Unification of Reaction Metrics II: Evaluation of Named Organic Reactions and Application to Reaction Discovery

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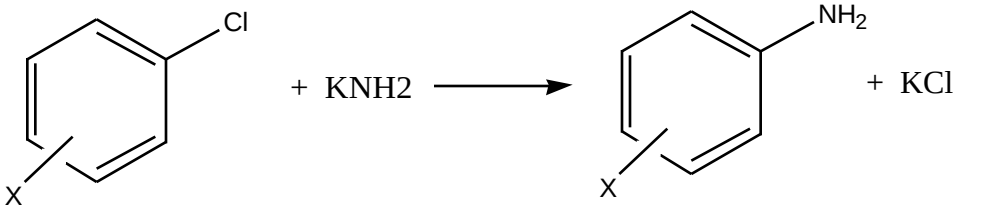
Supplementary Material

Table D10. Categorization of Named Substitution Reactions by Minimum Atom Economy and Maximum Environmental Impact Factor
(Reactions are listed alphabetically.)

Aniline synthesis
Hrutfiord, B.F.; Bunnett, J.F. *J. Am. Chem. Soc.* **1958**, 80, 2021
Panar, M.; Roberts, J.D. *J. Am. Chem. Soc.* **1960**, 82, 3629
Bunnett, J.F.; Hrutfriord, B.F. *J. Org. Chem.* **1962**, 27, 4152
Bunnett, J.F.; Kim, J.K. *J. Am. Chem. Soc.* **1970**, 92, 7464



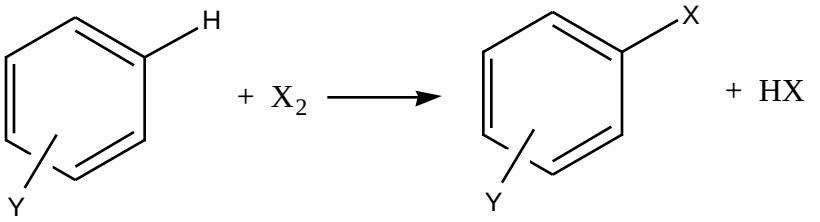
x + 107.45 55 x + 88 74.45

X = x (sum of substituents)

AE = [x + 88]/[x + 162.45]; **AE(min) = 0.56**; E = 74.45/[x + 88]; **E(max) = 0.80**

Aromatic Halogenation

Scheufelen, A. *Ann. Chem.* **1885**, 231, 152
Schramm, J. *Chem. Ber.* **1885**, 18, 607
Seelig, E. *Ann. Chem.* **1887**, 237, 129
Rilliet, A.; Ador, E. *Chem. Ber.* **1875**, 8, 1286
Mueller, H. *J. Chem. Soc.* **1862**, 15, 41



y + 73 2x y + x + 72 x + 1

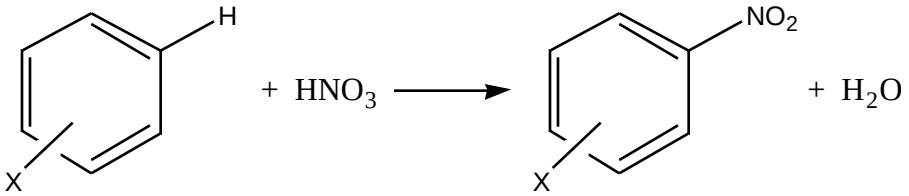
Y = y (sum of substituents); X = x (halogen)

AE = [x + y + 72]/[2x + y + 73]; E = [x + 1]/[x + y + 72]

X	E(max)	AE(min)
Cl	0.32	0.76
Br	0.52	0.66
I	0.63	0.61

Aromatic Nitration

Kopp, H. *Ann. Chem.* **1856**, 98, 367



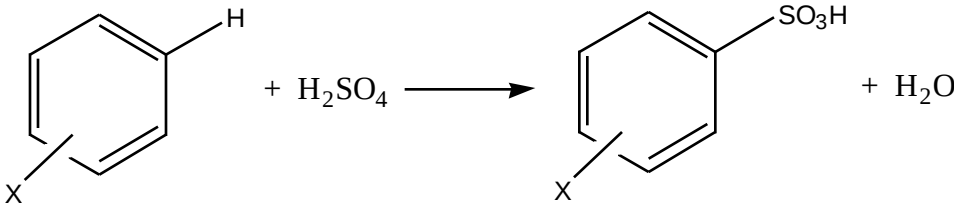
x + 73 63 x + 118 18

X = x (sum of substituents)

AE = [x + 118]/[x + 136]; **AE(min) = 0.87**; E = 18/[x + 118]; **E(max) = 0.15**

Aromatic Sulphonation

Ador, E.; Meyer, V. *Ann. Chem.* **1871**, 159, 1
Meyer, V.; Michler, W. *Chem. Ber.* **1875**, 8, 672
Barth, L.; Senhofer, C. *Chem. Ber.* **1875**, 8, 754
Ascher, M.; Meyer, V. *Chem. Ber.* **1871**, 4, 323
Noelting, E. *Chem. Ber.* **1875**, 8, 1091



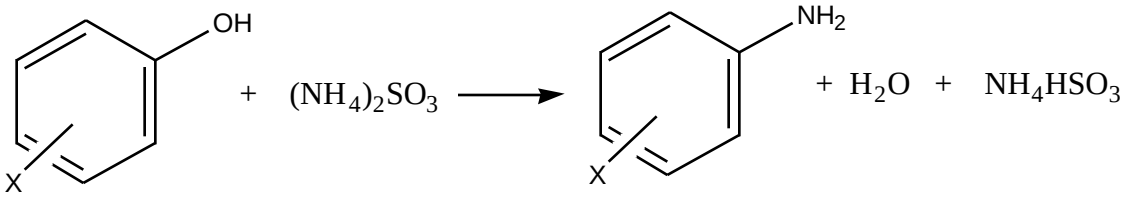
x + 73 98 x + 153 18

X = x (sum of substituents)

AE = [x + 153]/[x + 171]; **AE(min) = 0.90**; E = 18/[x + 153]; **E(max) = 0.11**

Bucherer reaction

Bucherer, T., *J. Prakt. Chem*. **1904**, 69, 49



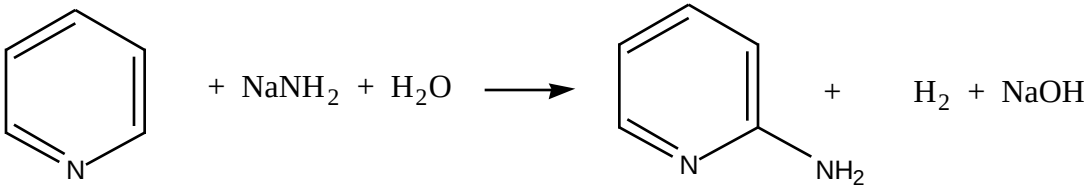
x + 89 116 x + 88 18 99

X = x (sum of substituents)

AE = [x + 88]/[x + 205]; **AE(min) = 0.43**; E = 117/[x + 88]; **E(max) = 1.33**

Chichibabin reaction

Chichibabin, A.E.; Zeide, O.A., *J. Russ. Phys. Chem. Soc*. **1914**, 46, 1216

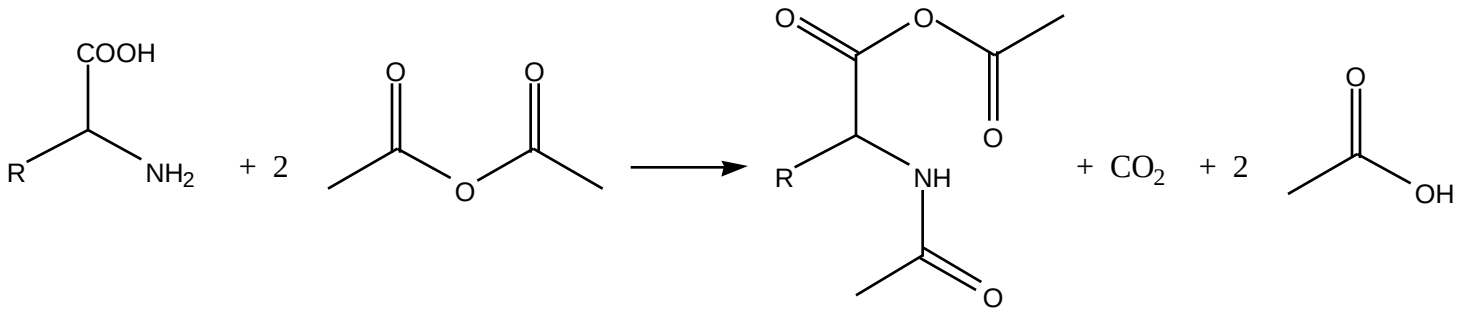


79 39 18 94 2 40

AE(min) = 0.69; E(max) = 0.45

Dakin-West reaction

Dakin, H.D.; West, R., *J. Biol. Chem*. **1928**, 78, 91; 745; 757



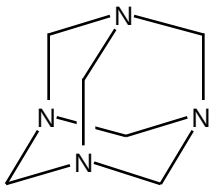
x + 74 204 x + 114 44 120

R = x

AE = [x + 114]/[x + 278]; **AE(min) = 0.41**; E = 164/[x + 114]; **E(max) = 1.43**

Delepine reaction

Délepine, M., *Bull. Soc. Chim. Fr.* **1895**, 13, 352



$$+ \; 4\ RCH_2X \; + \; 12\ HX \longrightarrow 4\ RCH_2NH_3^+\ X^- \; + \; 6\ CH_2X_2$$

140	4(x + y + 14)	12(x + 1)	4(x + y + 31)	6(2x + 14)

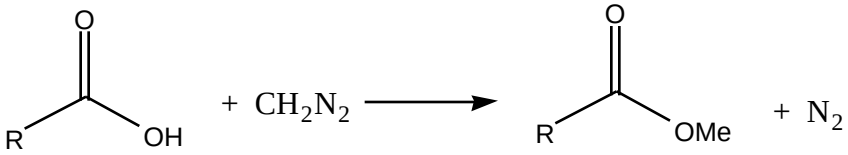
X = x (halide); R = y

AE = [4(x + y + 31)]/[16x + 4y + 208]; E = [6(2x + 14)]/[4(x + y + 31)]

X	**E(max)**	**AE(min)**
F	1.56	0.39
Cl	1.92	0.34
Br	2.35	0.30
I	2.54	0.28

Esterification with Diazomethane

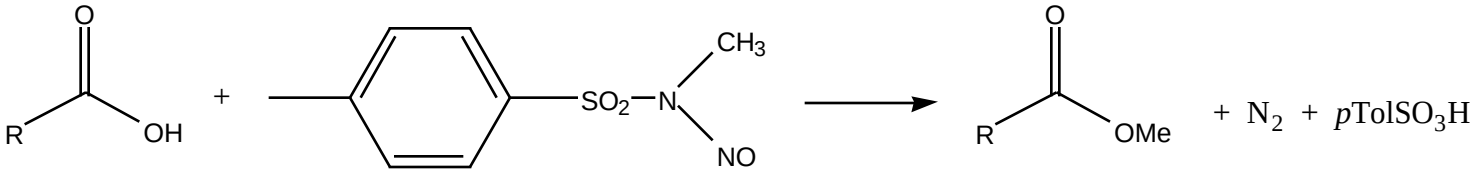
Herzig, J.; Pollak, J. *Monatsch. Chem.* **1908**, 29, 263
Wegschneidler, R.; Gehringer, H. *Monatsch. Chem.* **1909**, 29, 529
Bouveault, L.; Locquin, R. *Bull. Soc. Chim. Fr.* **1910**, 5[4], 1136
De Boer, T.J.; Backer, H.J. *Org. Synth. Coll. Vol. IV* **1963**, 250



x + 45 42 x + 59 28

R = x

AE = [x + 59]/[x + 87]; **AE(min) = 0.68**; E = 28/[x + 59]; **E(max) = 0.47**



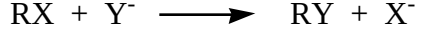
x + 45 214 x + 59 28 172

R = x

AE = [x + 59]/[x + 259]; **AE(min) = 0.23**; E = 200/[x + 59]; **E(max) = 3.33**

Finkelstein reaction

Perkin, W.H.; Duppa, B.F., *Ann. Chem*. **1859**, 112, 125
Finkelstein, H., *Chem. Ber*. **1910**, 43, 1528



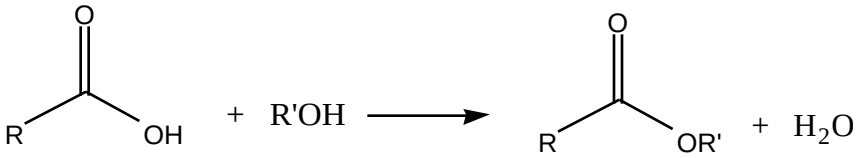
x + r y y + r x

AE = [y + r]/[x + y + r]; E = x/[y + r]

X	Y	E(max)	AE(min)	
Cl	Cl	0	1	(degenerate case)
Cl	Br	0.44	0.69	
Cl	I	0.28	0.78	
Br	Cl	2.25	0.31	
Br	Br	0	1	(degenerate case)
Br	I	0.63	0.61	
I	Cl	3.58	0.22	
I	Br	1.59	0.39	
I	I	0	1	(degenerate case)

Fischer esterification

Fischer, E.; Speier, A., *Chem. Ber*. **1895**, 28, 3252



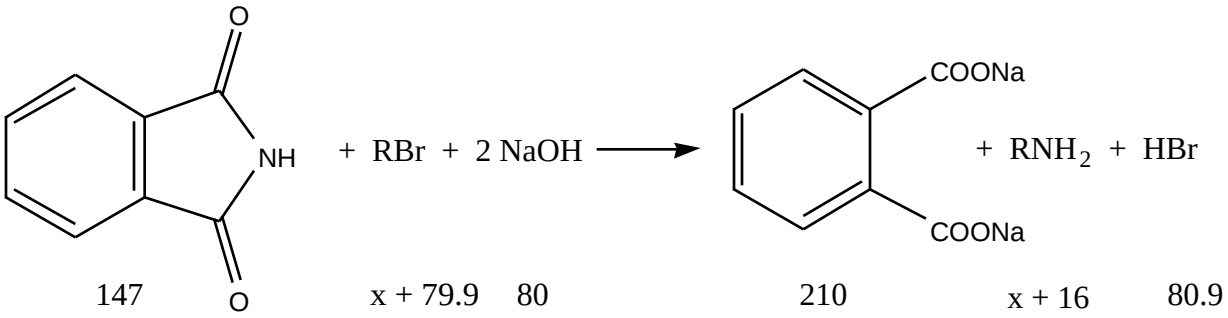
x + 45 y + 17 x + y + 44 18

R = x; R' = y

AE = [x + y + 44]/[x + y + 62]; **AE(min) = 0.72**; E = 18/[x + y + 44]; **E(max) = 0.39**

Gabriel synthesis

Gabriel, S., *Chem. Ber*. **1887**, 20, 2224



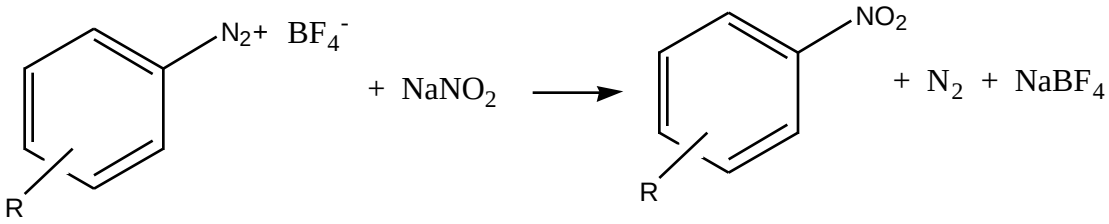
147 x + 79.9 80 210 x + 16 80.9

R = x

AE = [x + 16]/[x + 306.9]; **AE(min) = 0.055**; E = 290.9/[x + 16]; **E(max) = 17.11**

Gattermann reaction

Gattermann, L., *Chem. Ber*. **1898**, 31, 1149



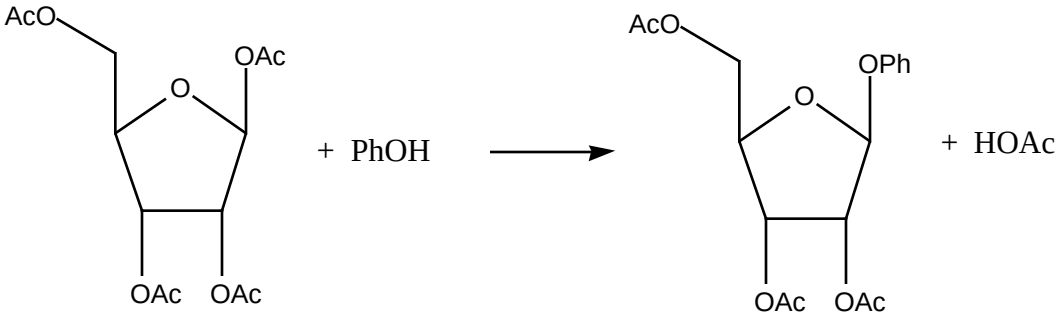
x + 187 69 x + 118 28 110

R = x (sum of substituents)

AE = [x + 118]/[x + 256]; **AE(min) = 0.47**; E = 138/[x + 118]; **E(max) = 1.12**

Helferich method

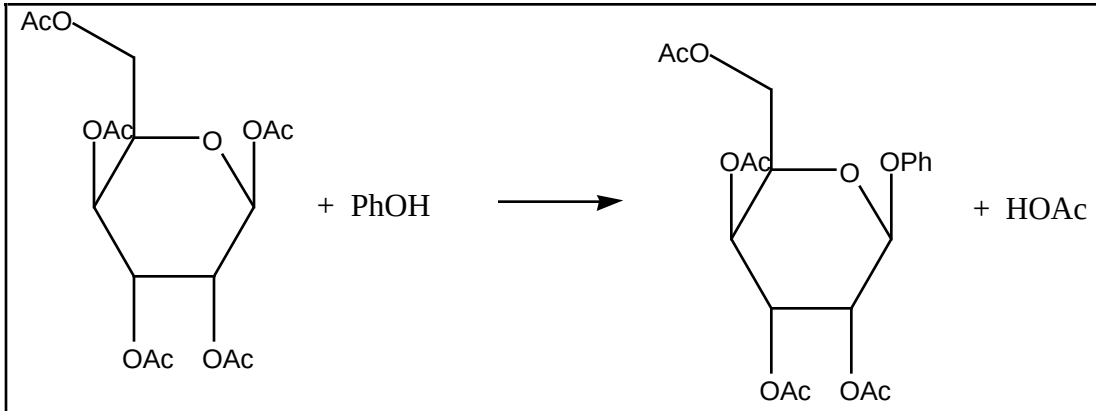
Helferich, B.; Schmitz-Hillebrecht, E. *Chem. Ber.* **1933**, 66, 378



318 94 454 60

5C sugars

AE = 0.88; E = 0.13

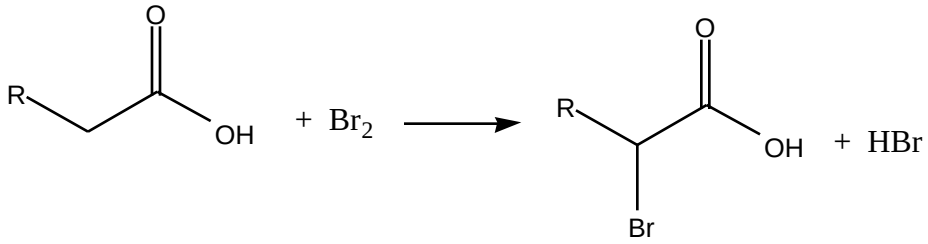


390 94 560 60

6C sugars

AE = 0.90; E = 0.11

Hell-Volhard-Zelinsky reaction
Hell, C., *Chem. Be*r. **1881**, 14, 891
Volhard, J., *Ann. Chem*. **1887**, 242, 141
Zelinsky, N., *Chem. Ber*. **1887**, 20, 2026



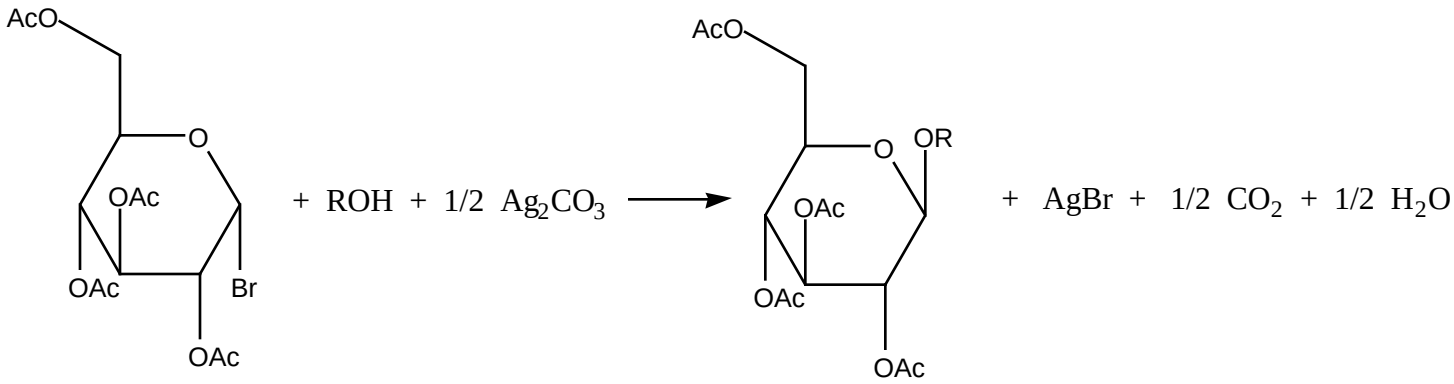
x + 59 159.8 x + 137.9 80.9

R = x

AE = [x + 137.9]/[x + 218.8]; **AE(min) = 0.63**; E = 80.9/[x + 137.9]; **E(max) = 0.58**

Koenigs-Knorr synthesis

Koenigs, W.; Knorr, E. *Chem. Ber.* **1901**, 34, 957



410.9 x + 17 138 x + 347 187.9 22 9

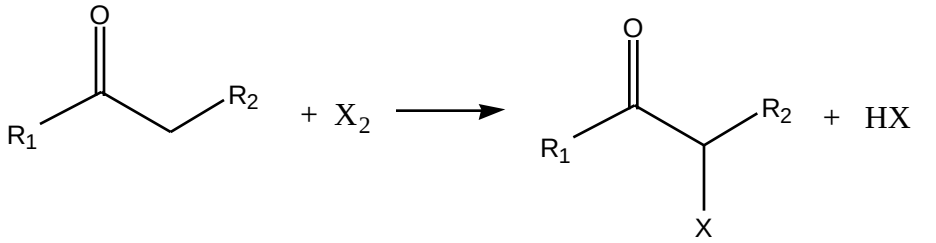
R = x

AE = [x + 347]/[x + 565.9]; **AE(min) = 0.61**; E = 218.9/[x + 347]; **E(max) = 0.62**

Lapworth reaction

Lapworth, A., *J. Chem. Soc.* **1903**, 83, 995

Lapworth, A., *J. Chem. Soc.* **1904**, 85, 1206



y + z + 42 2x x + y + z + 41 x + 1

R1 = y; R2 = z; X = x (halide)

AE = [x + y + z + 41]/[2x + y + z + 42]; E = [x + 1]/[x + y + z + 41]

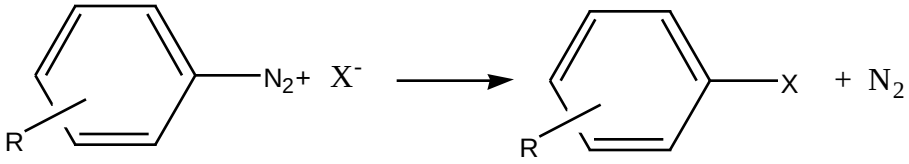
AE(min) = [x + 43]/[2x + 42]; **E(max) = [x + 1]/[x + 43]**

X	**E(max)**	**AE(min)**
Cl	0.46	0.68
Br	0.66	0.60
I	0.75	0.57

Sandmeyer reaction

Sandmeyer, T., *Chem. Ber*. **1884**, 17, 1633

Sandmeyer, T., *Chem. Ber*. **1884**, 17, 2650



x + y + 100 x + y + 72 28

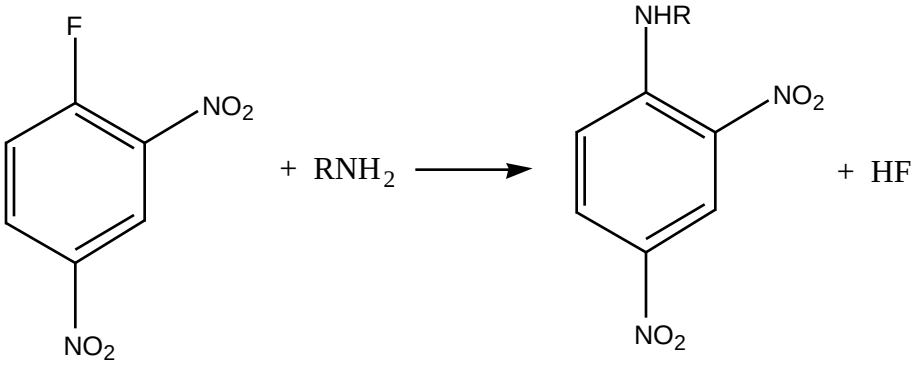
R = y (sum of substituents); X = x (halide)

AE = [x + y + 72]/[x + y + 100]; E = 28/[x + y + 72]

X	E(max)	AE(min)
Cl	0.25	0.80
Br	0.18	0.85
I	0.14	0.88

Sanger reaction

Sanger, F., *Biochem. J.* **1945**, 39, 507



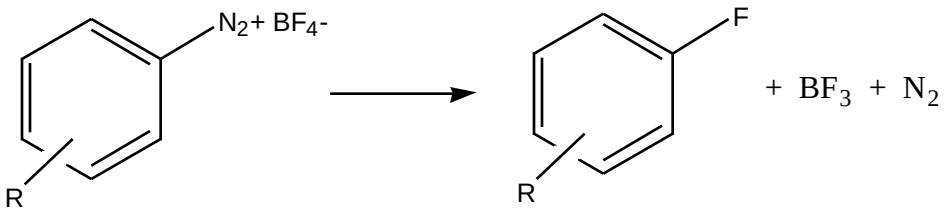
186 x + 16 x + 182 19

R = x

AE = [x + 182]/[x + 202]; **AE(min) = 0.90**; E = 20/[x + 182]; **E(max) = 0.11**

Schiemann reaction

Balz, G.; Schiemann, G., *Chem. Ber*. **1927**, 60, 1186



x + 187 x + 91 68 28

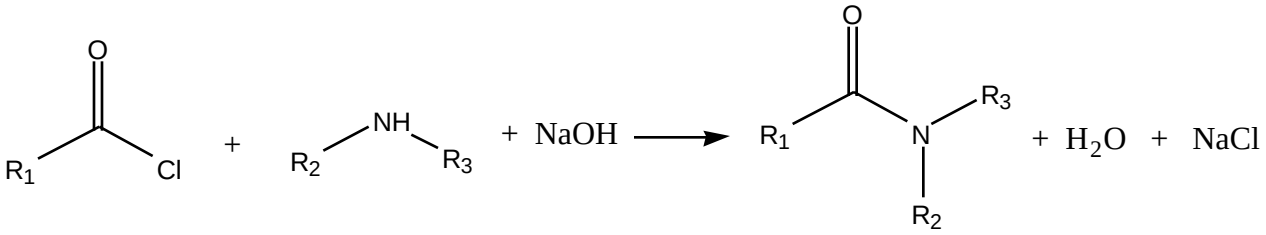
R = x (sum of substituents)

AE = [x + 91]/[x + 187]; **AE(min) = 0.50**; E = 96/[x + 91]; **E(max) = 1**

Schotten-Baumann reaction

Schotten, C., *Chem. Ber*. **1884**, 17, 2544

Baumann, E., *Chem. Ber*. **1886**, 19, 3218



x + 63.45 y + z + 15 40 x + y + z + 42 18 58.45

R1 = x; R2 = y; R3 = z

AE = [x + y + z + 42]/[x + y + z + 118.45]; **AE(min) = 0.37**; E = 76.45/[x + y + z + 42]; **E(max) = 1.70**

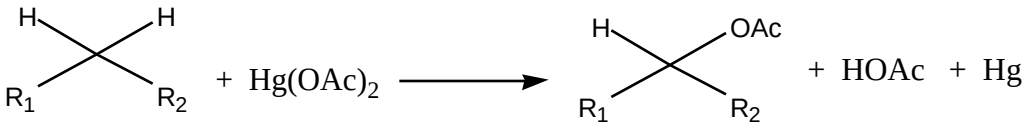
Synthesis of acetates via oxymercuration

Brook, A.G.; Wright, G.F. *Can. J. Res.* **1950**, 28B, 623

Wright, G.F. *Chemistry in Canada* **1950**, 2(9), 29

Wright, G.F. *Ann. N.Y. Acad. Sci.* **1957**, 65, 436

Abercrombie, M.J.; Rodgman, A.; Bharucha, K.R.; Wright, G.F. *Can. J. Chem.* **1959**, 37, 1328



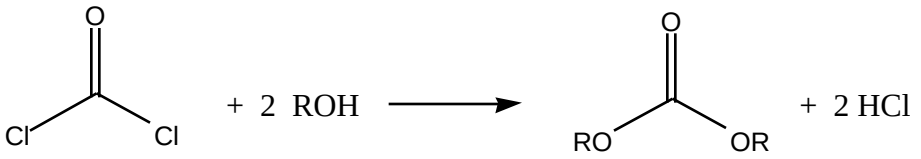
x + y + 14 319 x + y + 72 60 201

R1 = x; R2 = y

AE = [x + y + 72]/[x + y + 333]; **AE(min) = 0.22**; E = 261/[x + y + 72]; **E(max) = 3.53**

Synthesis of Carbonate diesters, Carbamates (Urethanes), and Ureas

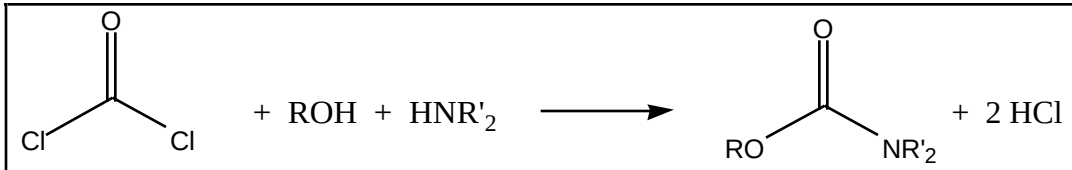
Kym, P. *J. Prakt. Chem.* **1907**, 75, 323
Friedrich Bayer & Co., US Pat. 935,017 (1909/09/28)
Friedrich Bayer & Co., US Pat. 935,018 (1909/09/28)
Friedrich Bayer & Co., DE Pat. 234,637 (1910/05/21)
Friedrich Bayer & Co., GB Pat. 1,012,433 (1910/05/21)
Abbott Labs, GB 255,971 (1925/05/06)
Miescher, K.; Kaeg, H., US Pat. 2,173,423 (1939/09/19)



98.9 2x + 34 2x + 60 72.9

R = x

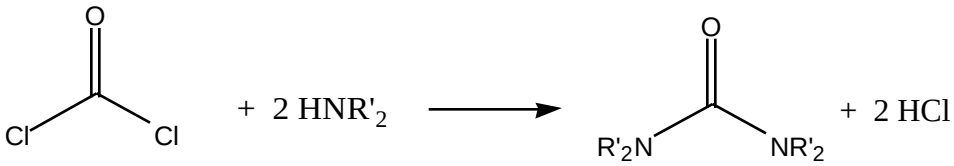
AE = [2x + 60]/[2x + 132.9]; **AE(min) = 0.46**; E = 72.9/[2x + 60]; **E(max) = 1.18**



98.9 x + 17 2y + 15 x + 2y + 58 72.9

R = x; R' = y

AE = [x + 2y + 58]/[2x + 130.9]; **AE(min) = 0.46**; E = 72.9/[x + 2y + 58]; **E(max) = 1.20**



98.9 2(2x + 15) 4x + 56 72.9

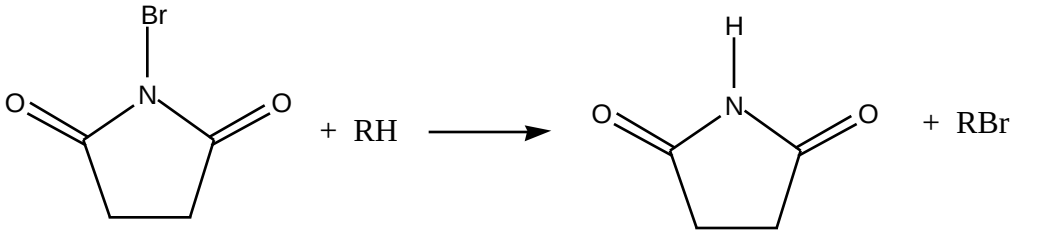
R' = x

AE = [4x + 56]/[4x + 128.9]; **AE(min) = 0.45**; E = 72.9/[4x + 56]; **E(max) = 1.22**

Wohl-Ziegler bromination

Wohl, A. *Chem. Ber.* **1919**, 52, 51

Ziegler, K.; Spath, E.; Schaaf, E.; Schumann, W.; Winkelmann, E. *Ann. Chem.* **1942**, 551, 80



177.9 x + 1 99 x + 79.9

R = x

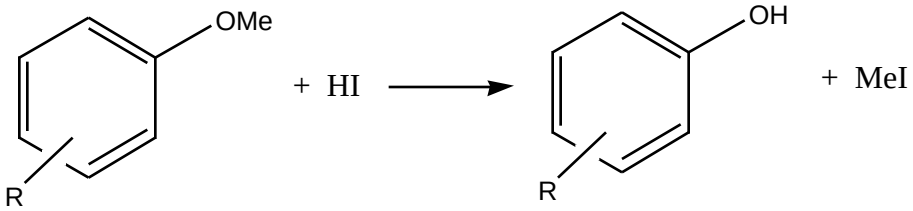
AE = [x + 79.9]/[x + 178.9]; **AE(min) = 0.45;** E = 99/[x + 79.9]; **E(max) = 1.22**

Zeisel determination

Zeisel, S. *Monatsch. Chem.* **1885**, 6, 989

Zeisel, S. *Monatsch. Chem.* **1886**, 7, 406

Zeisel, S.; Fanto, R. *Z. Anal. Chem.* **1903**, 42, 549



x + 103 128 x + 89 142

R = x (sum of substituents)

AE = [x + 89]/[x + 231]; **AE(min) = 0.40**; E = 142/[x + 89]; **E(max) = 1.53**