

Arilsulfatasi A: un nuovo potenziale target per la contraccezione. Progettazione razionale e sintesi chimica di potenziali inibitori.

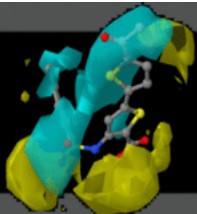


SAPIENZA
UNIVERSITÀ DI ROMA

Facoltà di Farmacia e Medicina
Corso di Laurea in Biotecnologie Farmaceutiche
Tesi Sperimentale in Chimica Farmaceutica
a.a. 2015/2016

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Matricola: 1230095

Relatore: Prof. Rino Ragno
Correlatore: Prof. Gilbert Kirsch



PREMESSA

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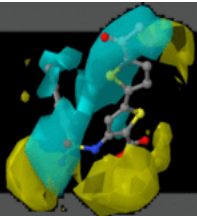


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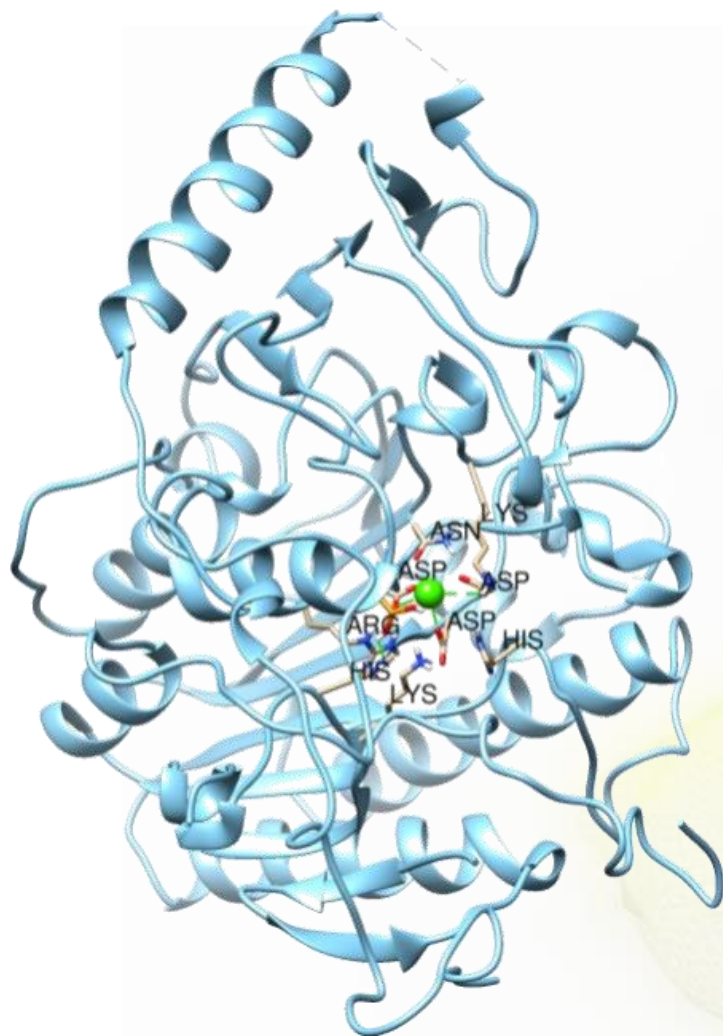
ROME CENTER FOR MOLECULAR DESIGN





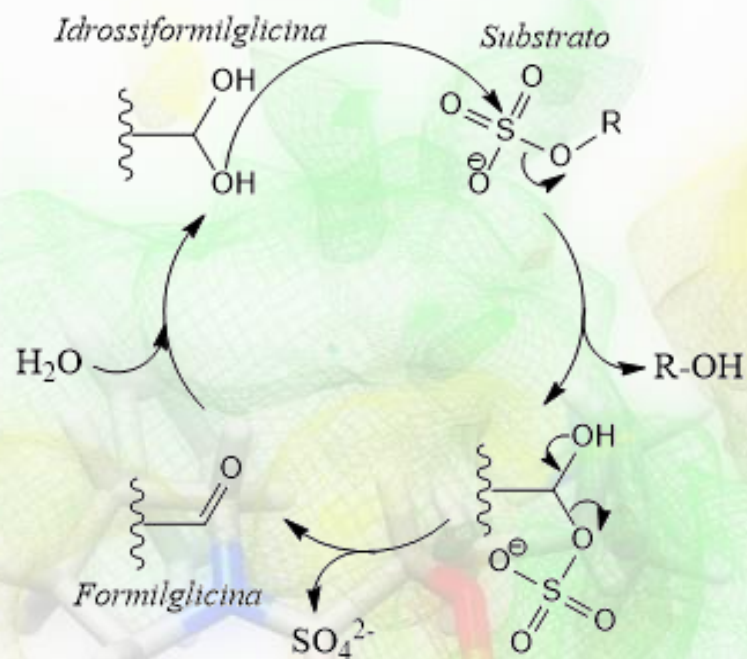
Introduzione : Arilsulfatasi A

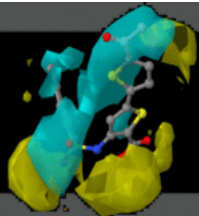
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Codice PDB: 1E33

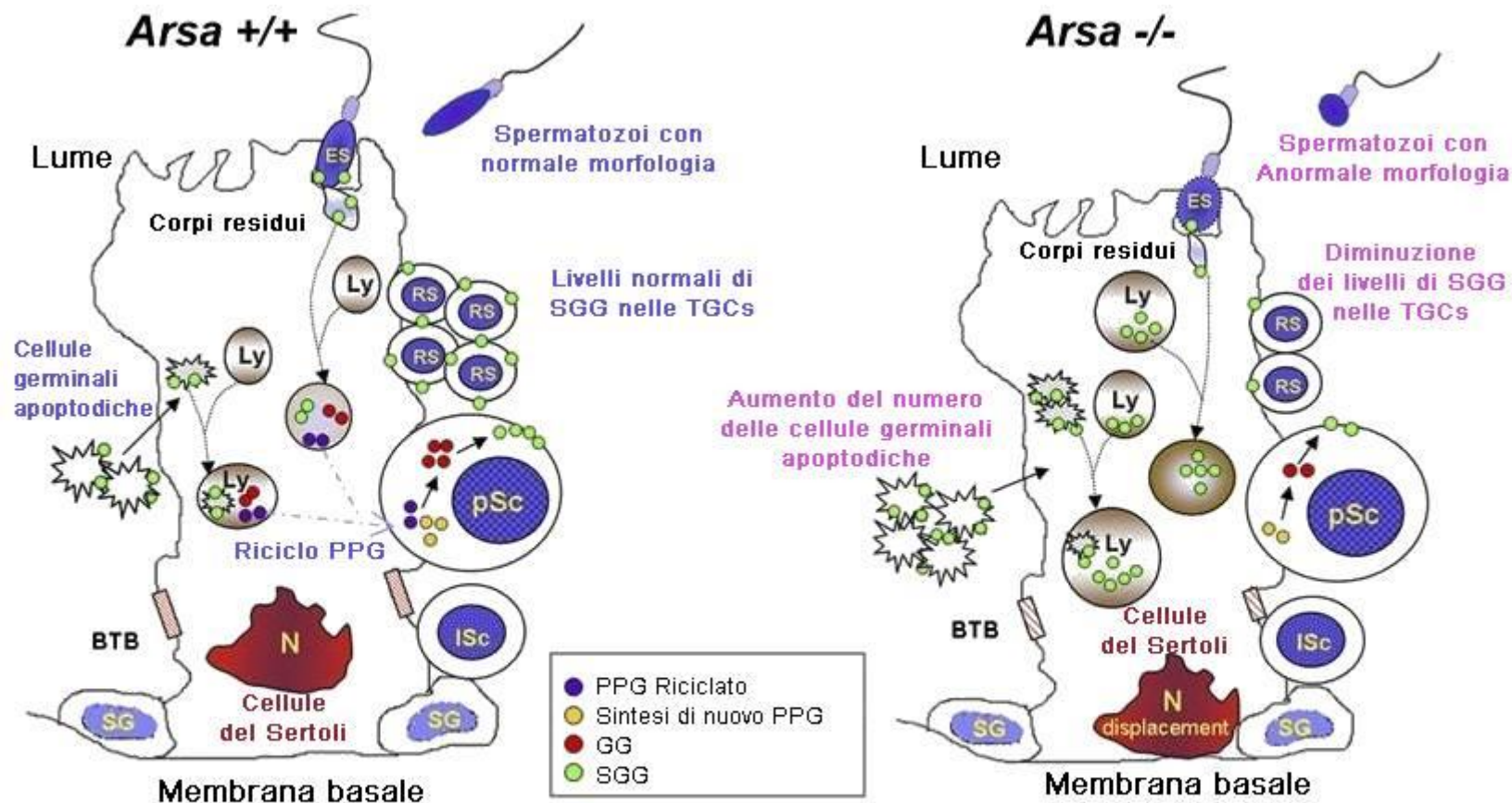
MECCANISMO D'AZIONE





Coinvolgimento nella spermatogenesi

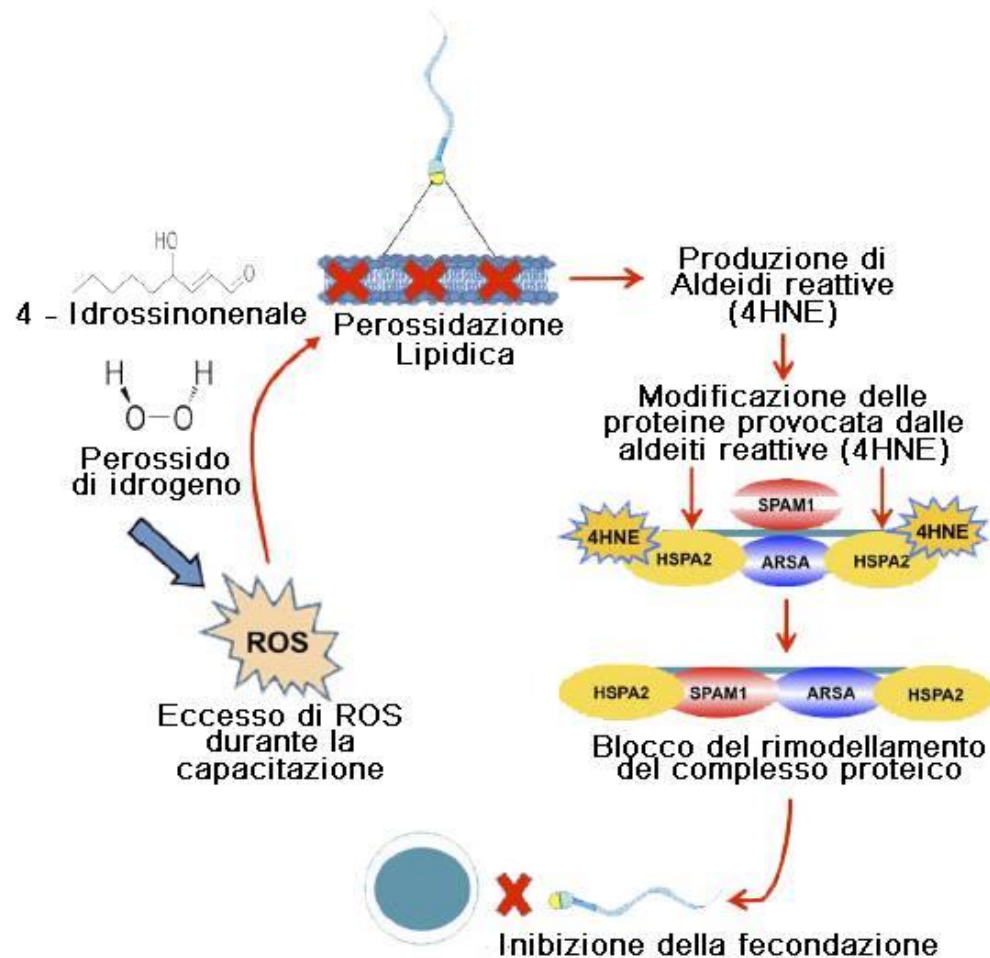
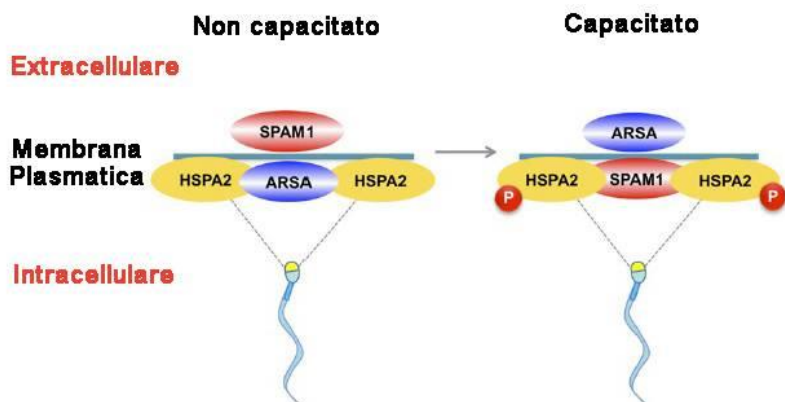
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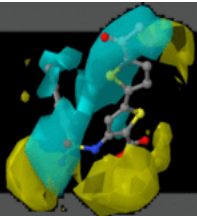
Referenza 1

Coinvolgimento nella fecondazione

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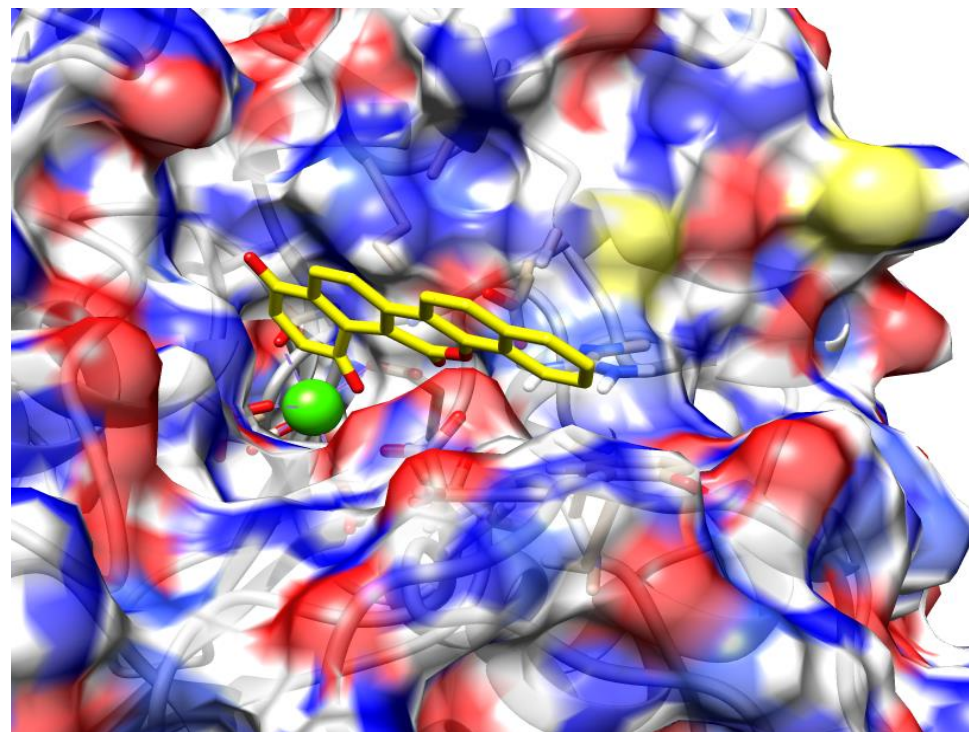
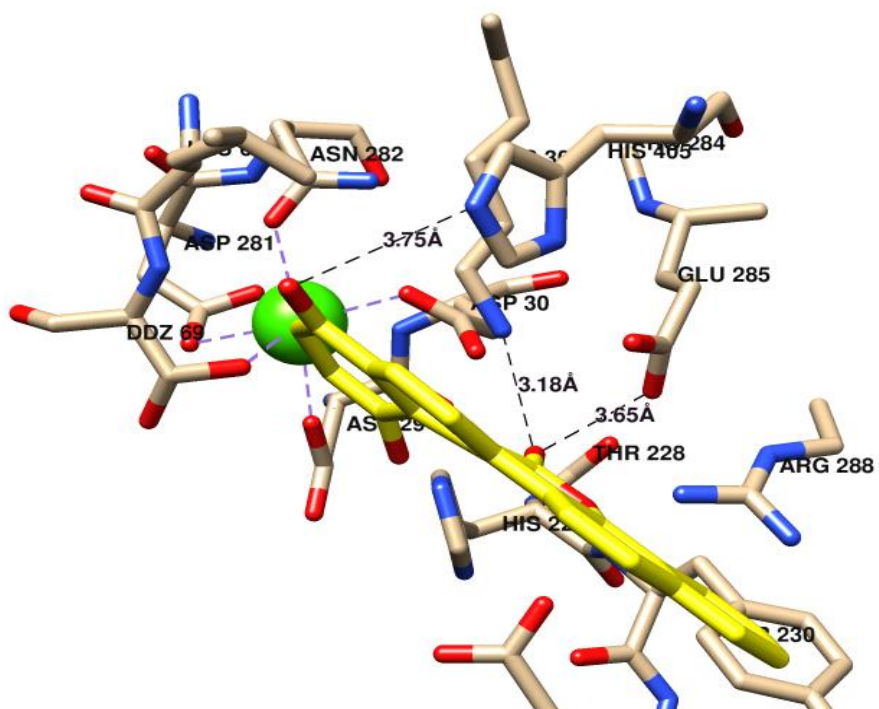


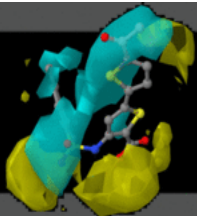
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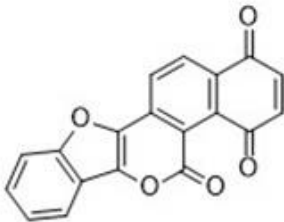
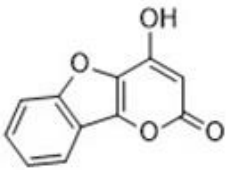
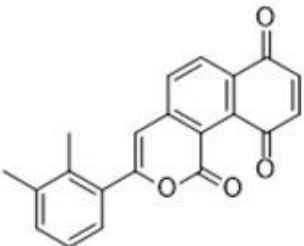
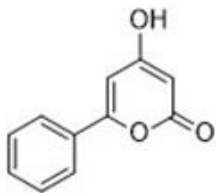
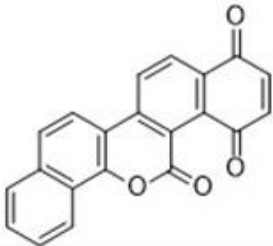
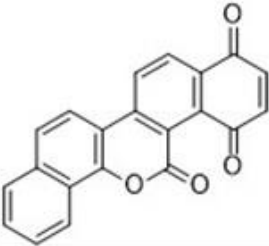


Drug Design

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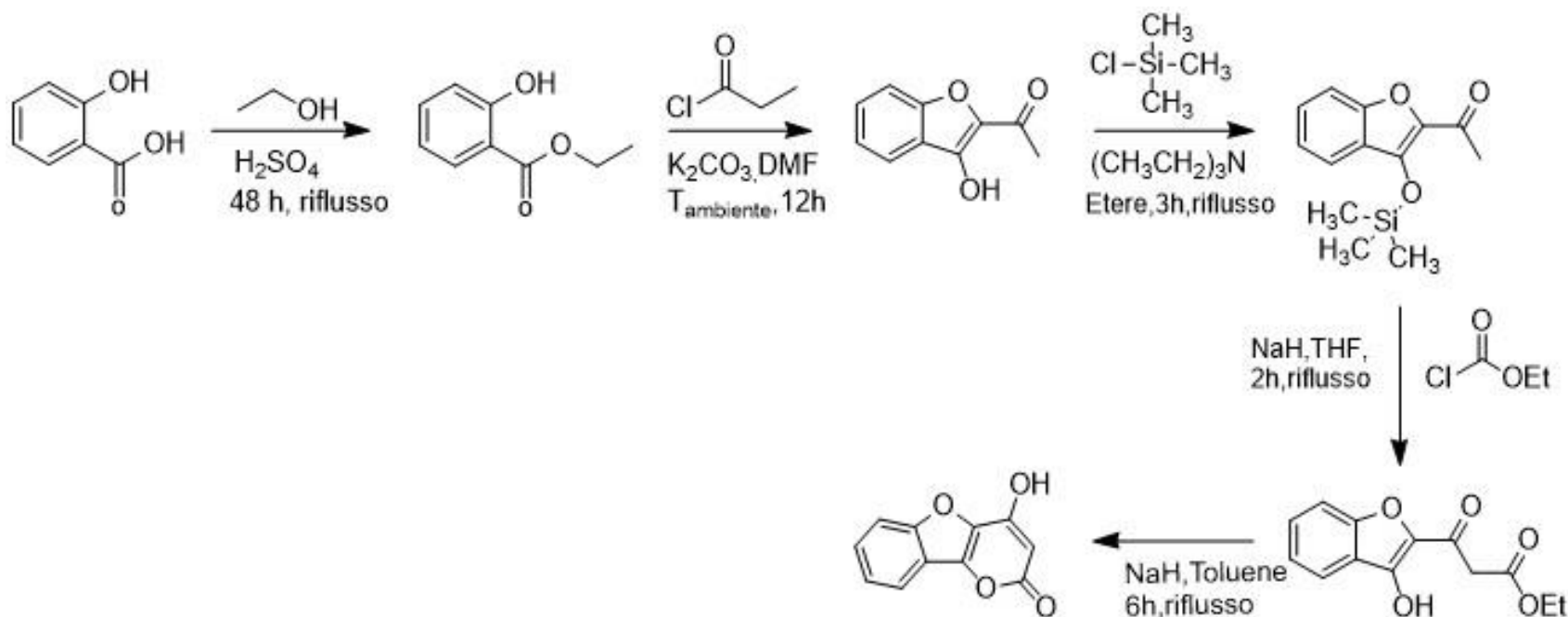




Obiettivo iniziale	Obiettivo rivalutato	Nome composto
		XU39
		XU49
		XU30

4-idrossi-2H-pirano[3,2-b]benzofuran-2-one

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Referenza 3-7



4-idrossi-2H-pirano[3,2-b]benzofuran-2-one

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Purificazione: Cristallizzazione

Solvente: Etanolo

Aspetto: Solido giallo

Resa: 23%

Punto di fusione: 232 ° C

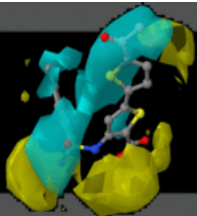
Peso molecolare: 202.65 g/mol



^1H NMR (400 MHz, CDCl_3) δ 5.33 (s, 1H, CH), 6.78-6.82 (t, H, CH_{benz}) J = 1.6 Hz, 6.89-6.91 (d, 1H, CH_{benz}) J = 1.2 Hz, 7.35-7.39 (t, 1H, CH_{benz}) J = 7.2 Hz, 7.76-7.79 (d, H, CH_{benz}) J = 1.6 Hz, 12.12 (OH)

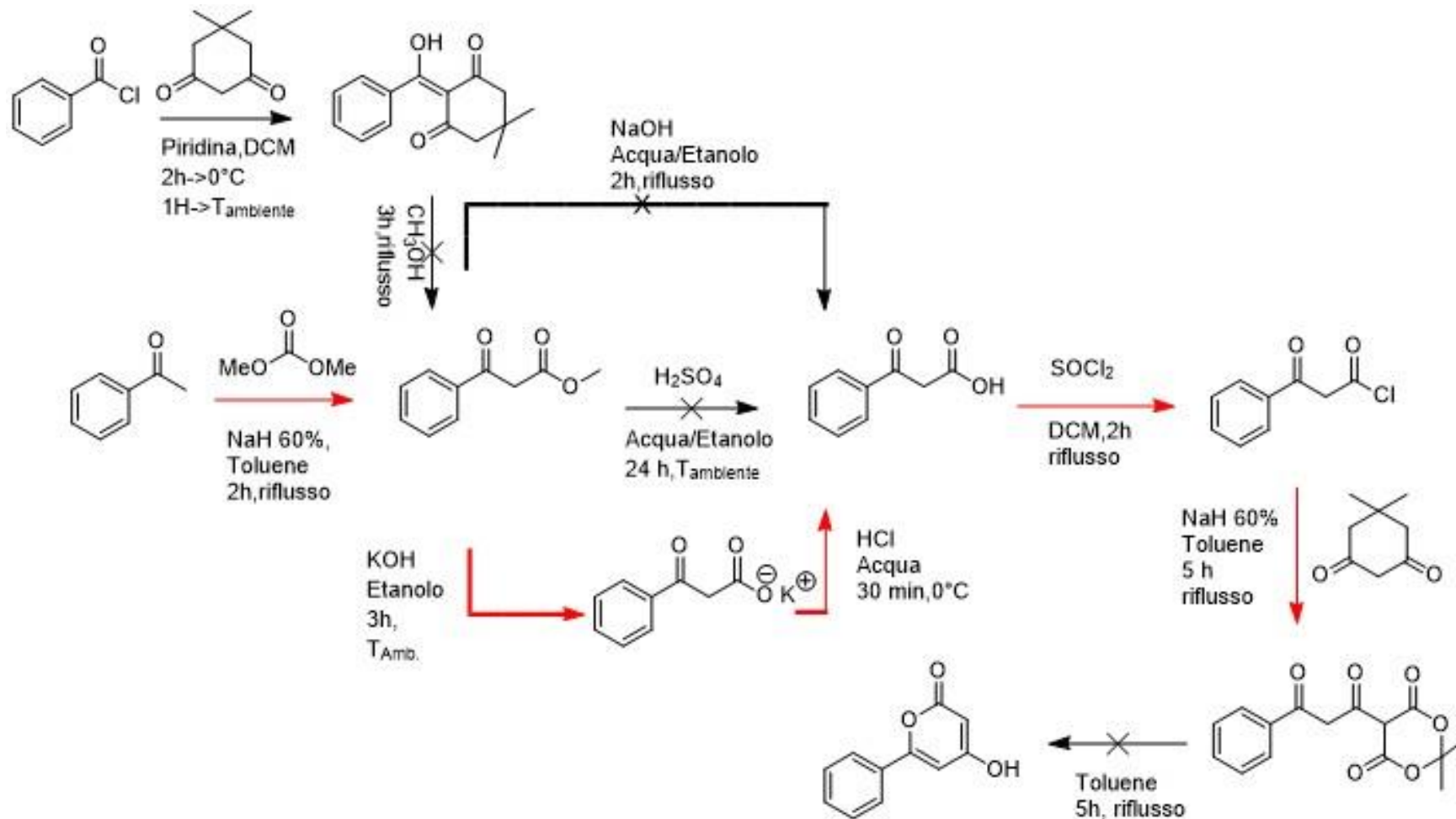
Analisi elementari

C (65.35%), H (2.99%), O (31.66%)

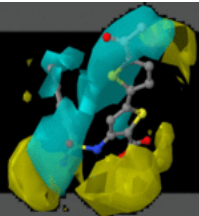


4-idrossi-6-fenil-2H-piran-2-one

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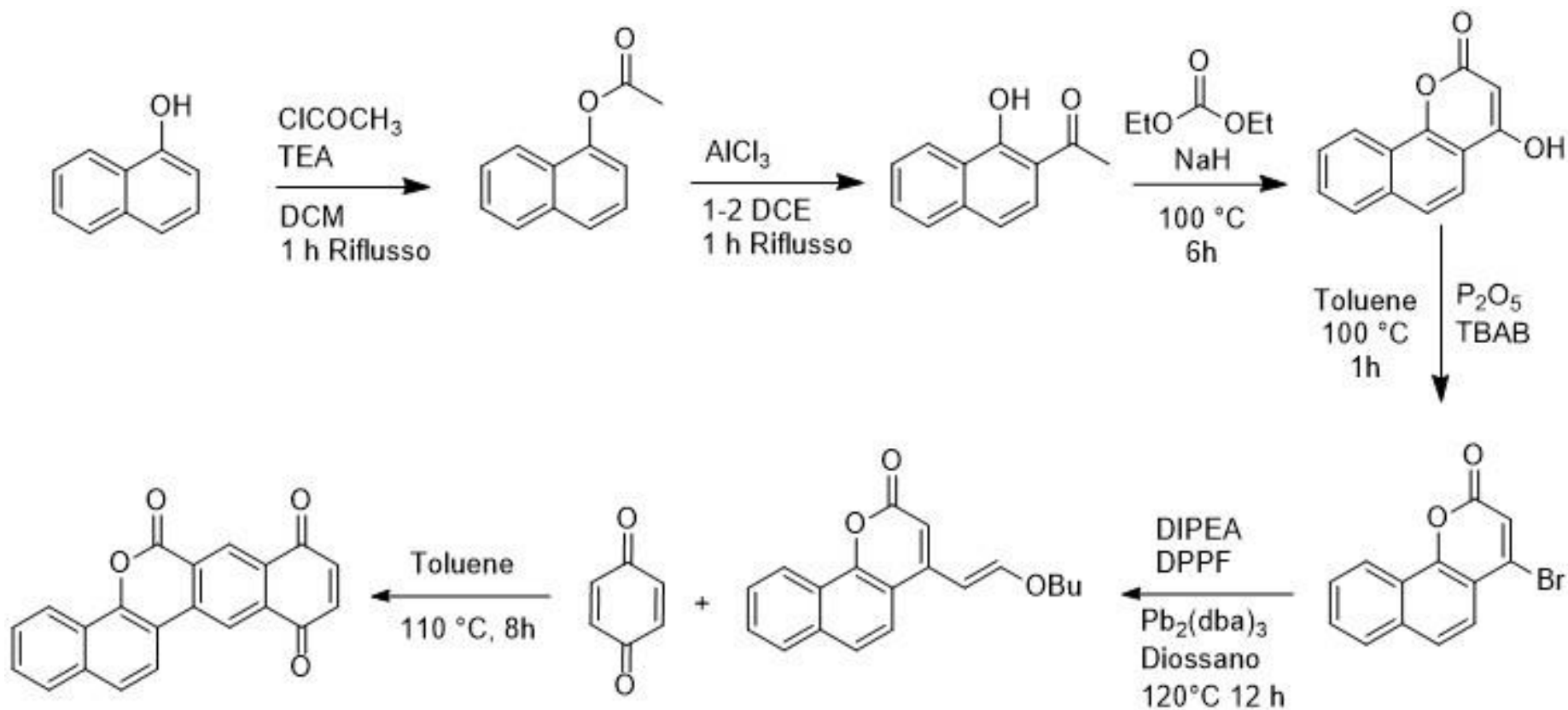


Referenze 8,9

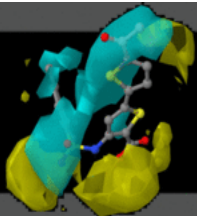


XU30

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Reference 10-12



XU30

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Purificazione: Cristallizzazione

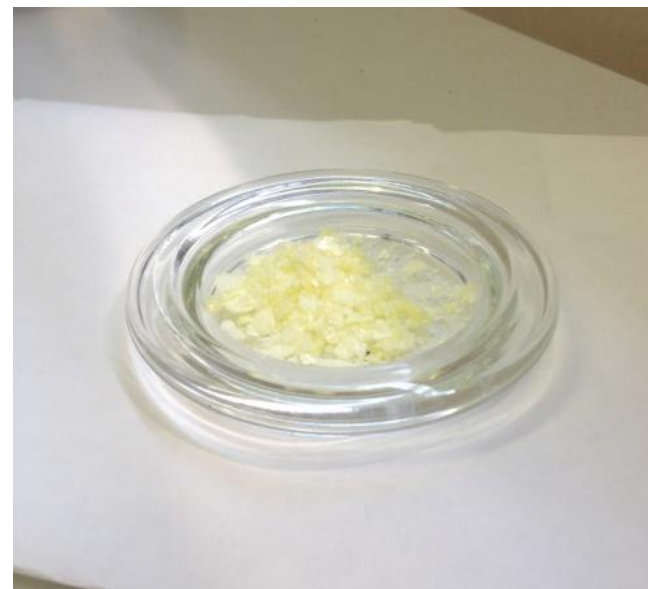
Solvente: Etanolo

Aspetto: Cristallo giallo

Resa: 58%

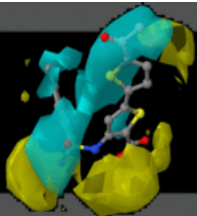
Punto di fusione: 167-169° C

Peso molecolare: 326.30 g/mol



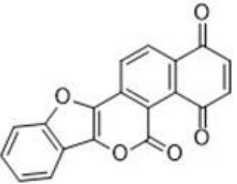
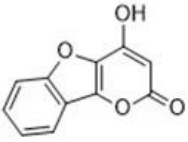
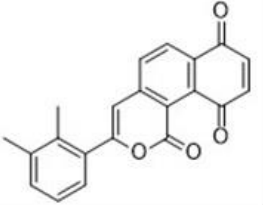
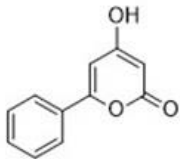
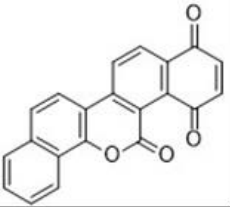
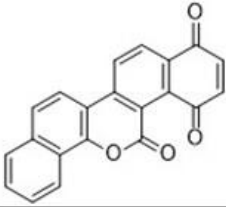
^1H NMR (400 MHz, DMSO- d_6) : δH 7.43-7.51 (m, 2H, 2 $\times$ CH), 7.65-7.71 (m, 1H, CH), 7.91-7.96 (m, 2H, 2 $\times$ CH), 8.06-8.09 (m, 1H, CH), 8.14-8.18 (m, 1H, CH), 8.43-8.46 (d, 1H, CH, J = 8.3 Hz), 8.51-8.54 (d, 1H, CH, J = 8.5 Hz), 8.84 (d, 1H, CH, J = 8.8 Hz).

^{13}C NMR (100 MHz, DMSO- d_6) : δC 116.6, 117.0, 119.0, 124.6, 124.8, 126.3, 126.4, 127.0, 131.2, 132.0, 132.6, 134.0, 134.7, 134.8, 135.3, 138.7, 140.6, 151.7, 156.7, 180.8, 183.1.



Conclusioni

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Obiettivo iniziale	Obiettivo rivalutato	Nome composto
		XU39
		XU49
		XU30

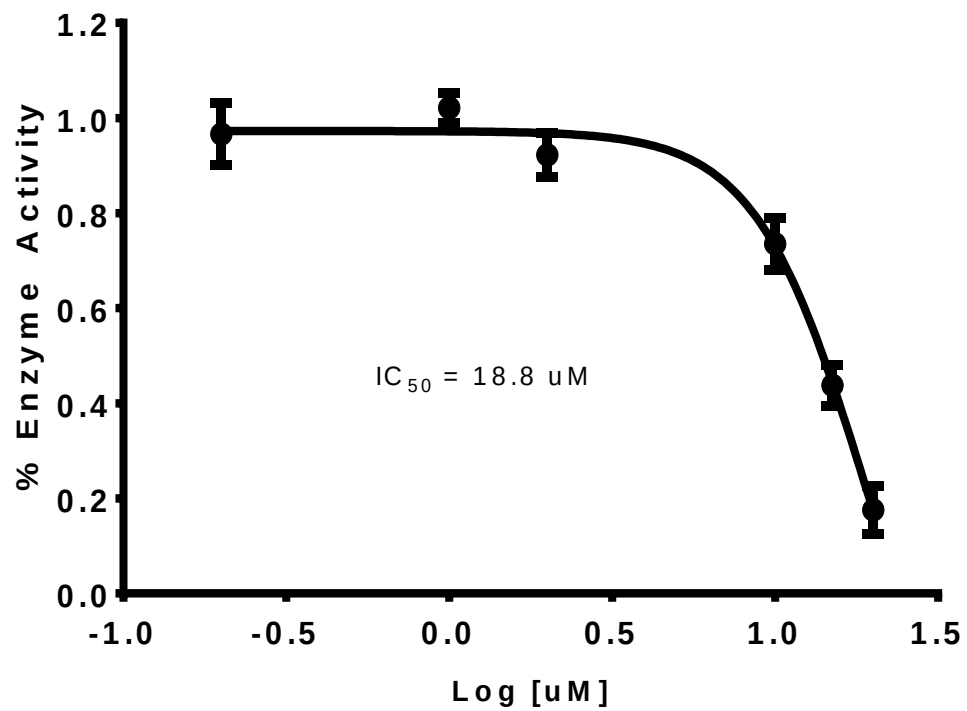


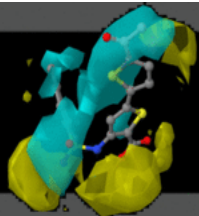


Conclusioni

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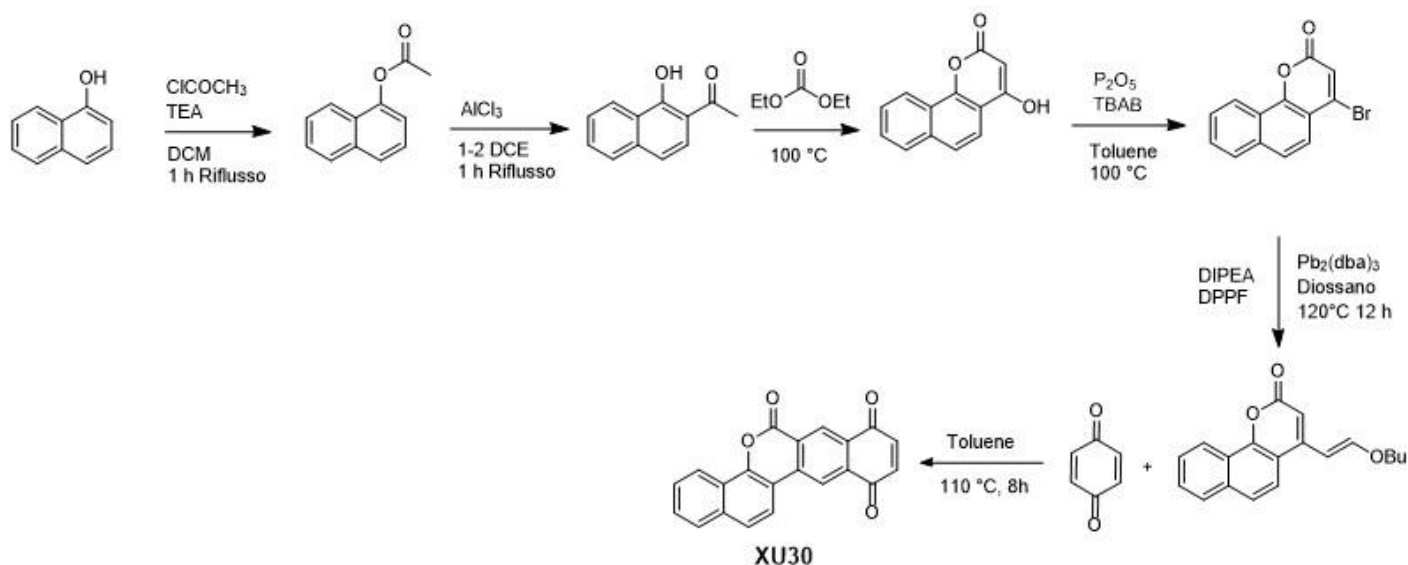
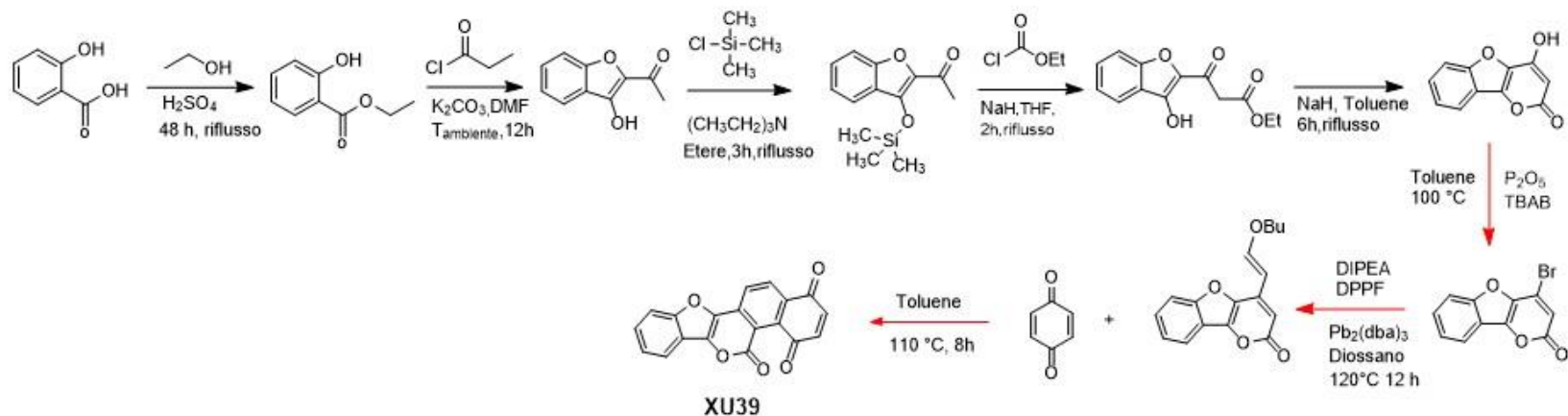
XU30

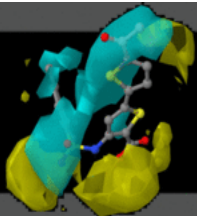




Prospettive future

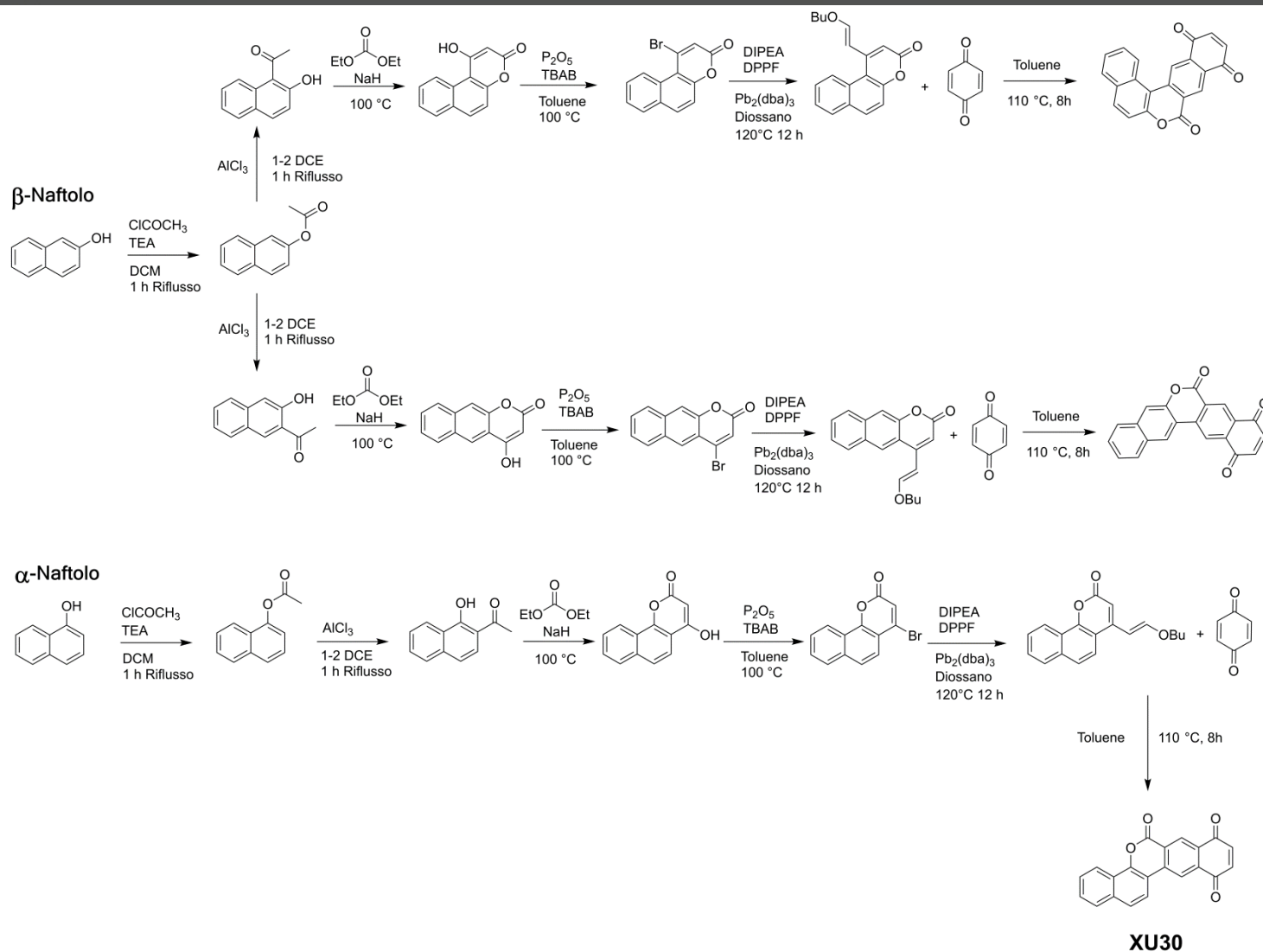
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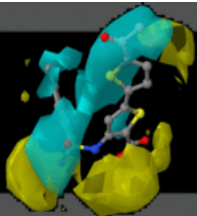




Prospettive future

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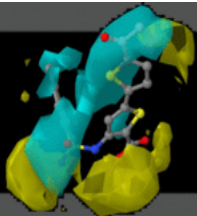


Grazie per l'attenzione

Riferimenti bibliografici:

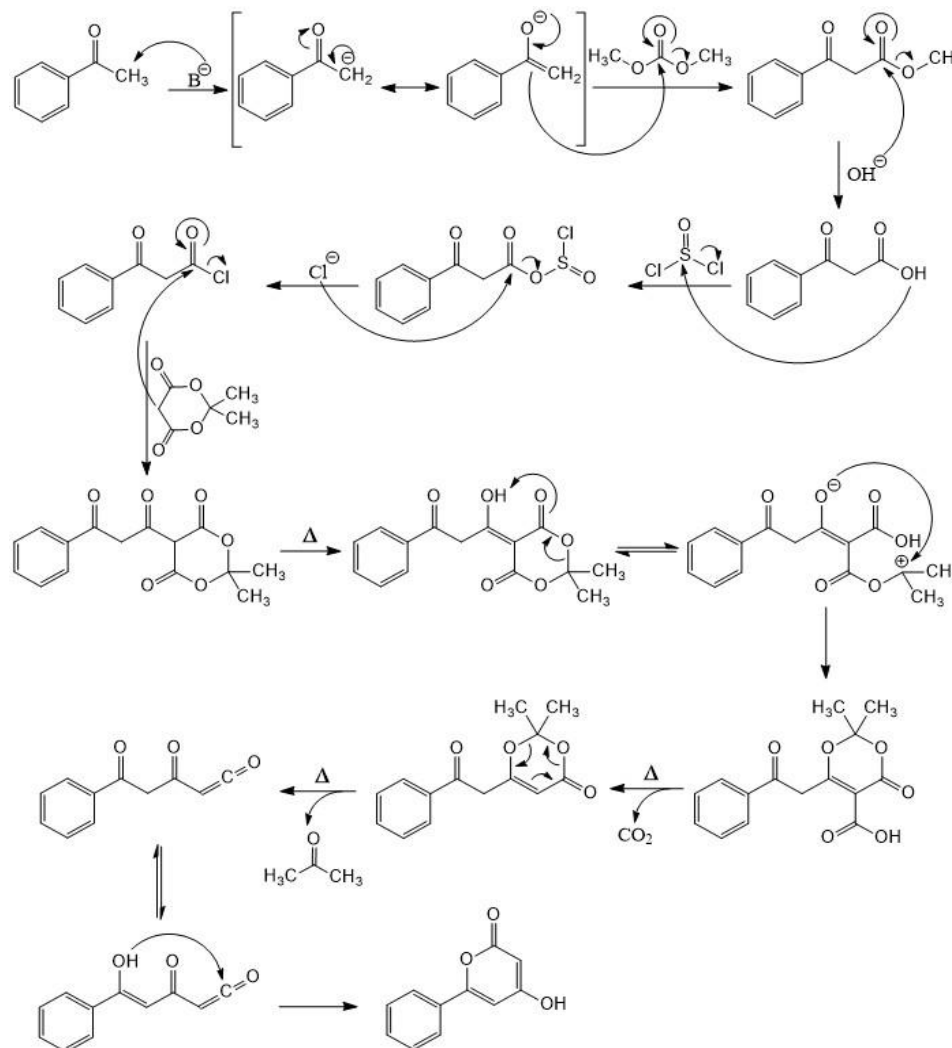
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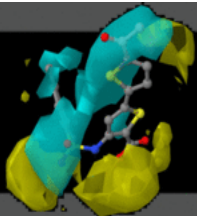




4-idrossi-6-fenil-2H-piran-2-one

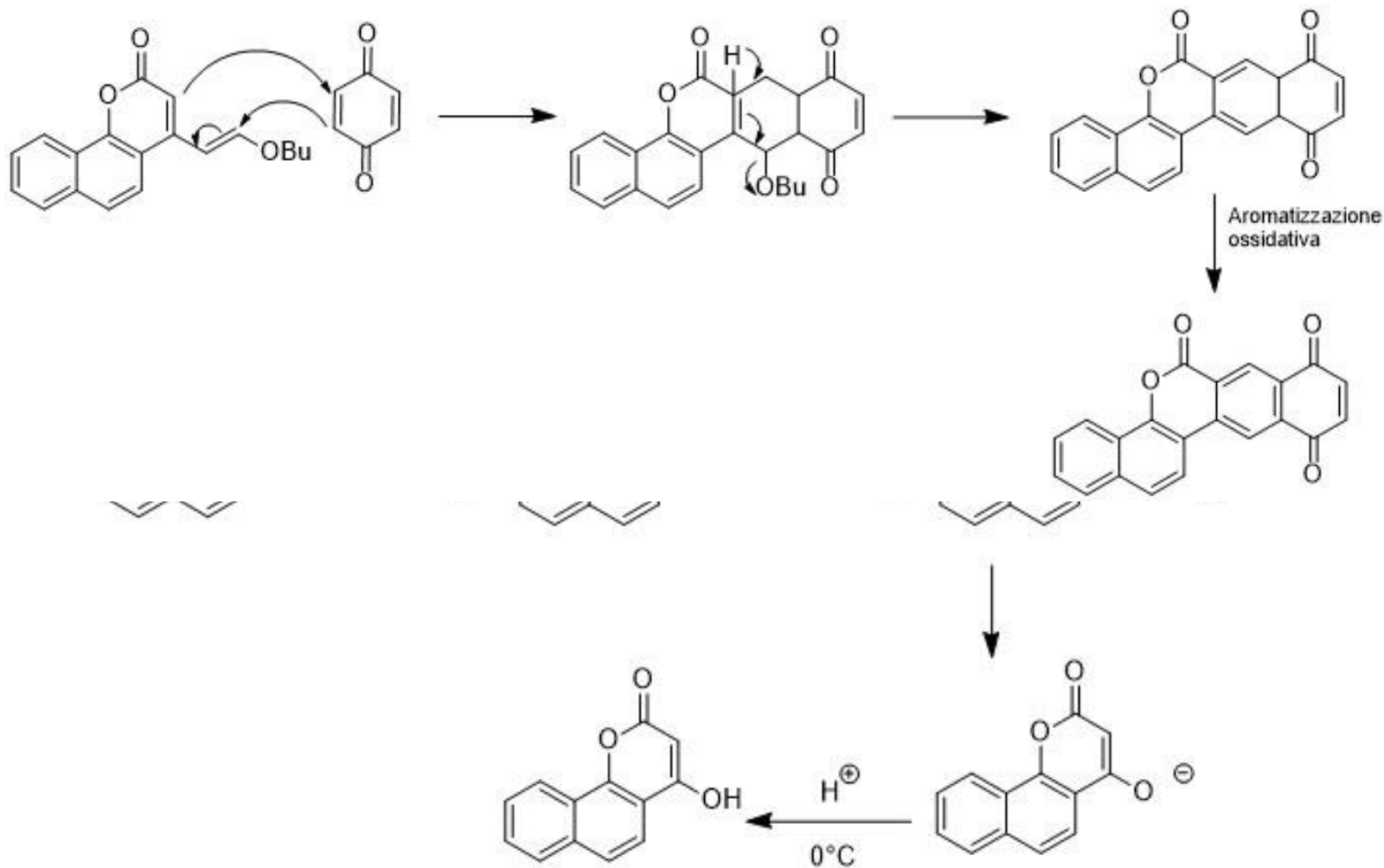
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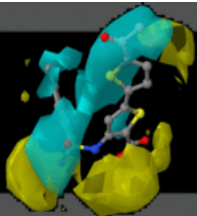


XU30

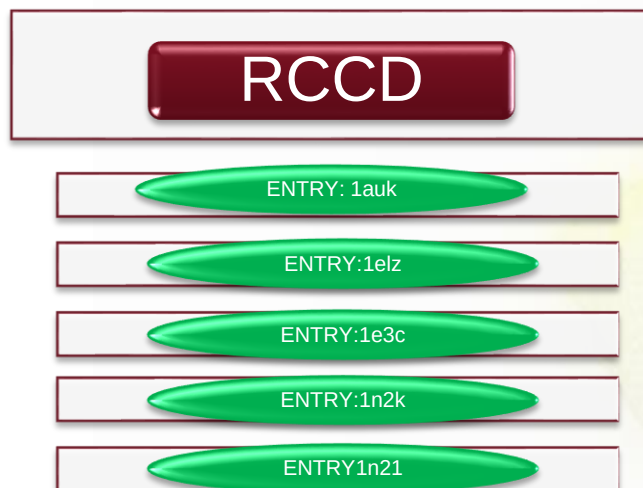
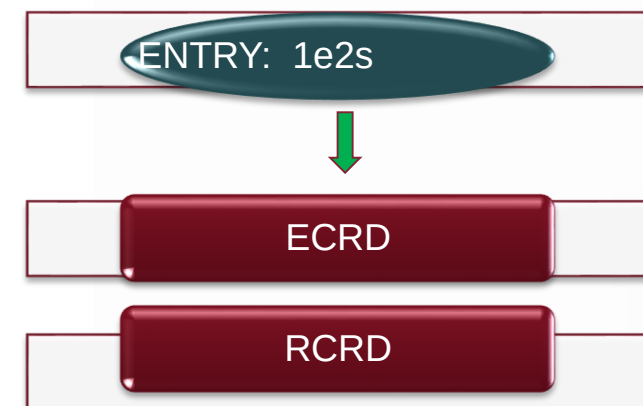
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Reference 10-12



Docking assestement



Programma di Docking	ECRD	RCRD
Autodock	1.276	1.139
Autodock Vina	0.595	0.605
Plants	1.140	1.095
Surflex	0.862	1.303
Paradocks	0.952	0.818

Docking Program	CODICI ENTRY IN PDB					
	1AUUK	1E1Z	1E33	1E3C	1N2K	1N2L
Autodock	1.071	1.289	0.996	0.823	2.380	3.005
Autodock Vina	0.818	3.019	2.632	2.701	5.725	5.193
Plants	0.867	1.132	1.809	1.172	7.956	7.024
Surflex	2.927	2.909	1.903	2.640	4.431	5.075
Paradocks	1.035	0.763	0.621	1.314	3.095	2.475



Drug Design

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