instrument Specord 75 in IR nujol as not otherwise stated. UV spectra were obtained on a ZEISS Specord UV-VIS instrument. Low-voltage routine mass spectra were obtained with the electron attachment mass spectrograph (Elektronenanlagerungs-Massenspektrograph) of the Research Institute 'Manfred von Ardenne', Dresden, using positive (10-16 eV) and negative (2-4 eV) ionization. The high resolution electron impact mass spectrum (EIMS) was obtained with an AE MS 902S spectrometer. The field desorption mass spectrum (FDMS) was obtained with a VARIAN MAT 311 instrument.

The $^{1}H$ NMR spectra were recorded on the Bruker spectrometer WP 200 at 200.13 MHz. The $^{13}C$ NMR spectra were run at 62.89 MHz on the Bruker spectrometer WM 250. The chemical shifts were measured using tetramethylsilane (TMS) as the internal standard. The NOE measurements were carried out with an undegassed sample of 5 at a concentration of 0.003 mol/l in pyridine $d_5$. For the NOE difference spectra b-d in Figure 2 the microprogram HOMNOEDF was used. The decoupler power was 50 dB below 0.2 W and 800-1200 transients were aquired. For the difference spectrum e a decoupler power of 42 dB was used and the program was modified in such a way[21] that each line of the doublet at $\delta$ 4.22 was irradiated consecutively 30 times during a total preirradiation time of 3.0 s; 8192 transients were accumulated. The $^{13}C$ subspectrum of 5, indicating the methine carbon atoms, was generated with the microprogram DEPT. A $\Theta$ = 90° pulse was used and the $\Delta$ delay corresponded to the coupling J ($^{1}H$, $^{13}C$) = 140 Hz. The relaxation delay was 2 s and 5190 transients were accumulated.

The photochemical reactions were performed in a Reading photoreactor (254 nm) with a quartz vessel at 15-20°C under argon. Column chromatography was performed on Woelm silica gel for partition.

### 3,13-Diacetyl-$GA_3$-(2'-hydroxy)propyl ester (2) and 3,13-diacetyl-$GA_3$-(1'-hydroxy)isopropyl ester (3)

A solution of tetraacetyl-$GA_3$ anhydride (1) (1 g, 1.2 mmol) was refluxed with dry 1,2-propanediol (3 ml) and dioxane (3 ml) for 5 hours. Removal under reduced pressure gave a gum, which was chromatographed on silica gel. Upon elution with benzene-ethyl acetate 85:15 at first the primary alcohol 3 (56 mg, 9 %) was obtained and was crystallised from benzene-n-hexane, m.p. 142-144°C; $[\alpha]_D^{25}$ +119.2° (c = 0.326); IR: $\nu_{max}$ 890, 1248, 1735, 1775, 3540 (broad) $cm^{-1}$. $^{1}H$ NMR ($CDCl_3$): 6.34, d, H(1), $J_{1,2}$ = 9.4; 5.86, dd, H(2), $J_{1,2}$ = 9.4, $J_{2,3}$ = 3.8; 5.32, d, H(3), $J_{2,3}$ = 3.8; 3.30, d, H(5), $J_{5,6}$ = 11.3; 2.74, d, H(6), $J_{5,6}$ = 11.3; 2.62, dt, H (15α), $J_{15\alpha,15\beta}$ = -15.0, $J_{15\alpha,17}$ = 2.0, $J_{15\alpha,17'}$ = 2.0; 4.94, s (broad), H(17); 5.03, d, H(17'), $J_{15\alpha,17'}$ = 2.0; 1,14, s, $H_3$(18); 3.65, t, H(1'a), $J_{1'a,2'}$ = 6.6, $J_{1'a,1'b}$ = -6.6; 3.07, t, H(1'b), $J_{1'b,2'}$ = 6.6, $J_{1'a,1'b}$ = -6.6; 5.08, m, H(2'), $J_{1'a,2'}$ = $J_{1'b,2'}$ = 6.6, $J_{2',3'H_3}$ = 6.5; 1.18, d, $H_3$(3'), $J_{2',3'H_3}$ = 6.5; 2.11, s, $H_3$ (OAc); 2.00, s, $H_3$(OAc). MS (positive ions): m/z 488 ($M^+$, 6 %), 446(28), 428(33), 413(25), 383(16), 368(10), 354(13), 342(13), 324(100), 266(93), 238(72), 221(100); MS (negative ions): m/z 488 ($M^-$,9), 444(16), 327(100). Calc. for $C_{26}H_{32}O_9$: C, 63.93; H, 6.61. Found: C, 63.80; H, 6.51.

Upon further elution with benzene-ethyl acetate 85:15 the secondary alcohol 2 (450 mg, 70 %) was obtained and was crystallized from benzene-n-hexane, m.p. 160-162°C; $[\alpha]_D^{23}$ +110.5° (c 0.323); IR: $\nu_{max}$ 890, 1248, 1730, 1775, 3430 (broad) $cm^{-1}$; $^{1}H$ NMR ($CDCl_3$): 6.38, d, H(1), $J_{1,2}$ = 9.3; 5.88, dd, H(2), $J_{1,2}$ = 9.3, $J_{2,3}$ = 3.8; 5.34, d, H(3), $J_{2,3}$ = 3.8; 3.33, d, H(5), $J_{5,6}$ = 11,2; 2.80, d, H(6) (major diastereomer), $J_{5,6}$ = 11.2; 2.82, d, H(6) (minor diastereomer); $J_{5,6}$ = 11.2; 4.96, s (broad), H(17); 4.97, s (broad), H(17); 5.10, s (broad), H(17'); 5.11, s (broad), H(17'); 1.16, s, $H_3$(18); 4.22, dd, H(1'a), $J_{1'a,2'}$ = 8.5, $J_{1'a,1'b}$ = -10.7; 4.45, dd, H(1'a), $J_{1'a,2'}$ = 2.7; $J_{1'a,1'b}$ = -11.2; 3.94, dd, H(1'b), $J_{1'b,2'}$ = 2.1; $J_{1'a,1'b}$ = -10.7; 3.83, dd, H(1'b), $J_{1'b,2'}$ = 6.9, $J_{1'a,1'b}$ = -11.2; 4.02 - 4.14, m, H(2'); 1.22, d, $H_3$(3'), $J_{2',3'}$ = 6.3; 1.24, d, $H_3$(3'), $J_{2',3'}$ = 6.3; 2.13, s, $H_3$(OAc); 2.02, s, $H_3$(OAc). $^{13}C$ NMR ($CDCl_3$)[22]: 70.6, C(1') (major diastereomer); 70.1, C(1') (minor diastereomer); 65.6, C(2'); 66.1, C(2'); 19.1, C(3'); 19.4, C(3'). MS (positive ions): m/z 446 ($M^+$-42, 8), 428(14), 413(8), 383(17), 352(17), 384(89), 266(71), 238(80), 220(100), 22(99); MS (negative ions): m/z 547($M^-$+59, 52), 488($M^-$, 27), 467(14), 444(39), 384(30), 324(92), 327(100) Calc. for $C_{26}H_{32}O_9$: C, 63.93; H, 6.61. Found: C, 63.71; H, 6.55.

Further elution of the column with ethyl acetate gave 3,13-diacetyl-$GA_3$[5] (405 mg).

### 3,13-Diacetyl-$GA_3$-(2'-oxo)propyl ester(4)

Hydroxy ester 2 (488 mg, 1 mmol) was stirred with PCC[6] (1.2 g, 5 mmol) in dry methylene chloride (5 ml) for 68 hours at room temperature. To the mixture ether (50 ml) was added, the organic layer separated and the remained dark residue treated three-times with ether (each 5 ml). The combined organic phase was shaken with water, separated, dried over sodium sulphate and evaporated to yield a gum, which was chromatographed on silica gel. Upon elution with benzene-ethyl acetate 9:1 the oxo ester 4 (273 mg, 56 %) was obtained and was crystallized from benzene-n-hexane, m.p. 187-188°C, $[\alpha]_D^{23}$ +182.5 (c 0.359); IR: $\nu_{max}$ 890, 1240, 1710, 1730, 1772 $cm^{-1}$; UV (methanol): $\lambda_{max}$ ($\varepsilon$) 275(60); $^1H$ and $^{13}C$ NMR see Table 1 and 2; MS (positive ions): m/z 486($M^+$, 9), 444(49), 426(47), 413(9), 381(22), 366(15), 352(20), 339(22), 322(63), 283(57), 265(64), 248(48), 238(64), 220(100); MS (negative ions): m/z 486($M^-$, 14), 429(100), 325(84), 284(45).

### Photolysis of 4

A solution of 4 (200 mg, 0.41 mmol) was irradiated in dry benzene (150 ml) for 5 hours. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel. Elution with benzene-ethyl acetate 8:2 gave starting 4 (53 mg). Upon elution with benzene-ethyl acetate 7:3 the photolactone 5 (79 mg, 56 %, based on consumed starting material) was obtained and was crystallized from acetone-n-hexane, m.p. 207-211°C (dec.); $[\alpha]_D^{22}$ +92.0° (c 0.3); IR (nujol): $\nu_{max}$ 900, 1245, 1730, 1740, 1775, 3430 $cm^{-1}$; IR (carbon tetrachloride, 2 mmol/l): $\nu_{max}$ 3475 $cm^{-1}$; $^1H$ and $^{13}C$ NMR see Table 1 and 2; FDMS: m/z 509$(M+Na)^+$, 487$(M+H)^+$, 486 ($M^+$); MS (negative ionization): m/z 545($M^-$-1+AcOH, 46), 486($M^-$, 65), 485($M^-$-1, 71), 441(40), 382(100), 354(86), 321(82), 278(95); EIMS: m/z 455.1698 ($C_{25}H_{27}O_8$ requires m/z 455.1706, $M^+-CH_3O$, 44), 444, 1808 ($C_{24}H_{28}O_8$ requires m/z 444.1784, $M^+-CH_2CO$, 28), 426(43), 412,1530 ($C_{23}H_{24}O_7$ requires m/z 412.1522, $M^+-CH_3COHCH_2O$); 396(29), 384(13), 322(49), 280(48), 238(88), 220(100); Calc. for $C_{26}H_{30}O_9$: C, 64.18; H, 6.22. Found: C, 63.98; H, 6.30.

### Triacetyl derivative 6

A solution of photolactone 5 (24 mg, 0.05 mmol) in a mixture of dry acetic anhydride (0.1 ml) and pyridine (0.2 ml) was left at room temperature for 24 hours. Removal of the solvent under reduced pressure gave a residue which was purified on a short silica gel column. Upon elution with benzene the triacetyl derivative 6 (24 mg, 92 %) was obtained and was crystallized from acetone-n-hexane, m.p. 134-136°C; $[\alpha]_D$ +79.3° (c 0.792); IR (chloroform): $\nu_{max}$ 895, 1245, 1735, 1777 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): 6.37, d, H(1), $J_{1,2}$ = 9.4; 5.87, dd, H(2), $J_{1,2}$ = 9.4, $J_{2,3}$ = 3.7; 5.42, d, H(3), $J_{2,3}$ = 3.7; 3.21, d, H(5), $J_{5,6}$ = 7.8; 2.80, d, H(6), $J_{5,6}$ = 7.8; 2.62, s (broad), H(15$\beta$); 5.29, d, H(17), $J_{15\beta,17}$ = 1.6; 5.32, d, H(17'), $J_{15\beta,17'}$ = 2.2; 4.52, d, H(1'a), $J_{1'a,1'b}$ = -12.4; 4.21, d, H(1'b), $J_{1'a,1'b}$ = -12.4; 1.40 and 1.60, 2x s, $H_3$(3'), $H_3$(18); 2.02, 2.03 and 2.11, 3x s, 3x $H_3$ (OAc). MS (positive ions): m/z 528($M^+$, 2), 486(2), 468(3), 455(10), 426(8), 364(30), 320(22), 304(41), 280(52), 260(51), 238(100), 220(73); MS (negative ions): m/z 528($M^-$, 40), 484(11), 364(100), 304(32).

### X-ray analysis of 4

For data collection a plate-shaped crystal of 4 (approximate dimensions 0.1x0.4x 0.5 mm) crystallized from acetone-n-hexane has been used. Crystal data: $C_{26}H_{30}O_9$, orthorhombic, a = 9.771(7), b = 13.640(8), c = 18.872(12) Å, Z = 4, $D_{calc}$ = 1.277 $gcm^{-3}$, space group $P2_12_12_1$, m.p. 187-188°C. The intensities of 2524 reflections were measured up to $\Theta = 25^{\circ}$ on a four-circle diffractometer CAD 4 with graphitemonochromated $MoK_{\alpha}$ radiation. 1716 reflections with $I > 3\sigma(I)$ were used for X-ray analysis. Corrections for Lorentz and polarization effects but not for absorption were applied.

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