



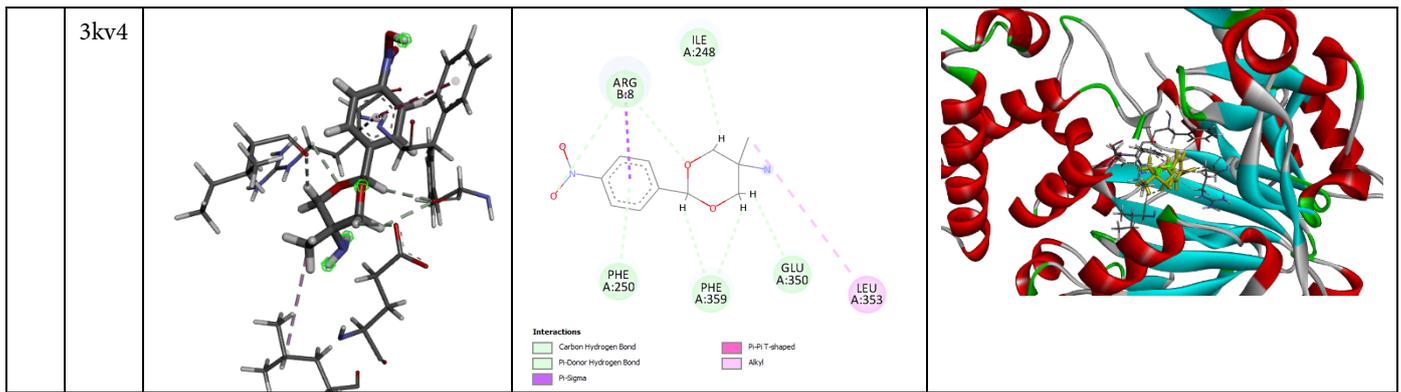
Innovative Piperidine-Catalyzation in Protecting Carbonyl Compounds with Implications for Angiogenesis and Inflammation

Mukhlif Mohsin Slaihimi^{1*}, Luay Ali Dhahi², and Abeer Hussein Ali³

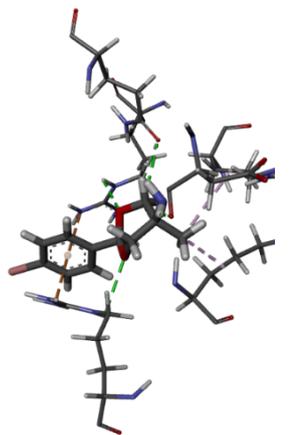
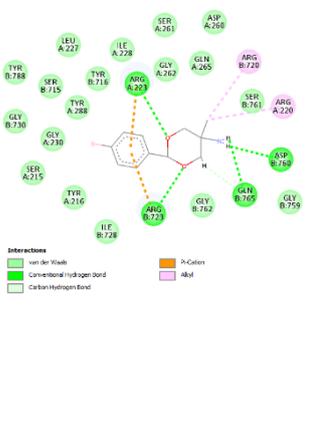
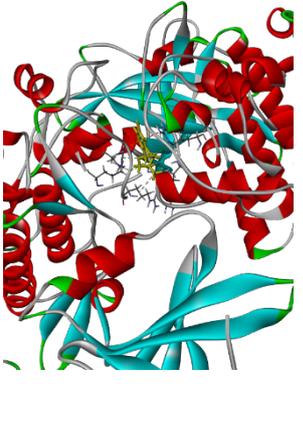
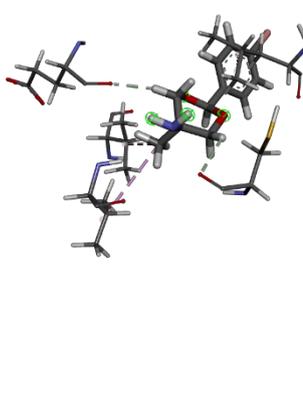
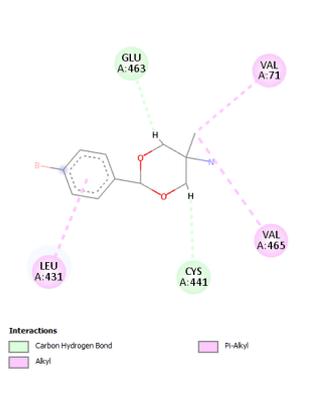
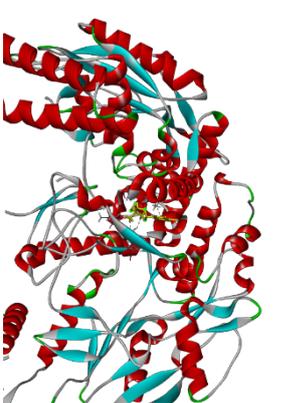
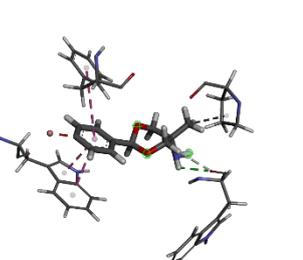
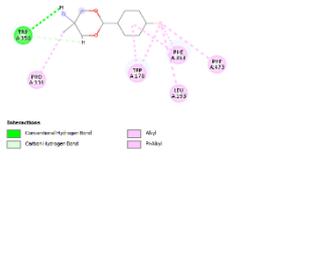
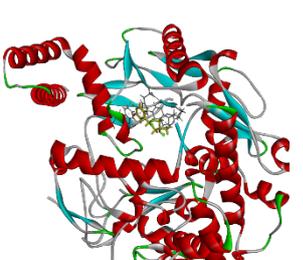
Supplementary Data

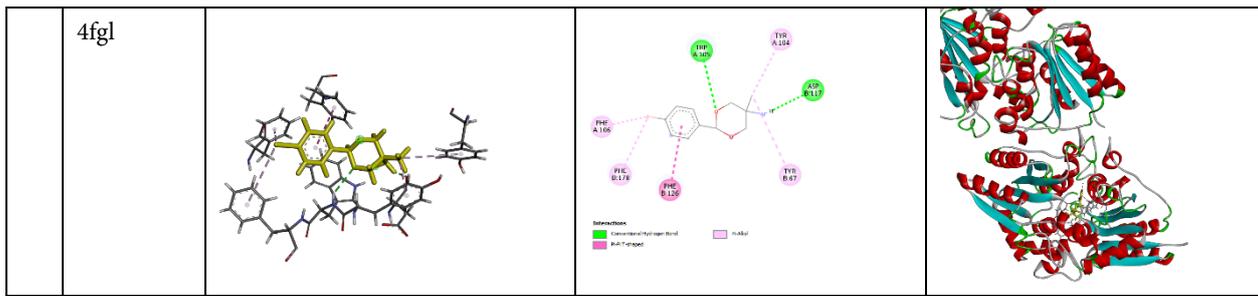
Supp Table 1. The top two affinities of A1 and A2 compounds among their predicted targets.

A1	1zkl		<p>Interactions</p> <ul style="list-style-type: none"> Conventional Hydrogen Bond Carbon-Hydrogen Bond Hydrophobic Pi-Pi Stacked Hyd 	
	5i6x		<p>Interactions</p> <ul style="list-style-type: none"> Conventional Hydrogen Bond Carbon-Hydrogen Bond Pi-Pi T-shaped Pi-Alkyl 	
A2	1s1p		<p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Pi-Pi Stacked Pi-Alkyl 	

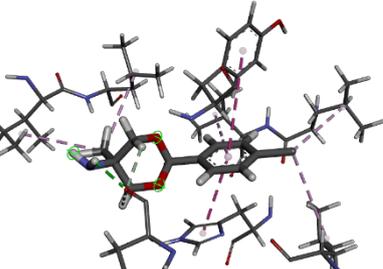
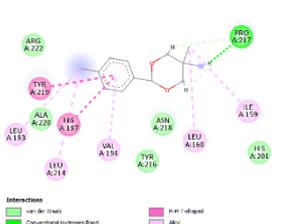
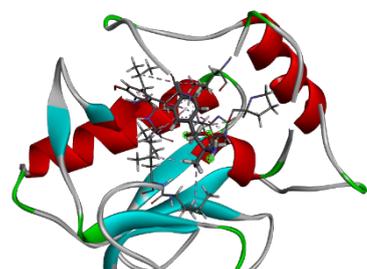
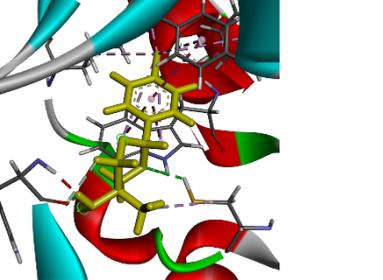
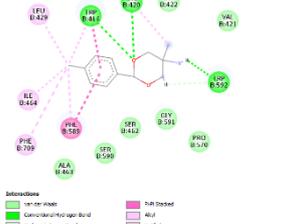
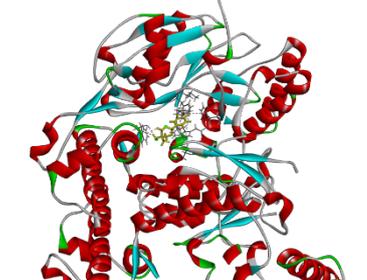
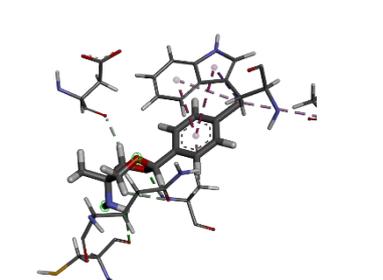
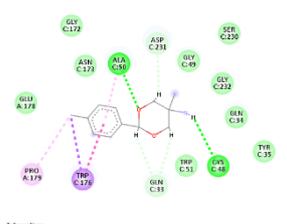
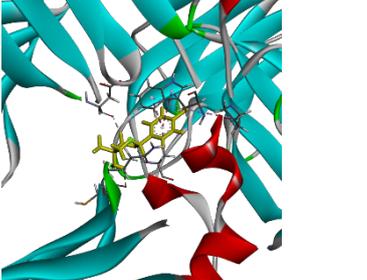
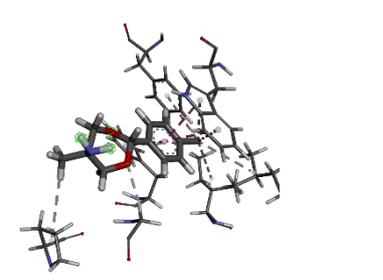
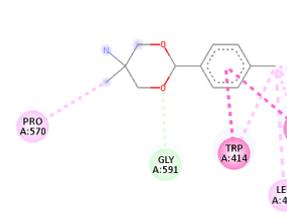
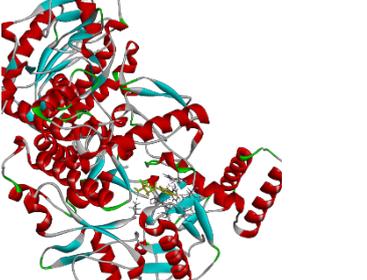


Supp Table 2. The top two affinities of B1 and B2 compounds among their predicted targets.

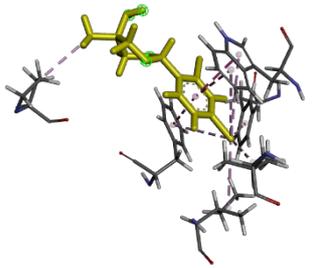
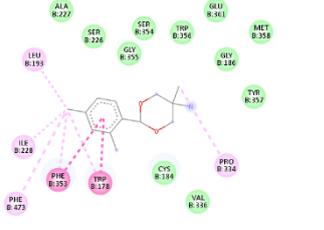
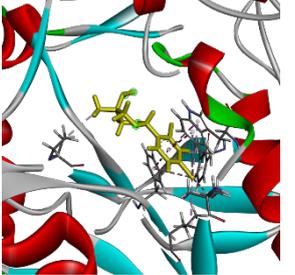
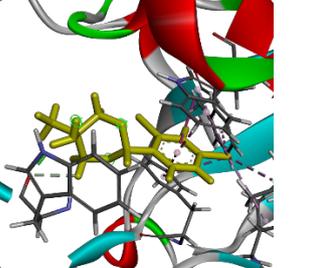
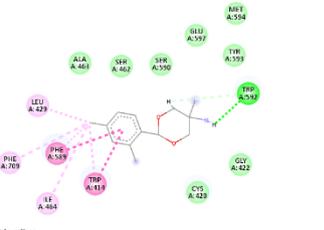
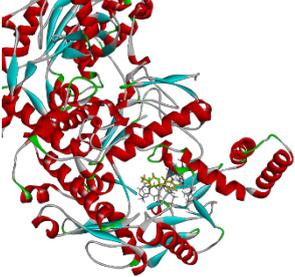
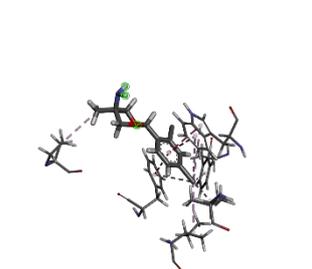
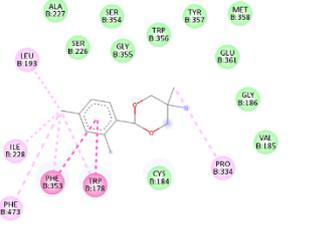
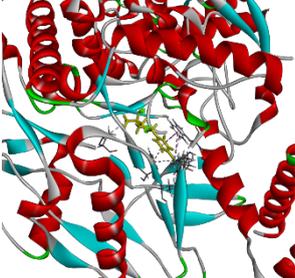
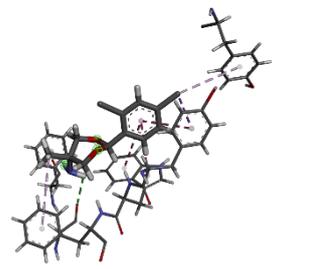
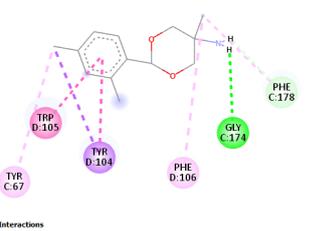
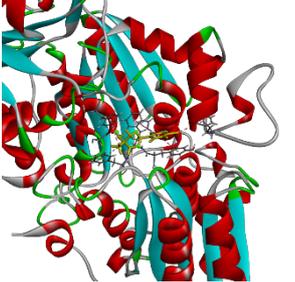
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	4d1p		 <p>Interactions</p> <ul style="list-style-type: none"> Carbon Hydrogen Bond Alkyl Pi-Alkyl 	
B2	4d1p		 <p>Interactions</p> <ul style="list-style-type: none"> Conventional Hydrogen Bond Carbon Hydrogen Bond Alkyl Pi-Alkyl 	



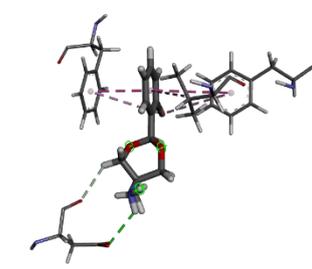
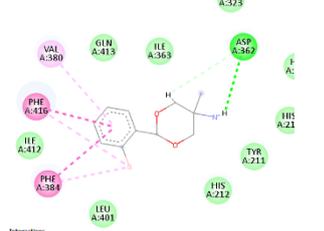
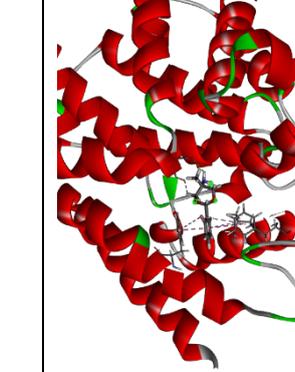
Supp Table 3. The top two affinities of C1 and C2 compounds among their predicted targets.

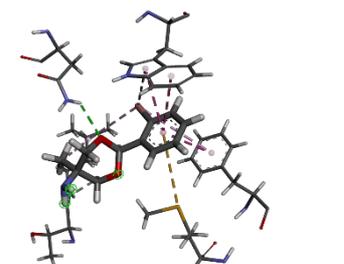
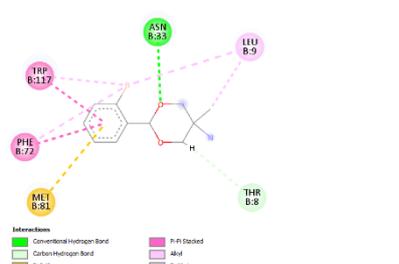
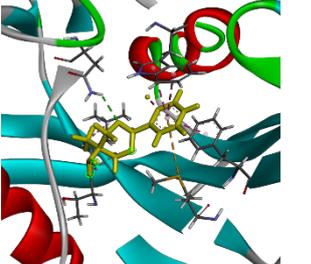
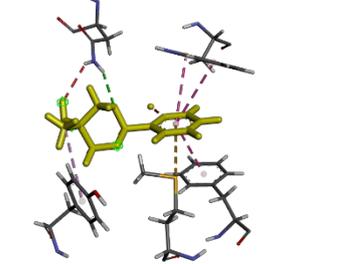
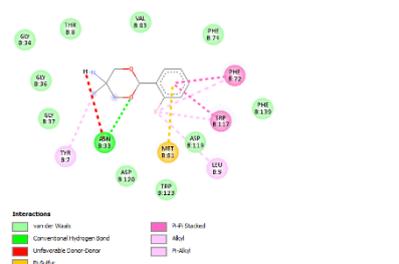
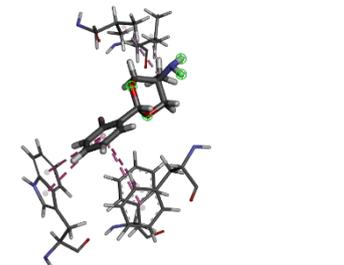
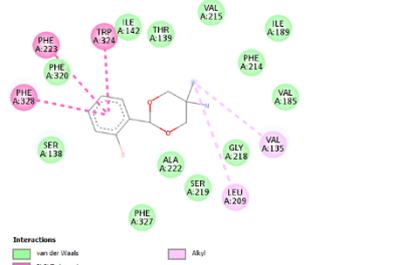
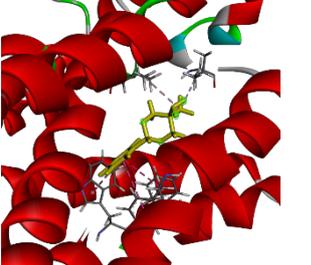
C1	1i76		 <p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon-Hydrogen Bond Hydrophobic Allyl Allyl Allyl 	
	6cid		 <p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon-Hydrogen Bond Hydrophobic Allyl Allyl Allyl 	
C2	6c98		 <p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon-Hydrogen Bond Hydrophobic Allyl Allyl Allyl 	
	6cid		 <p>Interactions</p> <ul style="list-style-type: none"> Carbon Hydrogen Bond Hydrophobic Allyl Allyl 	

Supp Table 4. The top two affinities of D1 and D2 compounds among their predicted targets.

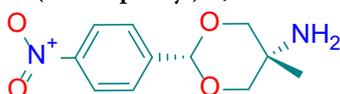
D1	4d1p		 <p>Interactions</p> <ul style="list-style-type: none"> Van der Waals Conventional Hydrogen Bond Pi-Donor Hydrogen Bond Carbon Hydrogen Bond Pi-Pi Stacked Alkyl Pi-Alkyl 	
	6cid		 <p>Interactions</p> <ul style="list-style-type: none"> Van der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond Pi-Pi Stacked Alkyl Pi-Alkyl 	
D2	4d1p		 <p>Interactions</p> <ul style="list-style-type: none"> Van der Waals Conventional Hydrogen Bond Pi-Donor Hydrogen Bond Carbon Hydrogen Bond Pi-Pi Stacked Alkyl Pi-Alkyl 	
	4fgl		 <p>Interactions</p> <ul style="list-style-type: none"> Conventional Hydrogen Bond Pi-Donor Hydrogen Bond Pi-Sigma Pi-Pi Stacked Pi-Pi T-shaped Pi-Alkyl 	

Supp Table 5. The top two affinities of E1 and E2 compounds among their predicted targets.

E1	1zkl		 <p>Interactions</p> <ul style="list-style-type: none"> Van der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond Pi-Pi Stacked Pi-Pi T-shaped Pi-Alkyl 	
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5ws7			
E2			
6bqh			

Cis-5-methyl-2-(4-nitrophenyl)-1, 3-dioxan-5-amine, A1

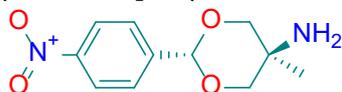


Cis-5-methyl-2-(4-nitrophenyl)-1,3-dioxan-5-amine

¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.16 (s, -CH₃), 3.27 (s, -NH₂), 3.33 (d, *J* = 8.0 Hz, 2H/(-CH₂)_{4,6}), 3.36 (d, *J* = 8.0 Hz, 2H/(-CH₂)_{4,6}), 4.94 (s, -CH), 7.71 (d, *J* = 8.0 Hz, 2H/H_{2,6})_{Ph}, 8.24 (d, *J* = 8.0 Hz, 2H/H_{3,5})_{Ph}.

¹³C-NMR (100 MHz, DMSO-*d*₆) δ 22.68, 65.61, 67.17, 73.41, 91.10, 123.88, 128.16, 147.74, 149.06.

Trans-5-methyl-2-(4-nitrophenyl)-1, 3-dioxan-5-amine, A2



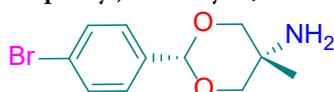
Trans-5-methyl-2-(4-nitrophenyl)-1,3-dioxan-5-amine

¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.08 (s, -CH₃), 3.26 (s, -NH₂), 3.42 (dd*, *J* = 4.0 Hz, 2H/(-CH₂)_{4,6}), 3.81 (dd*, *J* = 4.0 Hz, 2H/(-CH₂)_{4,6}), 5.58 (s, -CH), 7.70 (d, *J* = 8.0 Hz, 2H/H_{2,6})_{Ph}, 8.23 (d, *J* = 8.0 Hz, 2H/H_{3,5})_{Ph}.

*= superimposed signals

¹³C-NMR (100 MHz, DMSO-*d*₆) δ 22.25, 63.85, 65.97, 73.37, 90.50, 123.72, 128.03, 147.62, 148.75.

Cis-2-(4-bromophenyl)-5-methyl-1, 3-dioxan-5-amine, B1

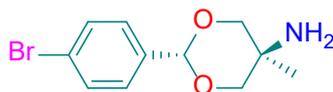


Cis-2-(4-bromophenyl)-5-methyl-1,3-dioxan-5-amine

¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.14 (s, -CH₃), 3.33 (s, -NH₂), 3.35 (d, *J* = 8.0 Hz, 2H/(-CH₂)_{4,6}), 3.37 (d, *J* = 8.0 Hz, 2H/(-CH₂)_{4,6}), 5.43 (s, -CH), 7.44 (d, *J* = 8.0 Hz, 2H/H_{2,6})_{Ph}, 7.46 (d, *J* = 8.0 Hz, 2H/H_{3,5})_{Ph}.

¹³C-NMR (100 MHz, DMSO-*d*₆) δ 22.75, 63.82, 66.24, 73.36, 91.47, 128.62, 128.76, 133.17, 140.22.

Trans-2-(4-bromophenyl)-5-methyl-1, 3-dioxan-5-amine, B2

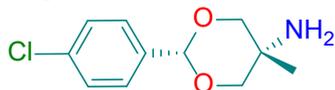


Trans-2-(4-bromophenyl)-5-methyl-1,3-dioxan-5-amine

¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.13 (s, -CH₃), 3.32 (s, -NH₂), 3.40 (dd', *J* = 4.0 Hz, 2H/(-CH₂)_{4,6}), 3.78 (dd', *J* = 4.0 Hz, 1H/(-CH₂)_{4,6}), 5.42 (s, -CH), 7.42 (d, *J* = 8.0 Hz, 2H/H_{2,6})_{Ph}, 7.45 (d, *J* = 8.0 Hz, 2H/H_{3,5})_{Ph}.

¹³C-NMR (100 MHz, DMSO-*d*₆) δ 22.54, 63.80, 65.51, 73.10, 90.87, 128.49, 128.65, 133.01, 140.01.

Cis-2-(4-chlorophenyl)-5-methyl-1,3-dioxan-5-amine, C1

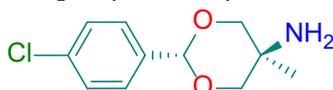


Cis-2-(4-chlorophenyl)-5-methyl-1,3-dioxan-5-amine

¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.15 (s, -CH₃), 3.35 (s, -NH₂), 3.36 (d, *J* = 8.0 Hz, 2H/(-CH₂)_{4,6}), 3.40 (d, *J* = 8.0 Hz, 2H/(-CH₂)_{4,6}), 5.43 (s, -CH), 7.41 (d, *J* = 8.0 Hz, 2H/H_{2,6})_{Ph}, 7.42 (d, *J* = 8.0 Hz, 2H/H_{3,5})_{Ph}.

¹³C-NMR (100 MHz, DMSO-*d*₆) δ 22.76, 63.81, 66.29, 73.41, 91.48, 128.57, 128.69, 133.26, 140.12.

Trans-2-(4-chlorophenyl)-5-methyl-1,3-dioxan-5-amine, C2

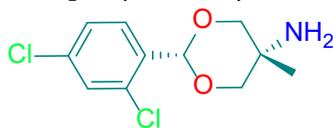


Trans-2-(4-chlorophenyl)-5-methyl-1,3-dioxan-5-amine

¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.14 (s, -CH₃), 3.34 (s, -NH₂), 3.42 (dd', *J* = 4.0 Hz, 2H/(-CH₂)_{4,6}), 3.80 (dd', *J* = 4.0 Hz, 2H/(-CH₂)_{4,6}), 5.43 (s, -CH), 7.39 (d, *J* = 8.0 Hz, 2H/H_{2,6})_{Ph}, 7.40 (d, *J* = 8.0 Hz, 2H/H_{3,5})_{Ph}.

¹³C-NMR (100 MHz, DMSO-*d*₆) δ 22.52, 63.79, 65.45, 73.10, 90.89, 128.49, 128.63, 133.10, 139.88.

Cis-2-(2,4-dichlorophenyl)-5-methyl-1,3-dioxan-5-amine, D1

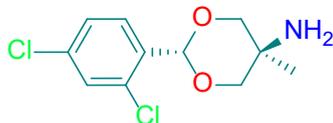


Cis-2-(2,4-dichlorophenyl)-5-methyl-1,3-dioxan-5-amine

¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.17 (s, -CH₃), 3.34 (s, -NH₂), 3.36 (d, *J* = 8.0 Hz, 1H/(-CH₂)_{4,6}), 3.40 (d, *J* = 8.0 Hz, 1H/(-CH₂)_{4,6}), 5.68 (s, -CH), 7.58 (dd, 1H/H₆)_{Ph}, 7.65 (s, 1H/H₃)_{Ph}, 7.67 (d, 1H/H₅)_{Ph}.

¹³C-NMR (100 MHz, DMSO-*d*₆) δ 22.53, 63.83, 66.14, 73.33, 88.81, 127.94, 129.18, 129.95, 133.99, 137.73.

Trans-2-(2,4-dichlorophenyl)-5-methyl-1,3-dioxan-5-amine, D1

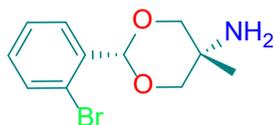


Trans-2-(2,4-dichlorophenyl)-5-methyl-1,3-dioxan-5-amine

¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.15 (s, -CH₃), 3.33 (s, -NH₂), 3.43 (dd', *J* = 4.0 Hz, 2H/(-CH₂)_{4,6}), 4.89 (dd', *J* = 4.0 Hz, 2H/(-CH₂)_{4,6}), 5.67 (s, -CH), 7.57 (dd, 1H/H₆)_{Ph}, 7.64 (s, 1H/H₃)_{Ph}, 7.66 (d, 1H/H₅)_{Ph}.

¹³C-NMR (100 MHz, DMSO-*d*₆) δ 22.15, 63.79, 65.33, 73.19, 88.17, 127.74, 129.07, 129.67, 133.82, 137.49.

Cis-2-(2-bromophenyl)-5-methyl-1,3-dioxan-5-amine, E1



Cis-2-(2-bromophenyl)-5-methyl-1,3-dioxan-5-amine

¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.19 (s, -CH₃), 3.43 (s, -NH₂), 3.34 (d, *J* = 8.0 Hz, 2H/(-CH₂)_{4,6}), 3.38 (d, *J* = 8.0 Hz, 2H/(-CH₂)_{4,6}), 5.64 (s, -CH), 7.26-7.31 (m, 1H/Ar-H)_{Ph}, 7.35-7.41 (m, 1H/Ar-H)_{Ph}, 7.57-7.64 (m, 2H/Ar-H)_{Ph}.

¹³C-NMR (100 MHz, DMSO-*d*₆) δ 22.57, 63.85, 66.03, 73.40, 91.33, 128.22, 128.44, 128.93, 130.75, 132.97, 139.86.

Trans-2-(2-bromophenyl)-5-methyl-1,3-dioxan-5-amine, E2



Trans-2-(2-bromophenyl)-5-methyl-1,3-dioxan-5-amine

¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.14 (s, -CH₃), 3.42 (s, -NH₂), 3.45 (dd[†], *J* = 4.0 Hz, 2H/(-CH₂)_{4,6}), 3.83 (dd[†], *J* = 4.0 Hz, 2H/(-CH₂)_{4,6}), 5.62 (s, -CH), 7.26-7.31 (m, 1H/Ar-H)_{Ph}, 7.35-7.41 (m, 1H/Ar-H)_{Ph}, 7.57-7.64 (m, 2H/Ar-H)_{Ph}.

¹³C-NMR (100 MHz, DMSO-*d*₆) δ 22.31, 63.83, 65.39, 73.12, 90.72, 128.17, 128.34, 128.77, 130.60, 132.89, 139.68.