



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07C 31/30	A1	(11) International Publication Number: WO 95/09141 (43) International Publication Date: 6 April 1995 (06.04.95)
(21) International Application Number: PCT/US94/09844 (22) International Filing Date: 2 September 1994 (02.09.94) (30) Priority Data: 08/129,818 30 September 1993 (30.09.93) US (71) Applicant: FMC CORPORATION [US/US]; 1735 Market Street, Philadelphia, PA 19103 (US). (72) Inventors: MORRISON, Robert, Charles; 1536 Stableview Drive, Gastonia, NC 28056 (US). KAMIENSKI, Conrad, William; 516 Eastwood Drive, Gastonia, NC 28054 (US). SCHWINDEMAN, James, Anthony; 3913 Melshire Lane, Charlotte, NC 28269 (US). (74) Agent: FELLOWS, Charles, C.; FMC Corporation, 1735 Market Street, Philadelphia, PA 19103 (US).		(81) Designated States: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, TJ, TT, UA, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: IMPROVED METHOD OF PREPARATION OF LITHIUM TERTIARY-BUTOXIDE (57) Abstract A process for quickly preparing easily separable solutions of lithium tertiary-alkoxides. Comprising the steps of reacting lithium metal in bulk form, containing less than 0.6 % by weight of sodium, with a tertiary alcohol in mole ratios of metal to alcohol ranging from 1 to 1 to 10 to 1 in a solvent selected from ethereal or hydrocarbon solvents under an inert atmosphere at elevated temperature for 1 to 10 hours, cooling the product and separating the product solution from the unreacted lithium metal in the reactor, and optionally adding solvent and sufficient lithium metal and alcohol to said unreacted metal in said reactor to maintain said mole ratio of lithium metal to alcohol, and continuing the reaction, thereby to form further lithium tert-alkoxide, and repeating said steps a number of times.		

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IMPROVED METHOD OF PREPARATION OF LITHIUM TERTIARY-BUTOXIDE

This invention concerns a process for preparing lithium tertiary
5 alkoxides by reacting lithium metal in gross or bulk form with a tertiary alcohol.

Alkali metal alkoxides and especially alkali metal tertiary alkoxides such as lithium tertiary butoxide are used in the preparation of pharmaceutical intermediates and in the synthesis of polymers and in
10 general organic synthesis. U.S. Patent 5,276,219 issued January 4, 1994 describes a process for preparing clear, suspensoid-free solutions of lithium tert-butoxide in tetrahydrofuran at reflux by reaction of lithium metal in finely divided dispersed particle form with an excess of tert-butyl alcohol.

Although lithium metal in a finely divided dispersed state reacts
15 rapidly with tert-butyl alcohol in THF medium, it is costly to produce, requiring the steps of (a) heating of bulk lithium metal and mineral oil to about 190-200°C in the presence of a dispersion aid, such as oleic acid, (b) stirring the resultant molten mixture at high speeds in a special dispersion unit to produce the required small particle sizes (generally less than 100
20 microns), then (c) cooling the product (preferably without stirring), and then finally (d) removing the mineral oil from the solidified lithium metal particles by washing several times with a volatile hydrocarbon solvent, such as hexane or pentane. The volatile hydrocarbon solvent can optionally be removed by purging with an inert gas such as argon, or more preferably, be
25 washed one or more times with tetrahydrofuran before reaction with the tert-butyl alcohol.

Besides being costly to produce, lithium dispersion also may add undesirable impurities to the subsequent lithium tert-butoxide product in THF such as, e.g., mineral oil and oleic acid breakdown products, and
30 volatile hydrocarbons.

Because of the extremely small sizes of the lithium metal particles, a high proportion of solid impurities, small in size may also be present after reaction with the alcohol is complete. Impurities on the lithium surface slow down the initial reaction. These impurities arise from side reactions with
35 traces of oxygen in the inert atmosphere, of traces of water in the solvent

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and alcohol, and with the solvent itself. These small solid impurities (including any unreacted lithium metal particles) cause filtration problems, although the use of an excess of the alcohol generally takes care of any unreacted lithium metal.

5 The present invention provides a process for quickly preparing easily separable solutions of lithium tert-alkoxides in an economically feasible time period (1 to 10 hours), comprising the steps of: reacting lithium bulk metal whose size exceeds 0.1 mm, containing less than 0.6% by weight of sodium, with a tertiary alkyl alcohol containing 3 to 10 carbon atoms in mole
10 ratios of lithium metal to alcohol ranging from 1 to 1 to 10 to 1 in an ethereal or hydrocarbon medium under an inert atmosphere at an elevated temperature between 40°C and 100°C, cooling the product and separating the product solution from the unreacted lithium metal in the reactor; the process is conveniently continued by adding additional solvent, sufficient
15 lithium metal and alcohol to the unreacted metal in the reactor to maintain the mole ratio of lithium metal to alcohol, and continuing the reaction, thereby to form further lithium tert-alkoxide, and repeating said steps a number of times. Optionally the reaction may be catalyzed with small amounts of a C₁ to C₃ alcohol. Lithium bulk metal and lithium in bulk form
20 are synonymous terminology as used in the description of this invention.

Unexpectedly, the process of the present invention overcomes problems experienced with the use of lithium metal in a finely divided (dispersed) state without experiencing an overly great increase in reaction time by the use of a sufficient excess of lithium metal in bulk form (over and
25 above the alcohol used) in the essential absence of any hydrocarbon or other (solid) impurities. Impurities on the lithium surface slow down the initial reaction. Surprisingly, the amount of lithium metal in bulk form needed to preserve a comparable overall reaction time when compared to lithium in dispersed form is only in the order of about three times. For
30 example, the surface area of one gram equivalent of lithium metal particles 20 microns in diameter is about 13,000 square centimeters, while the surface area of an equivalent amount of lithium metal cubes with dimensions of one centimeter by one centimeter by one centimeter is only 79 square centimeters, a one hundred sixty-six times greater surface area
35 for the dispersed lithium. One would therefore expect the relative amount

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of lithium in bulk form needed to give a overall reaction rate comparable to the dispersed lithium to be in the order of one hundred sixty-six times greater. Instead, only three equivalents of lithium metal in the form of cubes was found to react with one equivalent of the alcohol in a
5 comparable overall time (180 minutes) as did one equivalent of lithium metal dispersed to 20 micron diameter particles (135 minute overall reaction time). See Table I. Lithium tertiary butoxide in the tables I-V is abbreviated as LTB and elsewhere as lithium tert-butoxide and lithium t-butoxide.

10 After the reaction of one of the three equivalents of the bulk lithium metal is completed, the slightly hazy product solution can be easily decanted from the unreacted (floating) lithium metal and filtered quickly. Another reaction can be started in the same reactor, adding only another equivalent each of lithium metal and alcohol and the required amount of
15 solvent. When the process is to be repeated one or more times in the same reactor it is advantageous to immediately add additional solvent after the product of the preceding reaction is recovered. Surprisingly, the overall reaction time decreases still further in the second run (130 minutes) and then stays constant for the next two consecutive runs (120 minutes). This
20 decrease in time is thought to be due to preconditioning of the lithium metal. (Removal of surface impurities).

The ease of separation of the product solution from unreacted lithium metal is maintained in each subsequent run and there is no hazardous unreacted lithium to be disposed of as in the runs using dispersed lithium.

25 It is known that elevated sodium levels in the lithium metal used in preparing alkyllithiums are beneficial. For example W.N. Smith, Jr., in Journal of Organometallic Chemistry, 82 (1974) 1-6 recommends the use of 1% by weight of sodium in the lithium metal used to prepare tertiary butyllithium from tert-butyl chloride. It is also stated that lower levels of
30 sodium (0.02%) in the lithium metal resulted in no reaction with the alkyl chloride. It has unexpectedly been determined that at a sodium level of 0.69 weight percent sodium (in the lithium cubes) the overall reaction time is about 6 to 7 hours, whereas at a sodium level of 0.002%, the reaction time is 1.5 hours, everything else being equal.

35 In the case of dispersed lithium containing 0.79 weight percent

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sodium, the overall reaction rate is six hours as compared to a three hour reaction time for lithium dispersion containing 0.002 percent sodium.

In another embodiment of the invention, certain catalysts are used to speed up the overall reaction time of bulk lithium metal pieces with tert-butyl alcohol in THF solution. With a mole ratio of t-butyl alcohol to lithium metal of 1.1, addition of small amounts (2-5 mole % based on tert-butyl alcohol) of C1 to C3 alcohols decreases the reaction time by about one-half when using lithium metal rod pieces (1.27 centimeter diameter by one centimeter long). The ratio of lithium metal to tert alcohol can be 0.9 to 1 to 10 to 1.

It is quite unexpected that the size of the metal pieces used in the reaction with tert-butyl alcohol in tetrahydrofuran can be varied widely, depending on the batch size of the runs, without unduly affecting [reducing] the overall reaction time. Thus, any of the common commercially available sizes of lithium metal may be employed or segments [pieces] may be cut from these. For example, in a forty gallon size run to prepare 184 moles of product, ten one inch thick trapezoidal-shaped pieces of lithium were cut from each of four two pound trapezoidal ingots having dimensions of 2.5/3.5 inches (6.4/8.9cm) in width by 3.25 inches (8.3cm) in height by 10.5 inches (26.7cm) in length, and charged to the reactor, along with the requisite amount of tert-butyl alcohol (mole ratio Li/ROH=3) and THF solvent. The mixture was heated to reflux and required 4-5 hours to completion [average conversion of alcohol of 99+ % over seven consecutive runs]. This overall reaction time compares favorably to one mole laboratory runs using much smaller pieces of metal [see Table VI, P.P. Series 6].

Sizes of lithium metal available commercially are: one inch (2.5cm) diameter by 8 inch (20.3cm) long rods, one-half inch 1.3cm) by 6.5 inch (16.5cm) long rods, 2.25 inch (5.7cm) by 3.38 inch (8.6cm) long cylindrical ingots [1/4 lb], 3 inch (7.6cm) diameter by 3.8 inch (9.7cm) long cylindrical ingots [1/2 lb (227g)], 4 inch (10.2cm) diameter by 5 (12.7cm) inch long cylindrical ingots [1lb (454g)], and the two pound (908g) trapezoidal ingots mentioned above, as well as lithium metal dispersion, 30 weight per cent in mineral oil with 90% of the particles greater than 10 microns, but less than 50 microns, (average: 20 microns).

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The optimum size of the lithium bulk metal employed will depend upon the size of the reaction being carried out. Generally, the size of the pieces of lithium being employed will be such that the overall reaction time will be less than 8-10 hours. The pieces of metal should be easily visible as being discrete particles, i.e., not particles produced by a dispersion process as described above [less than 0.1 millimeter].

Table I compares the sizes of some lithium metal pieces and their surface area per gram against the overall reaction time, including the feed time of the alcohol, and the run size. Note the longer overall reaction time for lithium dispersion versus bulk lithium [same size run].

Generally, it is preferable to use excesses of such bulk metal relative to the tert-butyl alcohol in the range of 2:1 to 10:1, but, most preferably, 3:1 to 5:1.

Feeding the tert-butyl alcohol gradually rather than adding it all to the reactor initially lengthens the reaction time somewhat, but not inordinately so. Essentially, the alcohol reacts about as quickly as it is added after the first run of a consecutive series is completed. It is thought that this first run of the series serves to condition the metal and acts much like the catalyst activation. Thus, the second run of such a series, where all of the alcohol is added at once, is completed in a period of 130 minutes (see Table III series I), whereas, in a second run where the alcohol is added gradually over a period of 108 minutes, the reaction is complete in 155 minutes [see Table III, Series 2].

The reactions may be carried out at ordinary [atmospheric] pressure, but the atmospheric composition above the contents of the reaction vessel should be inert. Thus, the atmosphere should be dry and inert to lithium metal, i.e., most favorably be argon gas. Higher pressures, i.e., those above atmospheric, may be employed to raise the reaction temperature and thus, to further speed up the reaction.

Regardless of which size lithium pieces one employs, it is preferable to use a low sodium containing grade of lithium metal. Preferably, one should use a grade of lithium metal containing 0.001 to 0.6% by weight of sodium based on lithium; more preferable is a sodium level of less than 0.1%, and most preferable is a sodium level of 0.001 to 0.01 weight percent of the lithium metal. For example, employing lithium dispersion at a 1:1

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level with tert-butyl alcohol in THF medium, at a sodium level of 0.002 wt%, the reaction is essentially completed (>95%) in two to three hours time, whereas if the sodium level of the lithium metal used is 0.79 wt%, the reaction, to achieve above 90% completion, requires an additional 3-4 hours. The lithium metal in the latter case agglomerates to give larger pieces of less reactive lithium. At intermediate levels of sodium [0.19% and 0.38%] the reactions proceed more readily and are also completed in 2-3 hours [see Table II].

In the case of bulk metal, this effect is also evident. Tables III and IV present data at low (<0.01 wt%) and high (>0.6 wt%) sodium levels in the lithium metal employed. At the lower sodium level, overall reaction times are of the order of 1.5 to 3 hours and the reactions are complete, whereas at the higher sodium level, this reaction time is 6 to 7 hours and the reactions are incomplete. Less soluble surface impurities appear to coat the metal in the later case and slow down the rate of reaction, especially near the end.

Catalysts are employed to speed up the overall rate of the reaction. These are generally lower molecular weight C₁ to C₃ alcohols, particularly methanol, ethanol, and isopropanol. Catalyst levels should be in the range of 2-10 mole% based on tert-butyl alcohol reactant, and most preferably, 3-7 mole%.

Table V presents results using these catalysts in runs with lithium metal rod pieces (1.27 cm diameter by 0.5 cm long). The overall reaction times are cut from 332 minutes (5.5 hours) to 180 to 218 minutes (3-3.6 hours) using 4-5 mole% of catalysts methanol, ethanol or isopropanol. Other higher alcohols (C₄ and greater) may be used, but do not generally give as good results.

Alcohol reactants other than tert-butyl alcohol can be employed, such as, for example, C₄-C₁₀ tertiary alcohols, such as, e.g., tert-amyl alcohol, 3-methyl-3-hexanol, 3-ethyl-3-pentanol, and 4-methyl-4-heptanol.

Solvents which may be used in the process of this invention to prepare lithium tert alkoxides are ethers such as ethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, methyltetrahydrofuran, tetrahydropyran, and the like, and hydrocarbon solvents such as pentane, hexane, heptane, and toluene, and mixtures thereof. Although the most favored reaction

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temperature is the reflux temperature of the selected solvent, however, the reaction may be run below reflux, e.g., 40 to 100°C depending on the boiling point of the solvent. However, the least favorable temperatures are below about 40-45°C.

5 The reaction concentration of the product alkoxide being formed is generally limited by the solubility of the product in the solvent being employed. For example, the solubility of lithium tert-butoxide in tetrahydrofuran is approximately 2.4 moles per liter of solution. The preferred reaction concentration, however, is somewhat less than this, i.e.,
10 about 2.0 moles per liter of solution. Thus, it is best to carry out these reactions at concentration levels as high as possible without at the same time fostering a condition of insolubility of the product.

 The following examples further illustrate the invention.

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Exemplary Runs of Lithium tert-Butoxide Employing Bulk Lithium
[Table III, Series 1]

 A volume of 426 milliliters of dry tetrahydrofuran and 76.71 grams
20 [1.03 moles] of dry tert-butyl alcohol were added to a one liter three necked flask equipped with a mechanical stirrer, reflux condenser, thermometer, and gas inlet tube for provision of an argon atmosphere. The solution was heated to 61 degrees Centigrade and 24 pieces of lithium metal, cut into cubes with the approximate dimensions of one centimeter on each side
25 [21.53 grams, 3.10 gram equivalents], added to the flask as rapidly as possible. Heating was continued to bring the mixture to reflux with stirring. After 30 minutes, a sample of the solution was taken [4.24 grams] and analyzed for alkalinity content and extent of conversion of the alcohol present in the reactor to product lithium alkoxide. Conversion at this point
30 was 17.4%. Samples were taken at 60, 120, 150 and 180 minutes. Conversions were 37.6%, 84.4%, 92.6%, and 98.4%, respectively. After the 150 minute sample the metal pieces started losing their blue color and became shiny. At 180 minutes hydrogen evolution ceased and the heating was stopped. The shiny pieces were pitted. After the reaction mixture had
35 cooled to room temperature, the slightly cloudy solution was decanted away

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from the unreacted excess lithium metal pieces and stored in an argon-flushed bottle. A weight of 7.9 grams of tert-butyl alcohol [0.1068 moles] was added to the bottle. To the remaining pieces of lithium metal in the reaction flask was added 439 milliliters of tetrahydrofuran. After standing
5 overnight the solution contents of the bottle were clear.

Second consecutive run:

To the above reactor, containing lithium and tetrahydrofuran, was added another eight pieces of lithium metal in the form of 1x1x1 centimeter
10 [approximately] cubes [7.41 grams, 1.068 gram equivalents]. The reactor contents were heated to about 59°C and a solution of 79.1 grams [1.069 moles] of tert-butyl alcohol and 50 milliliters of tetrahydrofuran added all at once. The mixture was stirred and heated to reflux and, once again, samples removed to determine the extent of conversion at definite time
15 periods. At 20, 40, 100, and 130 minutes the conversions were 23%, 38%, 90%, and 99%, respectively. After cooling the reaction mass to room temperature the cloudy solution was decanted away from the remaining lithium metal into an argon-flushed bottle and 7.8 grams [0.1054 moles] of tert-butyl alcohol added to the bottle. A volume of 416 milliliters of
20 tetrahydrofuran was added to the reactor containing the remaining lithium metal. After standing overnight the solution contents of the bottle were clear.

Third consecutive run:

Another eight pieces of lithium metal [7.02 grams] in the form of
25 cubes was added to the above reactor from the second consecutive run, the mix heated to 53.7°C, 75.42 grams of t-butyl alcohol added and the reaction continued at reflux. Samples taken at 20, 60, 90, and 124 minutes showed conversions of 20, 52, 82, and 100%, respectively. The product
30 solution was decanted away from the metal as described above, and 432 ml of THF added to the remaining metal in the reactor.

Fourth consecutive run:

Eight pieces, 7.29 grams of lithium were added to the reactor, the
35 mix heated to 51.3°C, 77.8 grams of t-butyl alcohol added, and the reaction

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carried on at reflux. Conversions at 20, 40, 80, and 120 min were 26, 37, 72, and 100%, resp. The product solution was decanted away and 434 ml THF added to the reactor. The product solution was then filtered and a clear solution obtained with a filtration time of four minutes. The solids on the filter plate were washed with 104.2 grams of a solution of seven grams of t-butyl alcohol in tetrahydrofuran and dissolved completely indicating that they were undissolved lithium t-butoxide. Analysis of both clear solutions [main product and wash] showed recovered yields of 90.5% and 6.2%, resp. for a total yield of 96.7%, based on starting alcohol.

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Fifth consecutive run:

Eight pieces, 7.32 grams lithium added to reactor, mix heated to 62.9°C, 78.35 grams alcohol added, reaction heated to reflux. Conversions at 20, 40, 60, and 79 min were 39, 63, 87, and 96%. Product decanted and 421 ml THF added to reactor.

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Sixth consecutive run:

No further lithium metal added to this run. The mixture from the fifth consecutive run was heated to 55.9°C and 76.21 grams of t-butyl alcohol added [1.03 moles] all at once. The mixture was heated to reflux. Conversions at 20, 60, 80, and 180 min were 16, 28, 69, and 96%, resp. Product decanted and 7.8 grams of alcohol added to cloudy solution. The remaining metal in the flask was covered with 421 ml of THF. The next day the solution in the bottle was clear.

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Seventh consecutive run:

No further metal was added to this run. There should be only enough metal to react with another charge of alcohol. The reactor contents were heated to 62°C and 75.48 grams of alcohol added and then the reaction heated to reflux. Conversions at 60, 120, 180, 240, 270, 300 and 334 min were 35, 60, 83, 94.5, 95.7, 96.6 and 96.6%, resp.

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Note 1.: It was found on larger [pilot plant] runs where overall reaction times were somewhat slower due to a greater proportionate size of the bulk metal employed [see Table I] that the product solutions generated

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from consecutive 3X metal runs were essentially clear at the end of the reactions and did not require any further addition of tert-alcohol and overnight standing to effect clarification.

Note 2.: The lithium metal used in these runs contained 0.0035% sodium.

Comparative Single Run Employing Bulk Lithium [Table III]

10 In this run, only a single equivalent of lithium metal in the form of cubes is used instead of three equivalents as in consecutive runs 3-5 above. The object of the experiment is to determine the relative overall reaction times and also to compare the overall reaction time of this run with the seventh consecutive run above where only one equivalent of metal is used.

15 A solution of 84.57 grams of tert-butyl alcohol [1.141 moles] and 378 ml of tetrahydrofuran were heated to reflux and nine pieces [7.2 grams, 1.0375 g. eq] of lithium metal in the form of 1x1x1 cm cubes added as quickly as possible. The mixture was heated and stirred at reflux and samples removed periodically to determine conversion. At 60, 180, 300, 20 420 and 480 min conversions were 12, 35, 68, 91, and 97%, respectively.

Both the 3X equivalents run and the seventh consecutive run [above] were considerably faster than the comparative single run.

25 Comparative Runs Employing Lithium Dispersions [Table II]

Exemplary Run--The Preparation of Lithium t-Butoxide Using Low Sodium Containing Lithium Dispersion

30 A weight of 27.7 grams of a 30 weight percent lithium dispersion, wherein the lithium metal contained 0.0148% sodium, was washed three times with dry hexane and once with dry pentane and then was blown dry with argon gas. The dry metal powder weighed 8.86 grams [1.276 moles].
35 The metal was transferred to a one liter three necked flask equipped as

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described above with the aid of most of a charge of 525 ml of dry THF and heated to reflux. A weight of 95.4 grams of tert-butyl alcohol was diluted with the remaining THF [ca 50 ml] and slowly added to the stirred contents of the flask from a dropping funnel over a 46 min period. No agglomeration of the metal was noted during the reaction. Samples for analysis were withdrawn through a syringe filter at 30, 60, and 100 minutes. Conversions were 93.7, 98.8, and 99.7%, respectively. A cloudy, white solution was obtained.

Another, similar run was made, using a lithium dispersion made from lithium metal containing less than 0.01% sodium [# 8599]. Conversions after 15 and 135 min were 93 and 96%. The product solution required 2.5 hours to filter completely [slow filtration] compared to just several minutes for one of the bulk metal laboratory runs described above.

Comparative Run Using a High Sodium Containing Lithium Dispersion

A weight of 23.1 grams of a 30 weight percent lithium dispersion in mineral oil containing 6.93 grams [0.9986 gr. eq.] of lithium metal possessing a sodium content of 0.76% was transferred with the aid of 361 ml of dry THF to a one liter three necked flask equipped as above and heated to reflux. A solution of 81.4 grams [1.10 moles] of tert-butyl alcohol and 50 ml of dry THF was added to the contents of the flask over a 42 min period at reflux. The lithium metal particles agglomerated into bigger pieces. Samples of the product were filtered through a syringe filter and analyzed for total alkalinity. Conversions were 86.6 % [30 min], 90% [55 min], 92.3% [115 min], 92.5% [235 min], and 95.1% [330 min].

Exemplary Run--The Preparation of Lithium t-Butoxide Employing Bulk Lithium and a Catalyst

A weight of 81.3 grams [1.096 moles] of tert-butyl alcohol and 3.0 grams [0.05 moles] of isopropyl alcohol were mixed with 410 ml of tetrahydrofuran and heated to reflux [see apparatus description above].

A weight of 6.99 grams [1.007 moles] of lithium metal rods, 1.27 cm in diameter and one centimeter long was added to the refluxing solution all

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at once. The sodium content of the lithium metal was 0.0093%. The reaction was allowed to proceed for 30 minutes and a sample taken for total alkalinity in order to calculate the degree of conversion [39%]. Subsequent samples were taken at 60, 90, 120, 150 and 190 minutes, at which point
5 there was no longer any hydrogen release noted. The degree of conversion for these last five samples were 68, 79, 89, 93, and 96%.

A number of runs are catalogued in Table V using different catalysts as well as a comparative run with no catalyst.

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TABLE I

SYNTHESIS LTB IN THF EMPLOYING VARIOUS LITHIUM TYPES AND SIZES

SITE LAB	LITHIUM PIECES	LITHIUM DIMENSIONS	SURFACE AREA PER G LI (CM ² /G)	RUN SIZE MOLES	REACTION TIME-HRS.
	DISP (1)	10 micron	3770		
	DISP (1)	20 micron	1887	1	2
	DISP (1)	100 micron	1130		
LAB	CUBE (2)	1cmx1cmx1cm	8.1	1	2
LAB	ROD (2)	1.27cm diax1cm	9.7	1	1.5
P.P.	TRAP SLICES(2)	8.9cm/6.35cmx8.26cmx2.54cm	2.7	184	4 to 5

1. Mole ratio Lithium/t-butanol = 1
2. Mole ratio Lithium/t-butanol = 3

TABLE II

SYNTHESIS OF LTB IN REFLUXING THF EMPLOYING LITHIUM DISPERSION

EXP.No.	REAGENTS				CONDITIONS			RESULTS		
	LITHIUM		TBA(1) MOLES	THF MLS	TEMP °C	TBA Feed MIN.	CONC.(2) M.	CONV.(3) %	TIME(4) MIN.	
	% Na	MOLES								
8622	0.015	1.28	0.91	525	reflux(5)	46	18.3	98.8	106	
8617	0.190	1.52	0.91	627	reflux	45	17.9	98.0	145	
8620	0.380	1.22	0.91	501	reflux	45	16.2	100.0	165	
8601	0.760	1.00	0.91	411	reflux	42	17.6	95.1	372	

1. TBA = t-Butyl Alcohol
2. Concentration (molarity) at end of run.
3. Percent conversion at end of run. Based on lithium.
4. Time to complete reaction. Includes TBA feed time.
5. Reflux = 67 to 68°C.

TABLE III
SYNTHESIS OF LTB IN REFLUXING THF EMPLOYING BULK LITHIUM
LITHIUM CUBES - 1 CM SQUARE

		REAGENTS				CONDITIONS			RESULTS		
EXP.No.		LITHIUM		LITBA	TBA(1)	THF	Rx. TEMP	TBA Feed	CONC.(2)	CONV.(3)	TIME(4)
		% Na	MOLES	MOLE RATIO	MOLES	ml	oC	min	M.	%	MIN.
SERIES 1											
	8435	0.0035	3.10	3.0	1.03	425	reflux (5)	0	18.5	98.4	180
	8441	0.0035	1.07	3.2	1.07	439	reflux	0	18.4	98.7	130
	8443	0.0035	1.01	3.1	1.01	416	reflux	0	18.7	100.0	120
	8446	0.0035	1.05	3.3	1.05	432	reflux	0	18.6	100.0	120
	8453	0.0035	1.05	3.4	1.06	434	reflux	0	17.9	96.0	79
	8454	0.0035	0.00	2.2	1.02	421	reflux	0	17.9	95.8	180
	8459	0.0035	0.00	1.2	1.02	421	reflux	0	18.7	96.6	300
		TOTAL LI	7.28	TOTAL TBA	7.26				AVG.YIELD	97.9	
SERIES 2											
	8476	0.0035	3.05	2.9	1.07	439	reflux	129	17.9	97.8	310
	8477	0.0035	1.02	3.0	1.02	419	reflux	108	17.9	97.8	155
	8478	0.0035	1.01	3.0	1.01	414	reflux	106	17.8	97.2	140
	8482	0.0035	0.98	2.9	0.98	404	reflux	120	18	98.1	145
		TOTAL LI	6.06	TOTAL TBA	4.08				AVG.YIELD	97.7	
SERIES 3											
	8527	0.69	3.06	3.0	1.02	419	reflux	0	11.9	63.6	370
	8534	0.69	1.01	3.3	1.01	416	reflux	0	14.4	76.4	410
	8537	0.69	1.01	4.4	1.01	415	reflux	0	15.01	80.5	400
		TOTAL LI	5.08	TOTAL TBA	3.04				AVG.YIELD	73.5	
COMPARATIVE SINGLE RUN											
	8434	0.0035	1.04	0.91	1.14	427	reflux	0	17.1	96.7	480

1. TBA = t-Butyl Alcohol
2. Concentration (Molarity) at end of run.
3. Percent conversion at end of run. Based on lithium.
4. Time to complete reaction.
5. Reflux = 67 to 68oC.

TABLE IV
SYNTHESIS OF LTB IN REFLUXING THF EMPLOYING BULK LITHIUM
LITHIUM RODS -0.5" DIA X 1 CM LONG

EXP.No.	REAGENTS				CONDITIONS		RESULTS		
	LITHIUM	LITBA	TBA(1)	THF	Rx. TEMP	TBA Feed	CONC.(2)	CONV.(3)	TIME(4)
	% Na	MOLES	MOLE RATIO	MOLES	ml	oC	M.	%	MIN.
SERIES 1									
8396	<0.01	2.97	2.72	1.09	407	reflux (5)	19.2	103.4	215
8397	<0.01	0.99	2.96	1.09	407	reflux	19.3	105.3	153
8403	<0.01	1.00	2.98	1.10	411	reflux	18.4	97.4	100
8404	<0.01	1.00	2.98	1.10	411	reflux	18.4	101.4	60
	TOTAL U	5.96	TOTAL TBA	4.38			AVG. YIELD	101.88	
SERIES 2									
8436	<0.01	3.03	3.00	1.01	415	reflux	18.6	98.7	240
8442	<0.01	1.03	2.93	1.04	424	reflux	18.3	98.5	90
8444	<0.01	1.01	2.99	1.01	417	reflux	18.3	98.3	120
8447	<0.01	1.03	2.95	1.03	424	reflux	18.1	96.5	102
8452	<0.01	1.07	2.88	1.07	439	reflux	17.9	96.9	72
8455	<0.01	1.02	2.97	1.02	420	reflux	18.1	97.3	116
8460	<0.01	0.96	3.08	0.97	397	reflux	17.6	94.8	70
8461	<0.01	0.95	3.12	0.95	389	reflux	18.4	98.4	105
8462	<0.01	0.96	3.08	0.96	396	reflux	17.7	95.7	65
8464	<0.01	1.03	2.95	1.03	424	reflux	20.5	95.0	80
8466	<0.01	0.00	1.99	1.01	420	reflux	18.8	99.3	120
8467	<0.01	0.00	0.97	1.03	432	reflux	17.4	92.5	221
	TOTAL U	12.09	TOTAL TBA	12.12			AVG. YIELD	96.83	
SERIES 3									
8505	0.74	3.17	2.99	1.06	434	reflux	12.1	64.9	380
8511	0.74	1.05	3.36	1.05	434	reflux	12.7	68.8	340
8513	0.74	0.97	3.90	0.97	398	reflux	13.8	74.4	340
	TOTAL U	5.19	TOTAL TBA	3.08			AVG. YIELD	69.37	
COMPARATIVE SINGLE RUN									
8291	0.0093	1.03	0.94	1.10	370	reflux	18.1	97.1	332

1. TBA = t-Butyl Alcohol
2. Concentration (Molarity) at end of run.
3. Percent conversion at end of run. Based on lithium.
4. Time to complete reaction.
5. Reflux = 67 to 68oC.

TABLE V
SYNTHESIS OF LTB IN REFLUXING THF EMPLOYING BULK LITHIUM AND CATALYSTS
LITHIUM RODS

REAGENTS														CONDITIONS				RESULTS			
EXP.No.	LITHIUM				TBA(1) MOLES	CATALYST		THF ml	Rx. TEMP		TBA Feed mln	CONC.(2) M.	CONV.(3)		TIME(4) MIN.						
	TYPE	% Na	MOLES	Li/TBA		TYPE	MOLE%(5)		oC	%											
8311	ROD(7)	0.0093	1.03	0.94	1.10	methanol	5.14	410	reflux (6)	0	18.1	97.5	218								
8330	ROD(7)	0.0093	1.02	0.91	1.12	methanol	2.51	410	reflux	0	18.1	98.0	233								
8334	ROD(7)	0.0093	1.06	0.97	1.09	methanol	0.81	410	reflux	0	18.8	98.0	332								
8337	ROD(8)	0.0093	0.98	0.89	1.10	methanol	4.30	410	reflux	0	17.4	97.5	250								
8351	ROD(7)	0.0093	1.01	0.93	1.09	isopropanol	5.03	410	reflux	0	17.7	96.0	180								
8364	ROD(7)	0.0093	1.02	0.90	1.13	isopropanol	4.80	410	45	0	16.4	91.0	330								
8365	ROD(7)	0.0093	1.02	0.94	1.09	isopropanol	4.79	410	55	0	18.1	97.0	330								
8378	ROD(7)	0.0093	1.02	0.94	1.08	isobutanol	5.00	410	reflux	0	17.0	92.0	269								
8386	ROD(7)	0.0093	0.99	0.91	1.09	n-octanol	4.90	410	reflux	0	12.6	73.0	300								
8390	ROD(7)	0.0093	0.96	0.88	1.09	ethanol	4.30	410	reflux	0	16.7	97.0	180								
8391	ROD(7)	0.0093	0.99	0.89	1.11	s-butanol	4.71	405	reflux	0	19.4	100.0	330								
COMPARATIVE SINGLE RUN NO CATALYST																					
8291	ROD(7)	0.0093	1.03	0.94	1.10	NONE	NONE	370	reflux	0	18.1	97.1	332								

1. TBA = t-Butyl Alcohol
2. Concentration (molarity) at end of run.
3. Percent conversion at end of run. Based on lithium.
4. Time to complete reaction.
5. Based on TBA.
6. Reflux = 67 to 68°C.
7. Lithium rod 0.5" dia. x 1cm
8. Lithium rod 0.5" dia. x 4.6cm

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TABLE VI

SYNTHESIS OF LTB IN REFLUXING THF EMPLOYING BULK LITHIUM - SCALE-UP

LITHIUM TRAPS-CUT INTO 10 SLICES-8.9CM/6.35CM(WIDTH)X8.26CM(HT.)X2.54CM(THICK)

RUN NO.		REAGENTS						CONDITIONS			RESULTS		
		LITHIUM				TBA(1) MOLES	THF LBS.	TEMP °C	TBA Feed HRS	CONC.(2) M.	CONV.(3) %	TIME(4) MIN.	
		TYPE	% Na	MOLES	LI/TBA								
P.P. SERIES (6)													
9302	SL.TRAPS	0.0035	523	2.84	184	133.0	reflux (5)	1.5	18.9	93.7	435		
9303	SL.TRAPS	0.0035	196	2.91	184	148.0	reflux	1.3	17.9	97.2	355		
9304	SL.TRAPS	0.0035	183	2.90	184	148.0	reflux	1.3	18.1	97.1	265		
9305	SL.TRAPS	0.0035	196	3.00	182	148.0	reflux	1.2	17.3	94.1	300		
9306	SL.TRAPS	0.0035	183	3.01	182	148.3	reflux	0.8	18.1	97.0	325		
9307	SL.TRAPS	0.0035	183	3.01	182	148.3	reflux	0.7	18.6	99.4	210		
9308	SL.TRAPS	0.0035	183	3.02	182	148.3	reflux	1.2	18.7	96.7	230		
9309	SL.TRAPS	0.0035	0	1.70	216	174.8	reflux	1.5	20.4	100.0	210		
9310	SL.TRAPS	0.0035	0	0.70	216	174.8	reflux	1.5	9.0	48.2	620		
TOTAL LI			1647	TOTAL TBA		1712							

1. TBA = t-Butyl Alcohol
2. Concentration (molarity) at end of run.
3. Percent conversion at end of run. Based on lithium.
4. Time to complete reaction.
5. Reflux = 67 to 68°C.
6. Pilot plant runs

CLAIMS:

1. A process for preparing solutions of lithium tertiary-alkoxides characterized by the steps of reacting, in a reaction vessel, alkyl lithium bulk metal whose size exceeds 0.1 mm, containing less than 0.6% by weight of sodium, with a tertiary alcohol containing 3 to 10 carbon atoms, in mole ratios of metal to alcohol ranging from 1 to 1 to 10 to 1 in a solvent selected from ethereal or hydrocarbon solvents under an inert atmosphere at an elevated temperature between 34.6°C and 100°C for 1 to 10 hours, cooling the product lithium tertiary alkoxide and separating the lithium tertiary alkoxide solution from the unreacted lithium metal in the reaction vessel.
2. The process of Claim 1 characterized in that the tertiary alcohol is tertiary butyl alcohol the solvent is tetrahydrofuran and the lithium metal to tertiary alcohol ratio is 3 to 1.
3. The process of Claim 1 characterized in that the lithium bulk metal pieces are of a weight greater than 0.5 grams per piece and the sodium content of the lithium metal is less than 0.01 weight percent.
4. The process of Claim 2 characterized in that the elevated temperature is the boiling point of tetrahydrofuran.
5. The process of Claim 1 characterized in that the separation of the lithium tertiary alkoxide solution is carried out by decantation.
6. The process of claim 1 for preparing of lithium tert-alkoxides, further characterized in that adding 2-10 mole percent of C₁-C₃ alcohols to the reaction of lithium metal and a tertiary alcohol in an ethereal or hydrocarbon medium.
7. The process of Claim 6 characterized in that tert-alkoxide is lithium tert-butoxide, the C₁-C₃ alcohol catalyst is methyl alcohol and the solvent is tetrahydrofuran.
8. A process for preparing solutions of lithium tertiary-alkoxides characterized by the steps of reacting lithium bulk metal whose size exceeds 0.1 mm, containing less than 0.6% by weight of sodium, with a tertiary alkyl alcohol containing 3 to 10 carbon atoms in mole ratios of metal to alcohol ranging from 1 to 1 to 10 to 1 in a solvent selected from ethereal or hydrocarbon solvents under an inert atmosphere at elevated temperature between 34 and 100°C for 1 to 10 hours, cooling the product lithium tertiary

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alkoxide solution and separating the lithium tertiary alkoxide solution from the unreacted lithium metal in the reactor, adding additional solvent and sufficient lithium metal and alcohol to the unreacted metal in the reactor to re-establish the mole ratio of lithium metal to alcohol, and continuing the
5 reaction, thereby forming further lithium tertiary-alkoxide, and repeating these process steps a number of times.

9. The process of Claim 10 characterized in that the number of repetitions of said reaction steps is at least three.

10. The process of Claim 2 characterized in that the solvent added in
10 the repeated steps is added immediately after removal of the lithium tertiary alkoxide solution.

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INTERNATIONAL SEARCH REPORT

Int. application No.
PCT/US94/09844

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :C07C 31/30

US CL :568/851

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 568/851

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US,A, 3,971,833 (LENZ ET AL) 27 JULY 1971, SEE THE ABSTRACT; COLUMNS 2-4.	1-3,5-10
Y	COLLECTION CZECHOSLOV. CHEM. COMMUN., VOL. 35, ISSUED 1970, LOCHMAN ET AL, "PREPARATION OF SOME ALKOXIDES OF ALKALINE METALS", PAGES 733-736, ENTIRE DOCUMENT.	1-3,5-10

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

03 NOVEMBER 1994

Date of mailing of the international search report

06 JAN 1995

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Authorized officer

R. COOK

Facsimile No. (703) 305-3230

Telephone No. (703) 308-1235