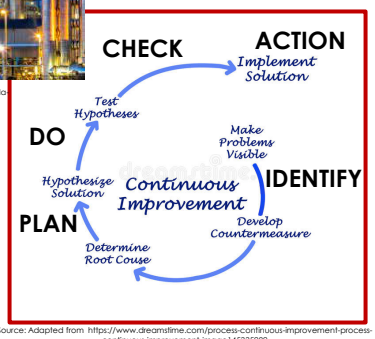
APPLICATION OF DESIGN EXPERT IN CLASSIC AROMATIC NITRATIONS

DSc Erika C.A.N.Chrisman – UFRJ/Brazil

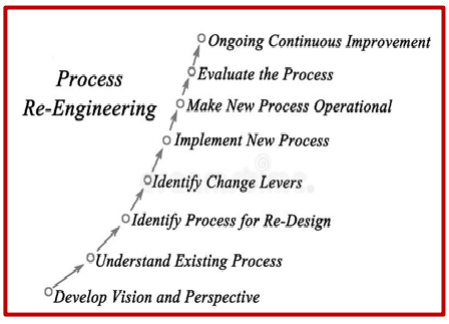
INTRODUCTION

Source:: https://exame.com/bussola/bussola-live-industria-quimica-em-risco-no-brasil/



Source: Adapted from https://www.dreamstime.com/process-continuous-improvement-process-continuous-improvement-image145335282

DOE



Source: Adapted from https://www.dreamstime.com/process-continuous-improvement-process-continuous-improvement-image145335282

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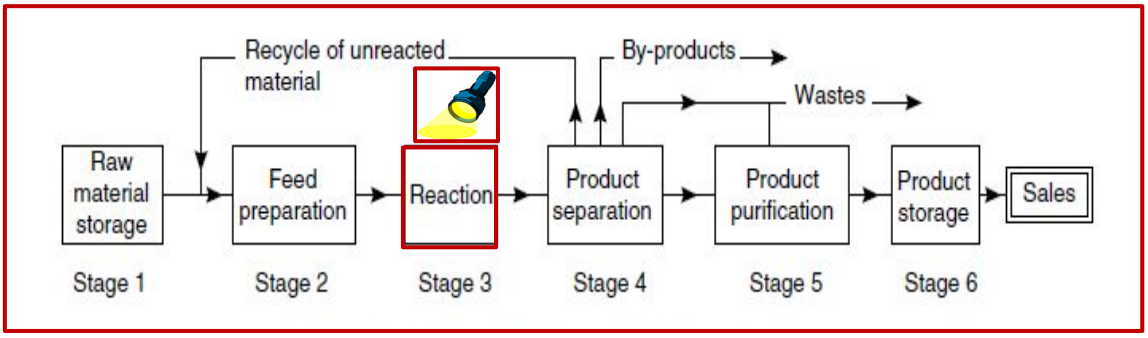
ANATOMY OF A CHEMICAL PROCESS



Source: Adaptive from https://chemicalprojects.net/2013/12/15/the-anatomy-of-a-chemical-manufacturing-process/

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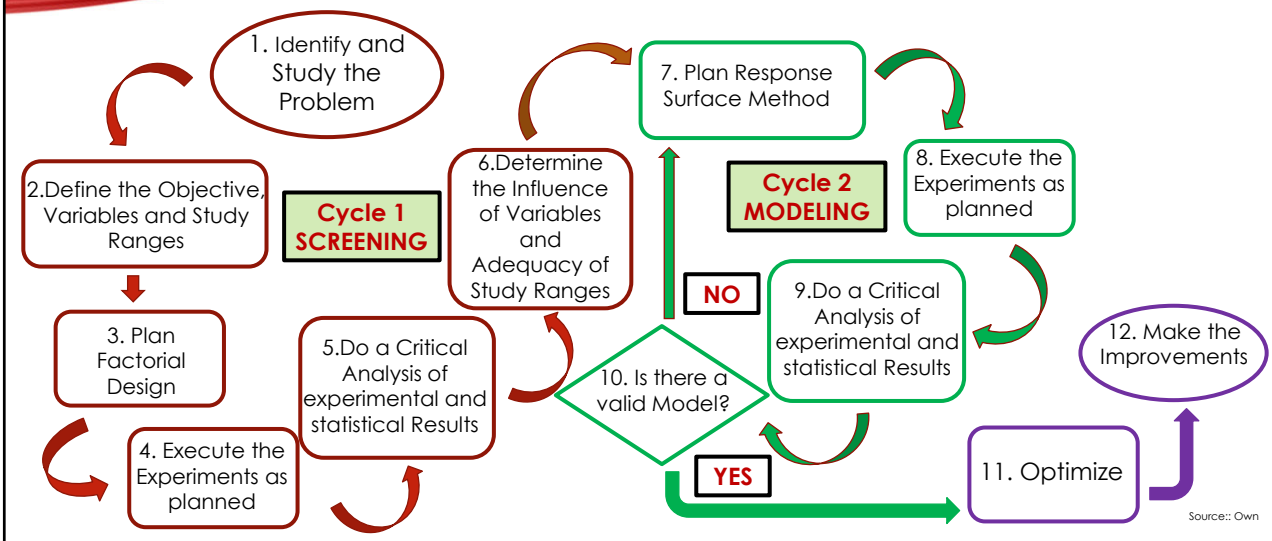
METHODOLOGY



Source:: Own

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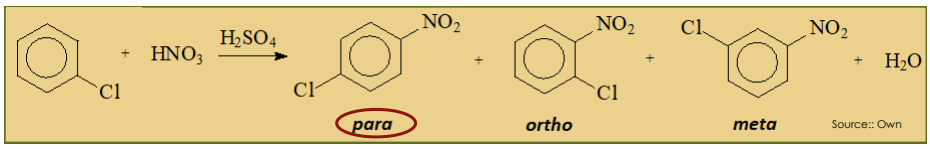
CASE STUDY 1

- Synthesis of *mono*-chloronitrobenzene



Literature **Yield**
75%

Literature **Selectivity** *(para : ortho)*
2 : 1

Source:: Own

Source: Adaptive from https://www.laboratuvar.org/pt/tekstil/kimyasal-ve-ekolojik-testler/azo-boyar-madde-testi/

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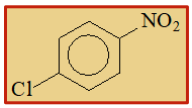
SEPARATION AND PURIFICATION PROCESSES



Literature **Selectivity** *(para : ortho)*
2 : 1

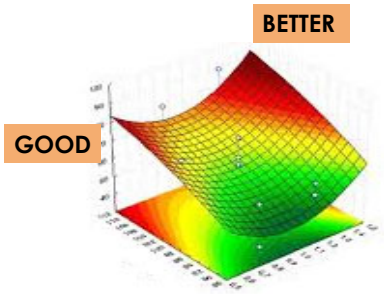
Source:: Own

Hard and involve

✓sequential steps of distillation and successive crystallizations

DECISION

APPLY THE DEVELOPED METHODOLOGY



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METHODOLOGY FA APPLIED

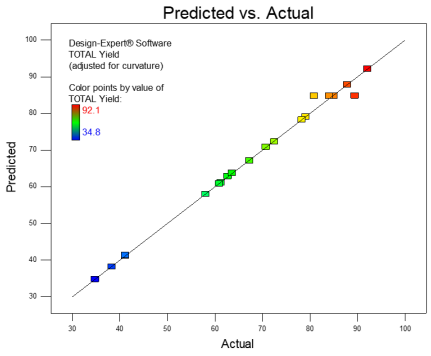
File Version	9.0.3.1	Factor
Study Type	Factorial	A
Design Type	2 Level Factorial	B
Center Point	4	C
Design Mode	4FI	D

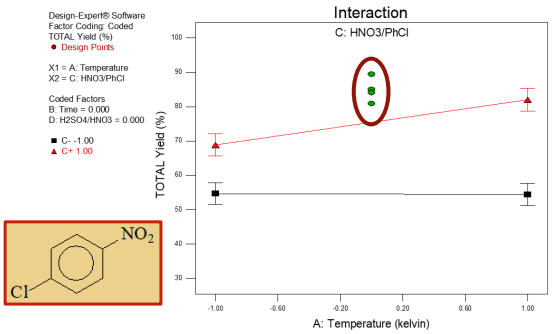
Name	Units
temperature	kelvin
time	minutes
HNO3/PhCl	
H2SO4/HNO3	

Response	Name	Units
R1	TOTAL Yield	%
R2	ORTO Isomer Yield	%
R3	PARA Isomer Yield	%
R4	para/orto isomer ratio	

ANOVA Summary

	Adjusted Model		Unadjusted Model	
	F-value	p-value	F-value	p-value
Model	807.24	< 0.0001	17.91	< 0.0001
Curvature	1455.46	< 0.0001		
Lack of Fit	0.15	0.8578	459.61	< 0.0001





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METHODOLOGY RSM APPLIED

TOTAL YIELD

ANOVA for Response Surface Reduced Cubic model

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F	
Model	14124.26	14	1008.88	853.54	< 0.0001	significant
A-temperature	*398.33*	*1*	*398.33*	*337.00*	*< 0.0001*	
B-time	*908.40*	*1*	*908.40*	*768.54*	*< 0.0001*	
C-HNO3/PhCl	*4536.11*	*1*	*4536.11*	*3837.71*	*< 0.0001*	
D-H2SO4/HNO3	*3920.15*	*1*	*3920.15*	*3316.58*	*< 0.0001*	
Residual	37.82	32	1.18			
Lack of Fit	*0.38*	*2*	*0.19*	*0.15*	*0.8578*	*not significant*

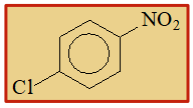
Std. Dev.	1.09	R-Squared	0.9973
Mean	64.75	Adj R-Squared	0.9962

para ISOMER YIELD

ANOVA for Response Surface Reduced Cubic model

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F
Model	9894.97	15	659.66	64.51	< 0.0001
A-temperature	*438.63*	*1*	*438.63*	*42.90*	*< 0.0001*
B-time	*1.10*	*1*	*1.10*	*0.11*	*0.7451*
C-HNO3/PhCl	*74.92*	*1*	*74.92*	*7.33*	*0.0114*
D-H2SO4/HNO3	*14.19*	*1*	*14.19*	*1.39*	*0.2487*
Pure Error	286.31	28	10.23		

Std. Dev.	3.14	R-Squared	0.9719
Mean	71.99	Adj R-Squared	0.9583



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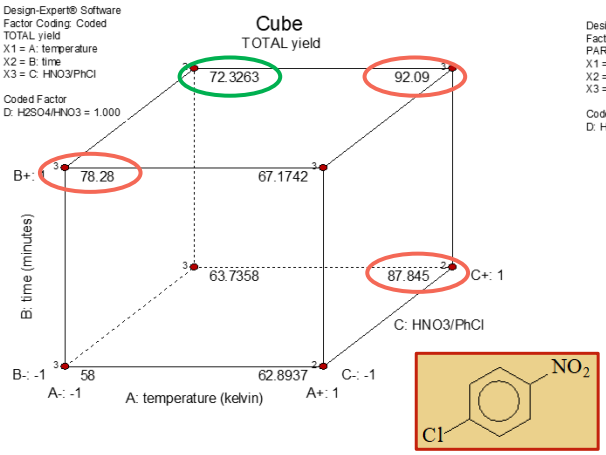
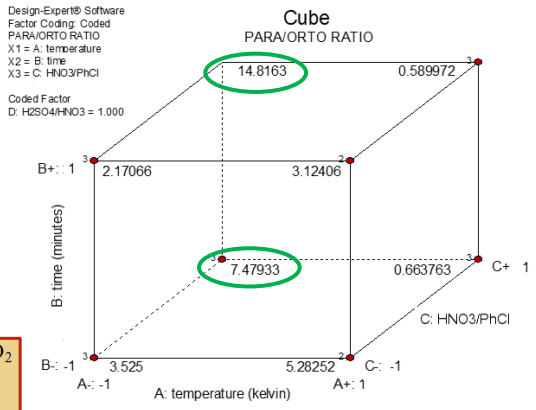
RESULTS MSR OF CASE 1

TOTAL YIELD



***Para/Ortho* Ratio YIELD**



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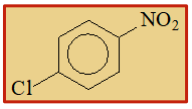
OPTIONS OF CASE STUDY 1

Literature **Yield**	Literature **Selectivity** *(para : ortho)*
75%	***2 : 1***



Std	Run	Factor 1 A:Temperature kelvin	Factor 2 B:Time minutes	Factor 3 C:HNO3/PhCl	Factor 4 D:H2SO4/HN...	Response 1 TOTAL Yield %	Response 2 ORTO Isome... %	Response 3 PARA Isomer... %	Response 4 para/orto iso...
47	11	1.000	1.000	1.000	1.000	92.1	64.11	34.75	0.542037
23	24	1.000	1.000	1.000	-1.000	79.07	11.9	86.84	7.29748
16	25	1.000	-1.000	1.000	-1.000	60.91	7.61	92.05	12.0959

AFTER OPTIMIZATION

Selectivity *(para : ortho)*	**Final Yield**
15 : 1	***88%***

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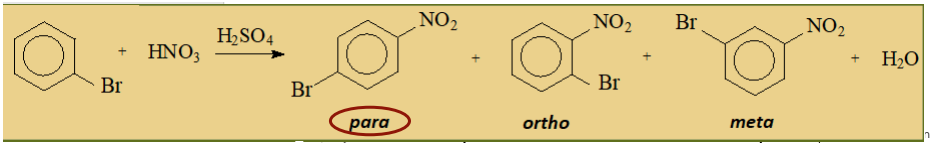
CASE STUDY 2

- Synthesis of *mono*-bromonitrobenzene



Literature **Yield**	Literature **Selectivity** (*para* : *ortho*)
79%	***3 : 1***

Source:: Own

Source: Adaptive from http://www.rubberpedia.com/antioxidantes-antiozonantes.php

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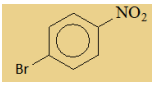
METHODOLOGY FA APPLIED

TOTAL YIELD

ANOVA Summary

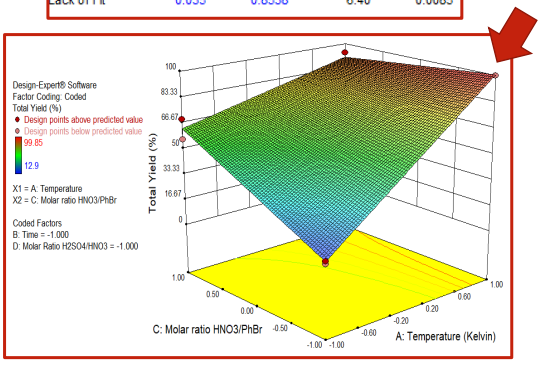
	Adjusted Model		Unadjusted Model	
	F-value	p-value	F-value	p-value
Model	94.72	< 0.0001	57.16	< 0.0001
Curvature	13.49	0.0017		
Lack of Fit	0.035	0.8538	6.40	0.0085

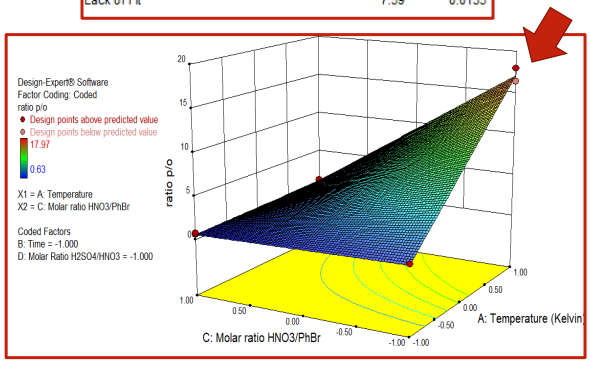


***Para/Ortho* Ratio YIELD**

ANOVA Summary

	Adjusted Model		Unadjusted Model	
	F-value	p-value	F-value	p-value
Model	43.65	< 0.0001	31.95	< 0.0001
Curvature	7.59	0.0135		
Lack of Fit			7.59	0.0135





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METHODOLOGY RSM APPLIED

TOTAL YIELD

Response 1 Total Yield
ANOVA for Response Surface Reduced Cubic model
Analysis of variance table [Partial sum of squares - Type III]

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F
Model	24188.63	13	1860.66	7.33	< 0.0001
A-Temperature	*2778.39*	*1*	*2778.39*	*10.95*	*0.0024*
B-Time	*2106.65*	*1*	*2106.65*	*8.30*	*0.0073*
C-Molar ratio HNO3/PhBr	*3490.30*	*1*	*3490.30*	*13.75*	*0.0008*
D-Molar Ratio H2SO4/HNO3	*4744.35*	*1*	*4744.35*	*18.69*	*0.0002*

***Para/Ortho* Ratio YIELD**

Response 4 ratio p/o
ANOVA for Response Surface 2FI model
Analysis of variance table [Partial sum of squares - Type III]

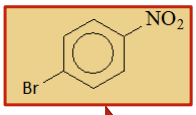
Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F
Model	367.75	10	36.77	4.12	0.0010
A-Temperature	*4.83*	*1*	*4.83*	*0.54*	*0.4669*
B-Time	*0.037*	*1*	*0.037*	*4.173E-003*	*0.9489*
C-Molar ratio HNO3/PhBr	*90.60*	*1*	*90.60*	*10.16*	*0.0031*
D-Molar Ratio H2SO4/HNO3	*70.33*	*1*	*70.33*	*7.89*	*0.0083*

Literature **Yield**

79%

Literature **Selectivity** (*para : ortho*)

3 : 1



Factor 1 A:Temperature Kelvin	Factor 2 B:Time minutes	Factor 3 C:HNO3/PhBr	Factor 4 D: H2SO4/HNO3	Response 1 Total Yield %	Response 2 p-Isomer Yield %	Response 3 o-isomer Yield %	Response 4 ratio p/o
1.000	-1.000	-1.000	-1.000	99.74	94.54	5.26	17.97
1.000	-1.000	-1.000	-1.000	99.78	94.04	5.73	16.41
-1.000	1.000	-1.000	-1.000	99.74	93.19	6.55	14.23

Source:: Own

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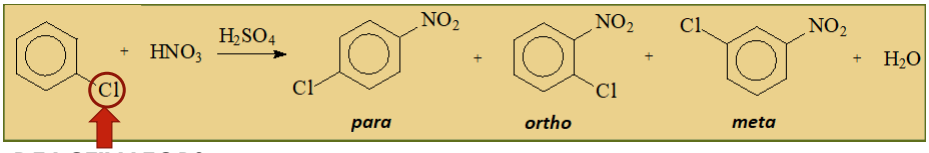
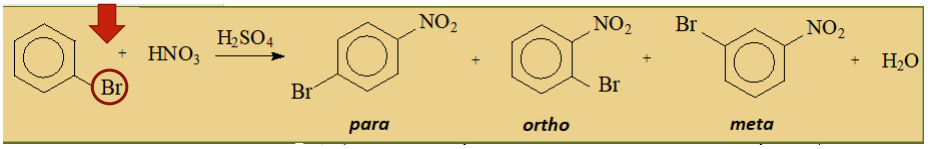
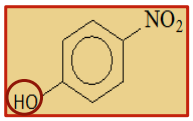
PRELIMINARY CONCLUSIONS

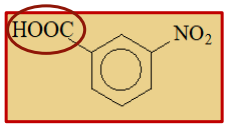
Nitration is a type of Electrophilic Aromatic Substitution reaction



DEACTIVATORS



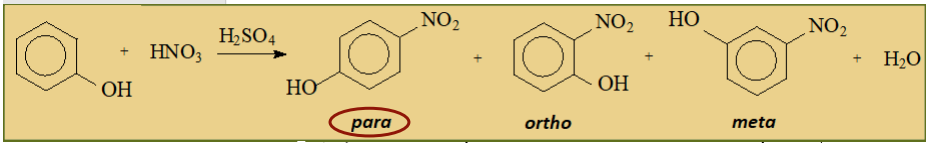




SourceAdaptive from https://www.apoven.com/tag-questions-linguistic-difference/

CASE STUDY 3

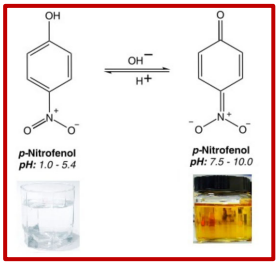
- Synthesis of *mono*-nitrophenol



Literature **Yield**
87%

Literature **Selectivity** *(para : ortho)*
2,3 : 1

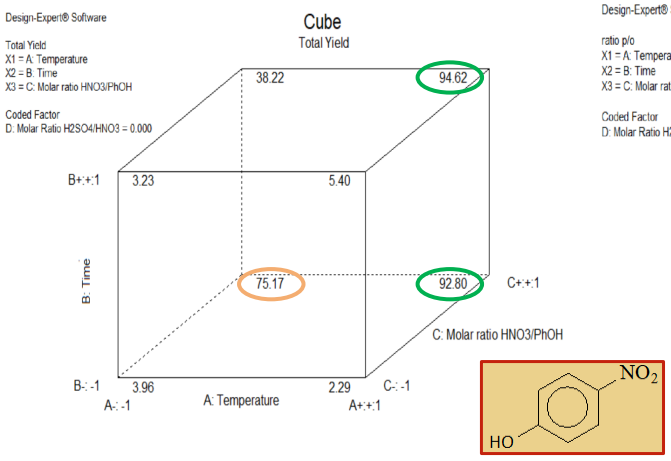
Source:: Own



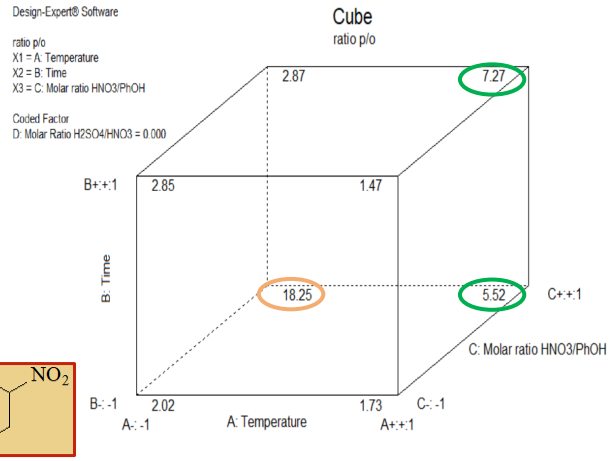
Source: Adaptive from https://maestrovirtuale.com/p-nitrofenol-caracteristicas-utilizacoes-e-toxicidade/

RESULTS MSR OF CASE 3

TOTAL YIELD



***Para/Ortho* Ratio YIELD**



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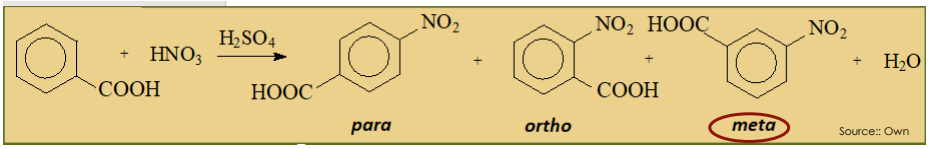
CASE STUDY 4



Literature **Yield**	Literature **Selectivity** *(meta : ortho)*	*meta* isomer **Purity**
85%	**24 : 1**	**96%**

Factor 1 A:Temperature Kelvin	Factor 2 B:Time minutes	Factor 3 C:Molar ratio H	Factor 4 D:Molar Ratio H	Response 1 Total Yield %	Response 2 p-Isomer Yield %	Response 3 m-isomer Yield %	Response 4 o-isomer Yield	Response 5 ratio m/o	Response 6 purity
1.000	-1.000	1.000	-1.000	99.25	1.22	71.16	26.88	2.64732	71.7
-1.000	-1.000	1.000	1.000	99.44	0.61	92.52	6.3	14.6857	93
1.000	-1.000	-1.000	1.000	96.53	0.14	96.34	0.04	2408.5	99.8

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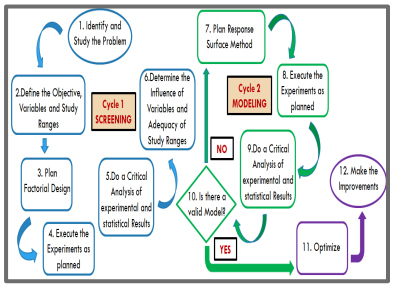
CONCLUSIONS

- ✓The proposed methodology presented very significant results in all cases.
- ✓The results were positive for both yield and selectivity improvement of chemical processes.
- ✓The focus on the chemical reaction stage provided positive impacts on subsequent stages with reduction and even elimination of steps.



Source:: Own

Source: https://www.statease.com/software/design-expert/

- ✓ The Design Expert used allowed both numerical and graphic evaluation of the influence of variables, in addition to the visualization of representative surfaces in each study.

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Thanks by your attention !

Contact and Questions

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