

INDEX

Index. This book has unique core content: detailed descriptions for processes intended to be used for large scale manufacturing. Precedent for the use of name reactions, reagents, solvents, and azeotropic distillations in manufacturing processes can be accessed using the indices below.

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REAGENT INDEX

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SOLVENT INDEX

Solvents used in processes described in this book can be separated into four groups: 1) common solvents routinely used in pharmaceutical manufacturing, 2) common solvents which are undesirable for scale up from an E H & S perspective, 3) common solvents often used as a catalyst or reagent, and 4) solvents used less frequently to achieve a specific solubility, stability, or reaction temperature objective. Solvents in groups 2, 3, and 4 are indexed in this section.

One surprising result of the analysis of the "hits" is that group 2 solvents chloroform, diisopropyl ether, and ether ether are still being used in some process R & D groups.

Group 1. Common solvents routinely used in pharmaceutical manufacturing

acetic acid
acetone
acetonitrile (ACN)
dichloromethane (DCM)
ethanol
ethyl acetate
heptane
hexanes
isopropanol (IPA)
methanol
methyl *tert*-butyl ether (MTBE)
N,N-dimethylformamide (DMF)
tetrahydrofuran (THF)
toluene

Group 2. Common solvents which are undesirable from an environmental health and safety perspective

1,4-dioxane, 19, 20, 24, 80, 102, 103, 113, 122, 137, 143, 170, 205, 222, 257, 265, 266, 269, 281, 329, 333, 336, 341, 342

benzene, 93, 233, 258, 260–262, 264, 290, 351
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Group 3. Common solvents often used as catalyst or reagent

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Group 4. Common solvents used less often to achieve a specific solubility, hydrolytic stability, or temperature objective.

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1,2-dimethoxyethane (DME), 32, 50, 81, 100, 174, 276, 324, 325, 350
1,3-dimethyl-2-imidazolidinone (DMEU), 50, 51
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cumene, 137, 229
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ethylbenzene, 326, 327
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isopropyl acetate, 145, 156
methyl isobutyl ketone (MIBK), 46, 121, 122, 156
N,N-dimethylacetamide (DMA), 35, 39, 43, 93, 156, 183, 185, 191, 222, 223, 231
N-methylpyrrolidinone (NMP), 39, 93, 146–148, 156, 185, 194, 197
PEG-X (X = 200/400/600/1500/4000), 16, 23, 27, 54, 55, 93, 99, 197
sulfolane, 40, 54, 55, 59
triglyme, 306, 307
xylenes, 137, 139–145, 155, 158, 161, 167, 229, 315, 321, 333

AZEOTROPE INDEX

This index keys on the term azeotrope used in process descriptions in the book.

The azeotropic distillations described can be separated into two groups: Group 1 distillations used to dry (separate water from) organic solutions and Group 2 distillations used to exchange one organic solvent for another. Group 1 azeotropic distillations are listed by organic solvent component. If there is more than one organic solvent, the mixture is indexed by the major component. Group 2 azeotropic distillations are indexed by initial solvent.

Group 1. Separation of water from organic solvents and organic solvent mixtures by azeotropic distillation

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heptane, 319

heptane-toluene (4:1), 323

heptane-toluene (9:1), 316

heptane-toluene-tetrahydrofuran (4.3:1.3:1), 318

hexane, 301

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methyl *tert*-butyl ether, 50, 142, 156

methyl *tert*-butyl ether-tetrahydrofuran (1.9:1), 320

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tetrahydrofuran-methyl *tert*-butyl ether (1.7:1), 320

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180, 198, 235, 299, 300, 310, 316, 318, 320–322,

329–331, 339, 348

Group 2. Separation of organic solvent mixtures by azeotropic distillation

ethanol to ethyl acetate 120¹

toluene to 1-propanol 87

toluene to ethanol 87, 159

1. The challenging separation of mixtures of ethyl acetate and ethanol can be achieved by adding a third solvent. Suitable third solvents include methyl *tert*-butyl ether and methyl formate. See: Berg, L. US 5,993,610 (11/30/1999).

