Supporting Information

for

Three-component reaction of 3-(diethoxyphosphoryl)coumarin, enolizable ketones and primary amines: Simple, stereoselective synthesis of benzo[1,3]oxazocine skeletons

Dariusz Deredas,[a] Łukasz Albrecht,[a] Waldemar Maniukiewicz,[b] Jakub Wojciechowski,[b] Wojciech M. Wolf,[b] Piotr Paluch[a,c] Tomasz Janecki,[a] Marek Różalski[d] Urszula Krajewska,[d] Anna Janecka,[e] and Henryk Krawczyk*[a]

[a] *Institute of Organic Chemistry, Technical University (Politechnika), Żeromskiego 116, 90-924 Łódź, Poland. Fax: +48(42)636 55 30; E-mail: henkrawc@p.lodz.pl*

[b] *Institute of General and Ecological Chemistry, Technical University (Politechnika), Żeromskiego 116, 90-924 Łódź, Poland.*

[c] *Centre of Molecular and Macromolecular Sciences, Polish Academy of Sciences, Sienkiewicza 112, 90-363 Łódź, Poland.*

[d] *Department of Pharmaceutical Biochemistry, Medical University of Łódź, Muszyńskiego 1, 90-151 Łódź, Poland*

[e] *Department of Biomolecular Chemistry, Medical University of Łódź, Mazowiecka 6/8, 92-215 Łódź, Poland*

Crystal structure determination of diethyl[(2S*,5S*,6S*)-3-benzyl-2-methyl-4-oxo-3,4,5,6-tetrahydro-2H-2,6-methanobenzo[g][1,3]oxazocin-5-yl]phosphonate 17. $C_{23}H_{28}NO_5P$. M_w= 429.43. Colourless single crystal 0.60 x 0.50 x 0.40 mm was grown from acetone n-hexane 1:1 mixture. Monoclinic, a= 9.1840(10), b= 18.429(2), c= 13.3004(15) Å, β= 94.728(2)°, V= 2243.5(4), $P2_1/c$, Z= 4, ρ_{calc}= 1.27 g cm^{-3}, μ= 0.156 mm^{-1}, $F(000)$= 912, semi-empirical absorption correction based on multiple scanned equivalent reflections (0.881 < T < 0.943), graphite monochromated Mo Kα radiation, λ= 0.71073 Å, T= 291 K, ω scans, 24377 reflections collected, $2\theta_{max}$= 50°, 3928 unique reflections (h= ±10, k= +21, l= +15), R_{int}= 0.030, 343 refined parameters, refinement on F^2, final R= 0.050 for all 3428 observed reflections [F_o > 4$\sigma(F_o)$], R_{all}= 0.057, $wR_{all}(F^2)$= 0.150, S= 1.03, $shift_{max}/su$= 0.02, $shift_{mean}/su$= 0.00, residual electron density $\Delta\rho_{max}$= 0.30 $\Delta\rho_{min}$= -0.31 e Å^{-3}. Hydrogen atoms were treated by a mixture of independent and contrained refinement. The C22 and C23 atoms of single ethoxy substitent are

disordered over two partially occupied positions, the higher occupied sites were refined with occupation factor 0.676(9). X-ray data were collected with Bruker SMART APEX II diffractometer. Computer programs used: data collection: *APEX2* [1], data reduction: *SAINT-Plus* [2], absorption collection: *SADABS* [3], structure solution, refinement and molecular graphics: *SHELXTL* [4], CCDC reference number 912211.

Crystal structure determination of diethyl [(3aR*,9R*,9aR*,10R*)-12-benzyl-11-oxo-2,3,9,9a-tetrahydro-1H-3a,9-(epiminoethano)cyclopenta[b]chromen-10-yl]phosphonate 19. $C_{25}H_{30}NO_5P$. M_w= 455.47. Colourless single crystal 0.40 x 0.30 x 0.20 mm was grown from diethyl ether solution. Triclinic, a= 10.2612(1), b= 11.1638(1), c= 11.3877(1) Å, α= 88.850(1), β= 70.398(1) γ= 70.439(1)°, V= 1151.71(2), P-1, Z= 2, ρ_{calc}= 1.31 g cm^{-3}, μ= 1.361 mm^{-1}, F(000)= 484, semi-empirical absorption correction based on multiple scanned equivalent reflections (0.658 < T < 0.754), graphite monochromated Cu Kα radiation, λ= 1.54178 Å, T= 293 K, ω scans, 24135 reflections collected, $2\theta_{max}$= 136°, 4032 unique reflections (h= ±12, k= ±13, l= ±13), R_{int}= 0.030, 292 refined parameters, refinement on F^2, final R= 0.040 for all 3997 observed reflections [$F_o > 4\sigma(F_o)$], R_{all}= 0.040, $wR_{all}(F^2)$= 0.109, S= 1.05, $shift_{max}/su$= 0.01, $shift_{mean}/su$= 0.00, residual electron density $\Delta\rho_{max}$= 0.42 $\Delta\rho_{min}$= -0.31 e Å^{-3}. Hydrogen atoms refined as riding on their parent atoms. X-ray data were collected with Bruker SMART APEX II diffractometer. Computer programs used: data collection: *APEX2* [1], data reduction: *SAINT-Plus* [2], absorption collection: *SADABS* [3], structure solution, refinement and molecular graphics: *SHELXTL* [4], CCDC reference number 912212.

Crystal structure determination of diethyl ((4aR*,9R*,9aR*,11R*)-13-benzyl-12-oxo-1,2,3,4,9,9a-hexahydro-4a,9-(epiminoethano)xanthen-11-yl)phosphonate 23. $C_{26}H_{32}NO_5P$. M_w= 469.50. Colourless single crystal 0.50 x 0.30 x 0.20 mm was grown from diethyl ether solution. Triclinic, a= 10.3639(19), b= 11.350(2), c= 11.563(2) Å, α= 87.909(5), β= 70.260(5) γ= 69.399(5)°, V= 1193.1(4), P-1, Z= 2, ρ_{calc}= 1.31 g cm^{-3}, μ= 1.330 mm^{-1}, F(000)= 500, semi-empirical absorption correction based on multiple scanned equivalent reflections (0.651 < T < 0.766), graphite monochromated Cu Kα radiation, λ= 1.54178 Å, T= 291 K, ω scans, 23765 reflections collected, $2\theta_{max}$= 136°, 4157 unique reflections (h= ±12, k= ±13, l= ±13), R_{int}= 0.049, 300 refined parameters, refinement on F^2, final R= 0.060 for all 4022 observed reflections

[$F_o > 4\sigma(F_o)$], R_{all}= 0.060, $wR_{all}(F^2)$= 0.175, S= 1.05, $shift_{max}/su$= 0.00, $shift_{mean}/su$= 0.00, residual electron density $\Delta\rho_{max}$= 0.57 $\Delta\rho_{min}$= -0.34 e Å^{-3}. Hydrogen atoms refined as riding on their parent atoms. X-ray data were collected with Bruker SMART APEX II diffractometer. Computer programs used: data collection: *APEX2* [1], data reduction: *SAINT-Plus* [2], absorption collection: *SADABS* [3], structure solution, refinement and molecular graphics: *SHELXTL* [4], CCDC reference number 912213.

Crystal structure determination of diethyl[(3R*,4R*,4aR*))-1-benzyl-4-(2-hydroxyphenyl)-2-oxo-1,2,3,4,4a,5,6,7-octahydroquinolin-3-yl]phosphonate 26. $C_{26}H_{32}NO_5P$. M_w= 469.50. Colourless single crystal 0.40 x 0.30 x 0.20 mm was grown from diethyl ether solution. Monoclinic, a= 12.4626(1), b= 8.2350(1), c= 12.6582(1) Å, β= 114.56(1)°, V= 1181.57(10), $P2_1$, Z= 2, ρ_{calc}= 1.32 g cm^{-3}, μ= 1.342 mm^{-1}, $F(000)$= 500, semi-empirical absorption correction based on multiple scanned equivalent reflections (0.648 < T < 0.874), graphite monochromated Cu Kα radiation, λ= 1.54178 Å, T= 100 K, ω scans, 12993 reflections collected, $2\theta_{max}$= 136°, 2299 unique reflections (h= ±14, k= ±9, l= ±14), R_{int}= 0.050, 305 refined parameters, refinement on F^2, final R= 0.042 for all 2299 observed reflections [$F_o > 4\sigma(F_o)$], R_{all}= 0.042, $wR_{all}(F^2)$= 0.118, S= 1.05, $shift_{max}/su$= 0.00, $shift_{mean}/su$= 0.00, residual electron density $\Delta\rho_{max}$= 0.47 $\Delta\rho_{min}$= -0.45 e Å^{-3}. Hydrogen atoms refined as riding on their parent atoms. X-ray data were collected with Bruker SMART APEX II diffractometer. Computer programs used: data collection: *APEX2* [1], data reduction: *SAINT-Plus* [2], absorption collection: *SADABS* [3], structure solution, refinement and molecular graphics: *SHELXTL* [4], CCDC reference number 912214.

Crystal structure determination of (3aS,9S,9aS)-10-methylene-12-[(R)-1-phenylethyl]-2,3,9,9a-tetrahydro-1H-3a,9-(epiminoethano)cyclopenta[b]chromen-11-one 33. $C_{23}H_{23}NO_2$. M_w= 345.43. Colourless single crystal 0.30 x 0.30 x 0.10 mm was grown from diethyl ether solution. Triclinic, a= 9.2805(1), b= 12.9476(1), c= 16.1252(2) Å, α= 99.392(1), β= 91.714(1) γ= 90.912(1)°,, V= 1910.35(4), $P1$, Z= 1, ρ_{calc}= 1.26 g cm^{-3}, μ= 0.635 mm^{-1}, $F(000)$= 778, semi-empirical absorption correction based on multiple scanned equivalent reflections (0.832 < T < 0.939), graphite monochromated Cu Kα radiation, λ= 1.54178 Å, T= 100 K, ω scans, 62988

reflections collected, $2\theta_{max}$= 136°, 12999 unique reflections (h= ±11, k= ±15, l= ±19), R_{int}= 0.023, 989 refined parameters, refinement on F^2, final R= 0.026 for all 12996 observed reflections [$F_o > 4\sigma(F_o)$], R_{all}= 0.026, $wR_{all}(F^2)$= 0.076, S= 1.05, $shift_{max}/su$= 0.00, $shift_{mean}/su$= 0.00, residual electron density $\Delta\rho_{max}$= 0.18 $\Delta\rho_{min}$= -0.13 e Å^{-3}. Flack parameter η= -0.070(7) [5]. Hydrogen atoms refined as riding on their parent atoms. Unit cell contains four symmetrically independent molecules of **33** augmented by a single cocrystalized diethyl ether moiety. X-ray data were collected with Bruker SMART APEX II diffractometer. Computer programs used: data collection: *APEX2* [1], data reduction: *SAINT-Plus* [2], absorption collection: *SADABS* [3], structure solution, refinement and molecular graphics: *SHELXTL* [4], CCDC reference number 912215.

Crystal structure determination of (3aR,9R,9aR)-10-methylene-12-[(S)-1-phenylethyl]-2,3,9,9a-tetrahydro-1H-3a,9-(epiminoethano)cyclopenta[b]chromen-11-one 38. $C_{23}H_{23}NO_2$. M_w= 345.43. Colourless single crystal 0.30 x 0.20 x 0.10 mm was grown from diethyl ether solution. Triclinic, a= 9.3543(1), b= 13.0737(2), c= 16.3819(2) Å, α= 99.063(1), β= 91.667(1) γ= 90.832(1)°, V= 1977.21(4), $P1$, Z= 1, ρ_{calc}= 1.22 g cm^{-3}, μ= 0.613 mm^{-1}, $F(000)$= 778, semi-empirical absorption correction based on multiple scanned equivalent reflections (0.861 < T < 0.941), graphite monochromated Cu Kα radiation, λ= 1.54178 Å, T= 291 K, ω scans, 35037 reflections collected, $2\theta_{max}$= 140°, 14073 unique reflections (h= ±11, k= ±15, l= ±20), R_{int}= 0.019, 989 refined parameters, refinement on F^2, final R= 0.036 for all 13950 observed reflections [$F_o > 4\sigma(F_o)$], R_{all}= 0.036, $wR_{all}(F^2)$= 0.107, S= 1.06, $shift_{max}/su$= 0.04, $shift_{mean}/su$= 0.00, residual electron density $\Delta\rho_{max}$= 0.17 $\Delta\rho_{min}$= -0.26 e Å^{-3}. Flack parameter η= 0.080(10) [5]. Hydrogen atoms refined as riding on their parent atoms. Unit cell contains four symmetrically independent molecules of **38** augmented by a single cocrystalized diethyl ether moiety. X-ray data were collected with Bruker SMART APEX II diffractometer. Computer programs used: data collection: *APEX2* [1], data reduction: *SAINT-Plus* [2], absorption collection: *SADABS* [3], structure solution, refinement and molecular graphics: *SHELXTL* [4], CCDC reference number 912216.

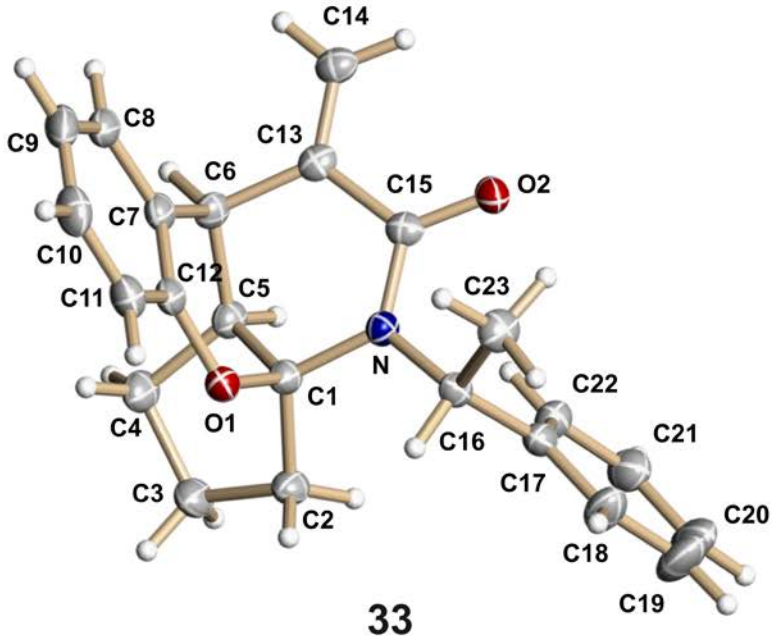
Crystal structure determination of diethyl [(3R,4R)-4-(2-hydroxyphenyl)-2-oxo-1-[(R)-1-phenylethyl)-1,2,3,4,5,6,7,8-octahydroquinolin-3-yl]phosphonate 43. $C_{27}H_{34}NO_5P$. M_w= 483.54. Colourless single crystal 0.40 x 0.30 x 0.20 mm was grown from benzene and n-heptane 3:1 mixture. Monoclinic, *a*= 15.3327(12), *b*= 9.0849(7), *c*= 19.0305(15) Å, β= 101.416(3)°, *V*= 2598.4(4), *P*1, *Z*= 2, ρ_{calc}= 1.24 g cm^{-3}, μ= 1.235 mm^{-1}, *F*(000)= 1032, semi-empirical absorption correction based on multiple scanned equivalent reflections (0.671 < *T* < 0.784), graphite monochromated Cu Kα radiation, λ= 1.54178 Å, *T*= 291 K, ω scans, 29553 reflections collected, $2\theta_{max}$= 136°, 9210 unique reflections (*h*= ±17, *k*= ±10, *l*= ±22), R_{int}= 0.032, 681 refined parameters, refinement on F^2, final *R*= 0.042 for all 9034 observed reflections [$F_o > 4\sigma(F_o)$], R_{all}= 0.043, $wR_{all}(F^2)$= 0.118, *S*= 1.03, $shift_{max}/su$= 0.00, $shift_{mean}/su$= 0.00, residual electron density $\Delta\rho_{max}$= 0.36 $\Delta\rho_{min}$= -0.21 e Å^{-3}. Flack parameter η= 0.010(14) [5]. Hydrogen atoms refined as riding on their parent atoms. Asymmetric unit contains two symmetrically independent molecules of **43**. The C27- C28 and C52 - C53 atom pairs of two ethoxy substitents are disordered over two partially occupied positions. The higher occupied sites were refined with occupation factor 0.54(2) and 0.550(8), respectively. X-ray data were collected with Bruker SMART APEX II diffractometer. Computer programs used: data collection: *APEX2* [1], data reduction: *SAINT-Plus* [2], absorption collection: *SADABS* [3], structure solution, refinement and molecular graphics: *SHELXTL* [4], CCDC reference number 912217.

Crystal structure determination of diethyl [(3S,4S)-4-(2-hydroxyphenyl)-2-oxo-1-[(S)-1-phenylethyl)-1,2,3,4,5,6,7,8-octahydroquinolin-3-yl]phosphonate 44. $C_{27}H_{34}NO_5P$. M_w= 483.54. Colourless single crystal 0.40 x 0.30 x 0.20 mm was grown from benzene and n-heptane 3:1 mixture. Monoclinic, *a*= 15.3297(2), *b*= 9.0879(1), *c*= 19.0093(3) Å, β= 101.437(1)°, *V*= 2595.69(6), *P*1, *Z*= 2, ρ_{calc}= 1.24 g cm^{-3}, μ= 1.236 mm^{-1}, *F*(000)= 1032, semi-empirical absorption correction based on multiple scanned equivalent reflections (0.643 < *T* < 0.793), graphite monochromated Cu Kα radiation, λ= 1.54178 Å, *T*= 291 K, ω scans, 29421 reflections collected, $2\theta_{max}$= 136°, 8887 unique reflections (*h*= ±18, *k*= ±10, *l*= ±21), R_{int}= 0.021, 681 refined parameters, refinement on F^2, final *R*= 0.034 for all 8719 observed reflections [$F_o > 4\sigma(F_o)$], R_{all}= 0.035, $wR_{all}(F^2)$= 0.096, *S*= 1.03, $shift_{max}/su$= 0.00, $shift_{mean}/su$= 0.00, residual electron density $\Delta\rho_{max}$= 0.35 $\Delta\rho_{min}$= -0.19 e Å^{-3}. Flack parameter η= 0.002(13) [5]. Hydrogen atoms refined as riding on their parent atoms. Asymmetric unit contains two symmetrically

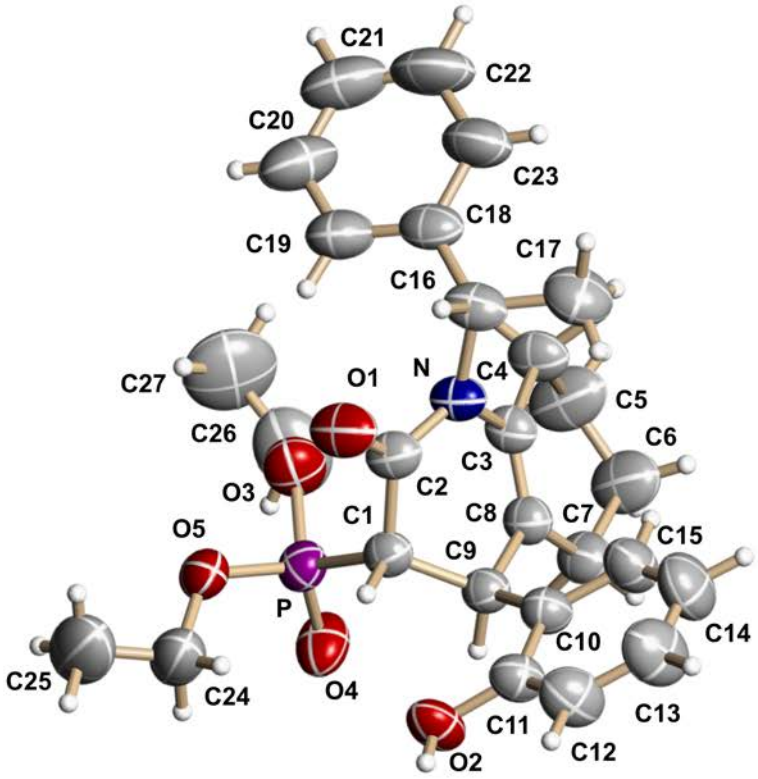
independent molecules of **44**. The C27- C28 and C52 - C53 atom pairs of two ethoxy substitents are disordered over two partially occupied positions. The higher occupied sites were refined with occupation factor 0.535(18) and 0.632(6), respectively. X-ray data were collected with Bruker SMART APEX II diffractometer. Computer programs used: data collection: *APEX2* [1], data reduction: *SAINT-Plus* [2], absorption collection: *SADABS* [3], structure solution, refinement and molecular graphics: *SHELXTL* [4], CCDC reference number 912218.

References:

1. *APEX2, Version 2010/3*, Bruker AXS Inc.,Madison,Wisconsin, 2010.
2. *SAINT-Plus, Version 7.68A*, Bruker AXS Inc., Madison, Wisconsin, 2009.
3. *SADABS – Bruker Nonius area detector scaling and absorption correction, Version 2008/1*, Bruker AXS Inc., Madison, Wisconsin, 2008.
4. G. M. Sheldrick, *SHELXTL, Version 2008/4*, Bruker AXS Inc.,Madison, Wisconsin, 2008.
5. H.D. Flack *Acta Crystallogr., Sect. A*, 1983, **39**, 876 - 881.



33



44

Fig. S1. Crystal structures of methylenelactam **33** and enamide **44**. Displacement ellipsoids are drawn at the 50% probability level.