Supplementary Material (ESI) for Green Chemistry


# A green protocol for palladium-catalysed Suzuki-Miyaura cross-coupling.

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## Supplementary Information

## INDEX

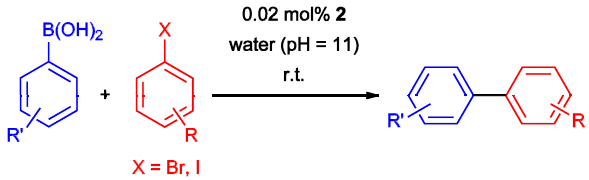
## 1. Procedures

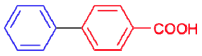
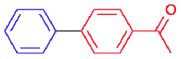
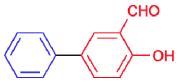
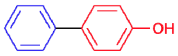
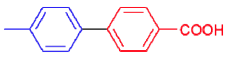
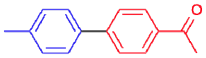
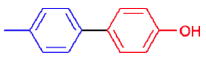
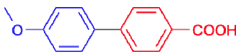
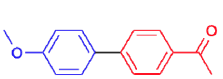
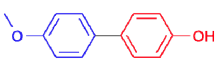
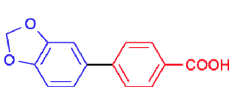
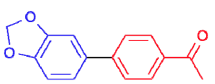
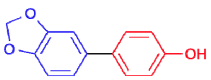
Crystallization of **4** *[Pd(μ-Cl)(P(Ph)$_2$OH(P(Ph)$_2$O]$_2$*

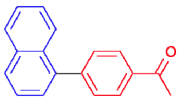
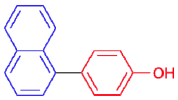
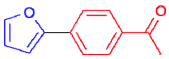
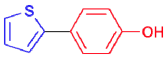
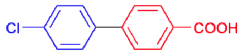
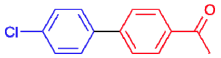
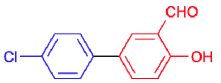
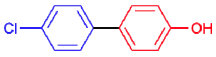
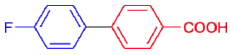
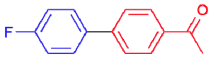
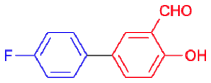
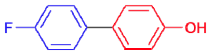
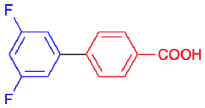
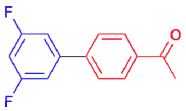
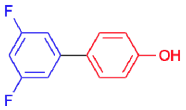
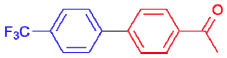
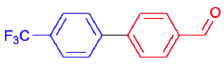
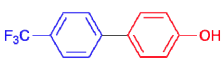
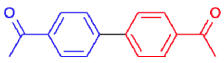
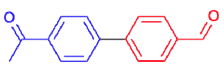
Crystals suitable for single-crystal X-ray analysis of complex **3** were grown in a solution of dichloromethane and aqueous ethanol at room temperature over several weeks according to a published procedure.[1]

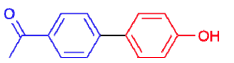
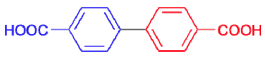
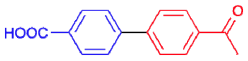
**2. Cross coupling products** were analysed for purity by GC-MS, $^1$H-NMR and elemental analysis. Analytical data correspond to the reported literature values. For respective literature, see table S1.

**Table S1** Suzuki cross-coupling products




| Entry | Product [a)] | Literature |
|---|---|---|
| 1 |  | G. M. Scheuermann, L. Rumi, P. Steurer, W. Bannwarth, R. Mülhaupt, *J. Am. Chem. Soc.* **2009**, *131*, 8262–8270. |
| 2 |  | J. K. Cho, R. Najman, T. W. Dean, O. Ichihara, C. Müller, M. Bradley, *J. Am. Chem. Soc.* **2006**, *128*, 6276–6277. |
| 3 |  | G. A. Morris and S.B. T. Nguyen, *Tetrahedron Letters* **2001**, *42*, 2093-2096. |
| 4 |  | R. Huang, K. H. Saughnessy, *Organometallics*, **2006**, *25*, 5105-4112. |
| 5 |  | P. Liu, W. Zhang, R. He, *Appl. Organometal. Chem.*, **2009**, *23*, 135-139. |
| 6 |  | J. K. Cho, R. Najman, T. W. Dean, O. Ichihara, C. Müller, M. Bradley, *J. Am. Chem. Soc.* **2006**, *128*, 6276–6277. |
| 7 |  | Haga, N.; Takayanagi, H. *J. Org. Chem.* **1996**, *61*, 735. |
| 8 |  | G. M. Scheuermann, L. Rumi, P. Steurer, W. Bannwarth, R. Mülhaupt, *J. Am. Chem. Soc.* **2009**, *131*, 8262–8270 |
| 9 |  | NMR $\delta_H$ (399.8 MHz, $CDCl_3$, r.t., [ppm]): 8.00 (2H, d, $^3J_{(H,H)}$ = 8.5 Hz), 7.65 (2H, d, $^3J_{(H,H)}$ = 8.5 Hz), 7.58 (2H, d, $^3J_{(H,H)}$ = 9.0 Hz), 7.00 (2H, d, $^3J_{(H,H)}$ = 8.5 Hz), 3.86 (3H, s), 2.61 (s, 3H). |
| 10 |  | G. M. Scheuermann, L. Rumi, P. Steurer, W. Bannwarth, R. Mülhaupt, *J. Am. Chem. Soc.* **2009**, *131*, 8262–8270. |
| 11 |  | NMR $\delta_H$ (399.8 MHz, $CDCl_3$, r.t., [ppm]): 12.99 (1H, s(br)), 7.96 (2H, d, $^3J_{(H,H)}$ = 8.3 Hz), 7.73 (2H, $^3J_{(H,H)}$ = 8.3 Hz), 7.33 (1H, s), 7.23 (1H, d, $^3J_{(H,H)}$ = 7.9 Hz), 7.03 (1H, d, $^3J_{(H,H)}$ = 8.3 Hz), 6.11 (2H, s). |
| 12 |  | K. M. Dawood, A. Kirschning, *Tetrahedron* **2005**, *61*, 12121-12130. |
| 13 |  | NMR $\delta_H$ (399.8 MHz, $CDCl_3$, r.t., [ppm]): 9.50 (1H, s(br)), 7.39 (2H, d, $^3J_{(H,H)}$ = 8.7 Hz), 7.13 (1H, s), 7.02 (1H, d, $^3J_{(H,H)}$ = 7.9 Hz), 6.92 (1H, d, $^3J_{(H,H)}$ = 8.3 Hz), |

| | | |
|---|---|---|
| | | 6.81 (2H, d, $^3J_{(H,H)}$ = 8.7 Hz), 6.02 (2H, s). |
| 14 |  | B. Inés, R. San Martin, F. Churruca, E. Domínguez, M. K. Urtiaga, M. I. Arriortura, *Organometallics* **2008**, *27*, 2833-2839. |
| 15 |  | N. A. Bumafin, D. A. Tsarev, *Tetrahedron Lett.* **1998**, *39*, 8155-8158. |
| 16 |  | A. Ohta, Y. Akita, T. Ohkuwa, M. Chiba, R. Fukunaga, A. Miyafuji, T. Nakata, N. Tani, Y. Aoyagi, *Heterocycles* **1990**, *31*, 1951. |
| 18 |  | M. P. Capparelli, R. E. DeSchepper, J. S. Swenton *J. Org. Chem.* **1987**, *52*, 4953-4961. |
| 19 |  | T. Kylmälä, N. Kuuloja, Y. Xu, K. Rissanen, R. Franzén, *Eur. J. Org. Chem.* **2008**, *23*, 4019-4024. |
| 20 |  | T. Kylmälä, N. Kuuloja, Y. Xu, K. Rissanen, R. Franzén, *Eur. J. Org. Chem.* **2008**, *23*, 4019-4024. |
| 21 |  | M. Braun, A. Hahn, M. Engelmann, R. Fleischer, W. Frank, C. Kryschi, S. Haremza, K. Kürschner, R. Parker, *Chem. Eur. J.* **2005**, *11*, 3405-3412. |
| 22 |  | R. J. Edsall, Jr., H. A. Harris, E. S. Manas, R. E. Mewshaw, *Bioorg. Med. Chem.* **2003**, *11*, 3457-3474. |
| 23 |  | S. L. Adamski-Werner, S. K. Palaninathan, J. C. Sacchettinin, J. W. Kelly, *J. Med. Chem*. **2004**, *47*, 355-374 |
| 24 |  | P. Liu, W. Zhang, R. He, *Appl. Organometal. Chem*., **2009**, *23*, 135-139. |
| 25 |  | W. L. Fitch, P. W. Berry, Y. Tu, A. Tabatabaei, L. Lowrie, F. Lopez-Tapia, Y. Liu, D. Nitzan, M. R. Masjedizadeh, A. Varadarajan, *Drug Metabolism and Disposition*, **2004**, *32*, 1482-1490. |
| 26 |  | S. L. Adamski-Werner, S. K. Palaninathan, J. C. Sacchettinin, J. W. Kelly, *J. Med. Chem***. 2004**, *47*, 355-374 |
| 27 |  | S. L. Adamski-Werner, S. K. Palaninathan, J. C. Sacchettinin, J. W. Kelly, *J. Med. Chem*. **2004**, *47*, 355-374 |
| 28 |  | F. Churruca, R. San Martin, B. Inés, I. Tellitu, E. Domínguez, *Adv. Synth. Catal.* **2006**, *348*, 1836-1840. |
| 29 |  | S. L. Adamski-Werner, S. K. Palaninathan, J. C. Sacchettinin, J. W. Kelly, *J. Med. Chem*. **2004**, *47*, 355-374 |
| 30 |  | NMR $\delta_H$ (399.8 MHz, $CDCl_3$, r.t., [ppm]): 8.06 (2H, d, $^3J_{(H,H)}$ = 8.4 Hz), 7.73 (s, 4H), 7.69 (2H, $^3J_{(H,H)}$ = 8.3 Hz), 2.66 (s, 3H). |
| 31 |  | NMR $\delta_H$ (399.8 MHz, DMSO-*d6*, r.t., [ppm]): 10.08 (1H, s), 8.04 (2H, d, $^3J_{(H,H)}$ = 6.8 Hz), 7.99-7.90 (4H, m), 7.87 (2H, d, $^3J_{(H,H)}$ = 8.4 Hz). |
| 32 |  | NMR $\delta_H$ (399.8 MHz, $CDCl_3$, r.t., [ppm]): 7.66 (2H, d, $^3J_{(H,H)}$ = 8.7 Hz), 7.63 (2H, $^3J_{(H,H)}$ = 8.6 Hz), 7.50 (2H, $^3J_{(H,H)}$ = 8.6 Hz), 6.94 (2H, $^3J_{(H,H)}$ = 8.6 Hz), 5.22 (s(br), 1H). |
| 33 |  | NMR $\delta_H$ (399.8 MHz, $CDCl_3$, r.t., [ppm]): 8.06 (4H, d, $^3J_{(H,H)}$ = 5.5 Hz), 7.73 (4H, $^3J_{(H,H)}$ = 5.6 Hz), 2.66 (s, 3H). |
| 34 |  | NMR $\delta_H$ (399.8 MHz, $CDCl_3$, r.t., [ppm]): 8.07 (2H, d, $^3J_{(H,H)}$ = 5.6 Hz), 7.98 (2H, $^3J_{(H,H)}$ = 5.4 Hz), 7.79 (2H, $^3J_{(H,H)}$ = 5.4 Hz), 7.74 (2H, $^3J_{(H,H)}$ = 5.5 Hz), 2.68 (s, 3H). |

| | | |
|---|---|---|
| 35 |  | NMR $\delta_H$ (399.8 MHz, DMSO-*d6*, r.t., [ppm]): 7.96 (2H, d, $^3J_{(H,H)}$ = 5.8 Hz), 7.72 (2H, $^3J_{(H,H)}$ = 5.7 Hz), 7.56 (2H, $^3J_{(H,H)}$ = 5.8 Hz), 6.84 (2H, $^3J_{(H,H)}$ = 5.8 Hz), 2.58 (s, 3H), 3.44 (s(br), 1H). |
| 36 |  | NMR $\delta_H$ (399.8 MHz, $CDCl_3$, r.t., [ppm]): 13.03 (2H, s(br)), 8.05 (4H, d, $^3J_{(H,H)}$ = 8.7 Hz), 7.86 (4H, $^3J_{(H,H)}$ = 8.3 Hz). |
| 37 |  | M. E. Sigman, T. Autrey, G. B. Schuster *J. Am. Chem. Soc.* **1988**, *110*, 4297-4305. |

Reaction conditions: 2 mmol (1 eq.) 4-bromophenol, 1.0 equiv. boronic acid, 20 ml buffer (1.0 M, $NaOH/NaHCO_3$, pH = 11), air, cat. (0.02 mol% palladacycle **2**). Reaction times not optimized

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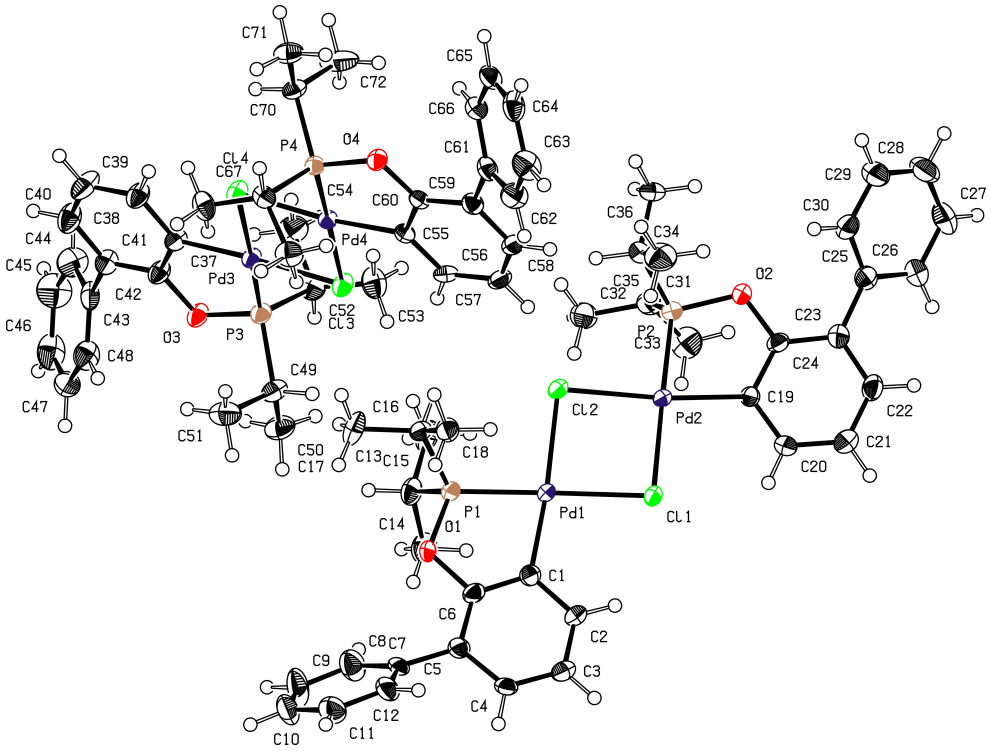
## 2. Crystal structure determination

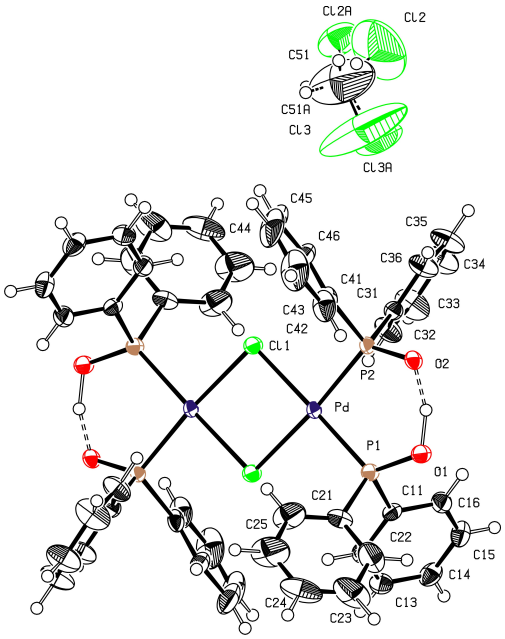
### Compound 2




| | |
|---|---|
| Operator: | *** Herdtweck *** |
| Molecular Formula: | $C_{36}\ H_{44}\ Cl_2\ O_2\ P_2\ Pd_2$ |
| Crystal Color / Shape | Colourless prism |
| Crystal Size | Approximate size of crystal fragment used for data collection: 0.10 × 0.18 × 0.36 mm |
| Molecular Weight: | 854.35 a.m.u. |
| $F_{000}$: | 3456 |
| Systematic Absences: | 00l: l≠4n |
| Space Group: | Tetragonal $P\,4_3$ (I.T.-No.: 78) |
| Cell Constants: | Least-squares refinement of 9794 reflections with the programs "APEX suite" and "SAINT" [2,3]; theta range 1.16° < $\theta$ < 25.32°; Mo($K\overline{\alpha}$); $l$ = 71.073 pm |
| | $a$ = 1760.26(6) pm |
| | $b$ = 1760.26(6) pm |
| | $c$ = 2374.70(9) pm |
| | $V$ = 7358.0(5)· $10^6$ $pm^3$; $Z$ = 8; $D_{calc}$ = 1.543 g $cm^{-3}$; Mos. = 0.74 |

| | |
|---|---|
| Diffractometer: | Kappa APEX II (Area Diffraction System; BRUKER AXS); rotating anode; graphite monochromator; 50 kV; 40 mA; l = 71.073 pm; Mo(K$\overline{\alpha}$) |
| Temperature: | (-150±1) °C; (123±1) K |
| Measurement Range: | 1.16° < $\theta$ < 25.32°; h: -18/17, k: -21/21, l: -28/28 |
| Measurement Time: | 2 × 5 s per film |
| Measurement Mode: | measured: 8 runs; 4676 films / scaled: 8 runs; 4676 films<br>$\varphi$– and $\omega$–movement; Increment: $\Delta\varphi/\Delta\omega$ = 0.50°; dx = 45.0 mm |
| LP - Correction: | Yes [3] |
| Intensity Correction | No/Yes; during scaling [3] |
| Absorption Correction: | Multi-scan; during scaling; $\mu$ = 1.240 mm$^{-1}$ [3]<br>Correction Factors: $T_{min}$ = 0.6644 $T_{max}$ = 0.7767 |
| Reflection Data: | 244559 reflections were integrated and scaled<br>305 reflections systematic absent and rejected<br>244254 reflections to be merged<br>13395 independent reflections<br>0.039 $R_{int}$: (basis $F_o^2$)<br>13395 independent reflections (all) were used in refinements<br>13028 independent reflections with $I_o > 2\sigma(I_o)$<br>99.7 % completeness of the data set<br>810 parameter full-matrix refinement<br>16.5 reflections per parameter |
| Solution: | Direct Methods [4]; Difference Fourier syntheses |
| Refinement Parameters: | In the asymmetric unit:<br>88 Non-hydrogen atoms with anisotropic displacement parameters |
| Hydrogen Atoms: | In the difference map(s) calculated from the model containing all non-hydrogen atoms, not all of the hydrogen positions could be determined from the highest peaks. For this reason, the hydrogen atoms were placed in calculated positions ($d_{C-H}$ = 95, 98, 100 pm). Isotropic displacement parameters were calculated from the parent carbon atom ($U_H$ = 1.2/1.5 $U_C$). The hydrogen atoms were included in the structure factor calculations but not refined. |
| Atomic Form Factors: | For neutral atoms and anomalous dispersion [5] |
| Extinction Correction: | no |
| Weighting Scheme: | $w^{-1} = \sigma^2(F_o^2)+(a*P)^2+b*P$<br>with a: 0.0315; b: 12.4448; P: [Maximum(0 or $F_o^2$)+2$*F_c^2$]/3 |
| Shift/Err: | Less than 0.001 in the last cycle of refinement: |
| Resid. Electron Density: | +1.72 $e_{0;}^-$/Å$^3$; -0.58 $e_{0;}^-$/Å$^3$ |
| R1: | $\Sigma(\|\|F_o\|-\|F_c\|\|)/\Sigma\|F_o\|$ |
| [$F_o > 4\sigma(F_o)$; N=13028]: | = 0.0273 |
| [all reflctns; N=13395]: | = 0.0287 |
| wR2: | $[\Sigma w(F_o^2-F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$ |
| [$F_o > 4\sigma(F_o)$; N=13028]: | = 0.0688 |
| [all reflctns; N=13395]: | = 0.0701 |
| Goodness of fit: | $[\Sigma w(F_o^2-F_c^2)^2/(NO-NV)]^{1/2}$ = 1.071 |
| Flack's Parameter : | $x$ = 0.368(16) |
| Remarks: | Refinement expression $\Sigma w(F_o^2-F_c^2)^2$<br>Twin refinement (twin operation: inversion) |
| Programs: | The program system "WinGX32" [8] with the programs: "PLATON" [7], "SHELXL-97" [6], "SIR92" [4] |

# Compound 3·2($CH_2Cl_2$)




| | |
|---|---|
| Operator: | *** Herdtweck *** |
| Molecular Formula: | $C_{50}\ H_{46}\ Cl_6\ O_4\ P_4\ Pd_2$<br>$C_{48}\ H_{42}\ Cl_2\ O_4\ P_4\ Pd_2,\ 2(C\ H_2\ Cl_2)$ |
| Crystal Color / Shape | Yellow plate |
| Crystal Size | Approximate size of crystal fragment used for data collection: 0.13 × 0.46 × 0.56 mm |
| Molecular Weight: | 1260.25 a.m.u. |
| $F_{000}$: | 1264 |
| Systematic Absences: | h0l: l≠2n; 0k0: k≠2n |
| Space Group: | Monoclinic $P\ 2_1/c$ (I.T.-No.: 14) |
| Cell Constants: | Least-squares refinement of 43743 reflections with the program "CRYSALIS" [2a]; theta range 2.77° < $\theta$ < 32.68°; Mo($K\alpha$); $l$ = 71.073 pm |
| | $a$ = 854.69(1) pm |
| | $b$ = 1517.43(2) pm $b$ = 100.4792(11)° |
| | $c$ = 2065.43(2) pm |
| | $V$ = 2634.04(5)· $10^6$ $pm^3$; $Z$ = 2; $D_{calc}$ = 1.589 g $cm^{-3}$ |
| Diffractometer: | Xcalibur™3; $k$-CCD (Area Diffraction System; OXFORD DIFFRACTIONS); sealed tube, graphite monochromator; 50 kV; 30 mA; l = 71.073 pm; Mo($K\alpha$) |
| Temperature: | (-120±1) °C; (153±1) K |
| Measurement Range: | 2.77° < $\theta$ < 25.35°; h: -10/10, k: -18/18, l: -24/24 |
| Measurement Time: | 20 s per film |
| Measurement Mode: | measured: 9 sets; 1192 films / scaled: 9 sets; 1192 films<br>$j$ and $w$movement; Increment: $Dj/Dw$ = 1.00°; dx = 50.0 mm |
| LP - Correction: | Yes [1a] |
| Intensity Correction: | No/Yes; during scaling [2a] |
| Absorption Correction: | No/Yes; during scaling; $m$ = 1.151 $mm^{-1}$ [2a] |
| | Correction Factors: $T_{min}$ = 0.5928 $T_{max}$ = 1.0000 |
| Reflection Data: | 73490 reflections were integrated |
| | 1123 reflections systematic absent and rejected |
| | 24281 reflections rejected (resolution limits 99.00 Å to 0.83 Å) |
| | 48086 reflections to be merged |
| | 0.019 $R_{int}$: (basis $F_o^2$) |
| | 4816 independent reflections (all) were used in refinements |
| | 4263 independent reflections with $I_o > 2s(I_o)$ |
| | 99.9 % completeness of the data set |
| | 322 parameter full-matrix refinement |

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|---|---|
| | 15.0 reflections per parameter |
| Solution: | Direct Methods [4]; Difference Fourier syntheses |
| Refinement Parameters: | In the asymmetric unit:<br>35 Non-hydrogen atoms with anisotropic displacement parameters<br>1 Hydrogen atoms with isotropic displacement parameters |
| Hydrogen Atoms: | The O-H atom positions was found in the difference map. The hydrogen position was refined with an individual isotropic displacement parameter. All other hydrogen atoms were placed in calculated positions ($d_{C-H}$ = 95, 99 pm). Isotropic displacement parameters were calculated from the parent carbon atom ($U_H$ = 1.2 $U_C$). The hydrogen atoms were included in the structure factor calculations but not refined. |
| Atomic Form Factors: | For neutral atoms and anomalous dispersion [5] |
| Extinction Correction: | $F_c$ (korr) = k$F_c$[1+ 0.001· $e$· $F_c^2$· $l^3$/sin(2$Q$)]$^{-1/4}$ SHELXL-97 [6]<br>$e$refined to $e$= 0.0023(2) |
| Weighting Scheme: | $w^{-1} = s^2(F_o^2)+(a*P)^2+b*P$<br>with a: 0.0209; b: 8.5912; P: [Maximum(0 or $F_o^2$)+2∗$F_c^2$]/3 |
| Shift/Err: | Less than 0.001 in the last cycle of refinement: |
| Resid. Electron Density: | +0.80 $e_{0;}^-$/Å$^3$; -0.90 $e_{0;}^-$/Å$^3$ |
| R1: | $S(\|\|F_o\|-\|F_c\|\|)/S\|F_o\|$ |
| [$F_o$ > 4$s$($F_o$); N=4263]: | = 0.0320 |
| [all reflctns; N=4816]: | = 0.0393 |
| wR2: | $[Sw(F_o^2-F_c^2)^2/Sw(F_o^2)^2]^{1/2}$ |
| [$F_o$ > 4$s$($F_o$); N=4263]: | = 0.0707 |
| [all reflctns; N=4816]: | = 0.0773 |
| Goodness of fit: | $[Sw(F_o^2-F_c^2)^2/(NO-NV)]^{1/2}$ = 1.084 |
| Remarks: | Refinement expression $Sw(F_o^2-F_c^2)^2$ |
| Programs: | The program system "WinGX32" [8] with the programs: "PLATON" [7], "SHELXL-97" [6], "SIR92" [4] |

## 4. References

[1] A. J. Carty, S. E. Jacobson, R. T. Simpson, N. J. Taylor, *J. Am. Chem. Soc.*, 1975, **97**, 7254-7262.

[2] APEX suite of crystallographic software. APEX 2 Version 2008.4. Bruker AXS Inc., Madison, Wisconsin, USA (2008).

[2a] CrysAlis Data Collection Software and Data Processing Software for Oxford Xcalibur diffractometer, Version 1.171, Oxford Diffraction Ltd., Oxfordshire, United Kingdom, 2005.

[3] SAINT, Version 7.56a and SADABS Version 2008/1. Bruker AXS Inc., Madison, Wisconsin, USA (2008).

[4] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, M. Camalli "**SIR92**", *J. Appl. Cryst.* 1994, **27**, 435-436.

[5] International Tables for Crystallography, Vol. C, Tables 6.1.1.4 (pp. 500-502), 4.2.6.8 (pp. 219-222), and 4.2.4.2 (pp. 193-199), A. J. C. Wilson, Ed., Kluwer Academic Publishers, Dordrecht, The Netherlands, 1992.

[6] G. M. Sheldrick, "**SHELXL-97**", University of Göttingen, Göttingen, Germany, (1998).

[7] A. L. Spek, "**PLATON**", A Multipurpose Crystallographic Tool, Utrecht University, Utrecht, The Netherlands, (2010).

[8] L. J. Farrugia, "**WinGX** (Version 1.70.01 January 2005) ", *J. Appl. Cryst.* 1999, **32**, 837-838.