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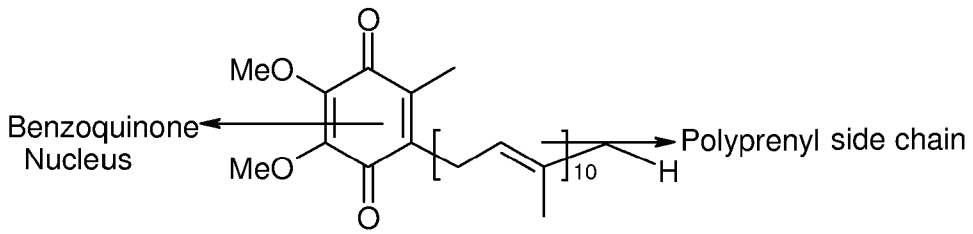
(54) **Title:** IMPROVED PROCESS FOR THE SYNTHESIS OF COQ_{10}



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(57) **Abstract:** The present invention relates to an improved process for the preparation of Coenzyme Q. Coenzyme Q_{10} or CoQ_{10} has the chemical name 2- [(all -trans)- 3, 7,l l,15,19,23,27,31,35,39-decamethyl-2, 6, 10, 14, 18, 22, 26, 30, 34, 38 - tetracontadecaenyl]-5,6-dimethoxy -3- methyl -1,4-benzoquinone and has the formula 1.

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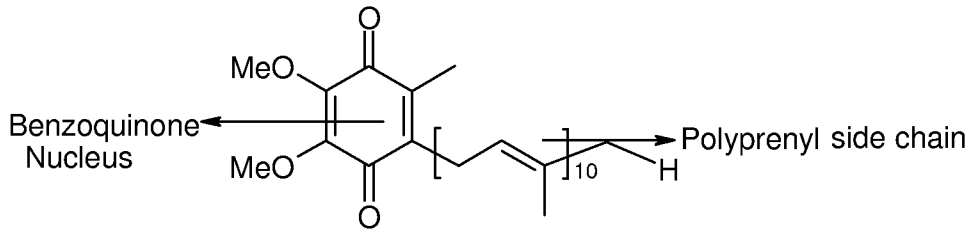
IMPROVED PROCESS FOR THE SYNTHESIS OF COQ_{10}

Field of Invention

The present invention relates to an improved process for the preparation of Coenzyme Q. Coenzyme Q_{10} or CoQ_{10} has the chemical name 2- [(all –trans)- 3, 7,11,15,19,23,27,31,35,39-decamethyl-2, 6, 10, 14, 18, 22, 26, 30, 34, 38 – tetracontadecaenyl]-5,6-dimethoxy -3- methyl -1,4-benzoquinone and has the formula **1**.



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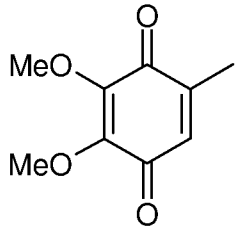
Background of the Invention

This coenzyme is present in virtually every cell in the human body and is known as the "miracle nutrient". It plays a vital role in maintaining human health and vigor and is involved in mitochondrial processes such as respiration, maintenance of heart muscle strength, enhancement of the immune system, quenching of free radical in the battle against ageing to name a few ("The miracle nutrient coenzyme" Elsevier/ North – Holland Biomedical Press, New York, 1986; "Coenzyme Q: Biochemistry, Bioenergetics, and clinical Applications of Ubiquinone" Wiley, New York, 1985; " Coenzyme Q, Molecular Mechanism in Health and Disease" CRC press).

As depicted above CoQ_{10} of the formula **1** comprises mainly of two moieties (i) the head group - "benzoquinone nucleus" and (ii) the "polyprenyl side chain" with ten isoprene units. The source of benzoquinone nucleus is 2,3-dimethoxy-5-methyl benzoquinone, CoQ_0, of the formula **2.**



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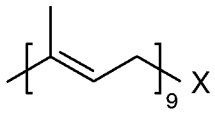
The source of the polyprenyl side chain is solanesol, a naturally occurring alcohol, containing nine isoprene units and having the formula **3** where X is -OH.



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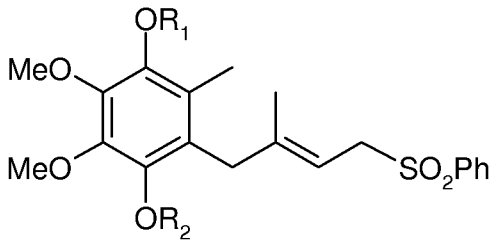
Literature reports several methods of semi synthetic preparation of CoQ_{10} (Strategies and Tactics in Organic Synthesis **4** 270 (2004), J Am. Chem. Soc. **118** , 5512 (1996), Huaxue Yu Nianhe **6** 267 (2002)).

One of the process involves condensing solanesyl bromide of nine isoprene units (compound of formula **3** where X is -Br) with CoQ_1 sulphone compound of formula **4** where R_1 and R_2 represents protecting groups,



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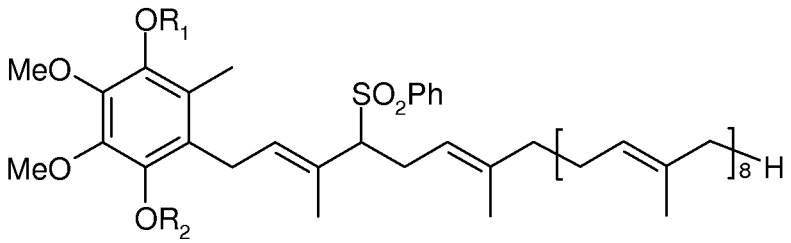
to achieve the desired polyprenyl carbon skeleton of CoQ_{10}, compound of formula **5** (J. Org. Chem. **44** 868 (1979) , US 4,270,003 (1981), Bull. Chem. Soc. Jpn. **55** 1325(1982), J. Org. Chem. **68** 7925 (2003), our co-pending Indian patent application No. 706/MUM/2006.



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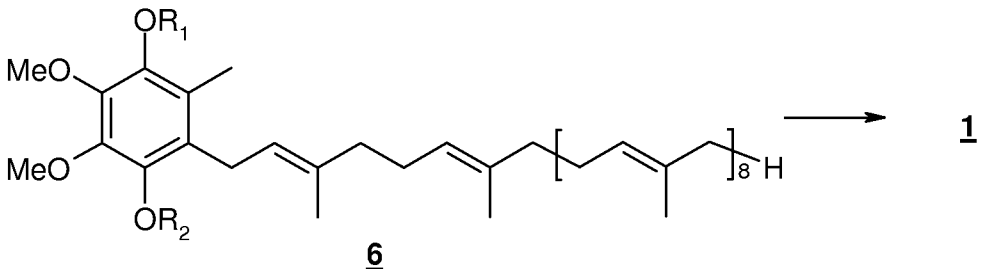
The next stage of the synthesis of CoQ_{10} involves removal of the sulphone to form compound of formula **6,** which is deprotected and oxidized subsequently to form CoQ_{10} compound of formula **1**.



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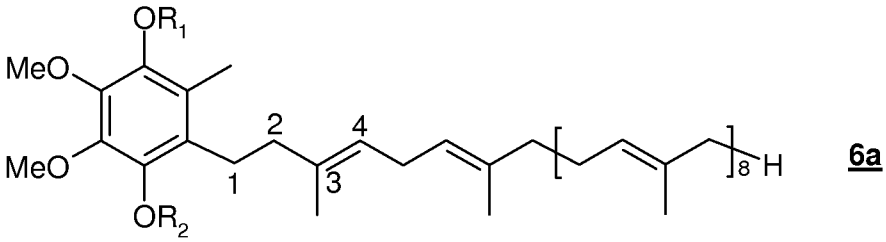
The key problem in synthesis by the above mentioned scheme is desulphonation. The sulphone is readily removed by reductive desulphonation by dissolving metal viz. sodium in THF/ ethanol or Li in ethylamine or methylamine (Chem.Soc.Chem Commun.(1982) 153, Bull. Chem. Soc. Jpn. **55** 1325(1982) our co-pending Indian patent application No. 706/MUM/2006).

But the stereochemical integrity of the double bond is lost in these free radical reactions giving rise to positional isomers.

The positional isomer formed from desulphonation of compound of formula **5** (where R_1 and R_2 represents protecting groups) where the sulphone is in carbon 4, is due to migration of double bond from 2,3 to 3,4 position (compound of formula **6a**).



6a

Stereoselective desulphonation is reported for compound of formula **5** where R_1 and R_2 are $-CH_3$, using lithium triethyl borohydride and diphenylphosphino ethane palladium chloride as catalyst. Compound of formula **6** (where R_1 and R_2 are methyl ($-CH_3$)) is treated with 1,2 Bis(diphenylphoshphinoethane) dichloropalladium (0.03g) and lithium triethylborohydride (1M, 2.2 ml) for 1 hour at 0^0 C. The mixture was quenched in ammonium chloride solution, extracted in ether and ether was evaporated to obtain the crude. The crude was purified by column chromatography to obtain 0.69 g of compound of formula **6** where R_1 and R_2 are $-CH_3$ in 77% yield.

Catalyst loading is 3%, and the yield obtained is only 77%. The catalyst being homogeneous is expensive and, with 3% loading and 77% yield makes the process cost ineffective. The literature does not specify about the extent of isomer formation.

The desulphonated compound of formula **6** where R_1 and R_2 are methyl (0.69 g) is treated with Ceric Ammonium Nitrate (0.84 g) in acetonitrile and water at 0^0 C for 30 minutes. The reaction was worked up and the crude purified by column chromatography to obtain CoQ_{10} compound of formula **1** in 61% yield.

Ceric Ammonium nitrate is an expensive reagent and used 1.2 times that of the starting material compound of formula **6** and therefore makes the process cost ineffective.

The present inventors have observed that the oxidation is not selective and gives rise to side reactions and generates impurities, and column purification cannot be avoided. Thus loss in purification is incurred and the yield of obtaining CoQ_{10} of pharmacopial standard is not more than 40%. This makes the process not industrially viable. Therefore CoQ_1 sulphone compound of formula **4** where R_1 and R_2 are $-CH_3$ is not suitable for synthesis of CoQ_{10} for industrial production.

The protecting group is a major contributing factor in CoQ_{10} synthesis. Among the various types of protecting groups, 2-methoxyethoxymethyl is reported to be of industrial use (Synthesis 469 (1981), US 4,270,003 (1981)).

Literature reports synthesis of CoQ_{10} with CoQ_1 sulphone compound of formula **4** using protecting groups both R_1 and R_2 as methoxyethoxymethyl and R_1 as methoxyethoxymethyl and R_2 as methyl (Bull. Chem. Soc. Jpn. 55 1325(1982, our co-pending Indian patent application No. 706/MUM/2006). The compound of formula **4** was coupled with solanesyl bromide to form compound of formula **5** (with both R_1 and R_2 as methoxyethoxymethyl, and R_1 as methoxyethoxymethyl and R_2 as methyl) .

Desulphonation of compounds of formula **5** (Both R_1 and R_2 are methoxyethoxymethyl and R_1 is methoxyethoxymethyl and R_2 is methyl respectively) was carried out using sodium and ethanol.

Literature does not specify the extent of positional isomer formed in desulphonated product compound of formula **6** (R_1 and R_2 as methoxyethoxymethyl and R_1 as methoxyethoxymethyl and R_2 as methyl respectively).

The present inventors have observed around 35% of positional isomers compound of formula **6** (R_1 and R_2 as methoxyethoxymethyl and R_1 as methoxyethoxymethyl and R_2 as methyl respectively) were formed. The respective isomers do not get separated in thin layer chromatography or high pressure liquid chromatography. The oxidation is done with isomers of compound of formula 6 (R_1 and R_2 as methoxyethoxymethyl and R_1 as methoxyethoxymethyl and R_2 as methyl respectively) and there is a substantial yield loss in purification after oxidation. The pharmacopeal passing CoQ_{10} can be obtained around 35 % yield only from the condensed compound of formula **5**. This makes the process, which has the potential of industrial application as cost ineffective.

The present inventors have also observed that selective desulphonation of compound of formula **5** (Both R_1 and R_2 as methoxyethoxymethyl and R_1 as methoxyethoxymethyl and R_2 as methyl respectively) with lithum triethyl borohydride using 1,2-bis-(diphenyl phoshphinoethane) dichloropalladium, and 1,4-bis-(diphenylphoshphinobutane) dichloropalladium does not go to completion even after 24 hrs and excess loading (>5%) of catalyst. Moreover 1,4-bis-(diphenylphoshphinobutane) dichloropalladium does not give any selectivity and produces around 40% of positional isomers which is more than found in using sodium and ethanol method.

Thus there is need to find a reagent for desulphonation in the above process in respect to reactivity and regioselectivity.

Literature reports deprotection of compound of formula **6** (R_1 and R_2 as methoxyethoxymethyl and R_1 as methoxyethoxymethyl and R_2 as methyl

respectively) to form CoQ_{10} hydroquinone compound of formula **6** (where R_1 and R_2 are hydrogen) and *in-situ* oxidation of CoQ_{10} hydroquinone to form CoQ_{10} compound of formula **1.** The oxidation was carried out *in-situ* in presence of methanolic potassium hydroxide solution in presence of oxygen.

The present inventors have observed that CoQ_{10} is sensitive to alkaline medium and neutralization with methanolic potassium hydroxide is not recommended for scale up. Also the employment of aerial oxidation does not take the reaction to completion.
Literature method of oxidation of CoQ_{10} hydroquinone compound of formula **7** (as described herein below) uses 2 molar equivalent of ferric chloride for one equivalent of hydroquinone (Chemistry Letters 1597 (1988)).
Using the above method the present inventors observed that 3 - 4 molar equivalent of ferric chloride for one equivalent of hydroquinone was required for taking the reaction to completion. Such large excess use of ferric chloride gives rise to effluent and also increases the heavy metal content in the oxidized product CoQ_{10}. Thus the process of oxidation of CoQ_{10} hydroquinone is not industrially clean.

Use of CoQ_{10} in broadband medical application is increasing day by day. A cost effective process is currently lacking.

The major cost-contributing factor for the preparation of CoQ_{10} is the cost of solanesol. Solanesol is obtained from natural sources namely tobacco and potatoes. The content of Solanesol in tobacco is very less (< 2%) and for using it as a starting material for the preparation of CoQ_{10} it requires a purity of minimum 95 %, which increases the cost of solanesol. The industrially feasible process would require the consumption coefficient of solanesol to be minimised.

The key point in the synthesis of CoQ_{10} is the choice of building block for "the benzoquinone nucleus" which features i) functional group for chain elongation and ii) protecting groups. One such "building block" for "the benzoquinone nucleus" utilizes i) CoQ_1 sulphones as nucleophilic functionality and ii) methoxyethoxymethyl and methoxyethoxymethyl and methyl, as protecting groups. The corresponding α-sulphonyl stabilized carbanions serve as nucleophilic partner in carbon carbon bond

formation to obtain the desired carbon skeleton of CoQ_{10} sulphone, with sulphone at carbon 4 of the polyprenyl chain. The sulphone has the advantage of easy removal and the drawback of inferior regioselectivity, at the end of reaction.

Thus the present invention relates to the improved process of i) desulphonation of CoQ_{10} sulphone with sulphone at carbon 4, containing dimethoxyethoxymethyl and monomethoxyethoxymethyl as protecting group and ii) oxidation of CoQ10 hydroquinone to CoQ_{10}

Objective of the invention

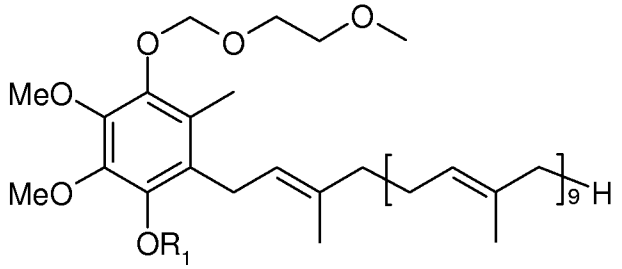
The main objective of the present invention is to provide an improved process for the desulfonation of CoQ10 sulphone of formula **5** to provide compound of formula **6** overcoming the drawbacks of the hitherto known process.

Another objective of the present invention is to provide an improved process for the preparation of CoQ_{10} of the formula **1**, given above overcoming the drawbacks of the hitherto known processes

Yet another objective of the present invention is to provide an improved process for the preparation of CoQ_{10} of the formula **1** given above which is useful for industrial application.

Summary of the Invention

A process for the preparation of compound of formula **6**



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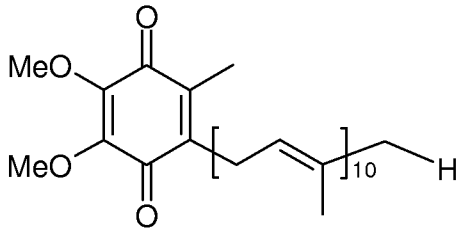
comprising desulfonating compound of formula **5** to obtain **6**

Also a process for the preparation of CoQ10 of formula **1**



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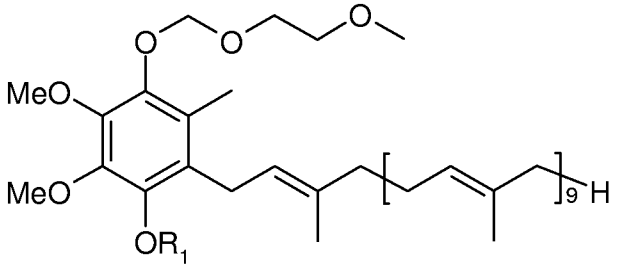
comprising desulfonating compound of formula **5** to obtain **6** which in turn is deprotected to obtain a compound of formula **7** followed by oxidation where R_1 represents $-CH_3$ or $-CH_2OCH_2CH_2OCH_3$ and R_2 is H or $-CH_3$.

Detailed Description of the Invention

The present invention provides a process for the preparation of a compound of formula **6**



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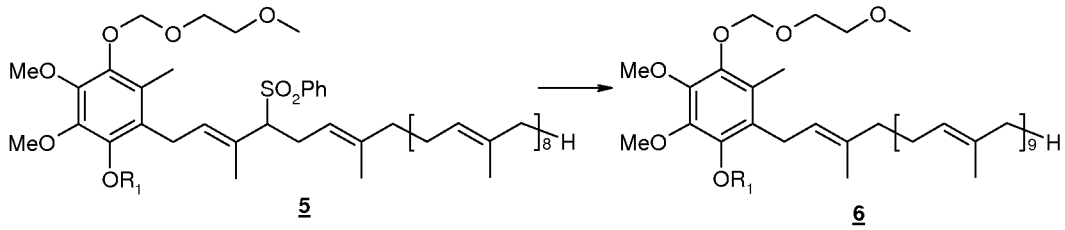
said process comprising the steps of:

i. desulphonating compound of formula **5** wherein R_1 represents $-CH_3$ or $-CH_2OCH_2CH_2OCH_3$ using lithium triethyl borohydrate in the presence of a catalyst and a solvent at a temperature in the range of $-10^{\circ}C$ to $25^{\circ}C$ for a period of 0.5 to 3 hours to obtain compound of formula **6** wherein R_1 represents $-CH_3$ or $-CH_2OCH_2CH_2OCH_3$,

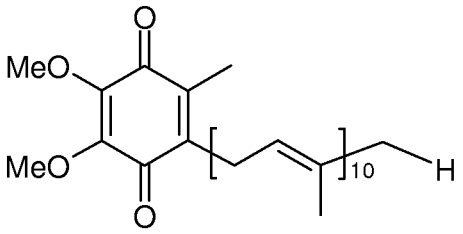
ii. isolating and purifying the compound of formula **6** formed by conventional methods.

The process of the present invention is shown in Scheme 1.



Scheme 1

The present invention also provides a process for the preparation of CoQ10 of the formula **1**



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said process comprising the steps of:

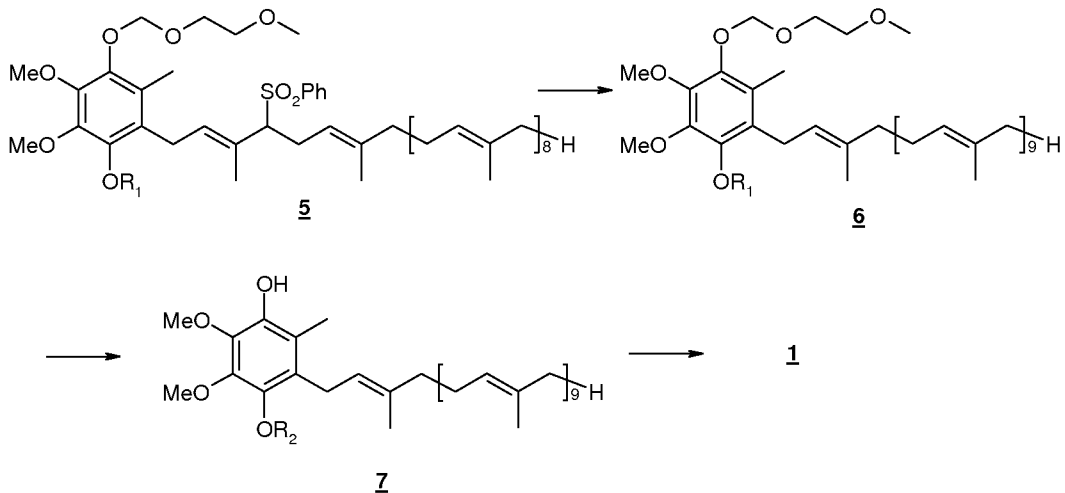
i. desulphonating compound of formula **5** wherein R_1 represents $-CH_3$ or $-CH_2OCH_2CH_2OCH_3$ using lithium triethyl borohydride in the presence of a catalyst and a solvent at a temperature in the range of –10°C to 25°C for a period of 0.5 to 3 hours to obtain compound of formula **6** wherein R_1 represents $-CH_3$ or $-CH_2OCH_2CH_2OCH_3$,

ii. deprotecting the compound of formula **6** wherein R_1 represents $-CH_3$ or $-CH_2OCH_2CH_2OCH_3$ by HBr in the presence of an alcohol as a solvent at a temperature in the range of 25°C to 100°C for a period of 0.5 to 3 hours to obtain a compound of formula **7** wherein R_2 is H or $-CH_3$,

iii. oxidising the compound of formula **7** by conventional method to form compound of formula **1** and

iv. isolating and purifying the compound of formula **1** formed by conventional methods.

The process of the present invention is shown in Scheme 2.



Scheme 2

Desulphonation of the compound of the formula **5** to obtain compound of formula **6** may be carried out by using lithium triethyl borohydride in a solvent selected from tetrahydrofuran, hexane, dioxane, xylol and the like in the presence of a catalyst such as 1,3-bis diphenyl phosphinopropane palladium chloride, at a temperature in the range of –10°C to 25°C for a period of 0.5 to 3 hours.

Deprotection of the compound of the formula **6** to get the compound of the formula **7** may be carried out using 48% hydrogen bromide in an alcohol such as ethanol, isopropyl alcohol, n-butyl alcohol and the like at a temperature in the range of 25°C to 100°C for a period of 0.5 to 3 hours.

The oxidation of the formula **7** may be carried out by known method of using ferric chloride at a molar ratio that is less than 1:1 in isopropanol as solvent in the presence of oxygen.

In the process of the present invention the undesired positional isomer is restricted to not more than 10% in the desulfonation reaction unlike the prior art where about 35% of the undesired positional isomer is obtained. Also the present invention provides for decreasing the molar quantity of ferric chloride, which increases the purity of the oxidized product and thereby increase the yield of CoQ_{10}.

The details of the various reactions conditions of the processes described above and those preferred ones are given below. The details of the process of the present invention are given in the Examples below which are provided for illustration only and therefore they should not be construed to limit the scope of the invention

Example 1: Preparation of 1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyltetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-3,4-dimethoxy-2,5-bis((2-methoxyethoxy)methoxy)-6-methylbenzene (6: R_1 = -$CH_2OCH_2CH_2OCH_3$)

Solution of 1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyl-4-(phenylsulfonyl)tetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-3,4-dimethoxy-2,5-bis((2-methoxyethoxy)methoxy)-6-methylbenzene (**5**: R_1 = -

$CH_2OCH_2CH_2OCH_3$) (5.9 g) in THF (120 ml) was treated with palladium chloride-diphenyl phosphino propane (168 mg) at 0 – 5 ^{0}C. Lithium triethyl borohydride 1M solution in THF (17.5 ml) was added to the mixture over a period of 30 minutes. The reaction was continued for 1 hour at 0 – 5 ^{0}C. The reaction was quenched in saturated ammonium chloride solution and THF layer separated. The THF layer was distilled to obtain the title compound (5g) in 97% yield (purity 90%)

Example 2: Preparation of 1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyltetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-3,4-dimethoxy-2,5-bis((2-methoxyethoxy)methoxy)-6-methylbenzene (6: R_1 = -$CH_2OCH_2CH_2OCH_3$)

Solution of 1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyl-4-(phenylsulfonyl)tetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-3,4-dimethoxy-2,5-bis((2-methoxyethoxy)methoxy)-6-methylbenzene (**5**: R_1 = -$CH_2OCH_2CH_2OCH_3$) (5.9 g) in THF (120 ml) was treated with palladium chloride-diphenyl phosphino propane (0.084 mg) at 0 – 5 ^{0}C. Lithium triethyl borohydride 1M solution in THF (17.5 ml) was added to the mixture over a period of 30 minutes. The reaction was continued for 1 hour at 0 – 5 ^{0}C. The reaction was quenched in saturated ammonium chloride solution and THF layer separated. The THF layer was distilled to obtain the title compound (5g) in 97% yield (purity 90%)

Example 3: Preparation of 1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyltetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-3,4-dimethoxy-2,5-bis((2-methoxyethoxy)methoxy)-6-methylbenzene (6: R_1 = -$CH_2OCH_2CH_2OCH_3$)

Solution of 1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyl-4-(phenylsulfonyl)tetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-3,4-dimethoxy-2,5-bis((2-methoxyethoxy)methoxy)-6-methylbenzene (**5**: R_1 = -$CH_2OCH_2CH_2OCH_3$) (5.9 g) in THF (120 ml) was treated with palladium chloride-diphenyl phosphino propane (168 mg) at 0 – 5 ^{0}C. Lithium triethyl borohydride 1M solution in THF (12.5 ml) was added to the mixture over a period of 30 minutes. The reaction was continued for 1 hour at 0 – 5 ^{0}C. The reaction was quenched in saturated ammonium chloride solution and THF layer separated. The THF layer was distilled to obtain the title compound (5g) in 97% yield (purity 90%)

Example 4: Preparation of 1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyltetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-3,4-dimethoxy-2,5-bis((2-methoxyethoxy)methoxy)-6-methylbenzene (6: R_1 = -$CH_2OCH_2CH_2OCH_3$)

Solution of 1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyl-4-(phenylsulfonyl)tetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-3,4-dimethoxy-2,5-bis((2-methoxyethoxy)methoxy)-6-methylbenzene (5: R_1 = -$CH_2OCH_2CH_2OCH_3$) (5.9 g) in hexane (120 ml) was treated with palladium chloride-diphenyl phosphino propane (168 mg) at 0 – 5 ^{0}C. Lithium triethyl borohydride 1M solution (17.5 ml) in hexane was added to the mixture over a period of 30 minutes. The reaction was continued for 1 hour at 0 – 5 ^{0}C. The reaction was quenched in saturated ammonium chloride solution and hexane layer separated. The hexane layer was distilled to obtain the title compound (5g) in 97% yield (purity 90%)

Example 5: Preparation of 1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyltetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-2,3,4-trimethoxy-5-((2-methoxyethoxy)methoxy)-6-methylbenzene (6: R_1 = -CH_3)

Solution of 1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyl-4-(phenylsulfonyl)tetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-2,3,4-trimethoxy-5-((2-methoxyethoxy)methoxy)-6-methylbenzene (5: R_1 = -CH_3) (45.0 g) in THF (675 ml) was treated with palladium chloride- diphenyl phosphino propane (790 mg) at 0 – 5 ^{0}C. Lithium triethyl borohydride 1M solution (142 ml) in THF was added to the mixture over a period of 30 minutes. The reaction was continued for 1 hour at 0 – 5 ^{0}C. The reaction was quenched in saturated ammonium chloride solution and THF layer separated. The THF layer was distilled to obtain the title compound (36 g) in 92 % yield (purity 90%).

Example 6: Preparation of 1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyltetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-2,3,4-trimethoxy-5-((2-methoxyethoxy)methoxy)-6-methylbenzene (6: R_1 = -CH_3)

Solution of 1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyl-4-(phenylsulfonyl)tetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-2,3,4-trimethoxy-5-((2-methoxyethoxy)methoxy)-6-methylbenzene (5: R_1 = -CH_3) (45.0 g) in THF (675 ml) was treated with palladium chloride- diphenyl phosphino propane (526 mg) at 0 – 5 ^{0}C. Lithium triethyl borohydride 1M solution (142 ml) in THF was added to the mixture over a period of 30 minutes. The reaction was continued for 1 hour at 0 – 5 ^{0}C. The reaction was quenched in saturated ammonium chloride solution and THF layer separated. The THF layer was distilled to obtain the title compound (36 g) in 92 % yield (purity 90%).

Example 7: Preparation of 1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyltetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-2,3,4-trimethoxy-5-((2-methoxyethoxy)methoxy)-6-methylbenzene (6: R_1 = -CH_3)

Solution of 1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyl-4-(phenylsulfonyl)tetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-2,3,4-trimethoxy-5-((2-methoxyethoxy)methoxy)-6-methylbenzene (5: R_1 = -CH_3) (45.0 g) in THF (675 ml) was treated with palladium chloride- diphenyl phosphino propane (526 mg) at 0 – 5 ^{0}C. Lithium triethyl borohydride 1M solution (109 ml) in THF was added to the mixture over a period of 30 minutes. The reaction was continued for 1 hour at 0 – 5 ^{0}C. The reaction was quenched in saturated ammonium chloride solution and THF layer separated. The THF layer was distilled to obtain the title compound (36 g) in 92 % yield (purity 90%).

Example 8: CoQ10 (1)

1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyltetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-3,4-dimethoxy-2,5-bis((2-methoxyethoxy)methoxy)-6-methylbenzene (6: R_1 = -$CH_2OCH_2CH_2OCH_3$) (4g) obtained according to Examples 1 – 4, was treated with HBr 48% (0.2 ml) and

Isopropyl alcohol (40 ml). The mixture was warmed to 60 ^{0}C for 1 hour, cooled and neutralized with sodium bicarbonate to obtain crude 2-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyltetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-5,6-dimethoxy-3-methylbenzene-1,4-diol (**7**: R_2 = H). This neutralized solution was treated with anhydrous ferric chloride 0.13 g in presence of oxygen for one hour to obtain CoQ10 of formula **1** (3.2 g).

Example 9: CoQ10 (1)

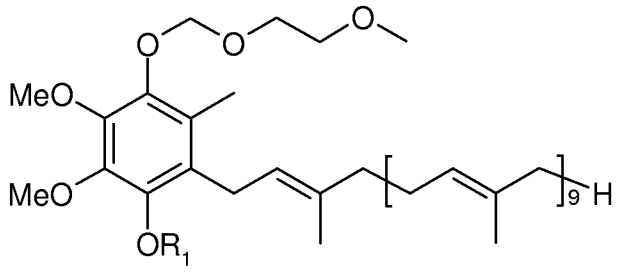
1-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyltetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-2,3,4-trimethoxy-5-((2-methoxyethoxy)methoxy)-6-methylbenzene (6: R_1 = -CH_3) (35 g) obtained according to Examples 5 – 7, was treated with HBr 48% (0.9 ml) and Isopropyl alcohol (250 ml). The mixture was warmed to 60 ^{0} C for 1 hour, cooled and neutralized with sodium bicarbonate to obtain crude 3-((2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyltetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-4,5,6-trimethoxy-2-methylphenol (**7**: R_2 = CH_3). This neutralized solution was treated with anhydrous ferric chloride 17 g in presence of oxygen for 4 hours to obtain CoQ10 of formula **1** (29 g).

Advantages

1. The undesired positional isomer to not more than 10% in the desulfonation reaction unlike the priorart where about 35% of the undesired positional isomer is obtained.
2. The molar quantity of ferric chloride was reduced, which increases the purity of the oxidized product and thereby increase the yield of CoQ_{10}.
3. CoQ10 was obtained in good overall yield as well purity.

We Claim:

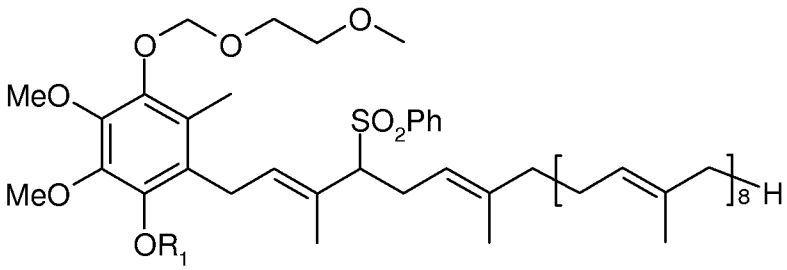
1. A process for the preparation of a compound of formula **6**



6

said process comprising the steps of:

i. desulphonating compound of formula **5**

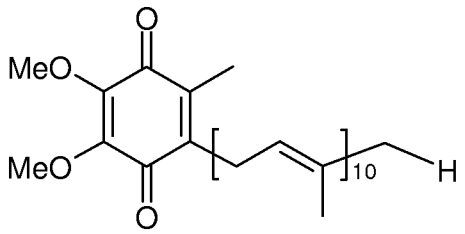


5

wherein R_1 represents $-CH_3$ or $-CH_2OCH_2CH_2OCH_3$ using lithium triethyl borohydrate in the presence of a catalyst and a solvent at a temperature in the range of $-10°C$ to $25°C$ for a period of 0.5 to 3 hours to obtain compound of formula **6** wherein R_1 represents $-CH_3$ or $-CH_2OCH_2CH_2OCH_3$,

ii. isolating and purifying the compound of formula **6** formed by conventional methods.

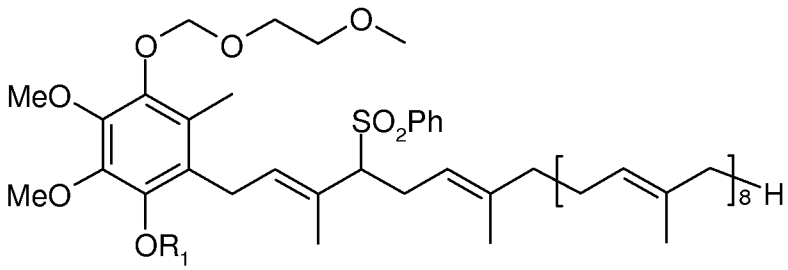
2. A process for the preparation of CoQ10 of the formula **1**



1

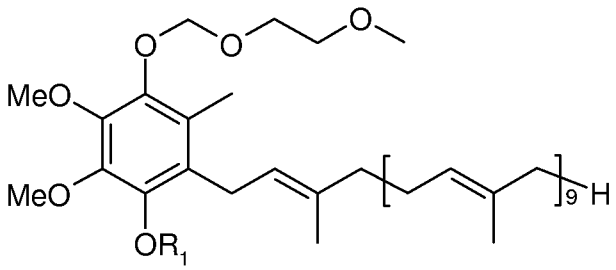
said process comprising the steps of:

i. desulphonating compound of formula **5**



5

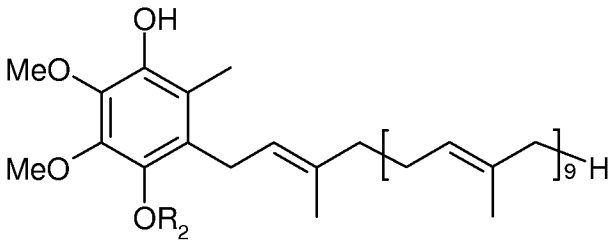
wherein R_1 represents $-CH_3$ or $-CH_2OCH_2CH_2OCH_3$ using lithium triethyl borohydrate in the presence of a catalyst and a solvent to obtain compound of formula **6**



6

wherein R_1 represents $-CH_3$ or $-CH_2OCH_2CH_2OCH_3$,

ii. deprotecting the compound of formula **6** wherein R_1 represents $-CH_3$ or $-CH_2OCH_2CH_2OCH_3$ by HBr in the presence of an alcohol as a solvent to obtain a compound of formula **7**



7

wherein R_2 is H or $-CH_3$,

iii. oxidising the compound of formula **7** by conventional method to form compound of formula **1** and

iv. isolating and purifying the compound of formula **1** formed by conventional methods.

3. The process as claimed in claims 1 and 2, wherein in step (i), the reaction is carried out at a temperature in the range of –10°C to 25°C for a period of 0.5 to 3 hours.

4. The process as claimed in claim 2, wherein in step (ii), the reaction is carried out at a temperature in the range of 25°C to 100°C for a period of 0.5 to 3 hours.

5. The process as claimed in claims 1 and 2, wherein the catalyst used in step (i) is 1,3-bis diphenyl phosphinopropane palladium chloride.

6. The process as claimed in claims 1 and 2, wherein the solvent used in step (i) is selected from tetrahydrofuran, hexane, dioxane and xylol.

7. The process as claimed in claim 2, wherein the alcohol used in step (ii) is selected from ethanol, isopropyl alcohol and n-butyl alcohol.

8. The process as claimed in claim 2, wherein the molar ratio of ferric chloride used in step (ii) is less than 1:1.