# $^{1}H$ and $^{13}C$ NMR Experiments and Chemical Shifts Calculations on Gossypol: a Compound Extracted from Cottonseeds

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***Abstract:*** *Gossypol is a yellow compound naturally occurring as a symmetrical binaphthyl dialdehyde, and is isolated from cottonseeds. It has been extensively studied because of its numerous important applications such as oral male contraceptive, antimalarial drug and potential drug for HIV infection. In this work we report the results of some $^{1}H$ and $^{13}C$ NMR experiments and chemical shift calculations on the gossypol geometry optimised structure. The $^{1}H$ and $^{13}C$ NMR measurements were carried out at a Bruker AMX 400 spectrometer using $CDCl_3$ as solvent and TMS as the internal standard. The NMR experiments were the normal 1D $^{1}H$ and $^{13}C$ spectra and DEPT, and 2D COSY, HSQC, ROESY, NOESY and HMBC measurements. A full geometry optimisation was carried out on gossypol, using the Hartree-Fock method with STO-3G basis set, without any symmetry constraints. It was performed with the program Chem 3D, part of the Chem Office package from CambridgeSoft.Com.. The NMR chemical shift calculations were done using the Gaussian 98 program. The Hartree-Fock method, with STO-3G, 6-21G and 6-31+G basis sets, without any polarization function was applied. All calculations were performed in the gas phase. Attempts to calculate the shifts using the Hartree-Fock (HF) and the Density Functional (B3LYP) methods, with a large basis set (6-311G) failed, probably due to computer hardware limitations. Good agreement between experimental and reference data, and the calculated results was achieved, except for the O**H***-7 proton, possibly due to its involvement in H-bonding. Evidence for the H-bonds is shown in the COSY spectrum.*

Gossypol, 2,2'-bis(8-formyl-1,6,7-trihydroxy-5-isopropyl-3-methylnaphtha-lene) is a yellow compound naturally occurring as a symmetrical binaphthyl dialdehyde (disesquiterpene) isolated from cottonseeds.[1] This compound has been extensively studied because of its numerous important applications including use as oral male contraceptive,[2] antimalarial drug[3] and as a potential drug for HIV infection[4]. In this work we report results of some $^{1}H$ and $^{13}C$ NMR experiments and chemical shift calculations on the gossypol geometry optimised structure.

The $^{1}H$ and $^{13}C$ NMR spectra were measured at 400.13 MHz and 100.61 MHz, respectively, on a Bruker AMX 400 spectrometer. $CDCl_3$ was used as solvent and TMS as internal standard. A full geometry optimisation was carried out on gossypol, using the Hartree-Fock method with STO-3G basis set,[5] without any symmetry constraints. It was performed with the program Chem 3D, part of the Chem Office package from CambridgeSoft.Com**.** The NMR chemical shift calculations were done using the Gaussian 98 program. The Hartree-Fock (HF) method, with the STO-3G, 6-21G and 6-31+G basis sets,

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without any polarization function was applied and the results are shown in table 1. All calculations were performed in the gas phase. Attempts to calculate the shifts using the HF and Density Functional (B3LYP) methods with a large basis set (6-311G) failed, probably due to computer hardware limitations.

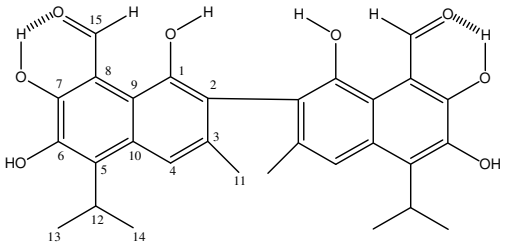

**Figure 1.** The gossypol structure showing the possible intramolecular H-bonds

Good agreement between experimental and reference data, and the calculated results was achieved (see table 1), except for the O**H**-7 proton, possibly due to its involvement in H-bonding (see Figure 1). Such H-bonding would explain the low field shifts for this OH proton. Evidence for the H-bonding is the observation of a scalar coupling correlation between O**H**-7 and **H**-15 in the COSY spectrum.

**Table 1.** Experimental and calculated $^{1}H$ and $^{13}C$ chemical shifts for gossypol

| Atom | RHF/STO-3G | RHF/3-21G | RHF/6-31+G | Literature values[6,7] | Our values |
|---|---|---|---|---|---|
| H1 | 3.49 | 5.69 | 4.75 | 5.80 | 5.80 |
| H4 | 8.01 | 8.41 | 8.25 | 7.80 | 7.80 |
| H6 | 3.21 | 4.44 | 5.90 | 6.35 | 6.40 |
| H7 | 9.07 | 10.86 | 11.38 | 15.10 | 15.00 |
| H11 | 1.96 | 2.73 | 2.08 | 2.12 | 2.18 |
| H12 | 2.58 | 3.11 | 3.50 | 3.80 | 3.90 |
| H13, H14 | 1.40 | 2.12 | 2.34 | 1.48 | 1.55 |
| H15 | 12.72 | 12.91 | 13.60 | 10.50 | 11.10 |
| C1 | 144.19 | 149.19 | 159.87 | 149.9 | 150.4 |
| C2 | 114.16 | 108.46 | 118.31 | 115.4 | 115.8 |
| C3 | 128.55 | 128.25 | 139.73 | 133.1 | 133.7 |
| C4 | 119.04 | 115.32 | 126.28 | 117.6 | 118.2 |
| C5 | 124.18 | 124.44 | 136.51 | 133.1 | 134.7 |
| C6 | 138.37 | 141.03 | 150.02 | 142.9 | 143.5 |
| C7 | 144.46 | 151.47 | 161.71 | 155.6 | 156.1 |
| C8 | 117.82 | 116.04 | 127.75 | 111.2 | 111.8 |
| C9 | 121.89 | 117.85 | 129.19 | 114.1 | 114.7 |
| C10 | 128.73 | 125.60 | 137.32 | 129.2 | 129.7 |
| C11 | 30.02 | 24.58 | 27.86 | 27.4 | 19.7 |
| C12 | 37.11 | 27.67 | 23.90 | 27.4 | 27.9 |
| C13, C14 | 26.73 | 22.42 | 25.91 | 19.8 | 20.5 |
| C15 | 164.24 | 194.41 | 215.11 | 198.2 | 199.3 |

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