Supplementary Material (ESI) for Green Chemistry

Photochemistry as a green synthetic method.

Environmental assessment of C-C bond forming reactions

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2.1.1 Reaction 1

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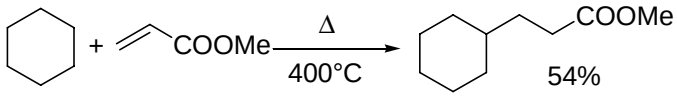
1. GENERAL

EATOS (**E**nvironmental **A**ssessment **T**ool for **O**rganic **S**ynthesis) software was downloaded from Professor J. O. Metzger web site (http://www.chemie.uni-oldenburg.de/oc/metzger/eatos/). Physical and environmental information (including risk and safety phrases, toxicity and ecological parameters) of considered compounds were obtained from the safety data sheets available on Sigma Aldrich web site (www.sigma-aldrich.com). The price of used compounds and materials (of reasonable purity) were obtained from Sigma Aldrich web site tooby chosing the largest quantity offered. The software affords plots of relevant parameters subdivided for the components (attached as .zip file). The figures are reported here as obtained from the application of the software, whereas in the manuscript these are rounded off.

2. TABLE OF PARAMETERS FOR REACTIONS 1-15.

ALKYLATION PROCESSES

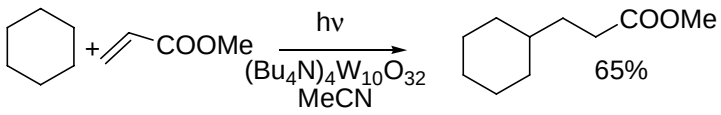
2.1.1. Reaction 1, Δ^1



Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
Methyl acrylate	0.90	0.80	4.70	2.80	16
Cyclohexane	0.90	-	2.30	-	37
Reagents	**1.80**	**0.80**	**7.00**	**2.80**	**53**
Cyclohexane[a]	44.7	44.7	111.7	119	857
Solvents	**44.7**	**44.7**	**111.7**	**119**	**857**
Methyl 3-cyclohexylpropanoate	-	-	-	-	-
Coupled products	-	-	-	-	-
Total value of parameters	**46.6**	**45.6**	**119**	**122**	**910**

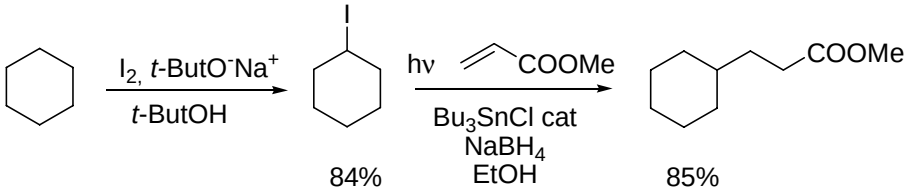
[a] Non stoichometric excess of cyclohexane was considered as solvent.

2.1.2. Reaction 2, hν[2]



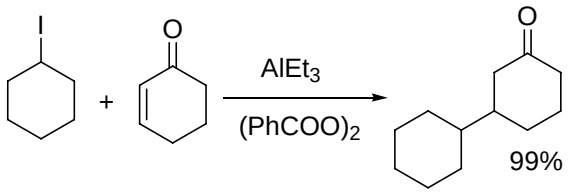
Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
Methyl acrylate	0.80	0.50	3.90	2.20	14
Cyclohexane	3.80	3.00	9.50	8.10	73
Reagents	**4.60**	**3.50**	**13.4**	**10.3**	**87**
Acetonitrile	142	142	426	284	2150
Solvent	**142**	**142**	**426**	**284**	**2150**
Methyl 3-cyclohexylpropanoate	-	-	-	-	-
Coupled products	-	-	-	-	-
Tetrabutylammonium decatungstate	-	0.50	1.40	0.50	195
Catalyst	-	**0.50**	**1.40**	**0.50**	**195**
Total value of parameters	**147**	**146**	**441**	**295**	**2432**

2.1.3. Reaction 3, hν[3,4]



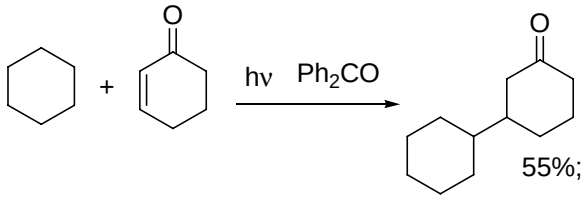
Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
Cyclohexane	5.80	5.20	5.80	20.9	24
Sodium *t*-butylate	0.70	-	3.00	-	129
Iodine	1.70	0.60	2.60	3.50	340
Methyl acrylate	2.50	1.90	2.50	10.0	44
$NaBH_4$	0.30	-	1.40	0.20	94
Reagents	**11.0**	**7.70**	**15.3**	**34.6**	**631**
Ethanol	4.60	4.60	9.10	13.7	90
Solvents	**4.60**	**4.60**	**9.10**	**13.7**	**90**
Bu_3SnCl	0.40	0.40	0.80	2.60	65
Catalyst	**0.40**	**0.40**	**0.80**	**2.60**	**65**
NaS_2O_3 2% aq	1.80	1.80	1.80	1.80	14
$MgSO_4$	0.30	0.30	0.30	2.20	16
Auxiliaries (reaction)	**2.10**	**2.10**	**2.10**	**4.00**	**30**
NaI	-	0.90	-	2.20	-
t-Butanol	-	0.40	-	0.40	-
$NaBH_3I$	-	1.00	-	1.00	-
Product/Coupled Product	-	**2.30**	-	**3.60**	-
Total value of parameters	**18.1**	**16.7**	**27.3**	**58.5**	**816**

2.1.4. Reaction 4, Δ^5.



Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
Iodocyclohexane	11.8	10.6	29.6	106	10768
2-Cyclohexen-1-one	0.50	-	2.7	-	746
Triethylaluminum	3.5	2.8	17.4	2.8	1289
Reagents	**15.8**	**13.4**	**49.7**	**109**	**12803**
Diethyl ether	39.9	39.9	139.6	120	1223
Solvent	**39.9**	**39.9**	**139.6**	**120**	**1223**
Benzoyl peroxide	2.7	2.7	15.0	10.9	185
Catalyst	**2.7**	**2.7**	**15.0**	**10.9**	**185**
HCl 37% aq	5.0	5.0	9.9	24.8	45
CH_2Cl_2	14.9	14.9	29.9	99.5	101
Auxiliaries (Reaction)	**19.9**	**19.4**	**39.8**	**124**	**146**
3-Cyclohexyl-methylpropanoate	-	-	-	-	-
Et_3AlI	-	1.3	-	1.3	-
Products-coupled products	**-**	**1.3**	**-**	**1.3**	**-**
Total value of parameters	**78.3**	**76.7**	**244.1**	**365**	**14357**

2.1.5. Reaction 5, hν[6]

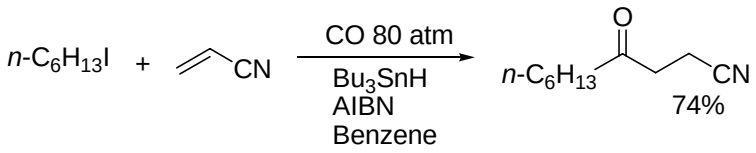


Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
Cyclohexane	0.84	-	2.10	-	16
2-Cyclohexen-1-one	1.0	0.0	3.40	-	1069
Reagents	**2.80**	**76.7**	**5.50**	**-**	**1085**
Cyclohexane[a]	76.7	76.7	191.7	307	1206
Solvents	76.7	76.7	191.7	307	1206
Benzophenone	1.8	1.8	1.8	9.4	95
Catalyst[b]	**1.8**	**1.8**	**1.8**	**9.4**	**95**
3-Cyclohexyl-methylpropanoate	-	-	-	-	-
Products-coupled products	**-**	**-**	**-**	**-**	**-**
Total value of parameters	**80.3**	**78.5**	**199**	**316**	**2386**

[a] Non stoichometric excess of cyclohexane was considered as solvent. [b] Photoproducts of benzophenone considered.

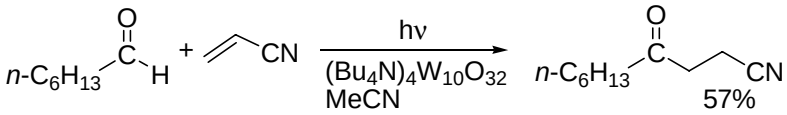
2.2. ACYLATION PROCESSES

2.2.1. Reaction 6, Δ^7



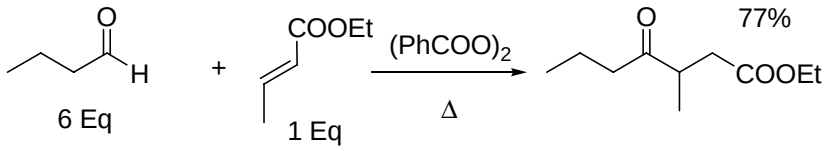
Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
Acrylonitrile	1.7	1.3	9.4	11.2	17
1-Iodohexane	1.7	-	5.1	-	613
Tributylhydride	3.3	0.90	13.2	9.4	3541
Carbon monoxide	98.7	98.4	543	984	2435
Reagents	**105**	**101**	**571**	**1005**	**6606**
Benzene	426	426	2344	3196	7795
Solvents	**426**	**426**	**2344**	**3196**	**7795**
AIBN	-	-	-	-	16
Catalyst	**-**	**-**	**-**	**-**	**16**
Tributyltin iodide	-	2.5	-	2.5	-
4-keto-decanitrile	-	0,0	-	-	-
Products-coupled products	**-**	**2.5**	**-**	**2.5**	**-**
Total value of parameters	**531**	**530**	**2915**	**4203**	**14417**

2.2.2. Reaction 7, hν[8]



Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
Acrylonitrile	1.20	0.80	1.80	2.20	12
Heptanal	0.60	-	3.10	-	62
Reagents	**1.80**	**0.80**	**4.90**	**2.20**	**74**
Acetonitrile	82.4	82.4	206	165	1248
Solvent	**82.4**	**82.4**	**206**	**165**	**1248**
Tetrabutylammonium decatungstate	0.70	0.70	1.40	0.70	286
Catalyst	**0.70**	**0.70**	**1.40**	**0.70**	**286**
4-keto-decanitrile	-	-	-	-	-
Products-coupled products	**-**	**-**	**-**	**-**	**-**
Total value of parameters	**84.9**	**83.9**	**212**	**168**	**1608**

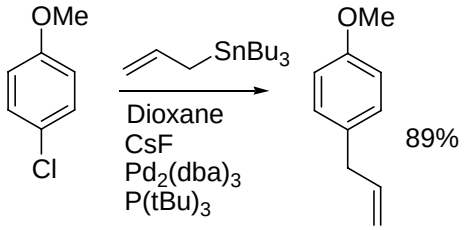
2.2.3. Reaction 8, Δ^9



Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
Ethyl crotonate	0.8	0.3	2.8	0.8	204
Butanal	3.0	2.6	4.6	14.1	110
Reagents	**3.8**	**2.9**	**7.4**	**14.9**	**314**
Benzoyl peroxide	0.2	0.2	0.9	0.2	9
Catalyst	**0.2**	**0.2**	**0.9**	**0.2**	**9**
Diethyl ether	1.0	1.0	3.4	2.9	30
Sodium bicarbonate $5\%_{aq}$	3.4	3.4	3.4	3.8	1
Auxiliaries (isolation)	**4.4**	**4.4**	**6.8**	**6.7**	**31**
4-Oxo-3-methylethyl-heptanoate	0.0	0.0	0.0	0.0	0
Product-coupled products	**0.0**	**0.0**	**0.0**	**0.0**	**0**
Total value of parameters	**8.4**	**7.5**	**15.1**	**21.8**	**354**

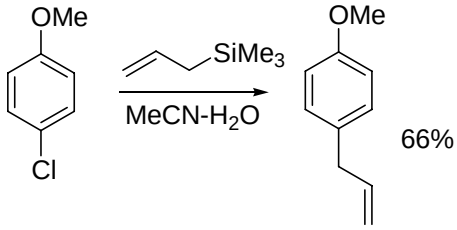
2.3 ARYLATION PROCESSES.

2.3.1. Reaction 9, Δ^{10}



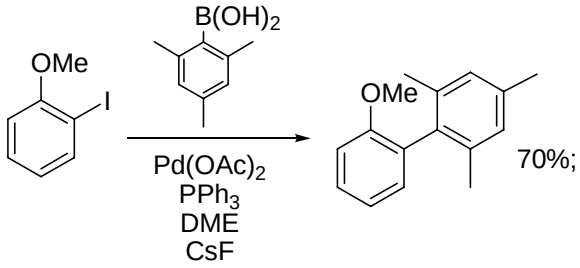
Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
4-Chloroanisole	1.1	0.2	4.3	0.2	1378
Allyltributyltin	2.7	0.4	14.6	3.8	7872
Reagents	**3.8**	**0.6**	**18.9**	**4.0**	**9250**
1,4-dioxane	10.2	10.2	51.0	40.8	95
Solvent	**10.2**	**10.2**	**51.0**	**40.8**	**95**
Tri(*t*-butyl)phosphine	0.1	0.1	0.7	0.1	2922
$Pd_2(dba)_3$	0.1	0.1	0.8	0.1	3009
Catalyst	**0.2**	**0.2**	**1.5**	**0.2**	**5931**
CsF	2.6	2.6	11.5	25.6	5458
Auxiliaries materials (reaction)	**2.6**	**2.6**	**11.5**	**25.6**	**5458**
Silica gel	3.8	3.8	3.8	3.8	113
Ethyl acetate	34.0	34.0	68.0	68.0	377
Auxiliaries materials (isolation)	**37.8**	**37.8**	**71.8**	**71.8**	**490**
4-Allylanisole	-	-	-	-	-
tributylchlorotin	-	2.20	-	18.7	-
Product-coupled products	-	**2.20**	-	**18.7**	-
Total value of parameters	**54.6**	**53.6**	**155**	**161**	**21224**

2.3.2. Reaction 10, hν[11]



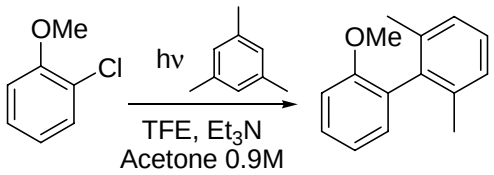
Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
4-Chloroanisole	1.5	0.9	6.6	8.9	1618
Allyltrimethylsilane	5.8	4.7	40. 9	46.7	19916
Reagents	**7.3**	**5.6**	**47.5**	**55.6**	**21534**
MeCN	66.4	66.4	199.3	133	1013
Water	17.1	17.1	17.1	17.1	1
Solvents	**83.5**	**83.5**	**216.4**	**151**	**1014**
CH_2Cl_2	40.6	40.6	81.3	271	277
Auxiliaries (isolation)	**40.6**	**40.6**	**81.3**	**271**	**277**
4-Allylanisole	-	-	-	-	-
Trimethylsilylchloride	-	0.70	-	0.70	-
Product-coupled products	**-**	**0.70**	**-**	**0.70**	**-**
Total value of parameters	**131**	**130**	**345**	**478**	**22800**

2.3.3. Reaction 11, Δ^{12}



Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
2-Iodoanisole	1.0	-	3.7	-	1676
Mesitylboronic acid	1.5	0.8	7.2	7.5	18386
Reagents	**2.5**	**0.8**	**10.9**	**7.5**	**20062**
Dimethoxyethane (DME)	5.2	5.2	28.7	28.7	295
Solvent	**5.2**	**5.2**	**28.7**	**28.7**	**295**
PPh_3	0.20	0.15	0.2	0.6	12
$Pd(OAc)_2$	0.05	0.05	0.2	-	2607
Catalyst	**0.2**	**0.2**	**0.4**	**0.6**	**2630**
CsF	2.9	2.9	12.9	24.4	4343
Auxiliaries Matherials	**2.9**	**2.9**	**12.9**	**24.4**	**4343**
2'-4'-6'-Trimethyl-2-methoxybiphenyl	-	-	-	-	-
$IB(OH)_2$	-	0.8	-	0.80	-
Product-coupled products	**-**	**0.8**	**-**	**0.80**	**-**
Total value of parameters	**10.8**	**9.9**	**52.9**	**62.0**	**27321**

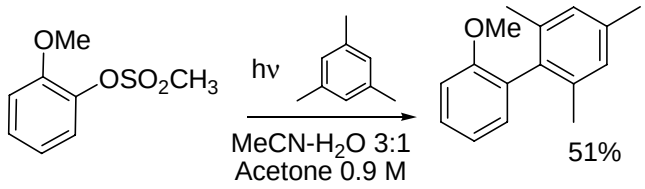
2.3.4. Reaction 12,hν[13]



66%;

Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
2-Chloroanisole	1.0	-	1.0	0.20	780
Mesitylene	16.1	15.3	24.1	61.2	1257
Reagents	**17.1**	**15.3**	**25.1**	**61.4**	**2037**
TFE	179	179	718	359	63012
Acetone	10.6	10.6	21.1	24.7	36
Solvents	**190**	**190**	**739**	**384**	**63048**
Triethylamine	0.7	0.70	2.4	0.7	38
Auxiliares (reaction)	**0.7**	**0.70**	**2.4**	**0.7**	**38**
2'-4'-6'-Trimethyl-2-methoxybiphenyl	-	-	-	-	-
Chloridric Acid	-	0.60	-	-	-
Product-coupled products	**-**	**0.60**	**-**	**-**	**-**
Total value of parameters	**208**	**206**	**766**	**446**	**65123**

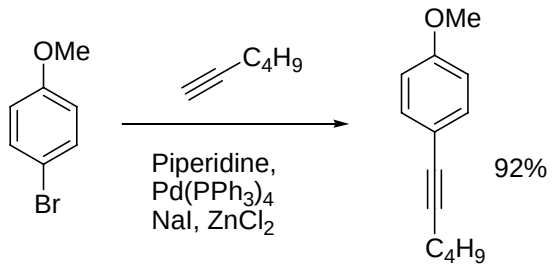
2.3.5. Reaction 13, hν[14]



Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
Guaiacol	1.10	-	1.60	-	83
Mesitylene	5.60	4.60	8.40	18.3	440
Methanesulfonylchloride	1.10	0.10	1.10	0.80	37
Triethylamine	1.30	0.40	4.60	0.40	73
Reagents	**9.10**	**5.10**	**15.7**	**19.5**	**633**
Acetonitrile	55.2	55.2	166	138	835
CH_2Cl_2	2.70	2.70	5.40	14.2	18
Water	23.4	23.4	23.4	23.4	1
Acetone	7.40	7.40	14.8	17.3	25
Solvents	**88.7**	**88.7**	**210**	**193**	**879**
2'-4'-6'-Trimethyl-2-methoxybiphenyl	-	-	-	-	-
Methanesulfonic acid	-	1.60	-	4.00	-
Trimethylammonium chloride	-	1.40	-	4.60	-
Product-coupled products	**-**	**3.00**	**-**	**8.60**	**-**
Total value of parameters	**97.8**	**96.8**	**226**	**221**	**1512**

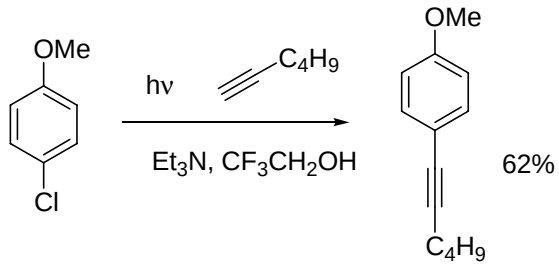
As hinted in the text, reactions 11-13 make use of different starting compounds (2-iodoanisole, 2-chloroanisole and guaiacol). However, the input parameters of the three compounds are quite similar and the output parameters are small or zero. Therefore, this difference has no major effect on the results, apart from an economical advantages in using less expensive guaiacol instead of halides. Anyway, major contribution to environmental and economical cost of reactions is given by nucleophile (eq. 11) or solvent (eq. 12 and 13) rather than the choise of aromatic derivative.

2.3.6. Reaction 14, Δ^{15}



Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
4-Bromoanisole	1.1	-	4.0	-	170
1-Hexyne	0.6	-	2.2	-	523
Reagents	**1.7**	**-**	**6.2**	**-**	**693**
Piperidine	6.7	6.7	23.3	26.6	344
Solvents	**6.7**	**6.7**	**23.3**	**26.6**	**344**
$Pd(PPh_3)_4$	0.4	0.4	2.8	0.4	15023
NaI	0.2	0.2	0.3	0.6	34
$ZnCl_2$	0.2	0.2	0.3	1.2	14
Catalysts	**0.8**	**0.8**	**3.4**	**2.2**	**15100**
NH_4Cl aq	30.8	30.8	33.8	63.8	152
CH_2Cl_2	81.8	81.8	164	546	559
Auxiliaries (isolation)	**113**	**113**	**198**	**610**	**711**
4-(1-Hexynyl)-anisole	-	-	-	-	-
HBr	-	0.4	-	2.1	-
Product-coupled products	**-**	**0.4**	**-**	**2.1**	**-**
Total value of parameters	**122**	**121**	**231**	**641**	**16800**

2.3.7. Reaction 15, hν[16]



Compounds	S^{-1}	E	E_{in}	E_{out}	€/Kg
4-Cloroanisole	1.2	-	5.5	-	1356
1-Hexyne	7.0	6.3	28.1	44.3	6584
Reagents	**8.2**	**6.3**	**33.6**	**44.3**	**7940**
2,2,2-Trifluoroethanol	238	238	715	1668	60140
Solvents	**238**	**238**	**715**	**1668**	**60140**
Triethylamine	0.9	-	3.0	2.0	20
Auxiliaries (Reaction)	**0.9**	**-**	**3.0**	**2.0**	**20**
4-(1-Hexynyl-anisole)	-	-	-	-	-
Chloridric acid	-	0.2	-	7.4	-
Product-coupled products	**-**	**0.2**	**0**	**7.4**	**-**
Total value of parameters	**247**	**245**	**752**	**1724**	**68100**

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