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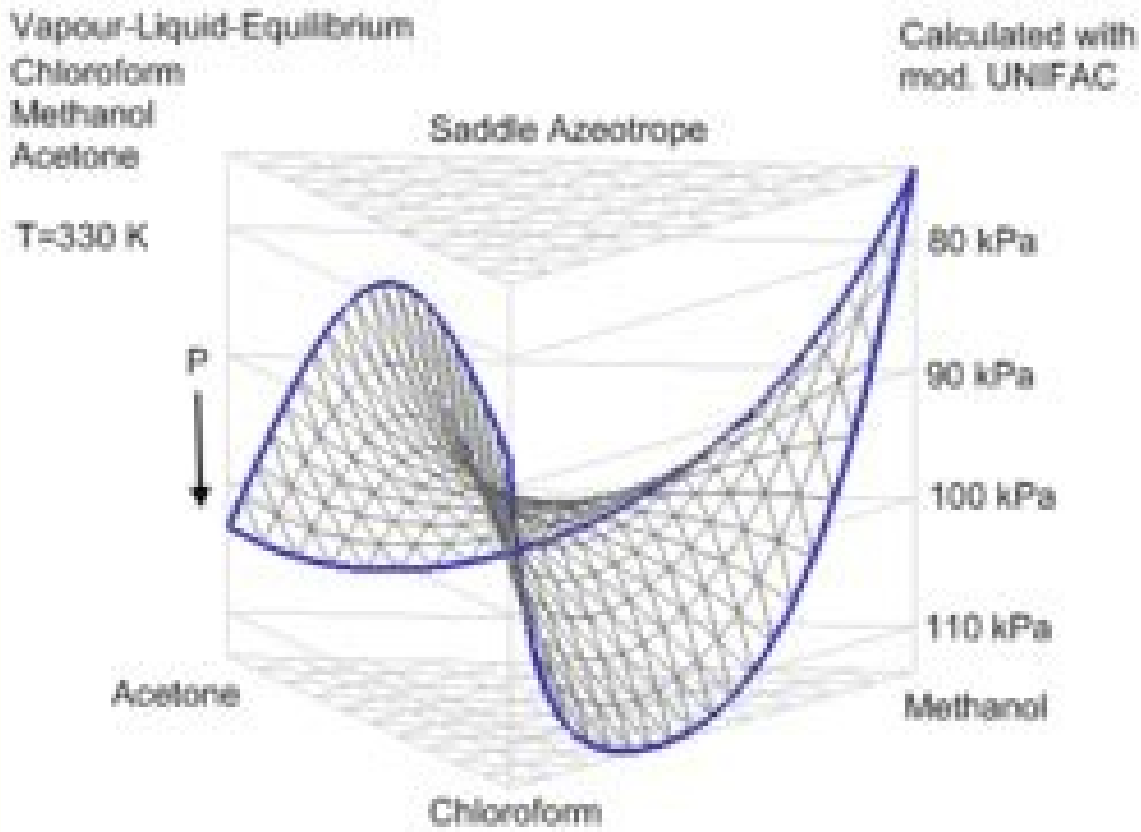
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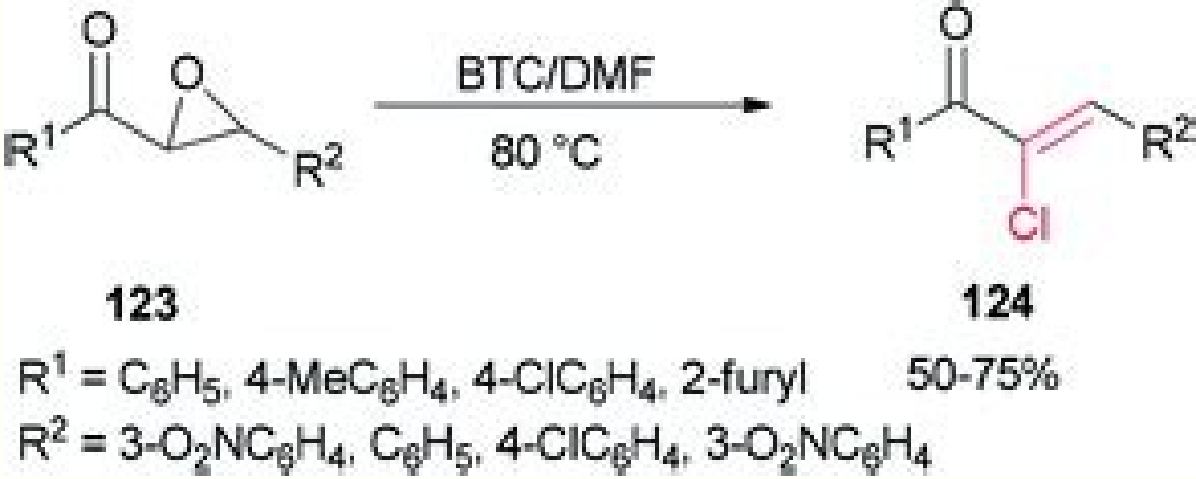
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Dimethylformamide azeotrope toluene

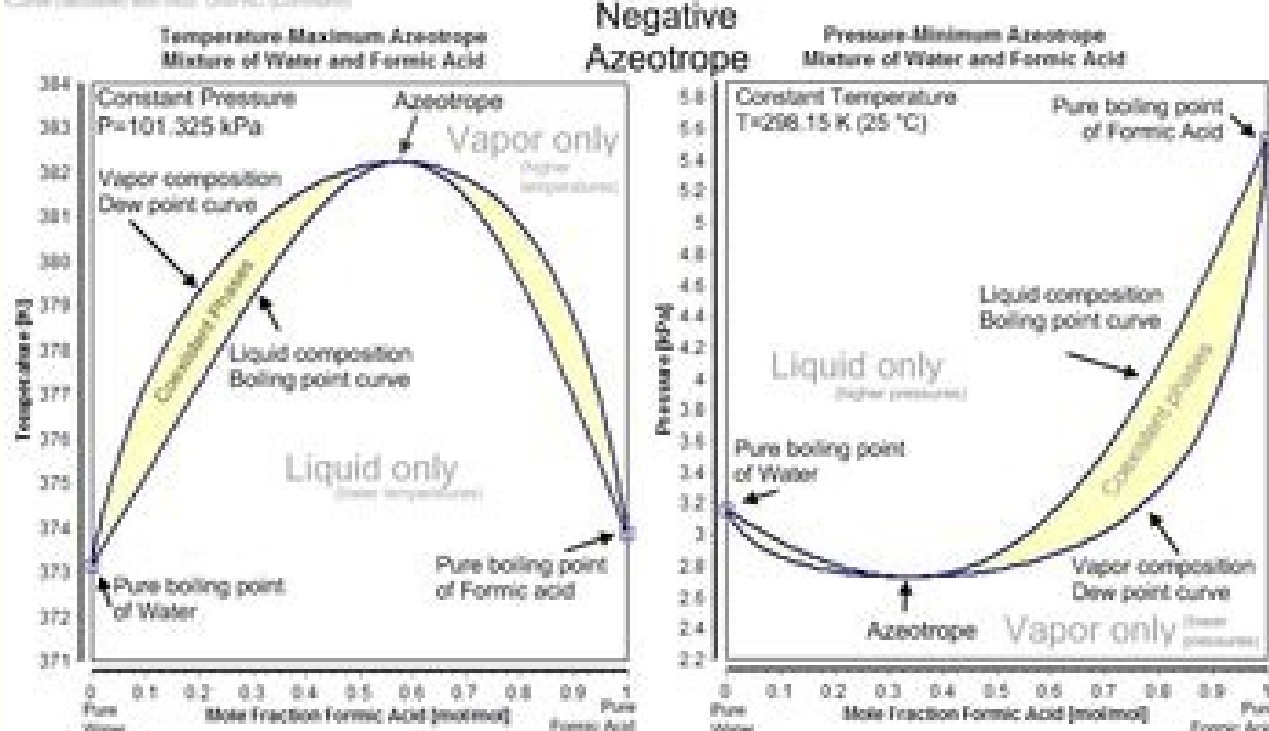
Does toluene dissolve in benzene. Does methanol form an azeotrope with water. Is toluene a good solvent for recrystallization. Dimethylformamide toluene azeotrope. Does toluene form an azeotrope with water.



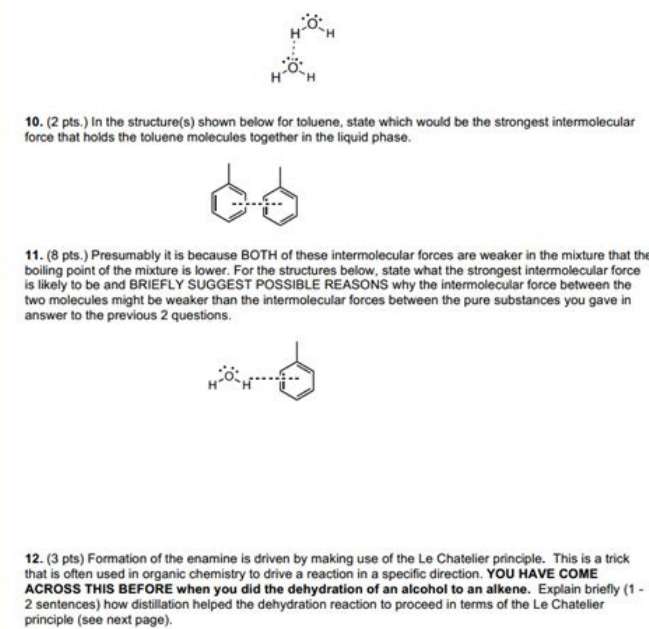
“Green Chromatography” Decision Tree See: Green Chem. (2014) 16, 4060 Extractions/work-up conditions If your material is not sensitive to base, potassium carbonate can be a better ‘salting out’ additive than the more usual sodium chloride. Potassium carbonate has very high solubility in water and of course higher ‘ionic strength’ to ‘push’ your organic material out of the water. Aqueous acetic acid wash can work better than HCl (aq) for purging low MW amines, such as Hünig’s base. Dipolar Aprotic Solvent (DAS) extractions: can often be problematic (either extracting product effectively, or carrying through of undesired DAS solvent). Process typically involves quench into water, followed by filtration or extraction to remove product. Org. Process Res.



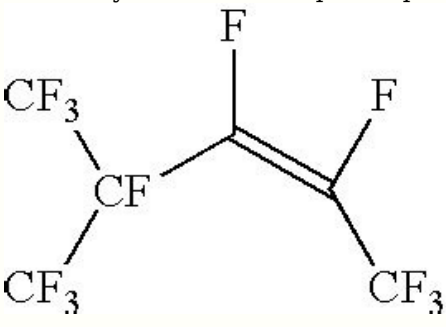
Dev., 2007, 11 (1), pp 160-164 Extract product with Least Polar solvents first (this will minimise levels of DMF / DMSO that follow your product) Heptanes or TBME works well (DMF is immiscible in these), Note: DCM gives poor results. DMF can be azeotropically removed using n-heptane, xylene and ethylbenzene. DMSO/Hünig’s Base (DIPEA) This can be used for extracting acids from DMSO mixtures, hence avoiding large (aq) volumes. Bonded/ion exchange resins Can be used as loose resins for scavenging or on purification machines standard to the industry There are now a number of bonded columns available to help you separate compounds that pose a challenge on simple silica gel. Added bonus is that these columns can be reused up to 20 times! Review of ion exchange resins: Chem. Rev., 2009, 109 (2), 515-529 SFC is not only for chiral separations Using alcohol solvents and CO2 recycling SFC has significantly less environmental impact than HPLC SFC can replace chlorinated solvent use for compounds with low solubility Recrystallizations Water wet solvents often solubilize compounds much better than dry solvents & should be considered when solubility screening. Note: You’ll be using water wet solvents for extraction! If your compound is soluble in a solvent when wet but insoluble when the solvent is dry this can be used to aid isolation or crystallization. Simply do your extractive work-up and azeotropically dry to crystallize your product. MEK (Methyl Ethyl Ketone) is particularly good for this. Reverse Phase Chromatography Purification of a variety of polar compounds on scale can now be easily carried out using C18 ISCO columns. less solvent/glass waste and shorter run time compared to multiple injections on prep HPLCs reusable columns reduce the amount of solid waste compared to silica columns no need to use DCM to purify polar compounds Silica Gel Chromatography Solubility: it is useful to note that solubility in mixed solvent systems is often non-linear – a compound may be much more soluble in a 50:50 mixture of solvents than it is in either of the individual solvents. Ref: Try using solvents mixtures (consider compatibilities) and running at higher concentration rather than simply diluting out (this can significantly aid workup efficiency and often lead to purification through evaporative crystallization). Pre-packed Silica Column reuse protocol: Using TLC as a guide, flush column with polar eluent to flush remaining material from column. Pre-columns/loading columns can be used as a way to minimize baseline material remaining on the column. Re-equilibrate with desired gradient mixture or flush with air to remove solvent for later use. Air pockets may form that will alter performance due to inconsistent packing of the stationary phase. DCM replacement in purification: DCM has an intrinsically high carbon footprint, is a greenhouse gas, has to be (expensively) scrubbed on incineration and chlorinated solvents have acute and chronic effects on human health. Solvent systems that can be used depending on solvents available include: 2.



3:1 iPrOAc and MeOH in heptanes: “Dilution of MeOH with i-PrOAc enables better separation between closely spaced peaks” GSK solvent guide Pfizer solvent guide Sanofi solvent guide Can be used effectively as a solvent for halogen displacements. Added bonus: product precipitated out of the reaction mixture. Alternative to most ethers as it has a much reduced tendency to form peroxides Alternative to DCM in silica chromatography MTBE forms azeotropes with water (52.6 °C; 96.5% MTBE) and methanol (51.3 °C; 68.6% MTBE) Caution: MTBE unstable toward strong acids, reacts dangerously with bromine, potential endocrine disruptor Obtained from agricultural waste via a green process Forms bi-layer with water unlike THF so that reactions can be worked up without solvent switching. Many reagents available in 2-MeTHF Worked better for Me-ester formation in the presence of an aniline than DCE and prevented need for TMS-diazomethane Suitable replacement to THF or Dioxane and may be a viable replacement to DCM in a variety of reactions including: Amide/Sulfonamide formation Boc protection Nickel-Catalyzed Suzuki-Miyaura Coupling: Org. Lett. 2013, 15, 3950 Lactone formation using CDI: OPRD August 27, 2013 Mitsunobu reaction, PPh3O crystallizes out and can be filtered off.



Heptanes Replacement for hexanes Better recrystallization solvent Can be used to azeotrope off DMF. Higher boiling point than EtOAc so that solvent removal from chromatography leaves solids instead of oils. Cyclohexanes also replacement for hexanes Sulfolane A highly stable alternative to DMSO, DMF, DMAC, and NMP The melting point of sulfolane can be lowered by addition of small amounts of water. Sulfolane with 3 vol % water has a melting point of 10 °C. Its viscosity is much higher than for the other dipolar aprotic solvents. However skin permeability of sulfolane is much lower than that of the other solvents. Due to the stability of sulfolane towards strong acidic conditions, even at high temperatures, it can be used with strong acids and also together with reagents such as phosphorous tri- and pentachloride or thionyl chloride. It has also been used as solvent for oxidations, nitrations, rearrangements, halogen exchange, phosphorylations, and condensation reactions Sulfolane is miscible with ester, ketone, and ether solvents in the same way as the other dipolar aprotic solvents. However sulfolane is not miscible with MTBE; in the case where the product acts as a detergent, addition of a small amount of water improves separation: Org. Proc. Res. Dev.



2012, 16 (7), pp 1273-1278 Dimethyl isosorbide A sustainable solvent in skin-care products and drug formulation can be a suitable replacement for THF and dioxane in some reactions. Its high boiling point offers a wider range of reaction temperatures, but it is completely soluble in water. IPAC Is also a great solvent for titrations and extractions, retains less water than EtOAc and it is less reactive! Lactic acid As solvent: Green Chemistry Journal article on various annulations run in lactic acid, acting as a solvent and promoter, outperforming conventional organic solvents and acetic acid: Lactic acid as an invaluable bio-based solvent for organic reactions Can be replaced with dimethyl carbonate in a free radical bromination with NBS TamiSolve® NxG May be suitable replacement for NMP and NEP Tamincos next-generation, high-performing, non-reprotoxic solvent Suitable NMP & NEP replacement (boiling point 241 °C) Favorable safety, health and environmental profile: No reprotoxicity, biodegradable, no bio-accumulation, not aquatotoxic, high flash point & low volatility Propylphosphonic Acid Anhydride (T3P) Useful for amide couplings, dehydrations (instead of POCl3) and heterocycle formation. Synlett, 2009, 3378-3382, Tetrahedron 65 (2009) 9989-9996. Air-stable version of AlMe3 called DABAL-Me3 An adduct of trimethylaluminum and DABCO (for Weinreb amidation of esters w/o the need of trimethyl aluminum, a highly flammable reagent Literature Reference for amide formation: Amide bond formation using an air-stable source of AlMe3.Method A: Reactions performed on a 0.50 mmol scale using amine (1.5 equiv), anhydrous THF, N2, 40 °C, 1 h followed by ester (1 equiv), reflux, 18 h. Method B: Reactions performed on a 0.50 mmol scale using amine (1.5 equiv), undried THF, open to air, 40 °C, 1 h followed by ester (1 equiv), reflux, 18 h. Metal based oxidizing agent alternative Stabilized IBX (SIBX, Aldrich-661384) SIBX can effectively oxidize alcohols to aldehydes and ketones, although sometimes heating is necessary. IBX alone is shock-sensitive and has been responsible for explosions, although they are believed to be due to residual potassium bromate left from its preparation. Neat

material should not be heated above 30°C, however, mixtures in dilute (i.e. b.p < 100°C) can safely be heated to around 80°C. Compatible with green solvents such as 2-MeTHF, toluene and EtOAcare compatible with SIBX use. Enzyme Laccase (Aldrich) Enzymatic oxidations to convert a zenzylic alcohol into the corresponding aldehyde. Zinc phthalocyanine (14320-04-8)(catalytic) Reduced nitro groups in the presence of acid, amide, ester, halogens, lactone, nitrile. N-benzyl, O-benzyl and hydroxy groups To a mixture of nitro compound (1.34 mmol) and zinc phthalocyanine (1 mol%) in PEG-400 (3 ml) was added hydrazine hydrate (2 equiv.). The reaction mixture was stirred at 100 °C for 8 h. Time was not optimized separately for all substrates. After completion of reaction, the reaction mixture was cooled to ambient temperature and 20 ml of ethyl acetate was added. PEG-400 was removed by washing with distilled water and ethyl acetate layer was dried under reduced pressure using rotatory evaporator and analyzed by GC-MS. Stable and efficient triflation 4-Nitrophenyl trifluoromethanesulfonate and K2CO3 in IPAC upon heating produces triflation cleanly. The added bonus is the precipitation of the resulting potassium 4-nitrophenolate, which can then be filtered off along with K2CO3. Suzuki–Miyaura Coupling over SiliaCat DPP-Pd valsartan synthesis The leach-proof and recyclable catalyst is available from Silicycle Replacement of expensive and potentially explosive HOBt With 2-hydroxypyridine in 2-MeTHF: J. Org. Chem. 2010, 75, 1155– 1161 Trifluoromethylation of heterocycles in water at room temperature Using a reaction medium containing nanoparticles consisting of commercially available TPGS-750-M in water, a combination of Langlois' reagent and t-BuOOH can be used to affect trifluoromethylation of several heterocyclic arrays, including heteroaromatics. These reactions take place at ambient temperatures, and the aqueous medium can be recycled. Dihydroxylations (or oxidative (C=C) cleavage in combination with NaIO4) can be effectively catalyzed using an immobilized OsO4 (EnCat 40 – Reaxa/Aldrich) allowing safer application of this reagent. In an added bonus, the catalyst can be effectively recycled (via filtration and washing process) on multiple occasions with little / no leaching detectable or effect on performance. TIP: Use efficient mixing (preferably overhead stir) for best performance. SMOPEX-301TM (J-M) A triphenylphosphine functionalized fiber support (initially developed as a metal scavenger) can be used very effectively as a reagent replacement for triphenylphosphine reactions (Mitsonobu, Halogenation of alcohols, Wittig, tetrazole formation, etc) often resulting in a far simplified workup procedure (avoiding chromatography). The resultant phosphine oxide can simply be removed by filtration. It is available in bulk (key for scale up), and has good filtration properties being a fiber based resin. Ref: Solubility of Inorganic component (e.g. BASE or Metal Catalyst salt) in DAS solvent can often lead to reactions stalling. As reactions proceed, inorganic salt by-products form (e.g. NaCl). Only a certain ion concentration can be supported (solubilised) by the solvent medium, hence active component e.g. CO32- concentration can drop significantly during the course of a reaction (large effect on reaction rate!). Process Tip: K2CO3 / Acetone reactions are well known for stalling on scale (or being slow). Consider adding: Phase Transfer Catalyst (Quaternary Ammonium Salts) Using Cs2CO3 – Increased organic solubility Using finer Mesh K2CO3 – increased surface area, combined with increased agitation rate. Quenching Reactions Water has a high surface tension, which makes it difficult to add in a controlled fashion. Controlled Addition of Water can be improved by using “wet organic mixtures” e.g. 10 % Water in THF. Very good for quenching very water-reactive reagents. Energy usage by the numbers Leaving your Buchi chiller on all day uses the same amount of electricity as 4 loads in a tumble dryer. Leaving your Buchi water bath on all day at 50oC uses the same amount of electricity as doing 6 loads of washing One rotary evaporator left on (unused) consumes the same amount of energy as 10 TV's left on Articles Figures Tables About An alternative process from U.S. Patent 3,635,946 A vigorously stirred reaction mixture consisting of 32.87 g (0.1 mol) of 5-fluorouracilmercury, 100 ml of dimethylformamide and 50 ml of toluene is dried by azeotropic distillation of toluene. It is then cooled to -40°C in a stream of dry nitrogen, and a solution of 21.3 g (0.2 mol) of 2-chlorofuranidin in 20 ml of dried dimethylformamide is gradually added to the stirred mixture, the temperature being maintained between -40°C and -30°C. After completion of the reaction (which is marked by complete dissolution of the starting 5-fluorouracilmercury) i.e. after about 3 to 4 hours, 60 to 80 ml of the solvent are distilled off in vacuo at a bath temperature not exceeding 35°C ... [Pg.1442] The various side reactions of the chemical cyclodehydration and because of the high cost for solvents, catalyst and cyclodehydration agent, researchers have been looking at more economic ways to manufacture bismaleimides. Efforts have been directed towards a catalytic cyclodehydration process via azeotropic distillation to avoid undesirable byproducts and to achieve improved yield of pure bismaleimide. The use of Lewis add/base salts based on p-toluene sulfonic acid, sulfuric add or trifluoroacetic add and dimethylformamide (DMF), N-methylpyrrolidone (NMP) and acetone as bases provided high yields of high purity bismaleimide (24). In another patent dimethyldialkylammoniummethane... [Pg.172] The anhydrous acetates of the rare earths have recently been prepared. Moeller et al. [355] obtained them for La, Dy, Ho, Er, Yb and Y by the azeotropic distillation of a mixture of hydrated acetates with N,N'-dimethylformamide (DMF) and benzene. In the case of Ce, Pr, Nd, Sm, Eu and Gd the same method gave a monosolvated acetate, M(C2HsO2)3 DMF. However, the anhydrous acetates of Ce, Pr, Nd, Sm, Eu and Gd can be prepared [355] by vacuum desolvation of the monosolvated compounds. A direct desolvation of the acetates in vacuum at –150° C was attempted by Witt and Onstott [389] after dissolution of the rare earth oxides in 50 per cent acetic acid, and anhydrous acetates of definite composition were obtained for La, Eu, Gd, Tb, Dy, Ho, Er, Tm, Lu and Y. [Pg.45] Note. (1) iV,iV-Dimethylformamide is azeotropically distilled from toluene (Section 4.1.26, p. 409). [Pg.1111] A previously prepared sample of 2 (Tinnemans et al., 1984) was dissolved in dimethylformamide and it was attempted to remove water by azeotropic distillation. Compound 2 was recovered unchanged, indicating the presence of coordinated water. The synthesis of compound 2 was carried out to give the correct product and elemental analysis. (Tail et al., 1978). [Pg.3] Under less vigorous conditions the acyclic monoamide (–amic acid) is formed and this can usually be converted into the cyclic imide by treatment with a mild dehydrating agent such as acetyl or thionyl chloride [77]. Alternatively, the reactants may be refluxed with triethylamine in benzene or toluene and the water formed in the reaction removed by azeotropic distillation [78]. The phthaloyl group has also been introduced into a-amino acids by heating with 0-carbethoxy-thiobenzoic acid in JV,JV-dimethylformamide at 80° [79], or at room temperature with JV-ethoxycarbonylphthalimide in the presence of sodium hydroxide [80]. [Pg.54] The principal route for production of isoprene monomer outside of the CIS is recovery from ethylene by-product C5 streams. This route is most viable where ethylene is produced from naphtha or gas oil and where several ethylene plants are located in relatively dose proximity to the isoprene plant. Although the yield of isoprene per mass of ethylene is quite low, there is enough ethylene produced to provide a large portion of demand. Because of the presence of -pentane in these streams which azeotropes with isoprene, extractive distillation must be used to recover pure isoprene. Acetonitrile is the most common solvent, but dimethylformamide is also used commercially. [Pg.468] C under argon. Methanol was removed azeotropically at 56 °C at a fast rate and as the boiling point began to rise, the distillation rate was reduced to 4 drops/min. and heating continued for 15h. The polymer thus prepared precipitated out of cyclohexane. The powdery polymer was crystalline with a melting point (DSC) of 212 °C. It was insoluble in the usual organic solvents such as methylene chloride, chloroform, ether, tetrahydrofuran, ethyl acetate, acetone, dimethylformamide, and dimethylsulfoxide. [Pg.88] Purification. For polymerization, butadiene that is at least 99 mol% pure is required. Although alkynes are the most troublesome impurities, separation of the butadiene from other C4 products is also necessary. Simple fractional distillation is effective for removing the light (C3) and heavy (C5) ends from butadiene, but not for removing the various C4 species because of the closeness of the boiling points to each other and to butadiene. Further complicating purification, butadiene forms azeotropes with re-butane and 2-butene. The most widely used recovery systems are extraction with aqueous cuprous ammonium acetate (CAA) and solvent extractions with furfural, acetonitrile, dimethylformamide, dimethylacetamide, or AT-methylpyrrolidnone (65,66). [Pg.864] Figure 3.3.21 Extractive distillation of the azeotropic system cyclohexane and benzene at Benzene 1 bar (a) y-x diagram without (dotted line) and with (short-dashed line) addition of50mol.% dimethylformamide (DMF) note that the content of DMF is not counted, that is,xç6H6= 1 –xçCHzi (b) typical process configuration. Adapted from Cmeihling and Brehm (1996). Polymer Synthesis. Polyethylene glycol (PEG) 600,1000, and 1500 were obtained from Aldrich Chemical Company and dried by azeotroping with toluene. Molecular weights for the polyethylene glycols were determined from hydroxyl numbers. DieSiylene glycol (DEG) from Fisher Scientific was purified by vacuum distillation over metallic sodium. Hexamethylene diisocyanate (HMDI) from Aldrich Chemical Company was vacuum distilled. Dicyclohexylmethane-4,4'-diisocyanate (DCDI) (Desmodur W) from Mobay Chemical Company was used as received. Dibutyltin bis-(2-ethylhexanoate) from Kodak was stored over phosphorus pentoxide. N,N'-dimethylformamide (DMF) from EM Science and 4-methyl-2-pentanone from Aldrich Chemical Company were dried over 3A molecular sieves. [Pg.87] See other pages where Dimethylformamide azeotropic distillation is mentioned: [Pg.669] [Pg.1659] [Pg.3150] [Pg.81] [Pg.504] [Pg.669] [Pg.669] [Pg.1442] [Pg.150] [Pg.150] [Pg.236] [Pg.26] [Pg.72] [Pg.121] [Pg.26] [Pg.215] [Pg.216] [Pg.157] [Pg.166] [Pg.25] [Pg.215] [Pg.148] [Pg.157] [Pg.28] [Pg.14] [Pg.71] [Pg.548] [Pg.70] See also in source #XX -- [Pg.92] Azeotrope distillation Azeotropic distillation Azeotropic distillation azeotropes Dimethylformamide Distillation azeotropes © 2019 chempedia.info