Electronic Supplementary Material (ESI) for Green Chemistry.


Supplementary Information

for

# Organic syntheses greenness assessment with multicriteria decision analysis

Marek Tobiszewski[a*], Witold Przychodzeń[b], Marta Bystrzanowska[a], Maria J. Milewska[b]

[a]Department of Analytical Chemistry, Faculty of Chemistry, Gdańsk University of Technology (GUT), 11/12 G. Narutowicza St., 80-233 Gdańsk, Poland.

[b]Department of Organic Chemistry, Faculty of Chemistry, Gdańsk University of Technology (GUT), 11/12 G. Narutowicza St., 80-233 Gdańsk, Poland.

* author for correspondence: marek.tobiszewski@pg.edu.pl

Table S1. Transformation of GHS Codes and Pictograms into points

| The Global Harmonized System (GHS) Codes and Pictograms | | | | | |
|---|---|---|---|---|---|
| | **Symbol** | **Pictogram** | **Name** | **Description** | **Points for assessment (0-10)** |
| **Physical hazards pictograms** | GHS01 |  | Exploding Bomb Explosives | Unstable explosives, Explosives, self-reactive substances and mixtures types A, B, organic peroxides types A,B | 5 |
| | GHS02 |  | Flame Flammables | Flammable gases cat. 1, aerosols cat. 1, 2, liquids cat. 1, 2, 3,4 and solids cat. 1, 2, self-reactive substances and mixtures types B, C, D, E, F, pyrophoric liquids and solids, combustible solids and liquids, self-heating substances and mixtures, substances and mixtures which in contact with water emit flammable gases, organic peroxides types B, C, D, E, | 8 |
| | GHS03 |  | Flame Over Circle Oxidizers | Oxidizing gases, liquidus and solids | 3 |
| | GHS04 |  | Gas Cylinder, Compressed Gases | Compressed gases, liquefied gases, refrigerated liquefied gases, dissolved gases | 2 |

| | | | | | |
|---|---|---|---|---|---|
| **Physical and health hazards pictograms** | GHS05 |  | Corrosion, Corrosives | Corrosive metals, explosives, flammable gases cat. 2, self-reactive substances and mixtures type G, organic peroxides type G, skin corrosion cat. 1A, 1B, 1C, serious eye damage cat. 1 | 3 |
| | GHS06 |  | Skull and Crossbones, Acute Toxicity | Acute toxicity cat. 1, 2, 3 (oral, dermal, inhalation) | 10 |
| **Health hazards pictograms** | GHS07 |  | Exclamation Mark, Irritant | Acute toxicity (oral, dermal, inhalation) cat. 4, skin irritation, eye irritation, skin sensitization, specific target organ toxicity following single exposure (respiratory tract irritation, narcotic effect) | 3 |
| | GHS08 |  | Health Hazard | Respiratory sensitization, germ cell mutagenicity cat. 1A, 1B, 2, carcinogenicity cat. 1A, 1B, 2, reproductive toxicity cat., 1A, 1B, 2, specific target organ toxicity following single exposure cat. 1, 2, specific target organ toxicity following repeated exposure cat. 1, 2, aspiration hazard cat. 1, 2 | 10 |
| **Environmental hazards pictograms** | GHS09 |  | Environment | Acute hazards to the aquatic environment cat. 1, chronic hazards to the aquatic environment cat. 1, 2, environmental toxicity cat. 1, 2 | 8 |

Table S2. List of alternatively used compounds for the purposes of chemicals characteristic for benzoic acid and γ-valerolactone synthesis.

| Original compound | | Changed compound | | Given points |
|---|---|---|---|---|
| CAS No. | Name | CAS No. | Name | |
| **Benzoic acid** | | | | |
| 13845-12-0 | dialuminium hexachloride | 12042-91-0 | dialuminium chloride pentahydroxide | 3 |
| 950206-91-4 | Copper, [1,3-bis[2,6-bis(1-methylethyl)phenyl]-1,3-dihydro-2H-imidazol-2-ylidene]iodo- | 578743-87-0 | 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene copper(I) chloride | 3 |
| 38609-76-6 | 3,5-bis(trifluoromethyl)pyridin-2-ol | 20857-47-0 | 3,5-bis(trifluoromethyl)pyridine | 21 |
| | water acidify; water basify | 7732-18-5 | water | 0 |
| **γ-Valerolactone** | | | | |
| | $CaLaRuSrO_6$ | 471-34-1 + 1312-81-8 + 12060-08-1 + 12036-10-1 | Mixture of: $CaCO_3$, $La_2O_3$, $Sc_2O_3$ and $RuO_2$ | 3 |
| | SBA-AM-IrTCPP/IrCP/IrTPP | 7439-88-5 + 917-23-7 | Iridium + meso-tetraphenylporphyrin | 11 |
| | $W(OTf)_6$ | 7440-33-7 | Mixture of tungsten + trifluoromethanesulfonate anion for transition metals | 11 |
| | ZnAl mixed oxide | 1314-13-2 + 1344-28-1 | Mixture of ZnO i $Al_2O_3$ | 19 |

Table S3. Numerical dataset for BA synthesis procedures

| No. | Characteristic of synthesis<br>Reactants/Solvent/Catalyst (Yes or No) | Reactants [point] | Atom Economy [%] | Efficiency [%] | Temperature [°C] | Pressure [MPa] | Time [h] | Solvent [point] | Catalyst [point] | Reagent [point] | Reference |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **1** | **Bz, $CO_2$/DMM/Cat** | 23 | 100 | 88 | 100 | 0 | 48 | 6 | 16 | 26 | [1] |
| **2** | **Bz, CO/TFA/Cat** | 51 | 91 | 100 | 2 | 0 | 20 | 6 | 3 | 16 | [2] |
| **3** | **Bz, $CO_2$/DMI, $H_2$Oa, $H_2$Ob/Cat** | 23 | 100 | 85 | 100 | 0 | 24.5 | 3 | 28 | 47 | [3] |
| **4** | **Bz, $CO_2$/-/Cat** | 23 | 100 | 86 | 10 | 1.9 | 12.5 | 0 | 3 | 6 | [4] |
| **5** | **Bz, $CO_2$/Bz/-** | 23 | 100 | 88 | 50 | 5.6 | 18 | 21 | 0 | 11 | [5] |
| **6** | **Bz, $CO_2$/THF/-** | 23 | 100 | 79 | 92 | 0 | 24 | 21 | 0 | 49 | [6] |
| **7** | **Bz, $CO_2$/-/Cat** | 23 | 100 | 61 | 60 | 2.9 | 48 | 0 | 6 | 3 | [7] |
| **8** | **Bz, OCl/$CS_2$, $H_2O$/-** | 42 | 59.5 | 66 | 4 | 0 | 22 | 21 | 0 | 30 | [8] |
| **9** | **Bz, FA/TFA, TFAA/Cat** | 42 | 98.4 | 53 | 10 | 0 | 48 | 12 | 3 | 16 | [9] |
| **10** | **Bz, $CO_2$/$H_2O$/Cat** | 23 | 100 | 20 | 60 | 0 | 12 | 0 | 6 | 0 | [10] |
| **11** | **Bz, CO/-/Cat** | 51 | 91 | 10 | 2 | 0 | 24 | 0 | 3 | 22 | [11] |
| **12** | **Bz, CO/TFA, TFAA/Cat** | 51 | 91 | 45 | 2 | 0 | 20 | 12 | 3 | 13 | [12] |
| **13** | **Bz, CO/HFIP, MeOH, $H_2$Oa/Cat** | 51 | 91 | 36 | 80 | 0 | 36 | 41 | 24 | 41 | [13] |
| **14** | **Bz, CO/$H_2O$, AcOH/Cat** | 51 | 91 | 42 | 110 | 0 | 62 | 11 | 43 | 16 | [14] |
| **15** | **Bz, BnOH/ACN/Cat** | 24 | 64 | 57 | 100 | 0 | 12 | 11 | 11 | 16 | [15] |
| **16** | **Bal$H_2O$/-** | 3 | 53.3 | 79 | 0 | 0 | 24 | 0 | 0 | 6 | [16] |
| **17** | **BrB, $CO_2$/CPME/-** | 21 | 60.7 | 100 | 63 | 0 | 0.5 | 11 | 0 | 8 | [17] |
| **18** | **Tol/$H_2O$/-** | 21 | 48.8 | 100 | 63 | 0.19 | 3 | 0 | 0 | 27 | [18] |

Abbreviation: ACN – acetonitrile, AcOH – acetic acid, Bal – benzaldehyde, BnOH - benzyl alcohol, BrB – bromobenzene, Bz – benzene, Cat – catalyst, CO - carbon monoxide, $CO_2$ - carbon dioxide, CPME - cyclopentyl methyl ether, $CS_2$ - carbon disulfide, DMI - dimethyl isosorbide, DMM – dimethoxymethane, FA - formic acid, $H_2O$ – water, $H_2$Oa – water acidified $H_2$Ob – water basified, HFIP - 1,1,1,3,3,3-hexafluoro-2-propanol, MeOH – methanol, OCl - oxalyl chloride, TFA - trifluoroacetic acid, TFAA - trifluoroacetic anhydride, THF – tetrahydrofuran, Tol – toluene

Table S4. Numerical dataset for GVL synthesis procedures

| No. | Characteristic of synthesis<br>Reactants/Solvent/Catalyst (Yes or No) | Reactants [point] | Atom Economy [%] | Efficiency [%] | Temperature [°C] | Pressure [MPa] | Time [h] | Solvent [point] | Catalyst [point] | Reagent [point] | Reference |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **1** | **Lev, $H_2$/DMF/Cat** | 16 | 84.7 | 100 | 80 | 0.9 | 12 | 21 | 11 | 0 | [19] |
| **2** | **Lev, $H_2$/H2O/Cat** | 16 | 84.7 | 100 | 80 | 3.4 | 5 | 0 | 3 | 0 | [20] |
| **3** | **Lev, TMDS/DCM/Cat** | 14 | 0.4 | 67 | 5 | 0 | 0.33 | 13 | 3 | 0 | [21] |
| **4** | **Lev, FA/$H_2O$/Cat** | 27 | 48.1 | 100 | 200 | 0 | 5 | 0 | 24 | 21 | [22] |
| **5** | **Lev, $H_2$/1,4-DX/Cat** | 16 | 84.7 | 100 | 180 | 0 | 2 | 21 | 31 | 0 | [23] |
| **6** | **Lev, IPA/IPA/Cat** | 17 | 42.4 | 41 | 120 | 0 | 0.008 | 11 | 8 | 0 | [24] |
| **7** | **o-VL/EMIM TfO/Cat** | 3 | 100 | 88 | 160 | 0 | 10 | 3 | 11 | 0 | [25] |
| **8** | **4-PA/PhCl/Cat** | 6 | 100 | 100 | 110 | 0 | 0.5 | 19 | 3 | 0 | [26] |
| **9** | **ML, *sec*-BuOH/*sec*-BuOH/Cat** | 14 | 36 | 100 | 130 | 0 | 0.5 | 11 | 8 | 0 | [27] |
| **10** | **FuOH, IPA/IPA/Cat** | 31 | 45.9 | 100 | 60 | 0 | 9 | 11 | 13 | 0 | [28] |
| **11** | **1,4-PDO, $O_2$/-/Cat** | 5 | 73.5 | 65 | 60 | 0 | 6 | 0 | 3 | 0 | [29] |
| **12** | **Lev, $H_2$/$H_2O$/Cat** | 16 | 84.7 | 100 | 10 | 5.9 | 13 | 0 | 18 | 0 | [30] |
| **13** | **Lev, FA/$H_2O$/Cat** | 27 | 48.1 | 74 | 120 | 1.4 | 6 | 0 | 19 | 0 | [31] |

Abbreviation: DCM – dichloromethane, 1,4-DX - 1,4-dioxane, DMF – dimethylformamide, EMIM TfO - 1-ethyl-3-methylimidazolium trifluoromethanesulfonate, FA - formic acid, FuOH - furfuryl alcohol, $H_2$ – hydrogen, $H_2O$ – water, IPA – isopropanol, Lev - levulinic acid, ML - methyl levulate, $O_2$ – oxygen, 4-PA - 4-pentenoic acid, 1,4-PDO - 1,4-pentanodiol, PhCl – chlorobenzene, *sec*-BuOH - 2-butanol, TMDS – tetramethyldisiloxane, o-VL - δ-valerolactone

[1] Gevorgyan, A., Hopmann, K. H., & Bayer, A. (2020). Formal C− H Carboxylation of Unactivated Arenes. *Chemistry–A European Journal*, *26*(27), 6064-6069. (DOI: 10.1002/chem.202000515)

[2] Lu, W., Yamaoka, Y., Taniguchi, Y., Kitamura, T., Takaki, K., & Fujiwara, Y. (1999). Palladium (II)-catalyzed carboxylation of benzene and other aromatic compounds with carbon monoxide under very mild conditions. *Journal of organometallic chemistry*, *580*(2), 290-294. (DOI: 10.1016/s0022-328x(98)01160-7)

[3] Gevorgyan, A., Hopmann, K. H., & Bayer, A. (2020). Exploration of new biomass-derived solvents: application to carboxylation reactions. ChemSusChem. (DOI: 10.1002/cssc.201903224)

[4] Device and method for preparing aromatic acid by direct carboxylation of carbon dioxide By Wang, Wentao et al. From Faming Zhuanli Shenqing, 108129296, 08 Jun 2018

[5] Olah, G. A., Török, B., Joschek, J. P., Bucsi, I., Esteves, P. M., Rasul, G., & Surya Prakash, G. K. (2002). Efficient chemoselective carboxylation of aromatics to arylcarboxylic acids with a superelectrophilically activated carbon dioxide− Al2Cl6/Al system. *Journal of the American Chemical Society*, *124*(38), 11379-11391. (DOI: 10.1021/ja020787o)

[6] Method for producing, via organometallic compounds, organic intermediate products By Meudt, Andreas From PCT Int. Appl., 2003033503, 24 Apr 2003

[7] Nemoto, K., Yoshida, H., Egusa, N., Morohashi, N., & Hattori, T. (2010). Direct carboxylation of arenes and halobenzenes with CO2 by the combined use of AlBr3 and R3SiCl. *The Journal of organic chemistry*, *75*(22), 7855-7862. (DOI: 10.1021/jo101808z)

[8] Villani, A. J., Etzkorn, F., Rotert, G. A., & Heys, J. R. (1988). Synthesis of 13C, 14C and 2H13C labeled adrenoceptor antagonists: 6-chloro-2, 3, 4, 5-tetrahydro-3-methyl-1H-3-benzazepine hydrochloride and its N-desmethyl analog. *Journal of Labelled Compounds and Radiopharmaceuticals*, *25*(12), 1339-1347. (DOI: 10.1002/jlcr.2580251208)

[9] Sakakibara, K., Yamashita, M., & Nozaki, K. (2005). An efficient Pd (II)-based catalyst system for carboxylation of aromatic C–H bond by addition of a phosphenium salt. Tetrahedron letters, 46(6), 959-962. (DOI: 10.1016/j.tetlet.2004.12.027)

[10] Gu, M. (2015). Carboxylation of Aromatics by CO 2 under "Si/Al Based Frustrated Lewis Pairs" Catalytic System. *Journal of Materials Science and Chemical Engineering*, *3*(01), 103. (DOI: 10.4236/msce.2015.31015)

[11] Sakakibara, K., Yamashita, M., & Nozaki, K. (2005). An efficient Pd (II)-based catalyst system for carboxylation of aromatic C–H bond by addition of a phosphenium salt. Tetrahedron letters, 46(6), 959-962. (DOI: 10.1016/j.tetlet.2004.12.027)

[12] Kalinovskii, I. O., Pogorelov, V. V., Gelbshtein, A. I., & Akhmetov, N. G. (2001). Oxidative carbonylation of aromatic hydrocarbons in the system containing Pd or Rh compound, trifluoroacetic acid and its anhydride, and MnO2 or Mn2O3. *Russian journal of general chemistry*, *71*(9), 1457-1462. (DOI: 10.1023/A:1013970406482)

[13] Wang, P., Verma, P., Xia, G., Shi, J., Qiao, J. X., Tao, S., ... & Yu, J. Q. (2017). Ligand-accelerated non-directed C–H functionalization of arenes. *Nature*, *551*(7681), 489-493. (DOI: 10.1038/nature24632)

[14] Yamada, S., Ohashi, S. I., Obora, Y., Sakaguchi, S., & Ishii, Y. (2008). Carboxylation of benzene with CO and O2 catalyzed by Pd (OAc) 2 combined with molybdovanadophosphates. *Journal of Molecular Catalysis A: Chemical*, *282*(1-2), 22-27. (DOI: 10.1016/j.molcata.2007.11.022)

[15] Mahajan, B., Aand, D., & Singh, A. K. (2018). Silver-Catalyzed Arylation of (Hetero) arenes via Oxidative Benzylic C− C Bond Cleavage of Benzyl Alcohols/Benzaldehyde. *ChemistrySelect*, *3*(43), 12336-12340. (DOI: 10.1002/slct.201803215)

[16] Geissman, T. A. (2004). The C annizzaro Reaction. *Organic reactions*, *2*, 94-113.

[17] Goldbach, M., Danieli, E., Perlo, J., Kaptein, B., Litvinov, V. M., Blümich, B., ... & Duchateau, A. L. (2016). Preparation of Grignard reagents from magnesium metal under continuous flow conditions and on-line monitoring by NMR spectroscopy. *Tetrahedron Letters*, *57*(1), 122-125. (DOI: 10.1016/j.tetlet.2015.11.077)

[18] Ambulgekar, G. V., Samant, S. D., & Pandit, A. B. (2004). Oxidation of alkylarenes to the corresponding acids using aqueous potassium permanganate by hydrodynamic cavitation. Ultrasonics sonochemistry, 11(3-4), 191-196. (DOI: 10.1016/j.ultsonch.2004.01.027)

[19] Anjali, K., Aswini, M. S., Aswin, P., Ganesh, V., & Sakthivel, A. (2019). Iridium Tetra (4-carboxyphenyl) Porphyrin, Calix [4] pyrrole and Tetraphenyl Porphyrin Complexes as Potential Hydrogenation Catalysts. *European Journal of Inorganic Chemistry*, *2019*(38), 4087-4094. (DOI: 10.1002/ejic.201900762)

[20] Hengne, A. M., & Rode, C. V. (2012). Cu–ZrO 2 nanocomposite catalyst for selective hydrogenation of levulinic acid and its ester to γ-valerolactone. *Green Chemistry*, *14*(4), 1064-1072. (DOI: 10.1039/c2gc16558a)

[21] Xie, H., Lu, J., Gui, Y., Gao, L., & Song, Z. (2017). (HMe2SiCH2) 2: A Useful Reagent for B (C6F5) 3-Catalyzed Reduction–Lactonization of Keto Acids: Concise Syntheses of (–)-cis-Whisky and (–)-cis-Cognac Lactones. *Synlett*, *28*(18), 2453-2459. (DOI: 10.1055/s-0036-1588488)

[22] Yu, Z., Lu, X., Xiong, J., Li, X., Bai, H., & Ji, N. (2020). Heterogeneous Catalytic Hydrogenation of Levulinic Acid to γ-Valerolactone with Formic Acid as Internal Hydrogen Source. *ChemSusChem*, *13*(11), 2916-2930. (DOI: 10.1002/cssc.202000175)

[23] Pinto, B. P., Fortuna, A. L. L., Cardoso, C. P., & Mota, C. J. (2017). Hydrogenation of levulinic acid (LA) to γ-Valerolactone (GVL) over Ni–Mo/C catalysts and water-soluble solvent systems. *Catalysis Letters*, *147*(3), 751-757. (DOI: 10.1007/s10562-017-1977-9)

[24] Al-Shaal, M. G., Calin, M., Delidovich, I., & Palkovits, R. (2016). Microwave-assisted reduction of levulinic acid with alcohols producing γ-valerolactone in the presence of a Ru/C catalyst. *Catalysis Communications*, *75*, 65-68. (DOI: 10.1016/j.catcom.2015.12.001)

[25] Xie, Z. Y., Deng, J., & Fu, Y. (2018). W (OTf) 6-Catalyzed Synthesis of γ-Lactones by Ring Contraction of Macrolides or Ring Closing of Terminal Hydroxyfatty Acids in Ionic Liquid. *ChemSusChem*, *11*(14), 2332-2339. (DOI: 10.1002/cssc.201800587)

[26] Zhou, Y., Woo, L. K., & Angelici, R. J. (2007). Solid acid catalysis of tandem isomerization-lactonization of olefinic acids. *Applied Catalysis A: General*, *333*(2), 238-244. (DOI: 10.1016/j.apcata.2007.09.013)

[27] Zhao, T., Ju, Z., Zhang, Y., Han, L., & Xiao, W. (2020). Specific role of aluminum site on the activation of carbonyl groups of methyl levulinate over Al (OiPr) 3 for γ-valerolactone

production. *Chemical Engineering Journal*, *390*, 124505. (DOI: 10.1016/j.cej.2020.124505)

[28] Yang, Z., Huang, Y. B., Guo, Q. X., & Fu, Y. (2013). RANEY® Ni catalyzed transfer hydrogenation of levulinate esters to γ-valerolactone at room temperature. *Chemical communications*, *49*(46), 5328-5330. (DOI: 10.1039/c3cc40980e)

[29] Kumar, N., Naveen, K., Bhatia, A., Muthaiah, S., Siruguri, V., & Paul, A. K. (2020). Solvent and additive-free efficient aerobic oxidation of alcohols by a perovskite oxide-based heterogeneous catalyst. *Reaction Chemistry & Engineering*, *5*(7), 1264-1271. (DOI: 10.1039/d0re00189a)

[30] Zhang, K., Meng, Q., Wu, H., Yuan, T., Han, S., Zhai, J., ... & Han, B. (2021). Levulinic acid hydrogenation to γ-valerolactone over single Ru atoms on a TiO 2@ nitrogen doped carbon support. *Green Chemistry*, *23*(4), 1621-1627. (DOI: 10.1039/d0gc04108d)

[31] Belguendouz, M. N., Gancedo, J., Rapado, P., Ursueguía, D., Patiño, Y., Faba, L., ... & Ordóñez, S. (2021). Selective synthesis of γ-valerolactone from levulinic and formic acid over ZnAl mixed oxide. *Chemical Engineering Journal*, *414*, 128902. (DOI: 10.1016/j.cej.2021.128902)