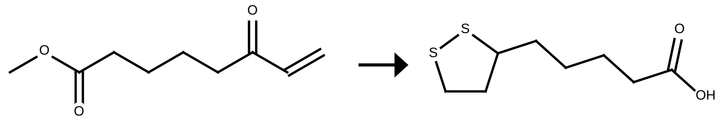

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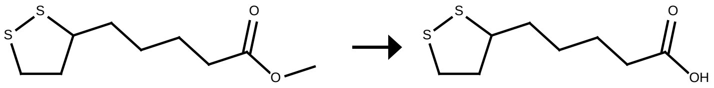
Yield	Conditions & References
	With cobalt polysulfide, hydrogen, sulfur, acetic acid, T= 175 °C , p= 58840.6 - 73550.8Torr , anschl. mit wss. NaOH und anschl. Behandeln der mit Eisen(III)-chlorid versetzten wss. Loesung mit Sauerstoff **Bullock et al.**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 1975,1976
	Reaction Steps: 2 2: acetic acid; hydrogen; cobalt polysulfide; sulfur / 175 °C / 58840.6 - 73550.8 Torr / anschl. mit wss. NaOH und anschl. Behandeln der mit Eisen(III)-chlorid versetzten wss. Lsg. mit Sauerstoff **With** cobalt polysulfide, hydrogen, sulfur, acetic acid **Bullock et al.**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 1975,1976
	Reaction Steps: 2 1: NaH 2: acetic acid; hydrogen; cobalt polysulfide; sulfur / 175 °C / 58840.6 - 73550.8 Torr / anschl. mit wss. NaOH und Behandeln der mit Eisen(III)-chlorid versetzten wss. Loesung mit Sauerstoff **With** cobalt polysulfide, hydrogen, sodium hydride, sulfur, acetic acid **Bullock et al.**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 1975,1976



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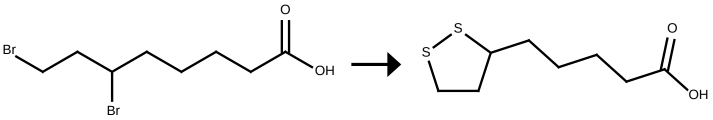
Yield	Conditions & References
70 %	**With** potassium hydroxide **in** methanol, Time= 24h, T= 20 °C **Chavan, Subhash P.; Shivsankar; Pasupathy**; Synthesis; nb. 8; (2005); p. 1297 - 1300; Art.No: Z20804SS
0.120 g	**With** potassium hydroxide **in** methanol, Time= 24h, Ambient temperature **Rao, A. V. Rama; Mysorekar, Sudha V.; Yadav, J. S.**; Synthetic Communications; **vol.** 17; nb. 11; (1987); p. 1339 - 1348



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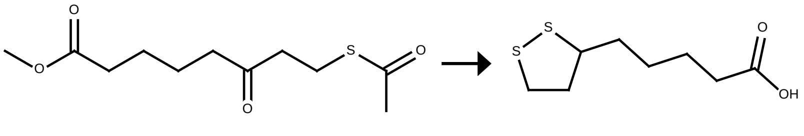
Yield	Conditions & References
65 %	**With** piperidinium thiotungstate **in** N,N-dimethyl-formamide, Time= 4h, T= 50 °C **Dhar; Chidambaram; Chandrasekaran**; Journal of Organic Chemistry; **vol.** 57; nb. 6; (1992); p. 1699 - 1702



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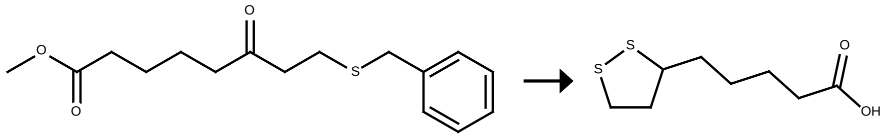
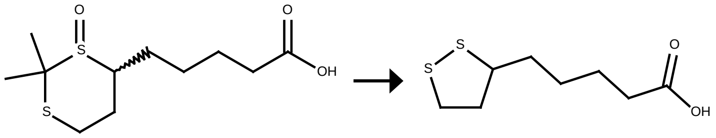
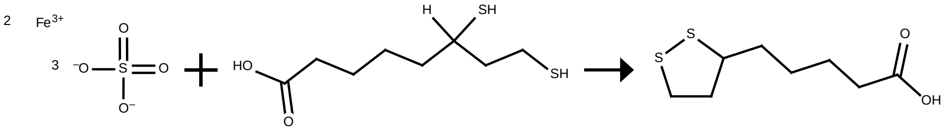
Yield	Conditions & References
	With cobalt polysulfide, hydrogen, sulfur, acetic acid, T= 175 °C , p= 58840.6 - 73550.8Torr , anschl. mit wss. NaOH und anschl. Behandeln der mit Eisen(III)-chlorid versetzten wss. Lsg. mit Sauerstoff **Bullock et al.**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 1975,1976



Yield	Conditions & References
	With cobalt polysulfide, hydrogen, sulfur, acetic acid, T= 175 °C , p= 58840.6 - 73550.8Torr , anschl. mit wss. NaOH und Behandeln der mit Eisen(III)-chlorid versetzten wss. Loesung mit Sauerstoff **Bullock et al.**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 1975,1976

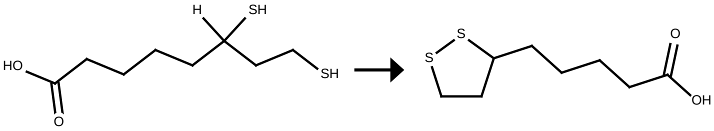


Yield	Conditions & References
69 %	**With** hydrogenchloride **in** benzene, Time= 7h, T= 50 °C **Chavan, Subhash P.; Kale, Ramesh R.; Pasupathy**; Synlett; nb. 7; (2005); p. 1129 - 1132; Art.No: D02905ST



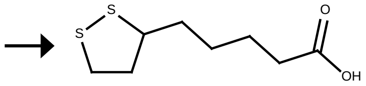
Yield	Conditions & References
	9 : Production of D,L-Thioctic Acid (IX) Example 9 Production of D,L-Thioctic Acid (IX) 8.0 grams (0.038 mole) of 6,8-dimercapto octanoic acid were added to 1.54 grams (0.038 mole) of sodium hydroxide in 90 ml of water and the solution formed adjusted to pH 9 with dilute aqueous sodium hydroxide. The solution was extracted twice, each time with 30 ml of methyl tertiary butyl ether, the aqueous solution separated off and the residual ether removed in a vacuum. The solution was diluted with 200 ml of water, 7 mg of iron (III) sulfate added and oxygen led in with stirring at room temperture. After 2.5 hours the reaction solution had reached a pH of 12.4, the supply of oxygen was ended and the precipitated iron salt filtered off. The clear yellow solution was acidified with 10percent hydrochloric acid at 5° C., to 10° C., further stirred for 1 hour at pH 1 and the precipitated crude product filtered off. The precipitate was washed with water, dried in a vacuum and recrystallized from ethyl acetate/hexane. After drying there were obtained 5.9 grams (75percent of theory) of 1,2-dithiolane-3-pentanoic acid as yellow crystals having a melting point of 61° C. to 62° C. ^{1} H-NMR 60 MHz ($CDCl_3$): δ1.3-2.30 (m, 8H); 2.15-2.80 (m, 2H); 3.18 (t, J=7Hz, 2H); 3.3-3.85 (m, 1H); 11.3 ppm (s, 1H). IR (KBr): δ3000-3250 (b, m) 2935 (s), 2865 (m), 2250-2800 (b, m), 1690 cm^{-1} (s). **With** sodium hydroxide **in** water

	Patent; **Degussa Aktiengesellschaft**; US4705867; (1987); (A) English



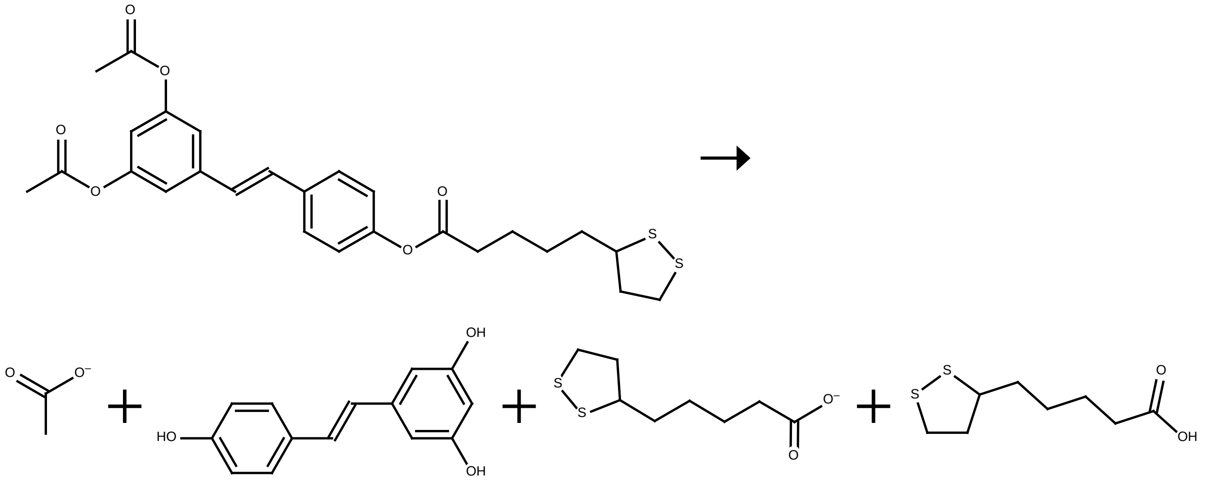
Yield	Conditions & References
	With water, iron(III) chloride, potassium carbonate, und Sauerstoff **Bullock et al.**; Journal of the American Chemical Society; **vol.** 76; (1954); p. 1828,1830
	With sodium hydroxide, water, iron(III) chloride, und Sauerstoff **Segre et al.**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 3503
	With flavopapain **in** dimethyl sulfoxide, T= 25 °C , ionic strength 0.1 (KCl), Tris buffer-HCl, EDTA (pH 7.3); oxidation with 7-acetyl-10-methylisoalloxasine (model flavin); relative rate enhancement, Rate constant **Fried, Herbert E.; Kaiser, E. T.**; Journal of the American Chemical Society; **vol.** 103; nb. 1; (1981); p. 182 - 184
	With semisynthetic "flavopapain" enzyme, T= 25 °C , with different catalysts and other additive; under anaerobic and aerobic conditions, Rate constant **Stewart, Kent D.; Radziejewski, Czestaw; Kaiser, E. T.**; Journal of the American Chemical Society; **vol.** 108; nb. 12; (1986); p. 3480 - 3483
	With bis(2-hydroxyethyl) disulfide **in** $d^{(4)}$-methanol, water-d2, T= 25 °C , phosphate buffer (0.5 mM, pH 7.0), Equilibrium constant **Houk,J.; Whitesides,G.M.**; Journal of the American Chemical Society; **vol.** 109; (1987); p. 6825

lipoic acid-polyethyleneglycol conjugate



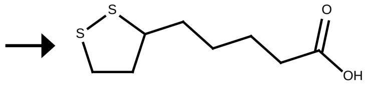
Yield	Conditions & References
	15 : Embodiment 15: hydrolysis of lipoic acid-polyethyleneglycol conjugate<i56> Stabilities in various temperatures, chemical and enzymatic hydrolysis conditions of lipoic acid-polyethyleneglycol conjugate of the present invention were tested.<i57> 0.5wtpercent of lipoic acid-polyethyleneglycol conjugate(embodiment 1~3) was dissolved in phosphate buffer(0.1M, pH 7.4) and reserved at 23°C and 37˚C respectively. And, lipoic acid-polyethyleneglycol conjugate(embodiment 1~3) was dissolved in phosphate buffer(0.1M, pH 7.4) containing porcine esterase and reserved at 37°C. Analytical reversed-phase HPLC was performed. The condition of HPLC was same in Embodiment 14.<158> A half-life period was determined using pseudo-first-order kinetics. As shown in Table 14, in 23˚C buffer solution the half-life period of lipoic acid-polyethyleneglycol conjugate(embodiment 1~3) was about 3,000hr, but that in 37°C was 800hr. And, the half-life period of lipoic acid- polyethyleneglycol conjugate in buffer containing porcine esterase was as short as 5hr. In the results, we know that hydrolyzable property of the ester bond of the lipoic acid-polyethyleneglycol conjugate. The conjugate of the present invention is characterized to be a soluble precursor of lipoic acid. **With** water, T= 23 - 37 °C , pH= 7.4, Aqueous phosphate buffer, Conversion of starting material **Patent**; **HAN-BUL COSMETICS CO., LTD.**; WO2007/105854; (2007); (A1) English
	15 : Embodiment 15: hydrolysis of lipoic acid-polyethyleneglycol conjugate<i56> Stabilities in various temperatures, chemical and enzymatic hydrolysis conditions of lipoic acid-polyethyleneglycol conjugate of the present invention were tested.<i57>

	0.5wtpercent of lipoic acid-polyethyleneglycol conjugate(embodiment 1~3) was dissolved in phosphate buffer(0.1M, pH 7.4) and reserved at 23°C and 37°C respectively. And, lipoic acid-polyethyleneglycol conjugate(embodiment 1~3) was dissolved in phosphate buffer(0.1M, pH 7.4) containing porcine esterase and reserved at 37°C. Analytical reversed-phase HPLC was performed. The condition of HPLC was same in Embodiment 14.<158> A half-life period was determined using pseudo-first-order kinetics. As shown in Table 14, in 23°C buffer solution the half-life period of lipoic acid-polyethyleneglycol conjugate(embodiment 1~3) was about 3,000hr, but that in 37°C was 800hr. And, the half-life period of lipoic acid- polyethyleneglycol conjugate in buffer containing porcine esterase was as short as 5hr. In the results, we know that hydrolyzable property of the ester bond of the lipoic acid-polyethyleneglycol conjugate. The conjugate of the present invention is characterized to be a soluble precursor of lipoic acid. **With** water, esterase, T= 37 °C , pH= 7.4, Aqueous phosphate buffer, Enzymatic reaction, Conversion of starting material **Patent**; **HAN-BUL COSMETICS CO., LTD.**; WO2007/105854; (2007); (A1) English



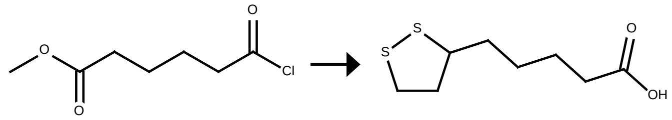
Yield	Conditions & References
	9.a :EXAMPLE 9Bio-Hydrolysisa.; Bio-Hydrolysis with the Cutaneous Enzymes Obtained by Tape StrippingThe precursors are solubilised in acetonitrile at a concentration of 1 g/l. For the bio-hydrolysis trials 50 µl of substrate and 50 µl of acetonitrile in 900 µl of enzymatic extract in the buffer at a chosen pH are added. The reaction mixtures are incubated at 35° C. without stirring and shielded from the light. The evolution of the bio-hydrolysis is determined by HPLC (high-performance liquid chromatography) with reverse phase polarity. The controls are effected in the same solutions without enzymatic extracts of skin, in order to determine the chemical stability of the products. b) Bio-Hydrolysis with Animal Cholesterol EsteraseThe enzyme used is the cholesterol esterase of bovine pancreas, of E.C. class 3.1.1.13 (SIGMA C-3766). The precursors are prepared as described in Example 9a. The results are presented in Table 1 below. **With** water, Stratum corneum; enzyme extract of **in** acetonitrile, Time= 48h, T= 35 °C , Enzymatic reaction, Darkness, Product distribution / selectivity **Patent**; **CHIMIE, Rhodia Chime; CHANEL PARFUMS BEAUTE**; US2009/215881; (2009); (A1) English

(+-)-6,8-bis-benzylsulfanyl-octanoic acid



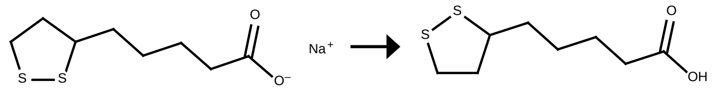
Yield	Conditions & References
	With sodium, toluene, und fluessiger NH_3, anschl. mit wss. HCl und wenig Eisen(III)-chlorid, anschl. mit Sauerstoff **Reed; Niu**; Journal of the American Chemical Society; **vol.** 77; (1955); p. 416,418
	With diethyl ether, sodium, und fluessigem NH_3, anschl. mit wss. HCl und Behandeln der mit Eisen(III)-chlorid versetzten wss. Loesung mit Sauerstoff

	Thomas; Reed; ; (1958); p. 1929 **Thomas; Reed**; Journal of the American Chemical Society; **vol.** 77; (1955); p. 5446



Yield	Conditions & References
	Reaction Steps: 3 1: aluminium chloride; 1,2-dichloro-ethane / anschliessendes Behandeln mit Wasser und Aethylacetat und Erwaermen der nicht-waessrigen Phase mit Natriumacetat 3: acetic acid; hydrogen; cobalt polysulfide; sulfur / 175 °C / 58840.6 - 73550.8 Torr / anschl. mit wss. NaOH und anschl. Behandeln der mit Eisen(III)-chlorid versetzten wss. Lsg. mit Sauerstoff **With** aluminium trichloride, cobalt polysulfide, hydrogen, sulfur, acetic acid, 1,2-dichloro-ethane **Bullock et al.**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 1975,1976
	Reaction Steps: 2 1: aluminium chloride; 1,2-dichloro-ethane / anschliessendes Behandeln mit Wasser und Aethylacetat und Erwaermen der nicht-waessrigen Phase mit Natriumacetat 2: acetic acid; hydrogen; cobalt polysulfide; sulfur / 175 °C / 58840.6 - 73550.8 Torr / anschl. mit wss. NaOH und anschl. Behandeln der mit Eisen(III)-chlorid versetzten wss. Loesung mit Sauerstoff **With** aluminium trichloride, cobalt polysulfide, hydrogen, sulfur, acetic acid, 1,2-dichloro-ethane **Bullock et al.**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 1975,1976
	Reaction Steps: 3 1: aluminium chloride; 1,2-dichloro-ethane / anschliessendes Behandeln mit Wasser und Aethylacetat und Erwaermen der nicht-waessrigen Phase mit Natriumacetat 2: NaH 3: acetic acid; hydrogen; cobalt polysulfide; sulfur / 175 °C / 58840.6 - 73550.8 Torr / anschl. mit wss. NaOH und Behandeln der mit Eisen(III)-chlorid versetzten wss. Loesung mit Sauerstoff **With** aluminium trichloride, cobalt polysulfide, hydrogen, sodium hydride, sulfur, acetic acid, 1,2-dichloro-ethane **Bullock et al.**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 1975,1976
	Reaction Steps: 3 1: $AlCl_3$; 1,2-dichloro-ethane / anschliessendes Behandeln mit H_2O und Aethylacetat und mit Natriumacetat 3: acetic acid; hydrogen; cobalt polysulfide; sulfur / 175 °C / 58840.6 - 73550.8 Torr / anschl. mit wss. NaOH und anschl. Behandeln der mit Eisen(III)-chlorid versetzten wss. Lsg. mit Sauerstoff **With** aluminium trichloride, cobalt polysulfide, hydrogen, sulfur, acetic acid, 1,2-dichloro-ethane **Bullock et al.**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 1975,1976
	Reaction Steps: 2 1: $AlCl_3$; 1,2-dichloro-ethane / anschliessendes Behandeln mit H_2O und Aethylacetat und mit Natriumacetat 2: acetic acid; hydrogen; cobalt polysulfide; sulfur / 175 °C / 58840.6 - 73550.8 Torr / anschl. mit wss. NaOH und anschl. Behandeln der mit Eisen(III)-chlorid versetzten wss. Loesung mit Sauerstoff **With** aluminium trichloride, cobalt polysulfide, hydrogen, sulfur, acetic acid, 1,2-dichloro-ethane **Bullock et al.**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 1975,1976
	Reaction Steps: 3 1: $AlCl_3$; 1,2-dichloro-ethane / anschliessendes Behandeln mit H_2O und Aethylacetat und mit Natriumacetat

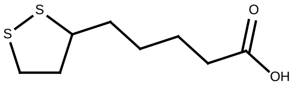
	2: NaH 3: acetic acid; hydrogen; cobalt polysulfide; sulfur / 175 °C / 58840.6 - 73550.8 Torr / anschl. mit wss. NaOH und Behandeln der mit Eisen(III)-chlorid versetzten wss. Loesung mit Sauerstoff **With** aluminium trichloride, cobalt polysulfide, hydrogen, sodium hydride, sulfur, acetic acid, 1,2-dichloro-ethane **Bullock et al.**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 1975,1976



Yield	Conditions & References
	1; 2 :30 g (0.145 moles) of thioctic acid are suspended in 1000 ml of water at 20^0C.19.4 g of 30percent aqueous sodium hydroxide (0.145 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 0-3^0C.5percent aqueous hydrochloric acid is added drop-wise over a 30 minute period until pH1 is achieved, to obtain precipitation of the product. EPO <DP n="5"/>The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35°C for 18 hours to provide 27.9 g of solvent-free thioctic acid. Test of solubility in chloroform (1 g in 10 ml of chloroform): cloudy solution with traces of polymer (undissolved lumps of various dimensions).EXAMPLE 2 (acidifying to pH 5.4 with HCI)30 g (0.145 moles) of thioctic acid are suspended in 1000 ml of water at 20°C. 20 g of 30percent aqueous sodium hydroxide (0.15 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 5°C.5percent aqueous hydrochloric acid is added drop-wise over a 30 minute period until pH5.4 is achieved, to obtain precipitation of the product.The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35°C for 18 hours to provide 24.7 g of solvent-free thioctic acid.Test of solubility in chloroform (1 g in 10 ml of chloroform): opalescent solution with traces of polymer (undissolved lumps of various dimensions). **With** hydrogenchloride **in** water, Time= 0.5h, pH= 1 - 5.4, Product distribution / selectivity **Patent**; **LABORATORIO CHIMICO INTERNAZIONALE S.P.A.**; WO2006/100229; (2006); (A1) English
	5; 6 :15 g (0.073 moles) of thioctic acid are suspended in 500 ml of water at 20°C. 10 g of 30percent aqueous sodium hydroxide (0.073 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 5°C.5percent aqueous methanesulfonic acid is added drop-wise over a 90 minute period until pH 2 is achieved, to obtain precipitation of the product. The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35°C for 18 hours to provide 13.7 g of solvent-free thioctic acid.Test of solubility in chloroform (1 g in 10 ml of chloroform): cloudy solution with traces of polymer (in lumps).EXAMPLE 6 (acidifying to pH 5.6 with 5percent methanesulfonic acid)15 g (0.073 moles) of thioctic acid are suspended in 500 ml of water at 20°C. 10 g of 30percent aqueous sodium hydroxide (0.073 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 5°C.5percent aqueous methanesulfonic acid is added drop-wise over a 90 minute period until pH 5.6 is achieved, to obtain precipitation of the product. EPO <DP n="7"/>The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35°C for 18 hours to provide 13.6 g of solvent-free thioctic acid. Test of solubility in chloroform (1 g in 10 ml of chloroform): slightly opalescent solution without evidence of polymer. **With** methanesulfonic acid **in** water, Time= 1.5h, pH= 2 - 5.6, Product distribution / selectivity **Patent**; **LABORATORIO CHIMICO INTERNAZIONALE S.P.A.**; WO2006/100229; (2006); (A1) English
	3; 4 :15 g (0.073 moles) of thioctic acid are suspended in 500 ml of water at 20^0C. 10 g of 30percent aqueous sodium hydroxide (0.073 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 5°C. 5percent aqueous sulfuric acid is added drop-wise over a 90 minute period until pH 2 is achieved, to obtain precipitation of the product.The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35°C for 18 hours to provide 13.5 g of solvent-free thioctic acid.Test of solubility in chloroform (1 g in 10 ml of chloroform): opalescent solution with traces of polymer (undissolved lumps of various dimensions). EPO <DP n="6"/>EXAMPLE 4 (acidifying to pH 5.6 with 5percent H_2SO_4)15 g (0.073 moles) of thioctic acid are suspended in 500 ml of water at 20°C. 1O g of 30percent aqueous sodium hydroxide (0.073 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 5°C.5percent aqueous sulfuric acid is added drop-wise over a 90 minute period until pH 5.6 is achieved, to obtain precipitation of the product.The solid is

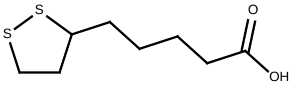
	filtered off and washed with water until the wash water is at neutral pH. The wet product is dried at 30-35°C for 18 hours to provide 13.8 g of solvent-free thioctic acid.Test of solubility in chloroform (1 g in 10 ml of chloroform): clear solution. **With** sulfuric acid **in** water, Time= 1.5h, pH= 2 - 5.6, Product distribution / selectivity **Patent**; **LABORATORIO CHIMICO INTERNAZIONALE S.P.A.**; WO2006/100229; (2006); (A1) English
	7; 8 :30 g (0.15 moles) of thioctic acid are suspended in 1000 ml of water at 20°C. 20 g of 30percent aqueous sodium hydroxide (0.15 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 5°C.8percent aqueous phosphoric acid is added drop-wise over a 90 minute period until pH2 is achieved, to obtain precipitation of the product.The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35^{0}C for 18 hours to provide 27.6 g of solvent-free thioctic acid.Test of solubility in chloroform (1 g in 10 ml of chloroform): opalescent solution with traces of polymer. EXAMPLE 8 (acidifying to pH 5.5 with 8percent H_3PO_4)90 g (0.437 moles) of thioctic acid are suspended in 2900 ml of water at 10°C. 62 g of 30percent aqueous sodium hydroxide (0.46 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 5°C. 8percent aqueous phosphoric acid is added drop-wise over a 90 minute period until pH5.5 is achieved, to obtain precipitation of the product.The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35^{0}C for 18 hours to provide 81 g of solvent-free thioctic acid.Test of solubility in chloroform (1 g in 10 ml of chloroform): clear solution.Melting point: 61 -62°C EPO <DP n="8"/>K.F. = 0.07percentPurity (HPLC): 99.9percentSolvents (cyclohexane, ethyl acetate, toluene): <5 ppm. **With** phosphoric acid **in** water, Time= 1.5h, pH= 2 - 5.5, Product distribution / selectivity **Patent**; **LABORATORIO CHIMICO INTERNAZIONALE S.P.A.**; WO2006/100229; (2006); (A1) English

(+-)-6,8-dibromo-octanoic acid ethyl ester →



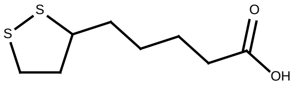
Yield	Conditions & References
	With ethanol, potassium thioacetate, anschl. mit KOH und Behandeln einer Lsg. des nach Ansaeuern mit wss. HCl isolierten Rktprod. in $CHCl_3$ mit einer wss. Lsg. von Jod und KI **Reed; Niu**; Journal of the American Chemical Society; **vol.** 77; (1955); p. 416,418

(+-)-6,8-dichloro-octanoic acid methyl ester →

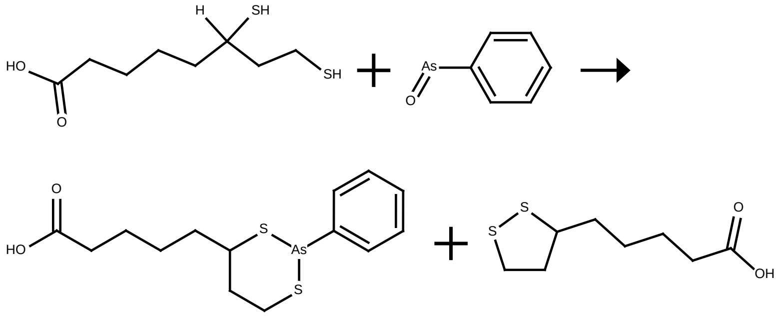


Yield	Conditions & References
	With ethanol, sodium disulfide **Acker; Wayne**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 6483,6485

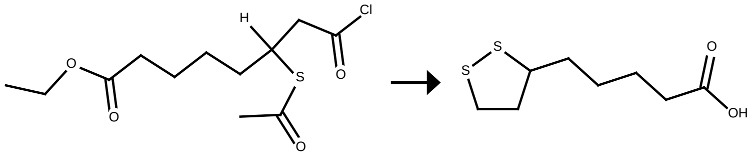
sodium-salt of/the/ (+-)-6,8-dichloro-octanoic acid →



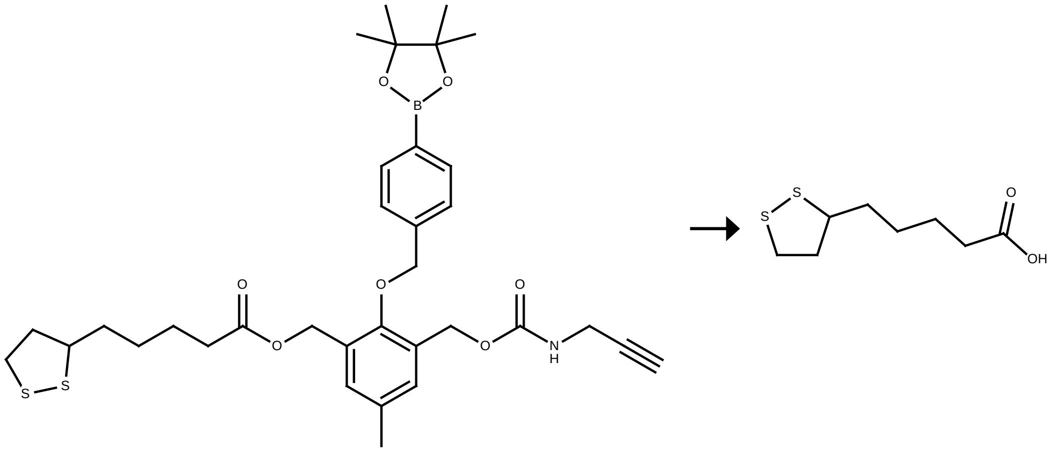
Yield	Conditions & References
	With ethanol, sodium disulfide **Acker; Wayne**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 6483,6485



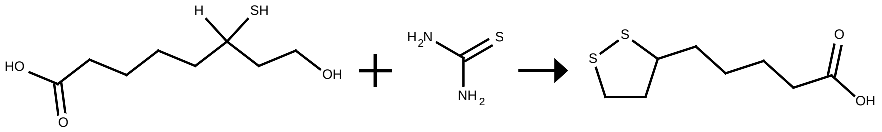
Yield	Conditions & References
9 %	**With** air **in** methanol, T= 20 °C **Ioannou, Panayiotis V.; Tsivgoulis, Gerasimos M.**; Monatshefte fur Chemie; **vol.** 145; nb. 6; (2014); p. 897 - 909



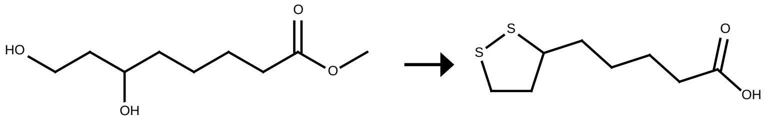
Yield	Conditions & References
	Reaction Steps: 2 1: sodium borate; dioxane / beim Erwaermen des Reaktionsprodukts mit wss.-methanol. Natronlauge und wenig Zink-Pulver 2: HBr; water / anschl. mit wss. NaOH und Behandeln einer Lsg. des nach Ansaeuern mit wss. HCl isolierten Rktprod. in $CHCl_3$ mit einer wss. Lsg. von Jod und KI **With** 1,4-dioxane, sodium borate, water, hydrogen bromide **Walton et al.**; Journal of the American Chemical Society; **vol.** 77; (1955); p. 5144,5146



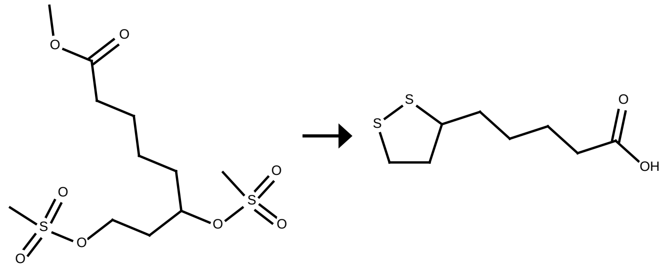
Yield	Conditions & References
	With dihydrogen peroxide **in** dimethylsulfoxide-d6, aq. phosphate buffer, Time= 70h, T= 37 °C , pH= 7.4 **Wu, Shaojue; Tan, Si Yu; Ang, Chung Yen; Luo, Zhong; Zhao, Yanli**; Chemical Communications; **vol.** 52; nb. 17; (2016); p. 3508 - 3511



Yield	Conditions & References
	With water, hydrogen bromide, anschl. mit wss. NaOH und Behandeln einer Lsg. des nach Ansaeuern mit wss. HCl isolierten Rktprod. in $CHCl_3$ mit einer wss. Lsg. von Jod und KI **Walton et al.**; Journal of the American Chemical Society; **vol.** 77; (1955); p. 5144,5146

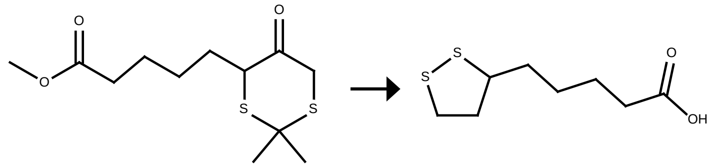


Yield	Conditions & References
	Reaction Steps: 3 1: Et_3N / CH_2Cl_2 / 0 °C 2: 257 mg / Na_2S*H_2O; sulfur / dimethylformamide / 24 h / 80 °C 3: 70 percent / aq. KOH / methanol / 24 h / 20 °C **With** sodium sulfide, potassium hydroxide, sulfur, triethylamine **in** methanol, dichloromethane, N,N-dimethyl-formamide **Chavan, Subhash P.; Shivsankar; Pasupathy**; Synthesis; nb. 8; (2005); p. 1297 - 1300; Art.No: Z20804SS
	Reaction Steps: 3 1: 80 percent / Et_3N / CH_2Cl_2 / 0 deg C, 0.5 h; RT, 3 h 2: 70 percent / Na_2S*H_2O, S / dimethylformamide / 24 h / 90 °C 3: 0.120 g / KOH / methanol / 24 h / Ambient temperature **With** sodium sulfide, potassium hydroxide, triethylamine **in** methanol, dichloromethane, N,N-dimethyl-formamide **Rao, A. V. Rama; Mysorekar, Sudha V.; Yadav, J. S.**; Synthetic Communications; **vol.** 17; nb. 11; (1987); p. 1339 - 1348

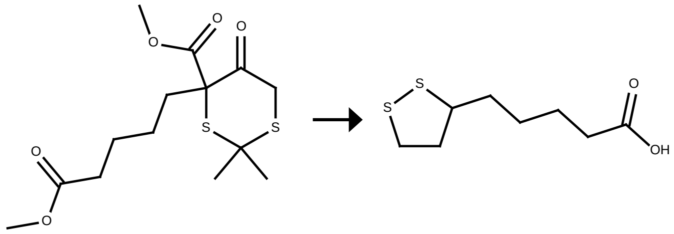


Yield	Conditions & References
	Reaction Steps: 2 1: 257 mg / Na_2S*H_2O; sulfur / dimethylformamide / 24 h / 80 °C 2: 70 percent / aq. KOH / methanol / 24 h / 20 °C **With** sodium sulfide, potassium hydroxide, sulfur **in** methanol, N,N-dimethyl-formamide **Chavan, Subhash P.; Shivsankar; Pasupathy**; Synthesis; nb. 8; (2005); p. 1297 - 1300; Art.No: Z20804SS
	Reaction Steps: 2 1: 70 percent / Na_2S*H_2O, S / dimethylformamide / 24 h / 90 °C 2: 0.120 g / KOH / methanol / 24 h / Ambient temperature

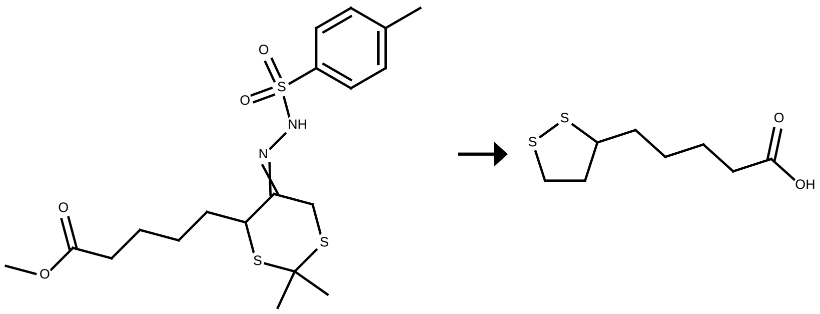
	With sodium sulfide, potassium hydroxide **in** methanol, N,N-dimethyl-formamide **Rao, A. V. Rama; Mysorekar, Sudha V.; Yadav, J. S.**; Synthetic Communications; **vol.** 17; nb. 11; (1987); p. 1339 - 1348



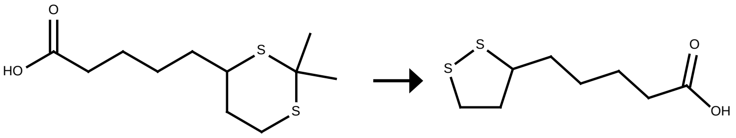
Yield	Conditions & References
	Reaction Steps: 4 1.1: 87 percent / methanol / 20 °C 2.1: NaOH / propan-2-ol / Heating 2.2: 73 percent / Et$_3$SiH / trifluoroacetic acid / 2 h / 0 - 20 °C 3.1: 68 percent / aq. NaIO$_4$ / methanol / 2 h / 0 °C 4.1: 69 percent / aq. HCl / benzene / 7 h / 50 °C **With** hydrogenchloride, sodium hydroxide, sodium periodate **in** methanol, isopropyl alcohol, benzene **Chavan, Subhash P.; Kale, Ramesh R.; Pasupathy**; Synlett; nb. 7; (2005); p. 1129 - 1132; Art.No: D02905ST



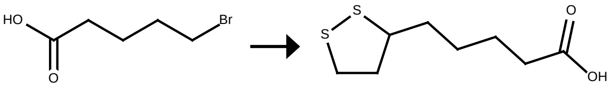
Yield	Conditions & References
	Reaction Steps: 5 1.1: 81 percent / aq. NaCl / dimethylsulfoxide / 135 - 140 °C 2.1: 87 percent / methanol / 20 °C 3.1: NaOH / propan-2-ol / Heating 3.2: 73 percent / Et$_3$SiH / trifluoroacetic acid / 2 h / 0 - 20 °C 4.1: 68 percent / aq. NaIO$_4$ / methanol / 2 h / 0 °C 5.1: 69 percent / aq. HCl / benzene / 7 h / 50 °C **With** hydrogenchloride, sodium hydroxide, sodium periodate, sodium chloride **in** methanol, dimethyl sulfoxide, isopropyl alcohol, benzene **Chavan, Subhash P.; Kale, Ramesh R.; Pasupathy**; Synlett; nb. 7; (2005); p. 1129 - 1132; Art.No: D02905ST



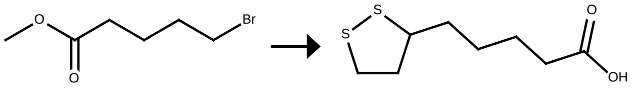
Yield	Conditions & References
	Reaction Steps: 3 1.1: NaOH / propan-2-ol / Heating 1.2: 73 percent / Et$_3$SiH / trifluoroacetic acid / 2 h / 0 - 20 °C 2.1: 68 percent / aq. NaIO$_4$ / methanol / 2 h / 0 °C 3.1: 69 percent / aq. HCl / benzene / 7 h / 50 °C **With** hydrogenchloride, sodium hydroxide, sodium periodate **in** methanol, isopropyl alcohol, benzene **Chavan, Subhash P.; Kale, Ramesh R.; Pasupathy**; Synlett; nb. 7; (2005); p. 1129 - 1132; Art.No: D02905ST



Yield	Conditions & References
	Reaction Steps: 2 1: 68 percent / aq. NaIO$_4$ / methanol / 2 h / 0 °C 2: 69 percent / aq. HCl / benzene / 7 h / 50 °C **With** hydrogenchloride, sodium periodate **in** methanol, benzene **Chavan, Subhash P.; Kale, Ramesh R.; Pasupathy**; Synlett; nb. 7; (2005); p. 1129 - 1132; Art.No: D02905ST

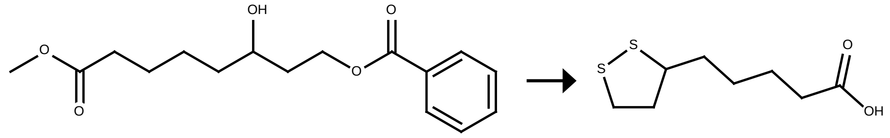


Yield	Conditions & References
	Reaction Steps: 2 1: 38 percent / LDA-TMEDA / tetrahydrofuran / 5 h / -78 °C 2: 69 percent / aq. HCl / benzene / 7 h / 50 °C **With** hydrogenchloride, N,N,N,N,-tetramethylethylenediamine, lithium diisopropyl amide **in** tetrahydrofuran, benzene **Chavan, Subhash P.; Kale, Ramesh R.; Pasupathy**; Synlett; nb. 7; (2005); p. 1129 - 1132; Art.No: D02905ST

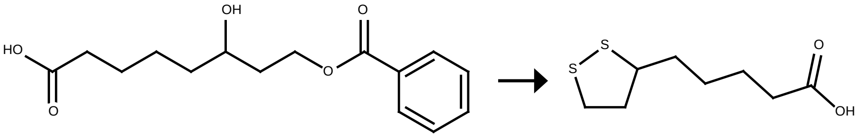


Yield	Conditions & References
	Reaction Steps: 6

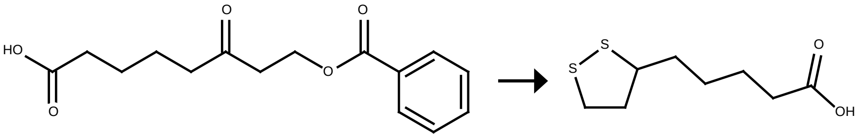
	1.1: 70 percent / K_2CO_3; Bu_4NHSO_4 / tetrahydrofuran / 20 °C 2.1: 81 percent / aq. NaCl / dimethylsulfoxide / 135 - 140 °C 3.1: 87 percent / methanol / 20 °C 4.1: NaOH / propan-2-ol / Heating 4.2: 73 percent / Et_3SiH / trifluoroacetic acid / 2 h / 0 - 20 °C 5.1: 68 percent / aq. $NaIO_4$ / methanol / 2 h / 0 °C 6.1: 69 percent / aq. HCl / benzene / 7 h / 50 °C **With** hydrogenchloride, sodium hydroxide, sodium periodate, tetra(n-butyl)ammonium hydrogensulfate, potassium carbonate, sodium chloride **in** tetrahydrofuran, methanol, dimethyl sulfoxide, isopropyl alcohol, benzene **Chavan, Subhash P.; Kale, Ramesh R.; Pasupathy**; Synlett; nb. 7; (2005); p. 1129 - 1132; Art.No: D02905ST



Yield	Conditions & References
	Reaction Steps: 4 1: 340 mg / NaOMe / methanol 2: Et_3N / CH_2Cl_2 / 0 °C 3: 257 mg / Na_2S*H_2O; sulfur / dimethylformamide / 24 h / 80 °C 4: 70 percent / aq. KOH / methanol / 24 h / 20 °C **With** sodium sulfide, potassium hydroxide, sodium methylate, sulfur, triethylamine **in** methanol, dichloromethane, N,N-dimethyl-formamide **Chavan, Subhash P.; Shivsankar; Pasupathy**; Synthesis; nb. 8; (2005); p. 1297 - 1300; Art.No: Z20804SS

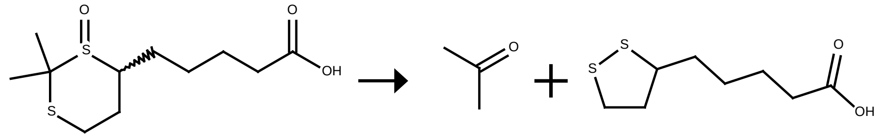


Yield	Conditions & References
	Reaction Steps: 5 1: diethyl ether 2: 340 mg / NaOMe / methanol 3: Et_3N / CH_2Cl_2 / 0 °C 4: 257 mg / Na_2S*H_2O; sulfur / dimethylformamide / 24 h / 80 °C 5: 70 percent / aq. KOH / methanol / 24 h / 20 °C **With** sodium sulfide, potassium hydroxide, sodium methylate, sulfur, triethylamine **in** methanol, diethyl ether, dichloromethane, N,N-dimethyl-formamide **Chavan, Subhash P.; Shivsankar; Pasupathy**; Synthesis; nb. 8; (2005); p. 1297 - 1300; Art.No: Z20804SS

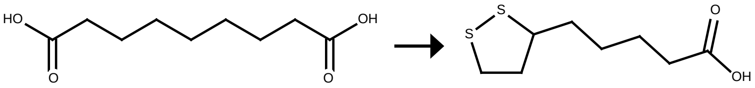


Yield	Conditions & References
	Reaction Steps: 6

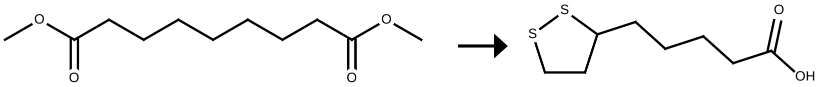
	1: 90 percent / $NaBH_4$ / methanol / 0 °C 2: diethyl ether 3: 340 mg / NaOMe / methanol 4: Et_3N / CH_2Cl_2 / 0 °C 5: 257 mg / Na_2S*H_2O; sulfur / dimethylformamide / 24 h / 80 °C 6: 70 percent / aq. KOH / methanol / 24 h / 20 °C **With** sodium sulfide, potassium hydroxide, sodium tetrahydroborate, sodium methylate, sulfur, triethylamine **in** methanol, diethyl ether, dichloromethane, N,N-dimethyl-formamide **Chavan, Subhash P.; Shivsankar; Pasupathy**; Synthesis; nb. 8; (2005); p. 1297 - 1300; Art.No: Z20804SS



Yield	Conditions & References
	With hydrogenchloride **in** benzene, Yield given **Menon; Kumar; Ravindranathan**; Tetrahedron Letters; **vol.** 28; nb. 44; (1987); p. 5313 - 5314

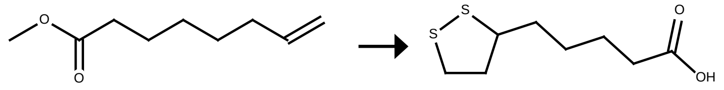


Yield	Conditions & References
	Reaction Steps: 8 1: 70 percent / H_2SO_4 conc. / 10 h / Heating 2: 84 percent / Ba(OH)2*8H_2O / methanol / Ambient temperature 3: 80 percent / Pb(OAc)4, Cu(OAc)2 / pyridine; benzene / 2 h / Heating 4: 1.) SeO_2, TBHP, 2.) Me_2S / 1.) CH_2Cl_2, 25 deg C, 30 h, 2.) AcOH, 4h 5: 1.) diborane, 2.) NaOAc, 30percent H_2O_2 / 1.) THF, 25 deg C, 2 h, 2.) THF-H_2O, 25 deg C, 2 h 6: 80 percent / Et_3N / CH_2Cl_2 / 0 deg C, 0.5 h; RT, 3 h 7: 70 percent / Na_2S*H_2O, S / dimethylformamide / 24 h / 90 °C 8: 0.120 g / KOH / methanol / 24 h / Ambient temperature **With** lead(IV) acetate, tert.-butylhydroperoxide, sodium sulfide, barium dihydroxide, potassium hydroxide, selenium(IV) oxide, copper diacetate, dimethylsulfide, sulfuric acid, dihydrogen peroxide, sodium acetate, triethylamine, diborane **in** pyridine, methanol, dichloromethane, N,N-dimethyl-formamide, benzene **Rao, A. V. Rama; Mysorekar, Sudha V.; Yadav, J. S.**; Synthetic Communications; **vol.** 17; nb. 11; (1987); p. 1339 - 1348

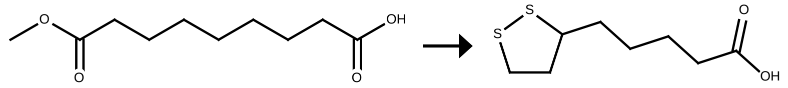


Yield	Conditions & References
	Reaction Steps: 7 1: 84 percent / Ba(OH)2*8H_2O / methanol / Ambient temperature 2: 80 percent / Pb(OAc)4, Cu(OAc)2 / pyridine; benzene / 2 h / Heating 3: 1.) SeO_2, TBHP, 2.) Me_2S / 1.) CH_2Cl_2, 25 deg C, 30 h, 2.) AcOH, 4h 4: 1.) diborane, 2.) NaOAc, 30percent H_2O_2 / 1.) THF, 25 deg C, 2 h, 2.) THF-H_2O, 25 deg C, 2 h 5: 80 percent / Et_3N / CH_2Cl_2 / 0 deg C, 0.5 h; RT, 3 h 6: 70 percent / Na_2S*H_2O, S / dimethylformamide / 24 h / 90 °C

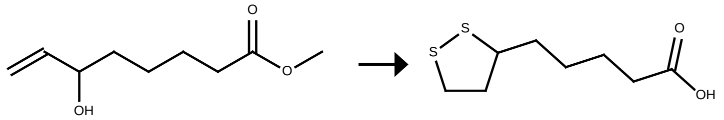
	7: 0.120 g / KOH / methanol / 24 h / Ambient temperature **With** lead(IV) acetate, tert.-butylhydroperoxide, sodium sulfide, barium dihydroxide, potassium hydroxide, selenium(IV) oxide, copper diacetate, dimethylsulfide, dihydrogen peroxide, sodium acetate, triethylamine, diborane **in** pyridine, methanol, dichloromethane, N,N-dimethyl-formamide, benzene **Rao, A. V. Rama; Mysorekar, Sudha V.; Yadav, J. S.**; Synthetic Communications; **vol.** 17; nb. 11; (1987); p. 1339 - 1348



Yield	Conditions & References
	Reaction Steps: 5 1: 1.) SeO_2, TBHP, 2.) Me_2S / 1.) CH_2Cl_2, 25 deg C, 30 h, 2.) AcOH, 4h 2: 1.) diborane, 2.) NaOAc, 30percent H_2O_2 / 1.) THF, 25 deg C, 2 h, 2.) THF-H_2O, 25 deg C, 2 h 3: 80 percent / Et_3N / CH_2Cl_2 / 0 deg C, 0.5 h; RT, 3 h 4: 70 percent / Na_2S*H_2O, S / dimethylformamide / 24 h / 90 °C 5: 0.120 g / KOH / methanol / 24 h / Ambient temperature **With** tert.-butylhydroperoxide, sodium sulfide, potassium hydroxide, selenium(IV) oxide, dimethylsulfide, dihydrogen peroxide, sodium acetate, triethylamine, diborane **in** methanol, dichloromethane, N,N-dimethyl-formamide **Rao, A. V. Rama; Mysorekar, Sudha V.; Yadav, J. S.**; Synthetic Communications; **vol.** 17; nb. 11; (1987); p. 1339 - 1348

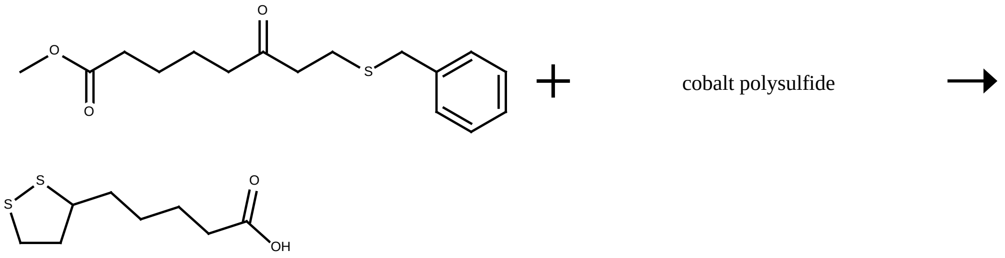


Yield	Conditions & References
	Reaction Steps: 6 1: 80 percent / Pb(OAc)4, Cu(OAc)2 / pyridine; benzene / 2 h / Heating 2: 1.) SeO_2, TBHP, 2.) Me_2S / 1.) CH_2Cl_2, 25 deg C, 30 h, 2.) AcOH, 4h 3: 1.) diborane, 2.) NaOAc, 30percent H_2O_2 / 1.) THF, 25 deg C, 2 h, 2.) THF-H_2O, 25 deg C, 2 h 4: 80 percent / Et_3N / CH_2Cl_2 / 0 deg C, 0.5 h; RT, 3 h 5: 70 percent / Na_2S*H_2O, S / dimethylformamide / 24 h / 90 °C 6: 0.120 g / KOH / methanol / 24 h / Ambient temperature **With** lead(IV) acetate, tert.-butylhydroperoxide, sodium sulfide, potassium hydroxide, selenium(IV) oxide, copper diacetate, dimethylsulfide, dihydrogen peroxide, sodium acetate, triethylamine, diborane **in** pyridine, methanol, dichloromethane, N,N-dimethyl-formamide, benzene **Rao, A. V. Rama; Mysorekar, Sudha V.; Yadav, J. S.**; Synthetic Communications; **vol.** 17; nb. 11; (1987); p. 1339 - 1348

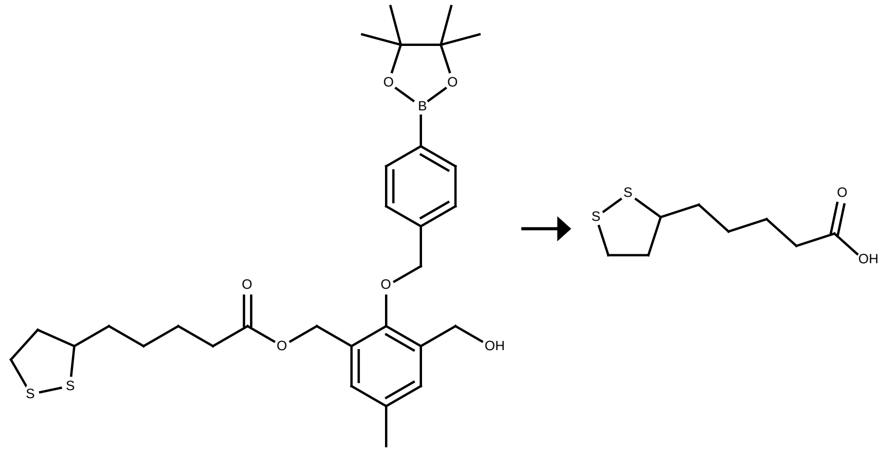


Yield	Conditions & References
	Reaction Steps: 4 1: 1.) diborane, 2.) NaOAc, 30percent H_2O_2 / 1.) THF, 25 deg C, 2 h, 2.) THF-H_2O, 25 deg C, 2 h 2: 80 percent / Et_3N / CH_2Cl_2 / 0 deg C, 0.5 h; RT, 3 h 3: 70 percent / Na_2S*H_2O, S / dimethylformamide / 24 h / 90 °C 4: 0.120 g / KOH / methanol / 24 h / Ambient temperature **With** sodium sulfide, potassium hydroxide, dihydrogen peroxide, sodium acetate, triethylamine, diborane **in** methanol, dichloromethane, N,N-dimethyl-formamide

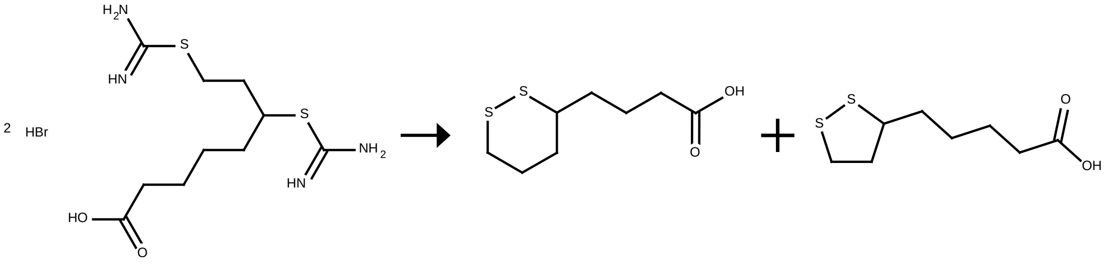
	Rao, A. V. Rama; Mysorekar, Sudha V.; Yadav, J. S.; Synthetic Communications; **vol.** 17; nb. 11; (1987); p. 1339 - 1348



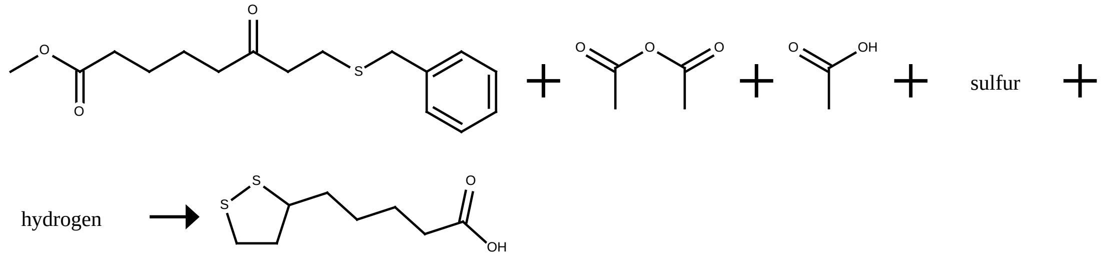
Yield	Conditions & References
	T= 190 °C , p= 63989.2Torr , anschliessend Erhitzen mit wss. KOH und Behandeln der mit $FeCl_3$ versetzten wss. Loesung des Reaktionsprodukts mit Sauerstoff **Bullock et al.**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 1975,1976



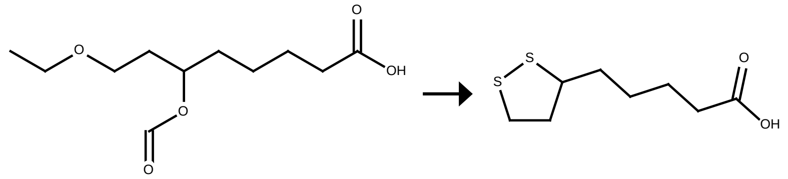
Yield	Conditions & References
	Reaction Steps: 3 1: dichloromethane / 20 °C 2: dichloromethane / 20 °C 3: dihydrogen peroxide / dimethylsulfoxide-d6; aq. phosphate buffer / 70 h / 37 °C / pH 7.4 **With** dihydrogen peroxide **in** dimethylsulfoxide-d6, aq. phosphate buffer, dichloromethane **Wu, Shaojue; Tan, Si Yu; Ang, Chung Yen; Luo, Zhong; Zhao, Yanli**; Chemical Communications; **vol.** 52; nb. 17; (2016); p. 3508 - 3511



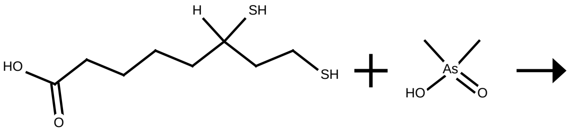
Yield	Conditions & References
	Stage 1: With potassium hydroxide, water, Time= 3h, Heating, Hydrolysis, Rearrangement **Stage 2: With** air, iron(III) chloride **in** water, Time= 2.5h, pH= 8.8 - 11.5, Oxidation, Cyclization, Title compound not separated from byproducts **Balkenhohl, Friedhelm; Paust, Joachim**; Zeitschrift fur Naturforschung - Section B Journal of Chemical Sciences; **vol.** 54; nb. 5; (1999); p. 649 - 654

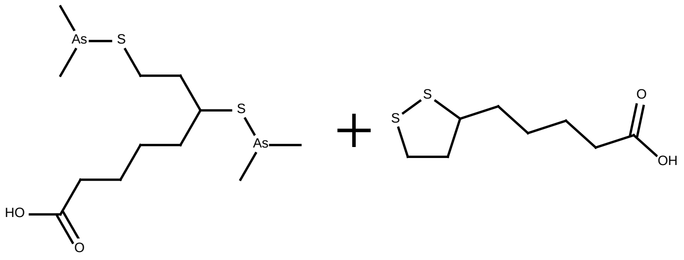


Yield	Conditions & References
	T= 190 °C , p= 63989.2Torr , anschliessend Erhitzen mit wss. KOH und Behandeln der mit $FeCl_3$ versetzten wss. Loesung des Reaktionsprodukts mit Sauerstoff **Bullock et al.**; Journal of the American Chemical Society; **vol.** 79; (1957); p. 1975,1976

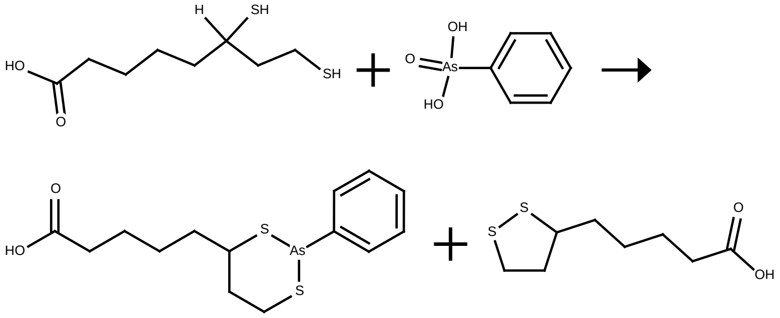


Yield	Conditions & References
	Reaction Steps: 2 1: HBr; H_2O / 20 h / 116 °C 2: KOH; H_2O / 3 h / Heating **With** potassium hydroxide, water, hydrogen bromide, 1: Substitution / 2: Hydrolysis **Balkenhohl, Friedhelm; Paust, Joachim**; Zeitschrift fur Naturforschung - Section B Journal of Chemical Sciences; **vol.** 54; nb. 5; (1999); p. 649 - 654
	Reaction Steps: 2 1.1: HBr; H_2O / 20 h / 116 °C 2.1: KOH; H_2O / 3 h / Heating 2.2: $FeCl_3$; air / H_2O / 2.5 h / pH 8.8 - 11.5 **With** potassium hydroxide, water, hydrogen bromide, 1.1: Substitution / 2.1: Hydrolysis / 2.2: Oxidation **Balkenhohl, Friedhelm; Paust, Joachim**; Zeitschrift fur Naturforschung - Section B Journal of Chemical Sciences; **vol.** 54; nb. 5; (1999); p. 649 - 654

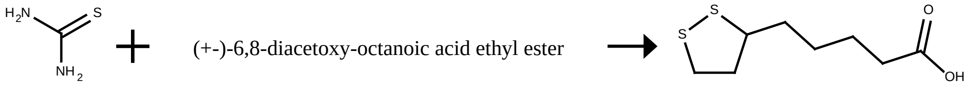




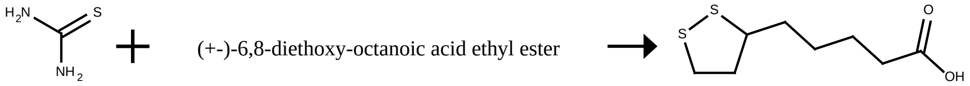
Yield	Conditions & References
	in tetrahydrofuran, Ambient temperature, Title compound not separated from byproducts **Von Doellen, Angelika; Strasdeit, Henry**; European Journal of Inorganic Chemistry; nb. 1; (1998); p. 61 - 66



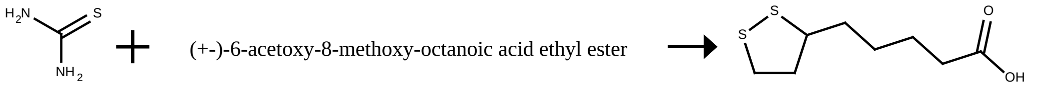
Yield	Conditions & References
	in tetrahydrofuran, Time= 24h, Ambient temperature **Von Doellen, Angelika; Strasdeit, Henry**; European Journal of Inorganic Chemistry; nb. 1; (1998); p. 61 - 66



Yield	Conditions & References
	With water, hydrogen iodide, anschl. mit wss. KOH und Behandeln einer mit K_2CO_3 neutralisierten und mit wenig Eisen(III)-chlorid versetzten wss. Loesung des Rktprod. mit Sauerstoff **Schmidt; Grafen**; Chemische Berichte; **vol.** 92; (1959); p. 1177,1183



Yield	Conditions & References
	With water, hydrogen iodide, anschl. mit wss. KOH und Behandeln einer mit K_2CO_3 neutralisierten und mit wenig Eisen(III)-chlorid versetzten wss. Loesung des Rktprod. mit Sauerstoff **Schmidt; Grafen**; Chemische Berichte; **vol.** 92; (1959); p. 1177,1183



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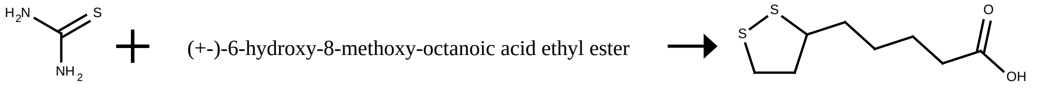
	With water, hydrogen iodide, anschl. mit wss. KOH und Behandeln einer mit K_2CO_3 neutralisierten und mit wenig Eisen(III)-chlorid versetzen wss. Loesung des Rktprod. mit Sauerstoff **Schmidt; Grafen**; Chemische Berichte; **vol.** 92; (1959); p. 1177,1183



Yield	Conditions & References
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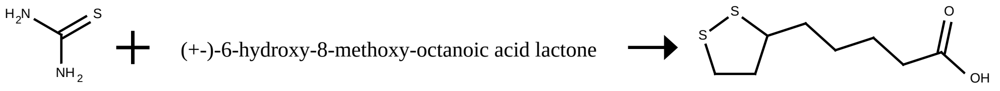
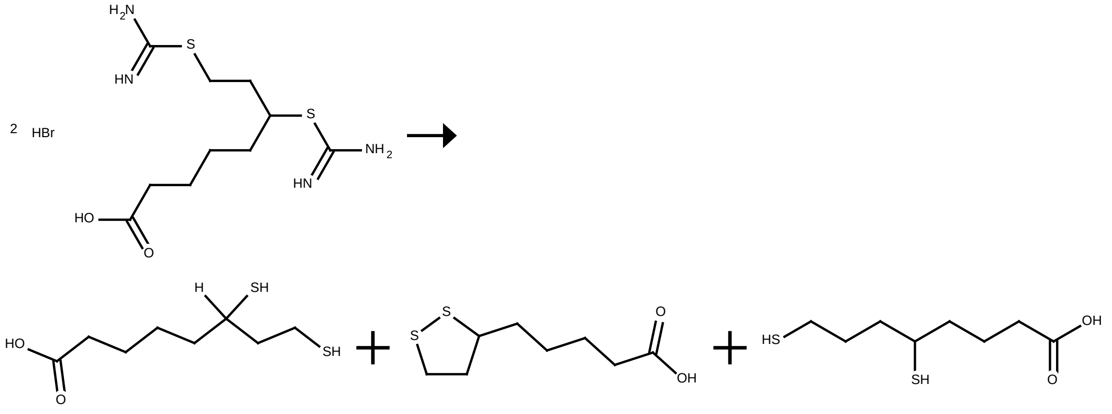
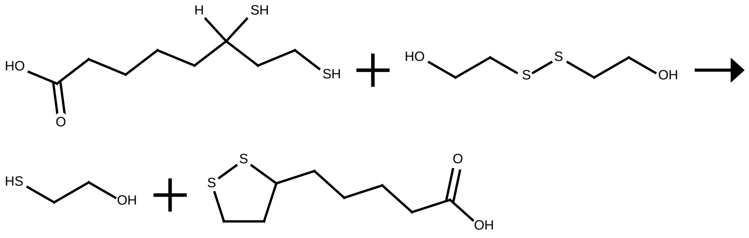


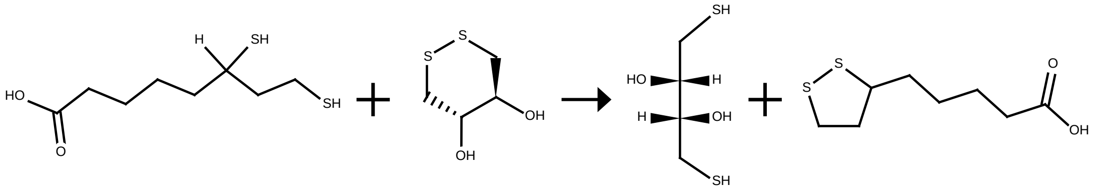
Yield	Conditions & References
	With water, hydrogen iodide, anschl. mit wss. KOH und Behandeln einer mit K_2CO_3 neutralisierten und mit wenig Eisen(III)-chlorid vesetzten wss. Lsg. des Rktprod. mit Sauerstoff **Schmidt; Grafen**; Chemische Berichte; **vol.** 92; (1959); p. 1177,1183



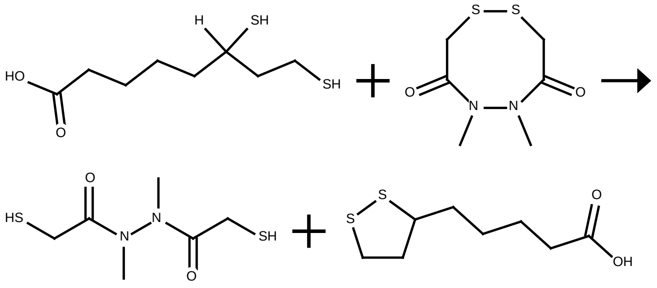
Yield	Conditions & References
	With potassium hydroxide, water, Time= 3h, Heating, Hydrolysis, Rearrangement; Cyclization, Title compound not separated from byproducts **Balkenhohl, Friedhelm; Paust, Joachim**; Zeitschrift fur Naturforschung - Section B Journal of Chemical Sciences; **vol.** 54; nb. 5; (1999); p. 649 - 654



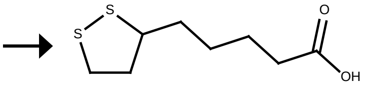
Yield	Conditions & References
	in water-d2, Time= 48h, phosphate buffer (pD 7.0); also in CD$_3$OD/D$_2$O, Equilibrium constant **Lees, Watson J.; Whitesides, George M.**; Journal of Organic Chemistry; **vol.** 58; nb. 3; (1993); p. 642 - 647



Yield	Conditions & References
	in water-d2, Time= 48h, phosphate buffer (pD 7.0); also in CD$_3$OD/D$_2$O, Equilibrium constant **Lees, Watson J.; Whitesides, George M.**; Journal of Organic Chemistry; **vol.** 58; nb. 3; (1993); p. 642 - 647



Yield	Conditions & References
	With buffer (pH 7.0, 2 mM EDTA, 0.1 M phosphate), Equilibrium constant **Singh, Rajeeva; Whitesides, George M.**; Journal of Organic Chemistry; **vol.** 56; nb. 7; (1991); p. 2332 - 2337



Yield	Conditions & References
	Lewis; Raphael; Journal of the Chemical Society; (1962); p. 4263 **Deguchi**; Yakugaku Zasshi; **vol.** 80; (1960); p. 933,936; ; nb. 24384; (1960) **Patent**; **Instituto Sieroterapico Italiano**; US2993056; (1957); ; **vol.** 56; nb. 331; (1962) **Patent**; **American Cyanamid Co.**; US2970161; (1953); ; nb. 18598; (1961)

Patent; **Res. Corp.**; US2975198; (1954); ; nb. 22137; (1961)
Tsuji et al.; Journal of Organic Chemistry; **vol.** 43; (1978); p. 3606
Patent; **Fujisawa Pharmaceutical Co., Ltd.**; JP4528; (1962); ; **vol.** 58; nb. 10205e; (1963)
Tursin et al.; J. Gen. Chem. USSR (Engl. Transl.); **vol.** 34; (1964); p. 3662,3711

Herstellung aus gleichen Teilen der unter a) und b) beschriebenen Enantiomeren

Walton et al.; Journal of the American Chemical Society; **vol.** 77; (1955); p. 5144,5146

Absorbable manganese, particularly manganese aspartate;
Soy isolate;
Vitamin K1 (a regulator of calcium metabolism);
Vitamin A;
Thioctic acid (alpha lipoic acid);

Patent; **Kosbab, John V.**; US2001/31744; (2001); (A1) English

2 : General Procedure for Coupling d- or l-Thioctic Acid and an OEG-Amine.
EXAMPLE 2
General Procedure for Coupling d- or l-Thioctic Acid and an OEG-Amine.
Racemic thioctic acid is resolved into its d- and l-isomers.

Patent; **Nelson, Deanna Jean**; US2003/44402; (2003); (A1) English
Patent; **Nelson, Deanna Jean**; US6756354; (2004); (B2) English

1; 2 : Example 1Repeat of Example 1 from the Degussa Patent; 30 g (0.145 moles) of thioctic acid are suspended in 1000 ml of water at 20° C. 19.4 g of 30percent aqueous sodium hydroxide (0.145 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 0-3° C.5percent aqueous hydrochloric acid is added drop-wise over a 30 minute period until pH 1 is achieved, to obtain precipitation of the product.The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35° C. for 18 hours to provide 27.9 g of solvent-free thioctic acid.Test of solubility in chloroform (1 g in 10 ml of chloroform): cloudy solution with traces of polymer (undissolved lumps of various dimensions).; Example 2Acidifying to pH 5.4 with HCl; 30 g (0.145 moles) of thioctic acid are suspended in 1000 ml of water at 20° C. 20 g of 30percent aqueous sodium hydroxide (0.15 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 5° C.5percent aqueous hydrochloric acid is added drop-wise over a 30 minute period until pH 5.4 is achieved, to obtain precipitation of the product.The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35° C. for 18 hours to provide 24.7 g of solvent-free thioctic acid.Test of solubility in chloroform (1 g in 10 ml of chloroform): opalescent solution with traces of polymer (undissolved lumps of various dimensions).

Stage 1: With sodium hydroxide **in** water, Time= 1h, T= 20 °C , pH= 9
Stage 2: With hydrogenchloride, water, Time= 0.5h, T= 0 - 5 °C , pH= 1 - 5.4, Purification / work up

Patent; **LABORATORIO CHIMICO INTERNAZIONALE S.p.A.**; US2008/227990; (2008); (A1) English

7; 8 : Example 7Acidifying to pH 2 with 8percent H_3PO_4 ; 30 g (0.15 moles) of thioctic acid are suspended in 1000 ml of water at 20° C. 20 g of 30percent aqueous sodium hydroxide (0.15 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 5° C.8percent aqueous phosphoric acid is added drop-wise over a 90 minute period until pH 2 is achieved, to obtain precipitation of the product.The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35° C. for 18 hours to provide 27.6 g of solvent-free thioctic acid.Test of solubility in chloroform (1 g in 10 ml of chloroform): opalescent solution with traces of polymer.; Example 8Acidifying to pH 5.5 with 8percent H_3PO_4 ; 90 g (0.437 moles) of thioctic acid are suspended in 2900 ml of water at 10° C. 62 g of 30percent aqueous sodium hydroxide (0.46 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 5° C.8percent aqueous phosphoric acid is added drop-wise over a 90 minute period until pH 5.5 is achieved, to obtain precipitation of the product.The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35° C. for 18 hours to

	provide 81 g of solvent-free thioctic acid.Test of solubility in chloroform (1 g in 10 ml of chloroform): clear solution.Melting point: 61-62° C.K.F.=0.07percentPurity (HPLC): 99.9percentSolvents (cyclohexane, ethyl acetate, toluene): <5 ppm. **Stage 1: With** sodium hydroxide **in** water, Time= 1h, T= 10 - 20 °C , pH= 9 **Stage 2: With** phosphoric acid, water, Time= 1.5h, T= 5 °C , pH= 2 - 5.5, Purification / work up **Patent**; **LABORATORIO CHIMICO INTERNAZIONALE S.p.A.**; US2008/227990; (2008); (A1) English
	5; 6 : Example 5Acidifying to pH 2 with 5percent Methanesulfonic Acid; 15 g (0.073 moles) of thioctic acid are suspended in 500 ml of water at 20° C. 10 g of 30percent aqueous sodium hydroxide (0.073 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 5° C.5percent aqueous methanesulfonic acid is added drop-wise over a 90 minute period until pH 2 is achieved, to obtain precipitation of the product.The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35° C. for 18 hours to provide 13.7 g of solvent-free thioctic acid.Test of solubility in chloroform (1 g in 10 ml of chloroform): cloudy solution with traces of polymer (in lumps).; Example 6Acidifying to pH 5.6 with 5percent Methanesulfonic Acid; 15 g (0.073 moles) of thioctic acid are suspended in 500 ml of water at 20° C. 10 g of 30percent aqueous sodium hydroxide (0.073 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 5° C.5percent aqueous methanesulfonic acid is added drop-wise over a 90 minute period until pH 5.6 is achieved, to obtain precipitation of the product.The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35° C. for 18 hours to provide 13.6 g of solvent-free thioctic acid.Test of solubility in chloroform (1 g in 10 ml of chloroform): slightly opalescent solution without evidence of polymer. **Stage 1: With** sodium hydroxide **in** water, Time= 1h, T= 20 °C , pH= 9 **Stage 2: With** methanesulfonic acid, water, Time= 1.5h, T= 5 °C , pH= 2 - 5.6, Purification / work up **Patent**; **LABORATORIO CHIMICO INTERNAZIONALE S.p.A.**; US2008/227990; (2008); (A1) English
	3; 4 : Example 3Acidifying to pH 2 with 5percent H_2SO_4 ; 15 g (0.073 moles) of thioctic acid are suspended in 500 ml of water at 20° C. 10 g of 30percent aqueous sodium hydroxide (0.073 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 5° C.5percent aqueous sulfuric acid is added drop-wise over a 90 minute period until pH 2 is achieved, to obtain precipitation of the product.The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35° C. for 18 hours to provide 13.5 g of solvent-free thioctic acid.Test of solubility in chloroform (1 g in 10 ml of chloroform): opalescent solution with traces of polymer (undissolved lumps of various dimensions).; Example 4Acidifying to pH 5.6 with 5percent H_2SO_4 ; 15 g (0.073 moles) of thioctic acid are suspended in 500 ml of water at 20° C. 10 g of 30percent aqueous sodium hydroxide (0.073 moles) are added drop-wise over a 1 hour period to obtain a solution at pH 9. The solution is filtered under vacuum through a paper filter and cooled to 5° C.5percent aqueous sulfuric acid is added drop-wise over a 90 minute period until pH 5.6 is achieved, to obtain precipitation of the product.The solid is filtered off and washed with water until the wash water is at neutral pH.The wet product is dried at 30-35° C. for 18 hours to provide 13.8 g of solvent-free thioctic acid.Test of solubility in chloroform (1 g in 10 ml of chloroform): clear solution. **Stage 1: With** sodium hydroxide **in** water, Time= 1h, T= 20 °C , pH= 9 **Stage 2: With** sulfuric acid, water, Time= 1.5h, T= 5 °C , pH= 2 - 5.6, Purification / work up **Patent**; **LABORATORIO CHIMICO INTERNAZIONALE S.p.A.**; US2008/227990; (2008); (A1) English