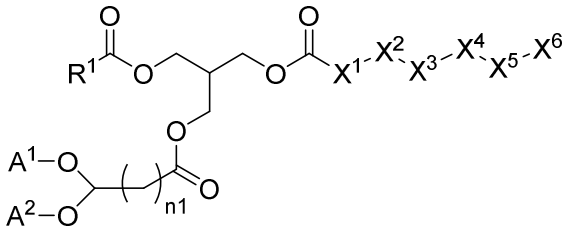
WHAT IS CLAIMED IS:

1. A compound of Formula (I):



(I)

wherein:

R^1 is C_9-C_{20} alkyl or C_9-C_{20} alkenyl with 1-3 units of unsaturation;

X^1 and X^2 are each independently absent or selected from –O–, –NR^2– and $-(CH)_a-$ (X^7), wherein each R^2 is independently hydrogen or C_1-C_6 alkyl;

each a is independently an integer between 1 and 6;

X^3 and X^4 are each independently absent or selected from the group consisting of: 4- to 8-membered heterocyclyl optionally substituted with 1 or 2 C_1-C_6 alkyl groups, 5- to 6-membered heteroaryl optionally substituted with 1 or 2 C_1-C_6 alkyl groups, 5- to 6-membered aryl optionally substituted with 1 or 2 C_1-C_6 alkyl groups, 4- to 7-membered cycloalkyl optionally substituted with 1 or 2 C_1-C_6 alkyl groups, –O– and –NR^3–, wherein each R^3 is a independently a hydrogen atom or C_1-C_6 alkyl and wherein X^1-X^2-X^3-X^4 does not contain any oxygen-oxygen, oxygen-nitrogen or nitrogen-nitrogen bonds;

X^5 is –$(CH_2)_b$–, wherein b is an integer between 0 and 6;

X^6 is hydrogen, C_1-C_6 alkyl, 5- to 6-membered heteroaryl optionally substituted with 1 or 2 C_1-C_6 alkyl groups, or –NR^4R^5, wherein R^4 and R^5 are each independently hydrogen or C_1-C_6 alkyl; or alternatively R^4 and R^5 join together with the nitrogen to which they are bound to form a 4- to 7-membered heterocyclyl optionally substituted with 1 or 2 C_1-C_6 alkyl groups, wherein the heterocyclyl optionally includes an additional heteroatom selected from oxygen, sulfur, and nitrogen;

each X^7 is independently hydrogen, hydroxyl or –NR^6R^7, wherein R^6 and R^7 are each independently hydrogen or C_1-C_6 alkyl; or alternatively R^6 and R^7 join together with the nitrogen to which they are bound to form a 4- to 7-membered

heterocyclyl optionally substituted with 1 or 2 C_1-C_6 alkyl groups, wherein the heterocyclyl optionally includes an additional heteroatom selected from oxygen, sulfur, and nitrogen;

at least one of X^1, X^2, X^3, X^4, and X^5 is present;

A^1 and A^2 are each independently selected from the group consisting of: C_5-C_{12} haloalkyl, C_5-C_{12} alkenyl, C_5-C_{12} alkynyl, (C_5-C_{12} alkoxy)-$(CH_2)_{n2}$–, (C_5-C_{10} aryl)-$(CH_2)_{n3}$– optionally ring substituted with one or two halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, or C_1-C_6 alkoxy groups, and (C_3-C_8 cycloalkyl)-$(CH_2)_{n4}$– optionally ring substituted with 1 or 2 C_1-C_6 alkyl groups; or alternatively A^1 and A^2 join together with the atoms to which they are bound to form a 5- to 6-membered cyclic acetal substituted with 1 or 2 C_4-C_{10} alkyl groups;

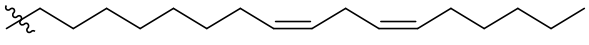
n1, n2 and n3 are each individually an integer between 1 and 4; and

n4 is an integer between zero and 4.

2. The compound of claim 1, wherein A^1 and A^2 are each independently C_5-C_{12} alkenyl, or wherein A^1 and A^2 are each independently C_5-C_{12} haloalkyl.

3. The compound of claim 1, wherein A^1 and A^2 are each independently (C_5-C_{10} aryl)-$(CH_2)_{n3}$– optionally ring substituted with one or two halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, or C_1-C_6 alkoxy groups, or wherein A^1 and A^2 are each independently (C_3-C_8 cycloalkyl)-$(CH_2)_{n4}$– optionally ring substituted with 1 or 2 C_1-C_6 alkyl groups.

4. The compound of claim 1, wherein A^1 and A^2 are each independently C_5-C_{12} alkynyl, A^1 and A^2 are each independently (C_5-C_{12} alkoxy)-$(CH_2)_{n2}$–, or A^1 and A^2 join together with the oxygen atoms to which they are bound to form a 5- to 6-membered cyclic acetal substituted with 1 or 2 C_4-C_{10} alkyl groups.

5. The compound of any one of claims 1-4, wherein R^1 is C_9-C_{20} alkenyl with 2 units of unsaturation, optionally wherein R^1 is .

6. The compound of any one of claims 1-3, wherein

X^1 is absent, and X^2 is , wherein X^7 is optionally: hydrogen, hydroxyl and a is 1, or –NR^6R^7 and a is 1;

X^1 is –O–, and X^2 is , wherein X^7 is optionally: hydrogen, hydroxyl and a is 1, or –

NR^6R^7 and a is 1; or

X^1 is  , and X^2 is  , wherein X^7 is optionally: hydrogen, hydroxyl and a is 1, or – NR^6R^7 and a is 1.

7. The compound of any one of claims 1-6, wherein X^3 is absent or X^3 is 4- to 8-membered heterocyclyl optionally substituted with 1 or 2 C_1-C_6 alkyl groups.

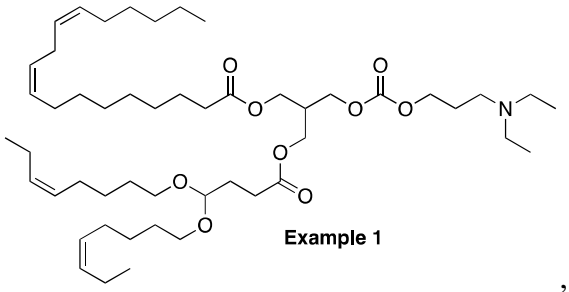
8. The compound of any one of claims 1-7, wherein X^4 is absent.

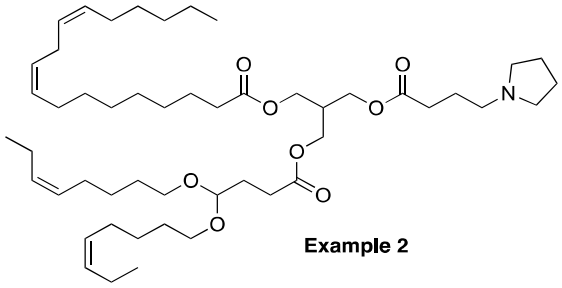
9. The compound of any one of claims 1-8, wherein

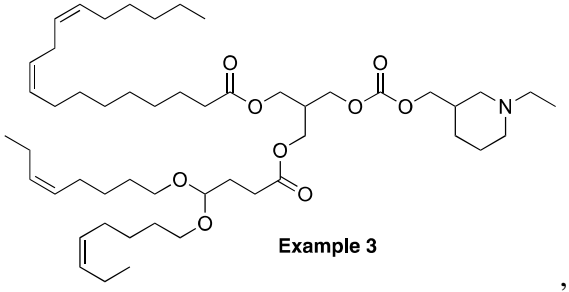
b is an integer between 1 and 6; and

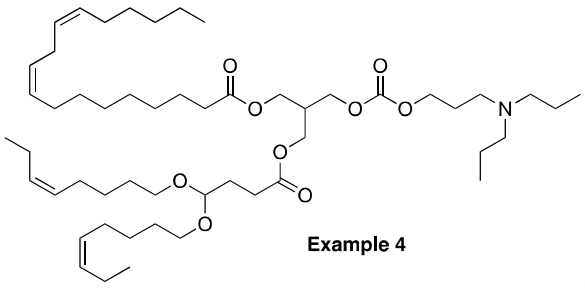
X^6 is hydrogen or NR^4R^5, optionally wherein R^4 and R^5 join together with the nitrogen to which they are bound to form a 4- to 7-membered heterocyclyl optionally substituted with 1 or 2 C_1-C_6 alkyl groups.

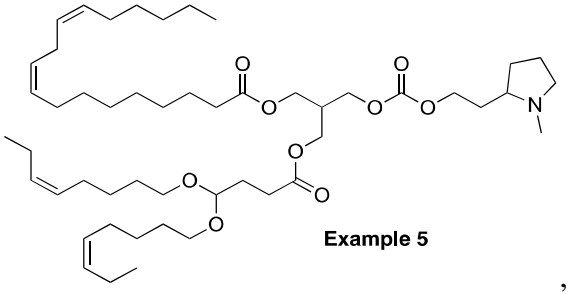
10. The compound of claim 1, wherein the compound is any one of examples 1-148

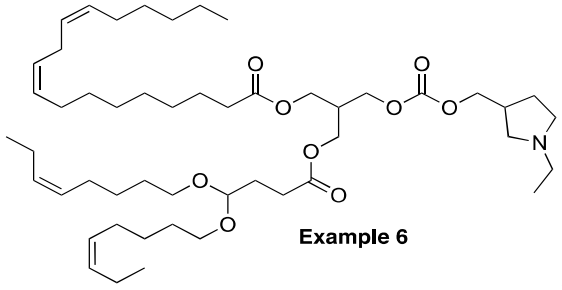


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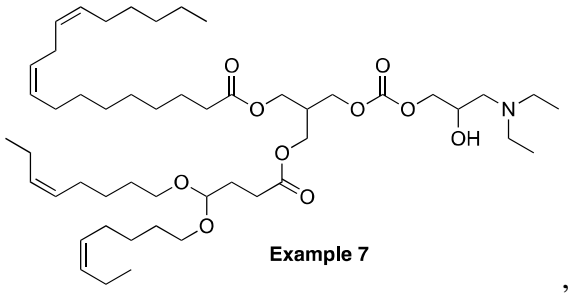
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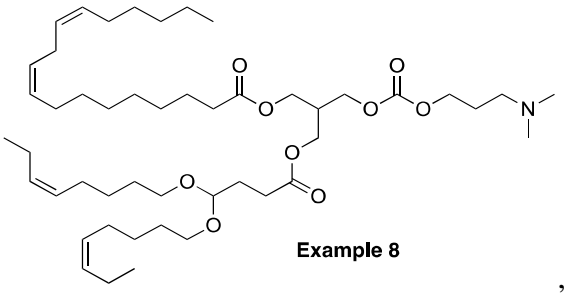
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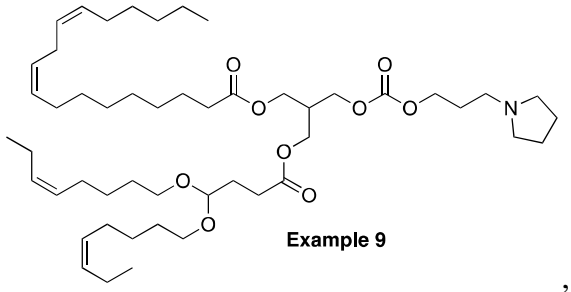
Example 7

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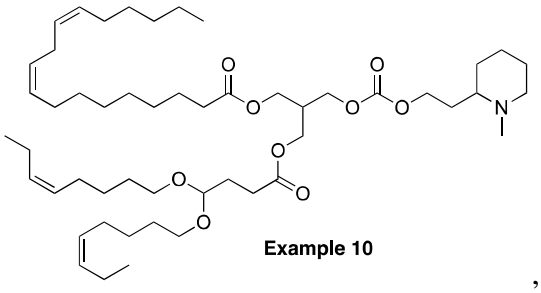
Example 8

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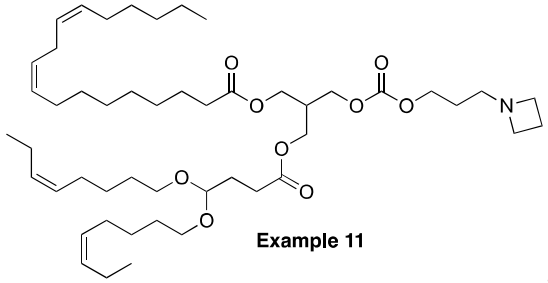
Example 9

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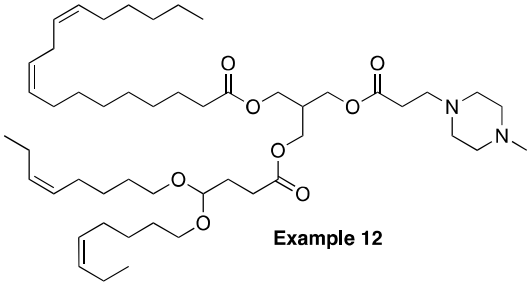
Example 10

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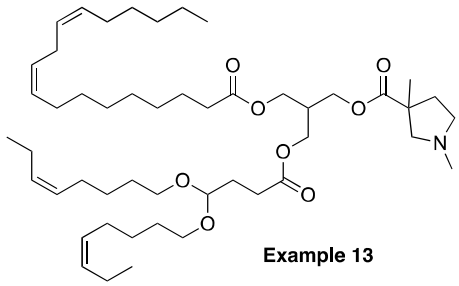
Example 11

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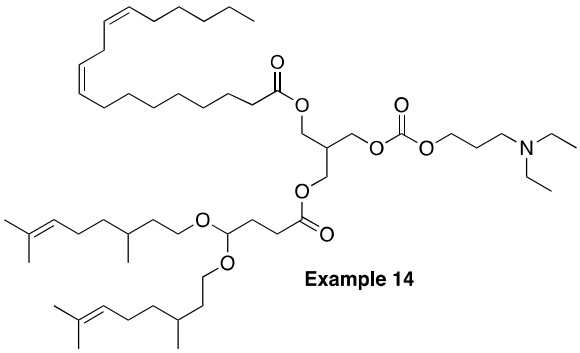
Example 12

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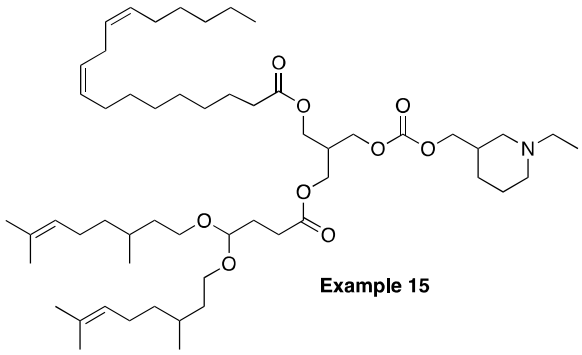
Example 13

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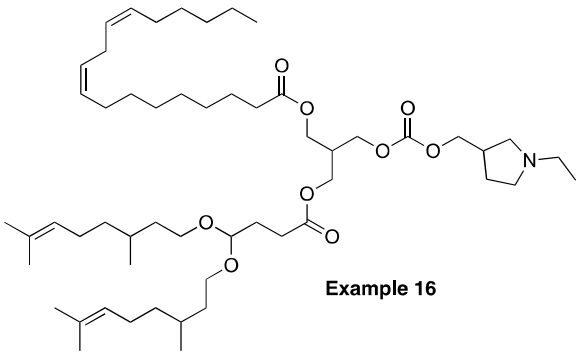
Example 14

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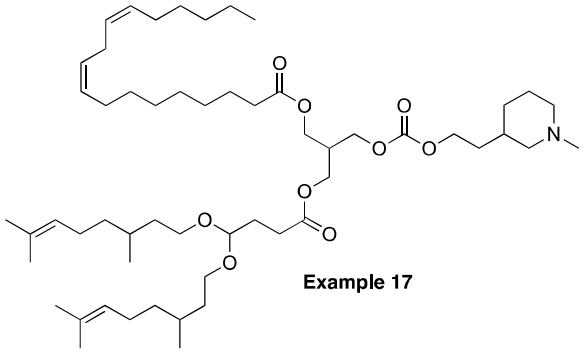
Example 15

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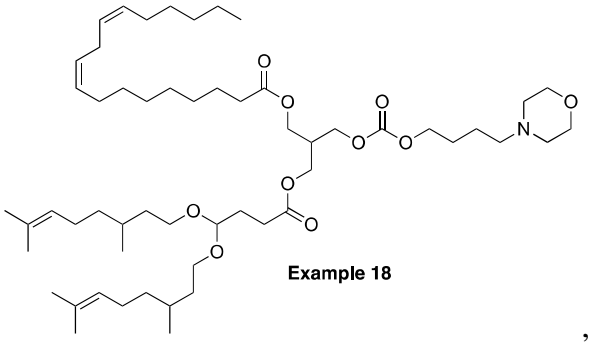
Example 16

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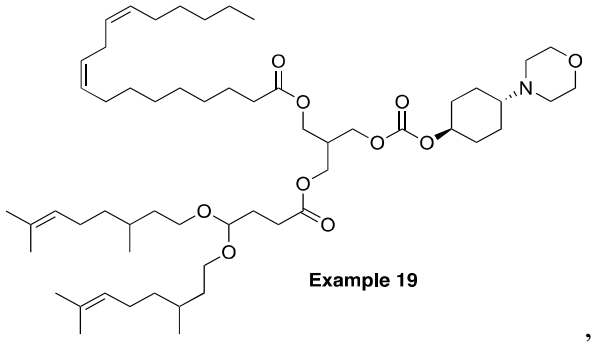
Example 17

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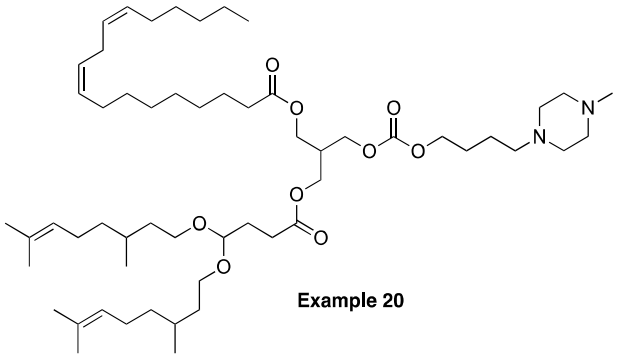
Example 18

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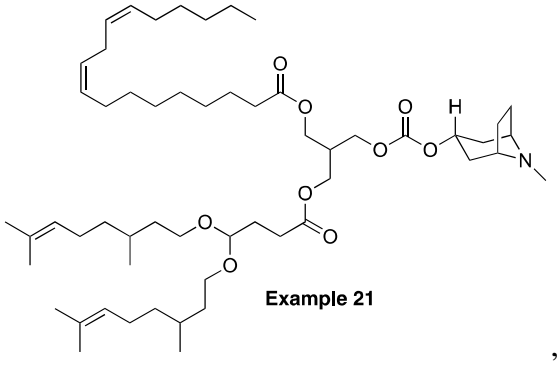
Example 19

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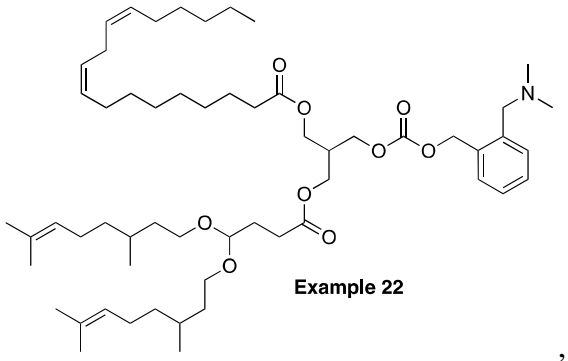
Example 20

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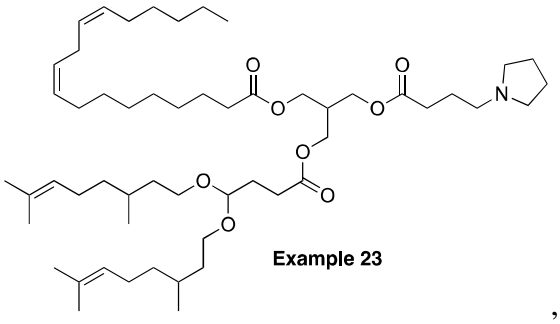
Example 21

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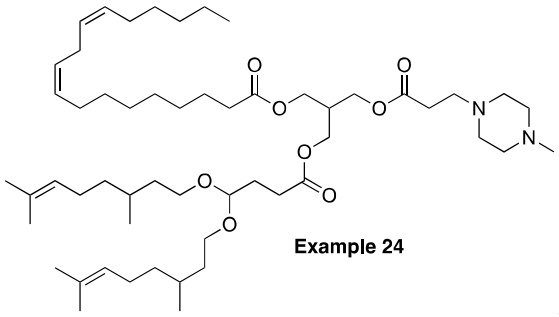
Example 22

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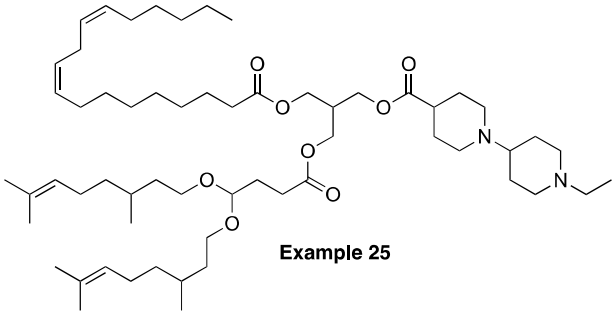
Example 23

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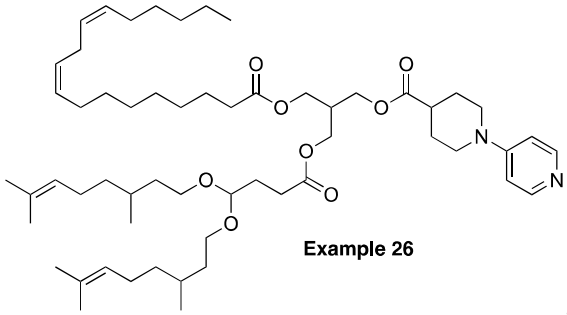
Example 24

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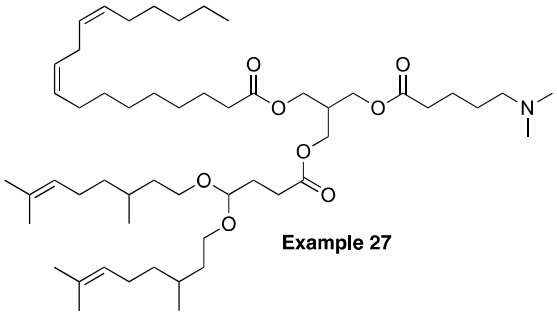
Example 25

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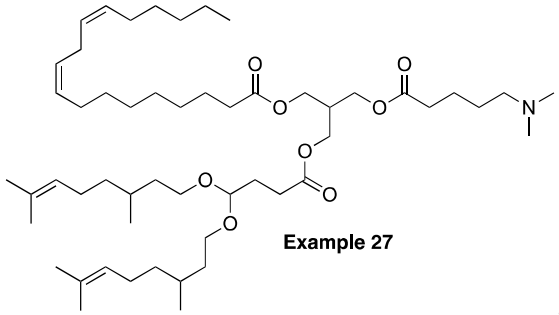
Example 26

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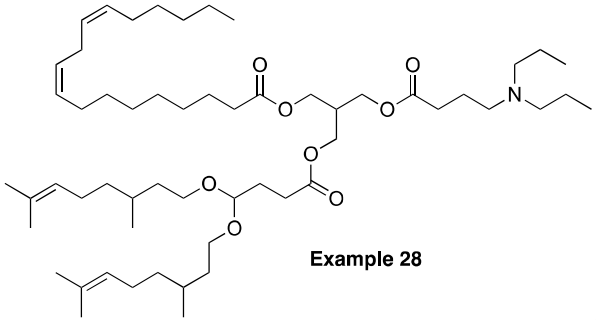
Example 27

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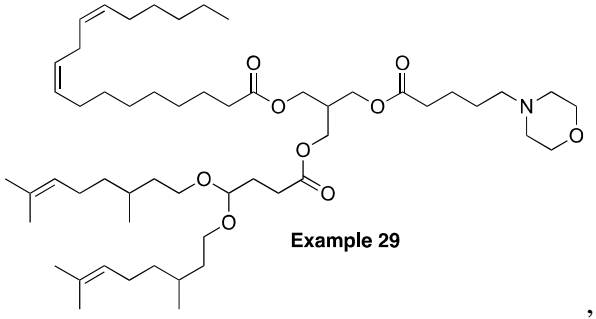
Example 27

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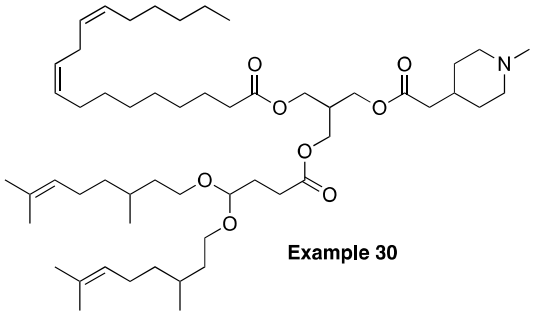
Example 28

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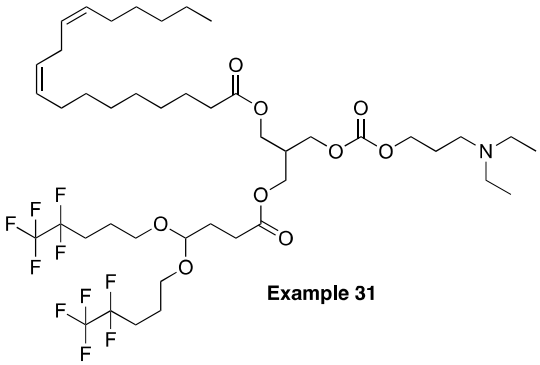
Example 29

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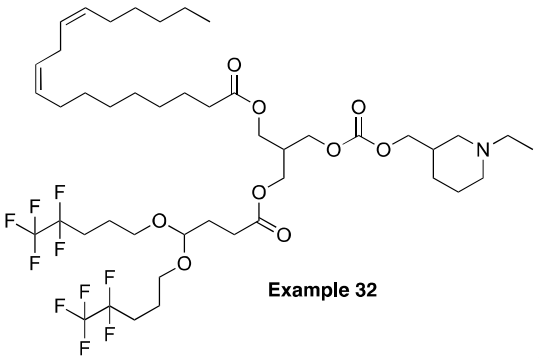
Example 30

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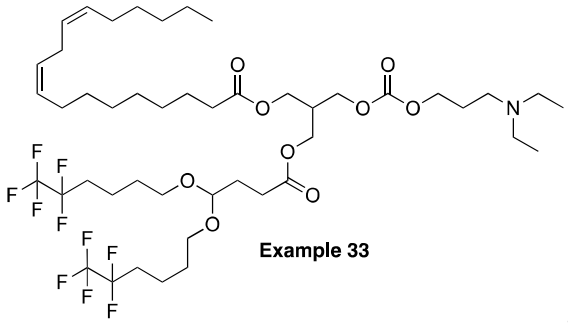
Example 31

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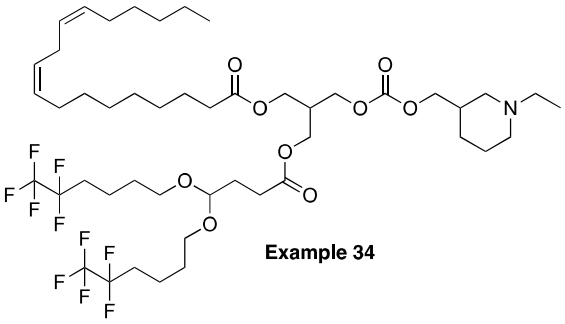
Example 32

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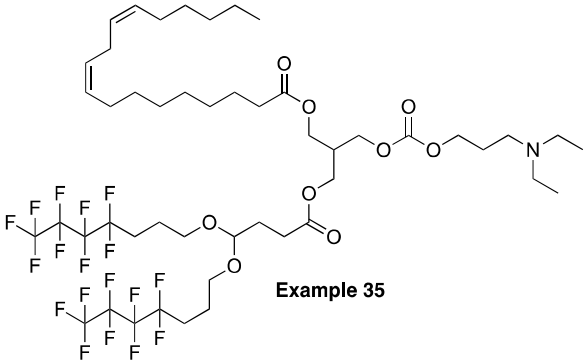
Example 33

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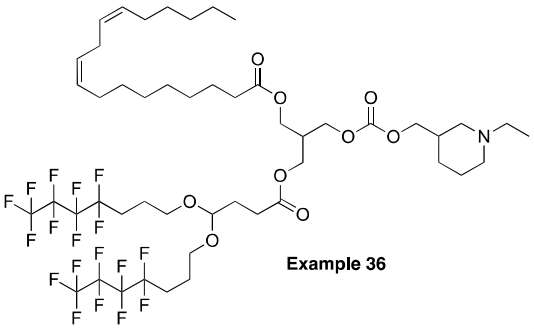
Example 34

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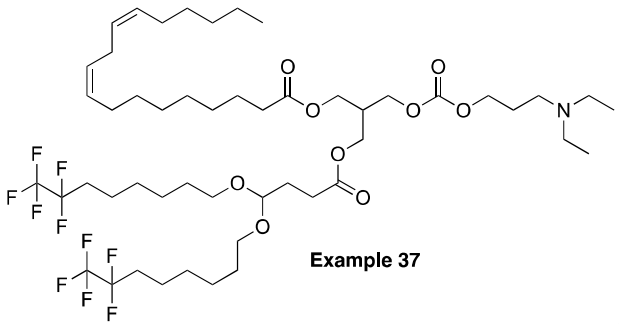
Example 35

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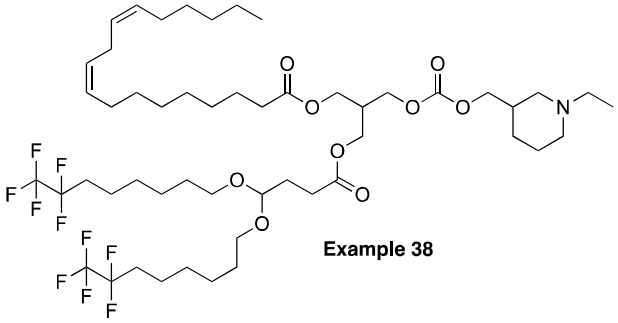
Example 36

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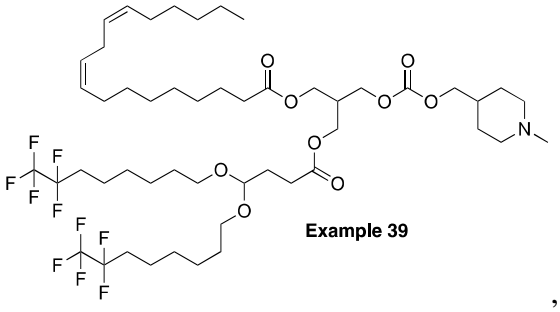
Example 37

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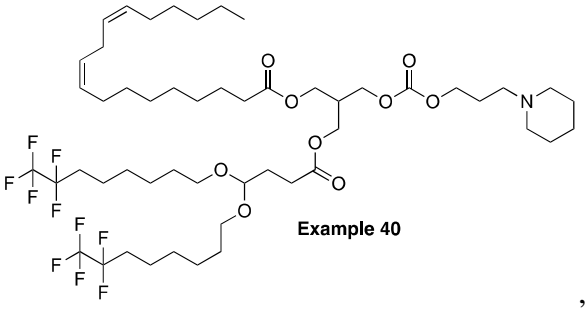
Example 38

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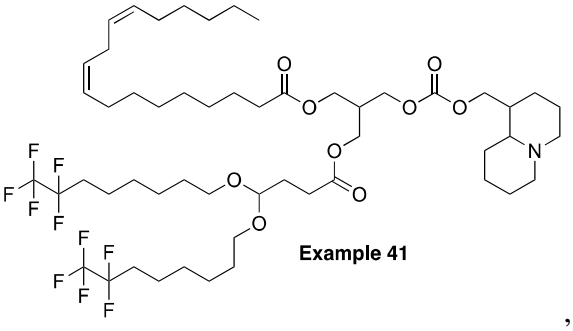
Example 39

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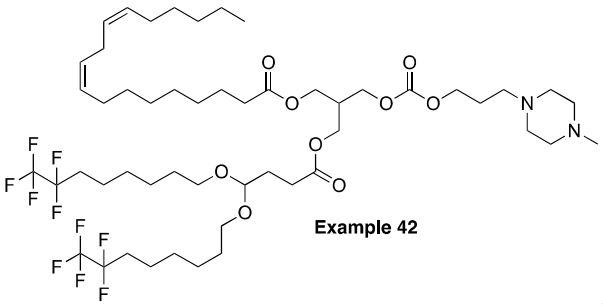
Example 40

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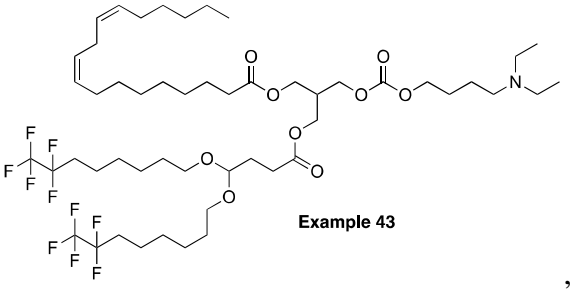
Example 41

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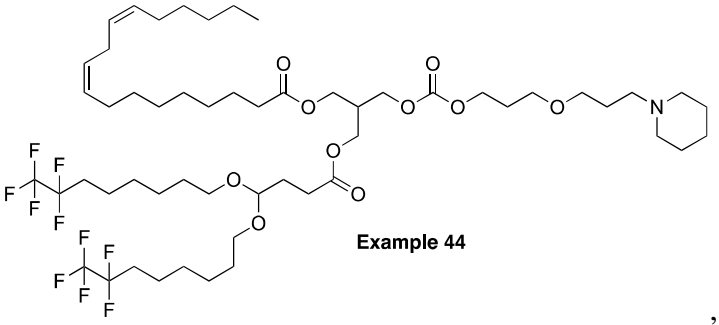
Example 42

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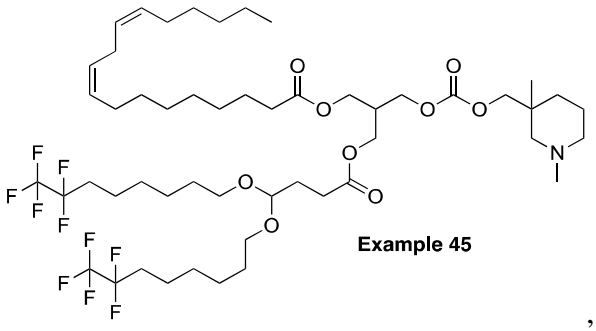
Example 43

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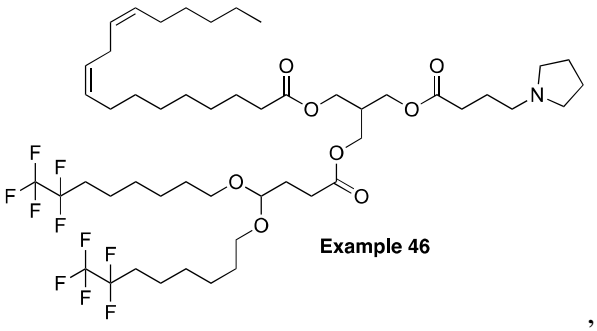
Example 44

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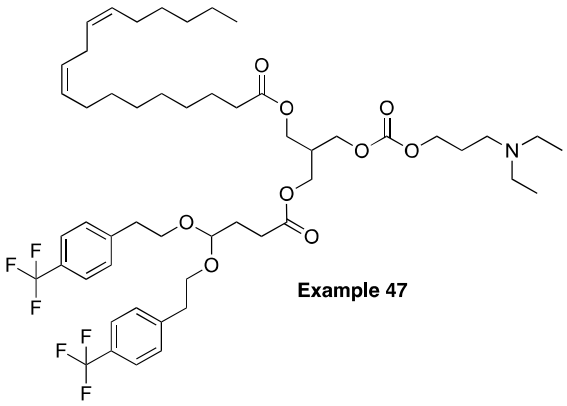
Example 45

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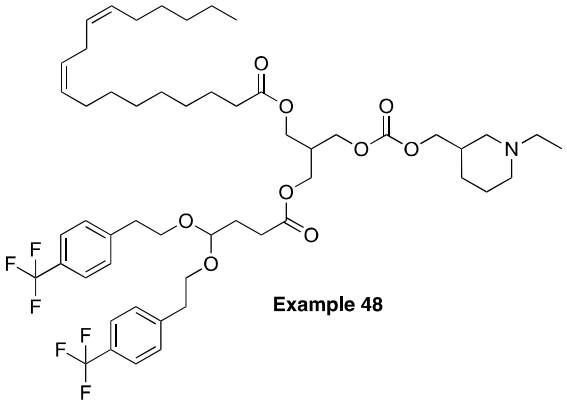
Example 46

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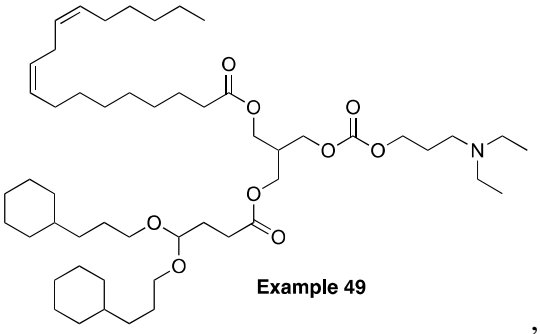
Example 47

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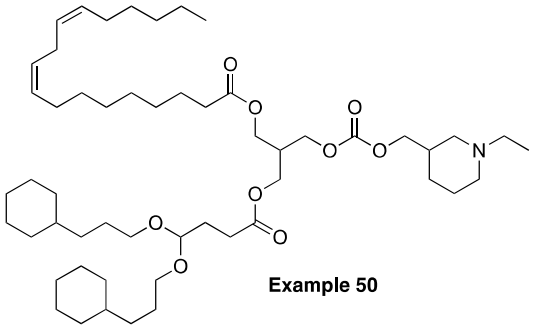
Example 48

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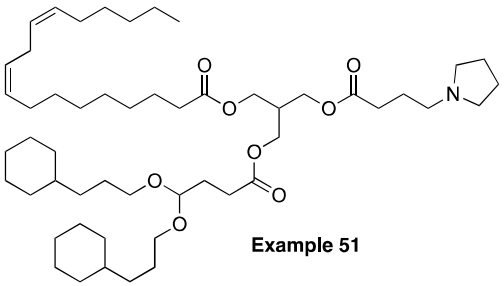
Example 49

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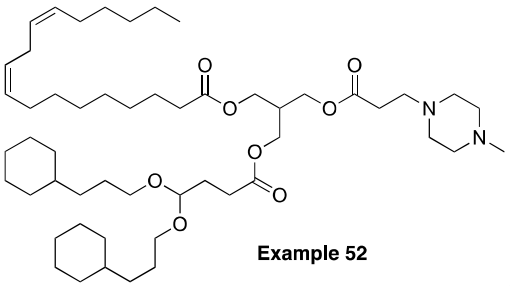
Example 50

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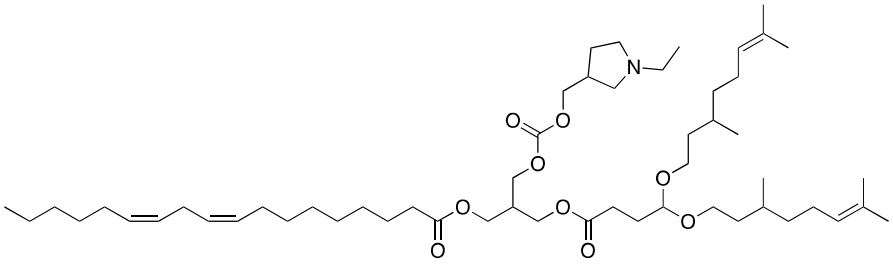
Example 51

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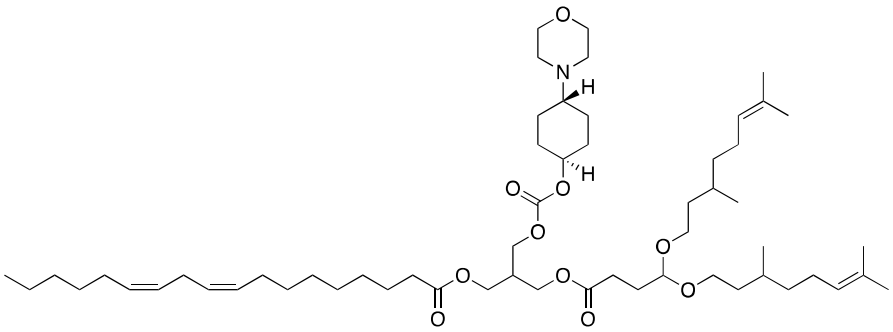
Example 52

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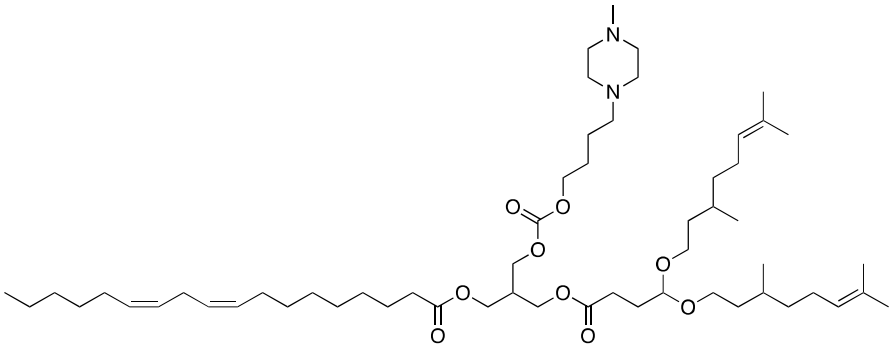
Example 53

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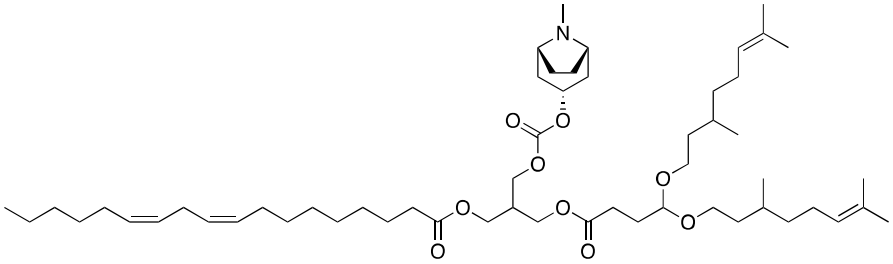
Example 54

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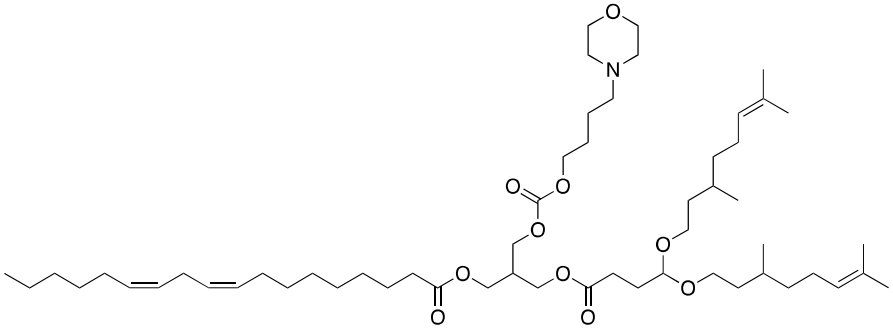
Example 55

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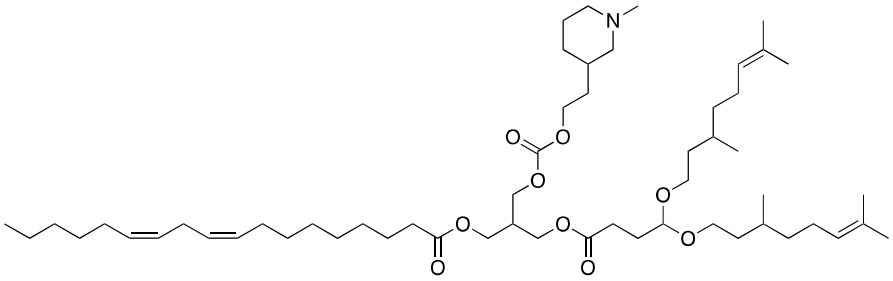
Example 56

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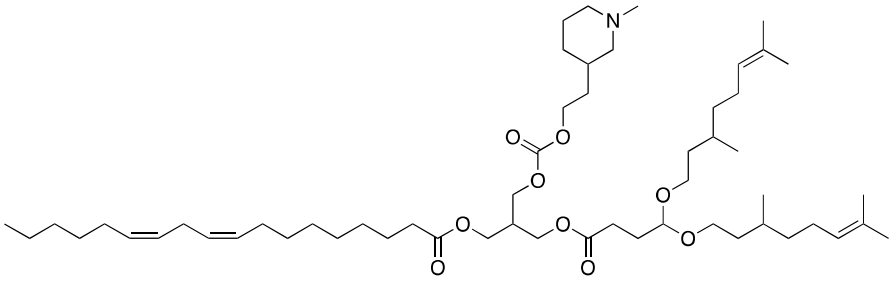
Example 57

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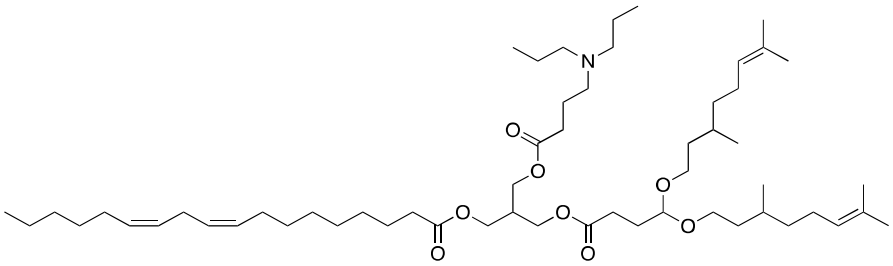
Example 58

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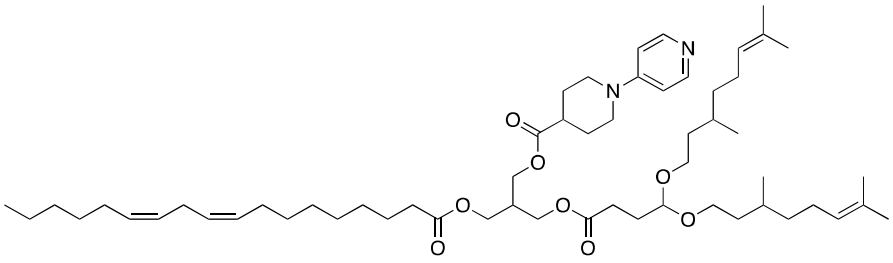
Example 58

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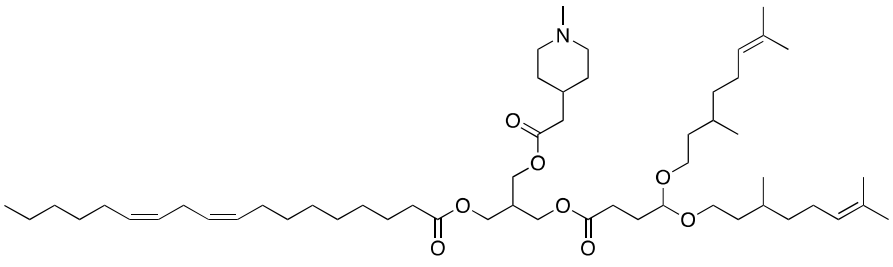
Example 60

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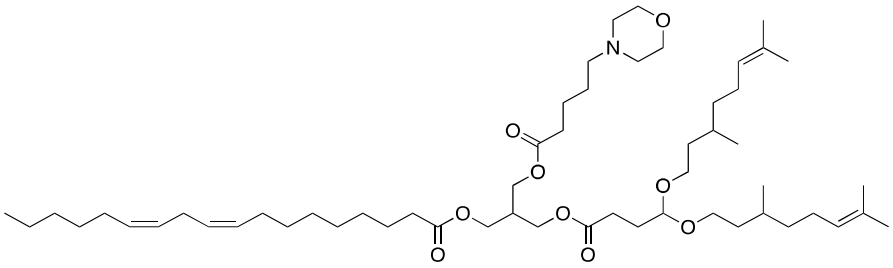
Example 61

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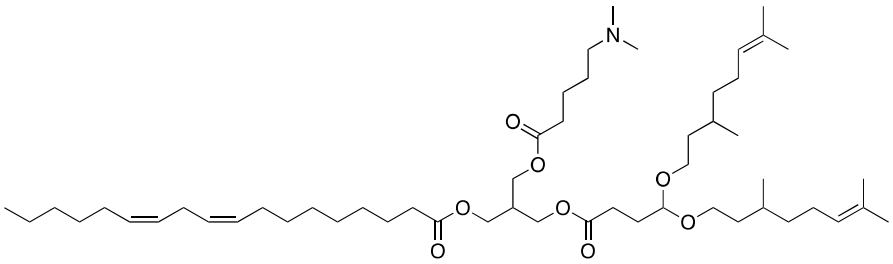
Example 62

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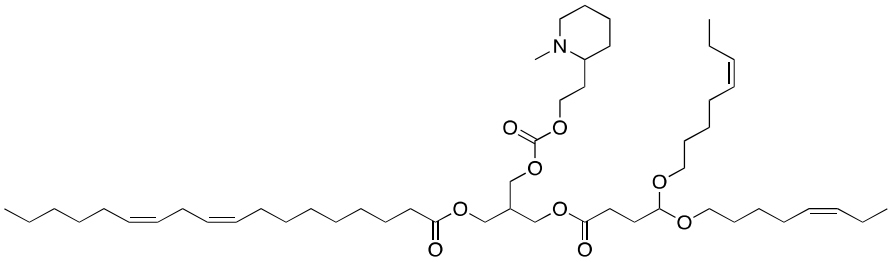
Example 63

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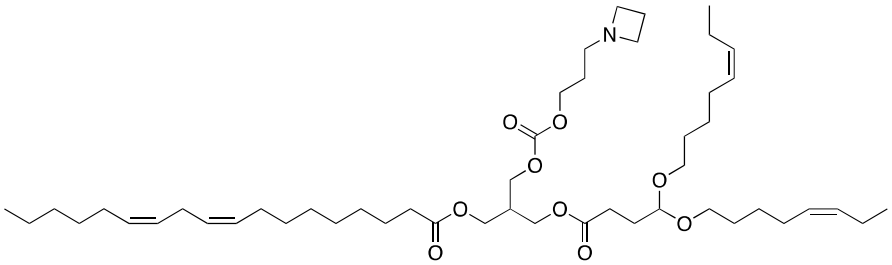
Example 64

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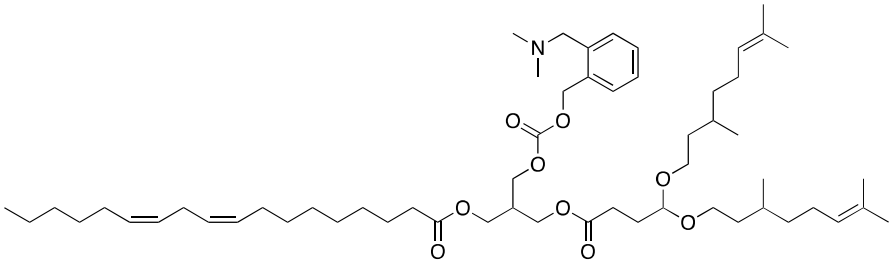
Example 65

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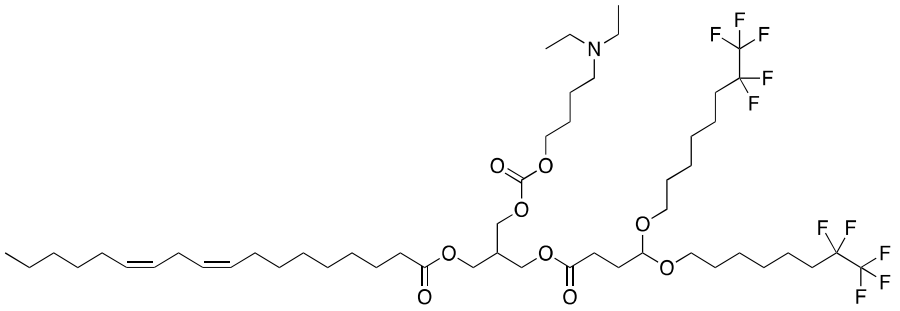
Example 66

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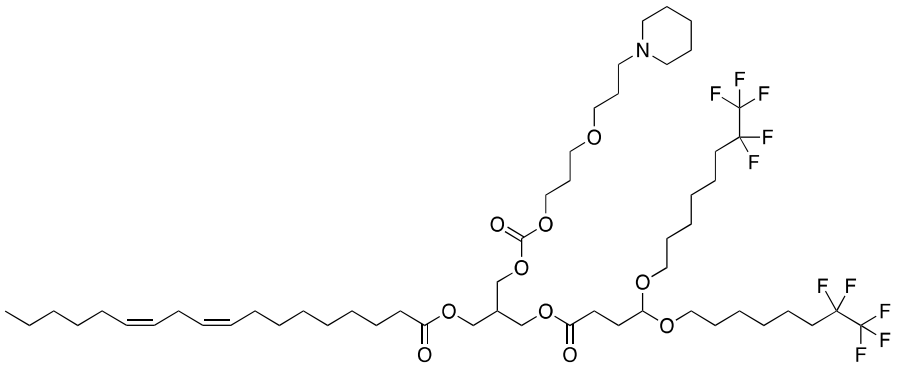
Example 67

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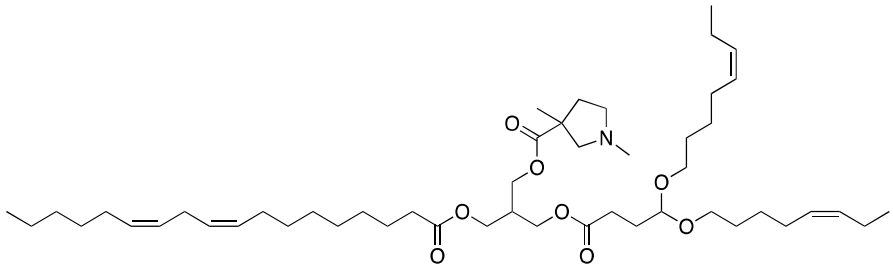
Example 68

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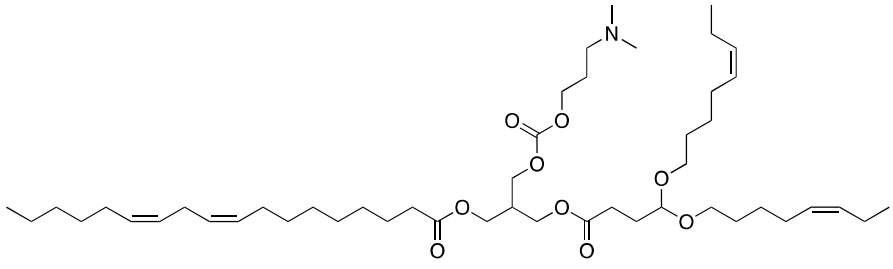
Example 69

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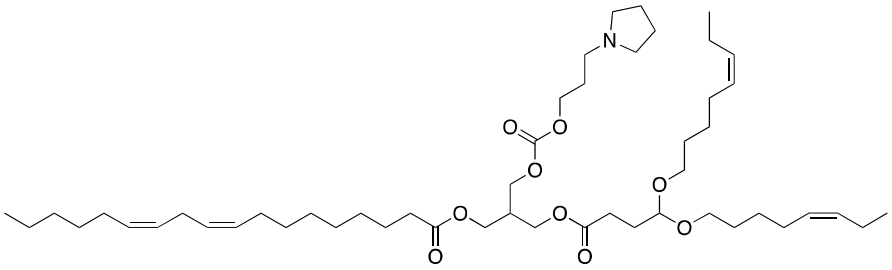
Example 70

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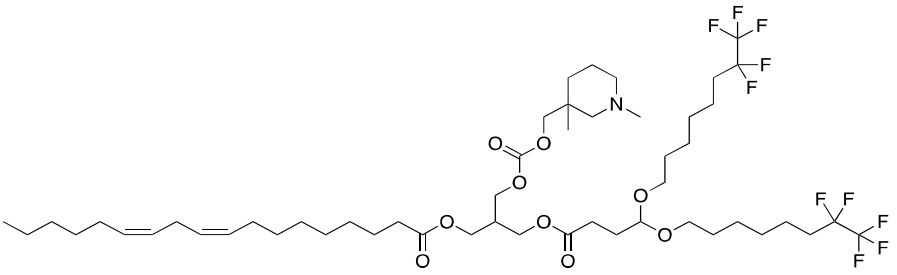
Example 71

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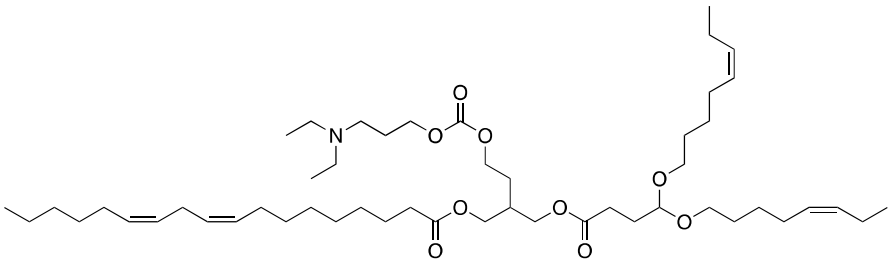
Example 72

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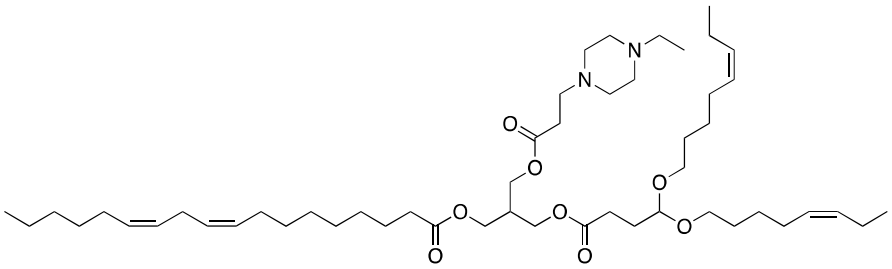
Example 73

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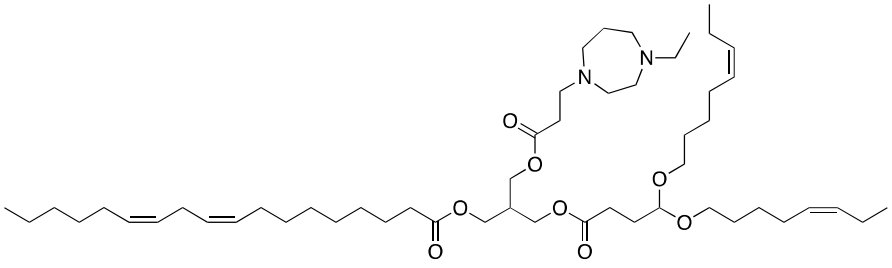
Example 74

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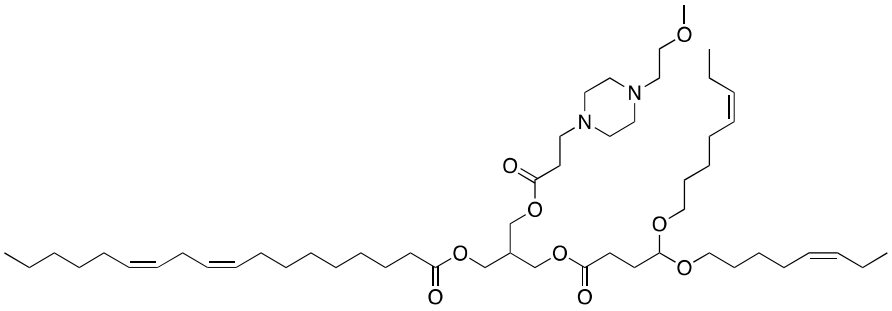
Example 75

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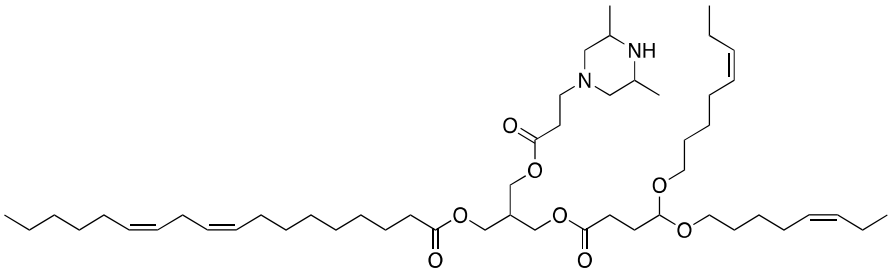
Example 76

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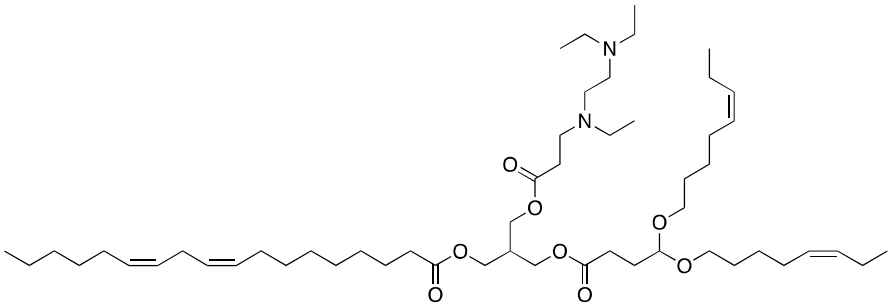
Example 77

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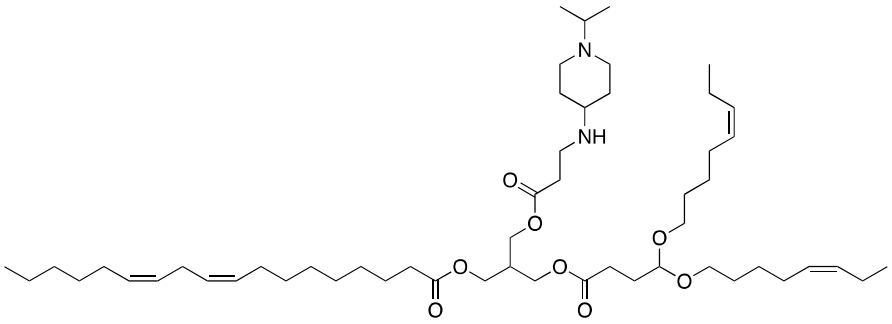
Example 78

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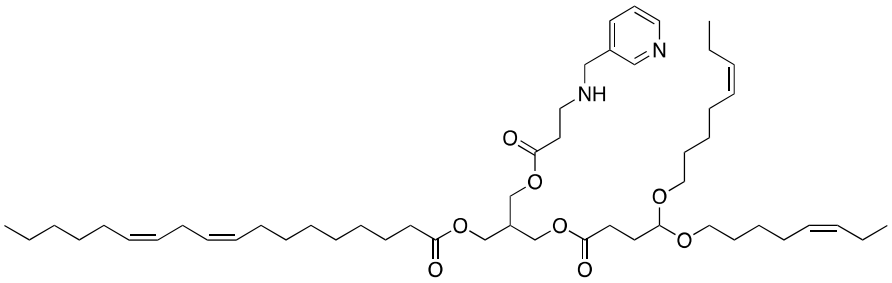
Example 79

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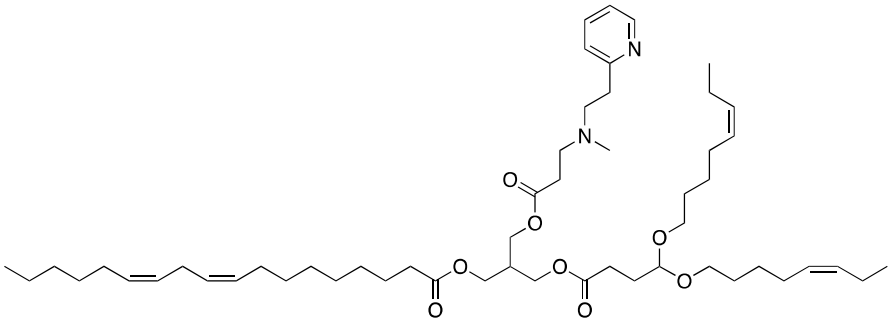
Example 80

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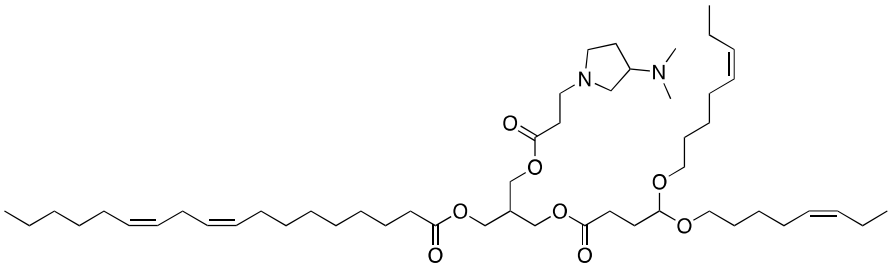
Example 81

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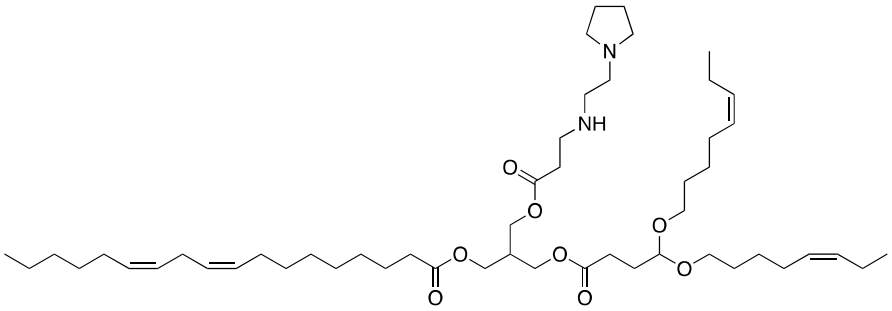
Example 82

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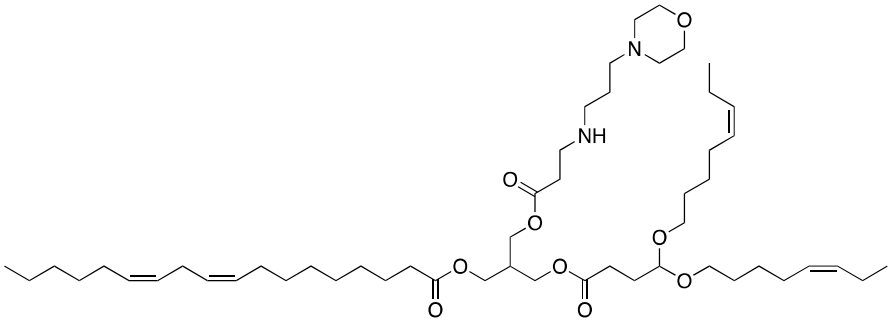
Example 83

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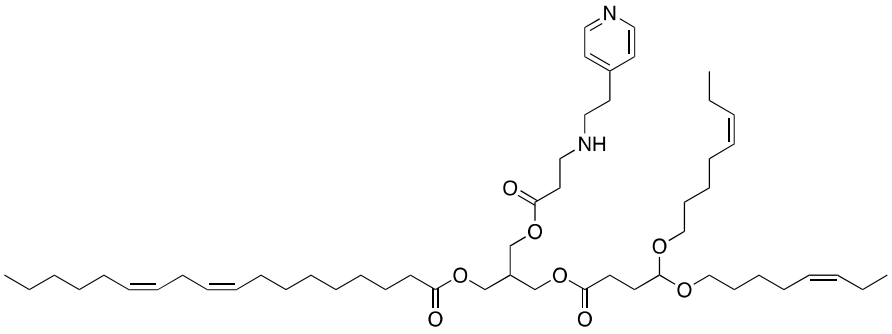
Example 84

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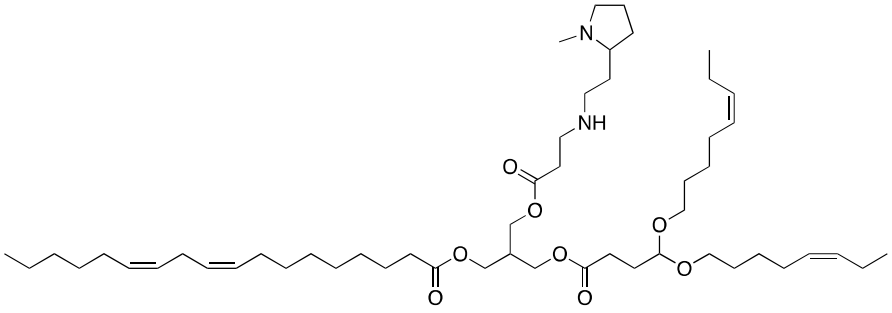
Example 85

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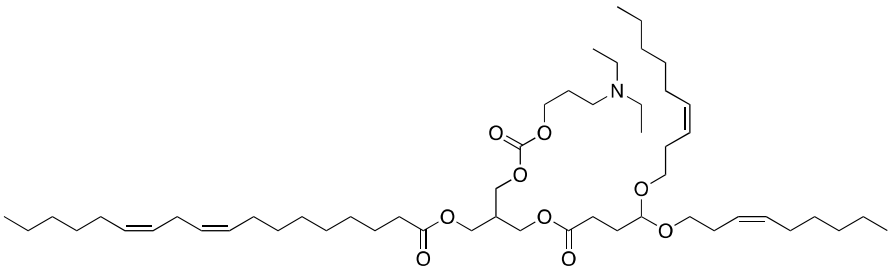
Example 86

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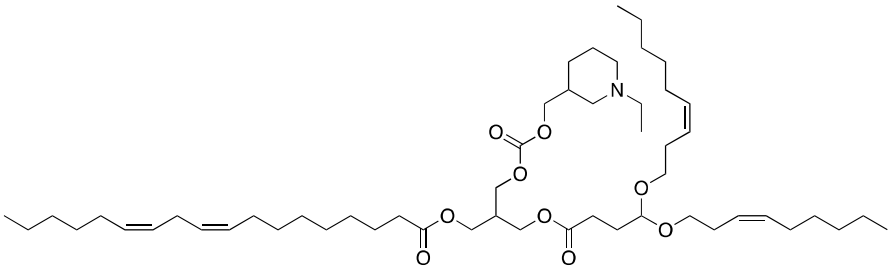
Example 87

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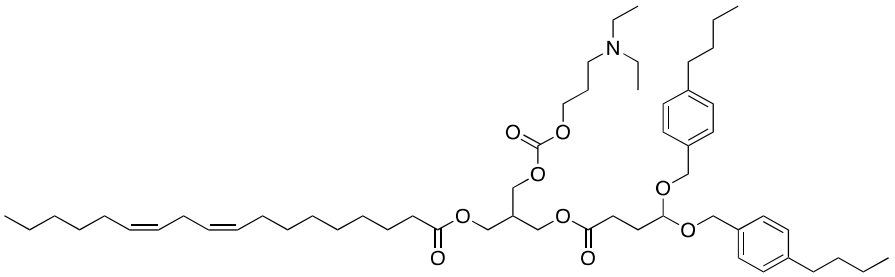
Example 88

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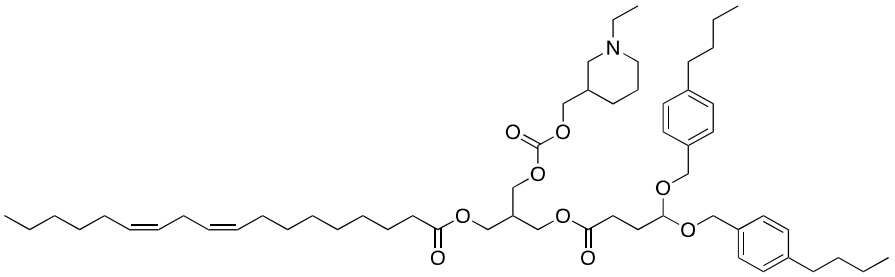
Example 89

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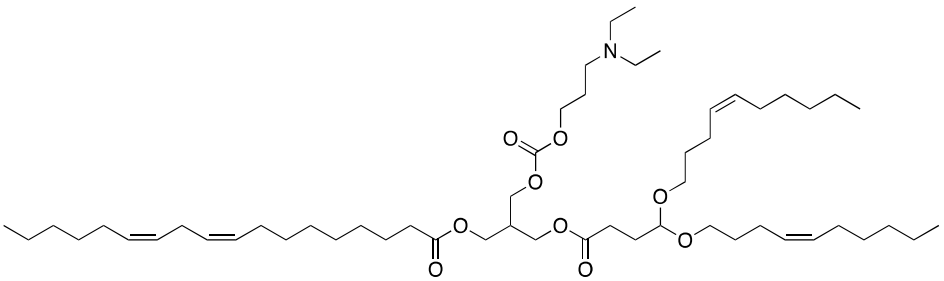
Example 90

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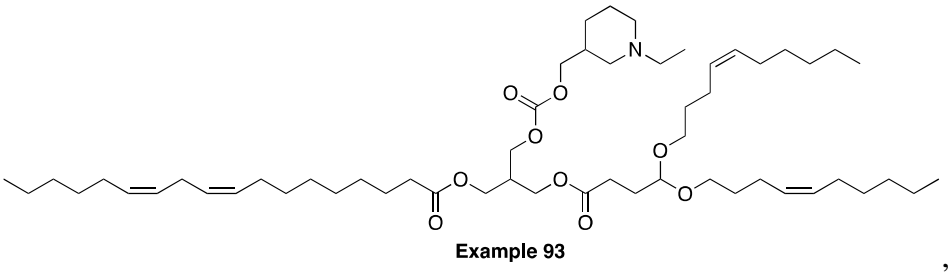
Example 91

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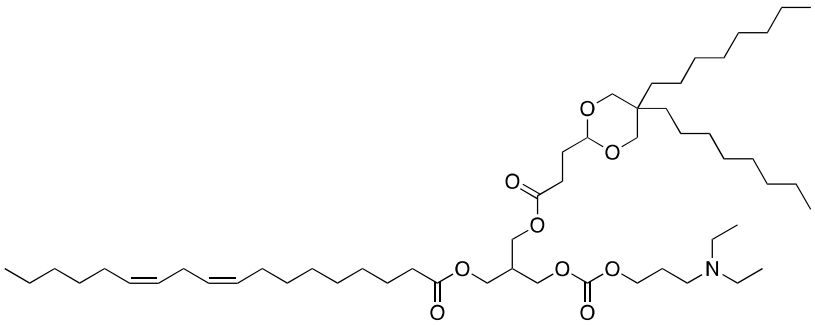
Example 92

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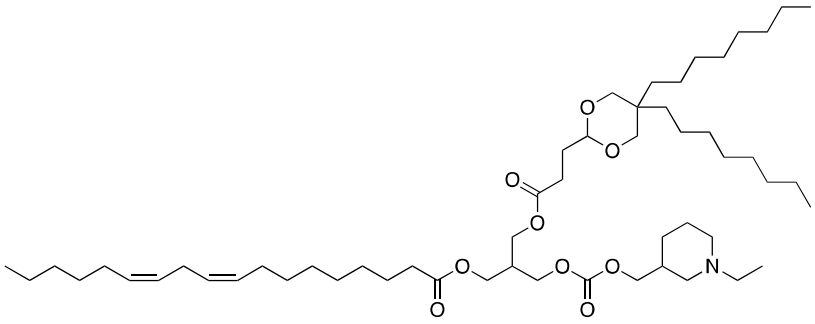
Example 93

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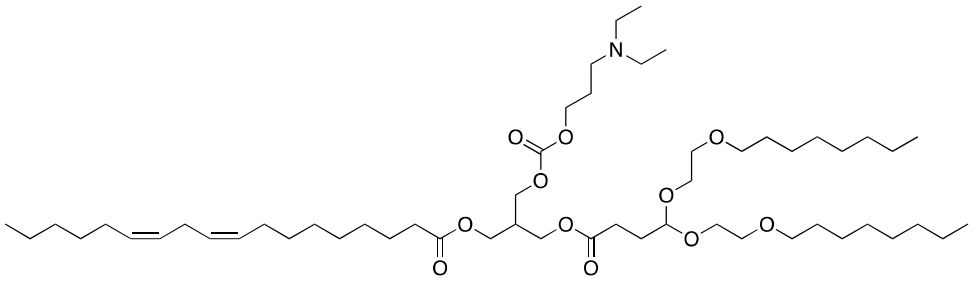
Example 94

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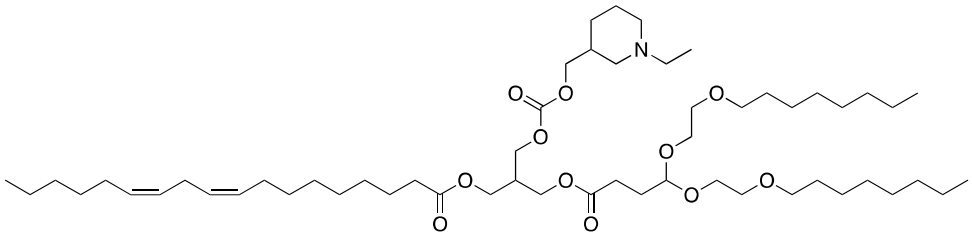
Example 95

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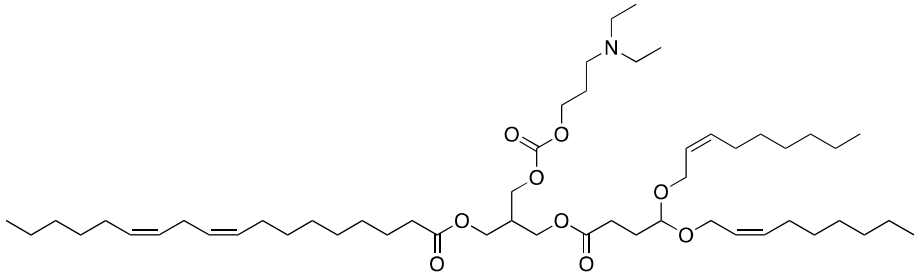
Example 96

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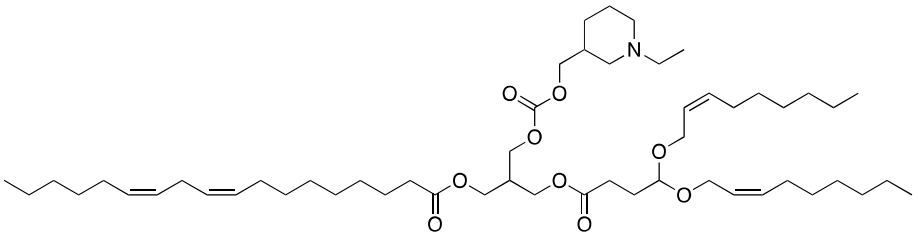
Example 97

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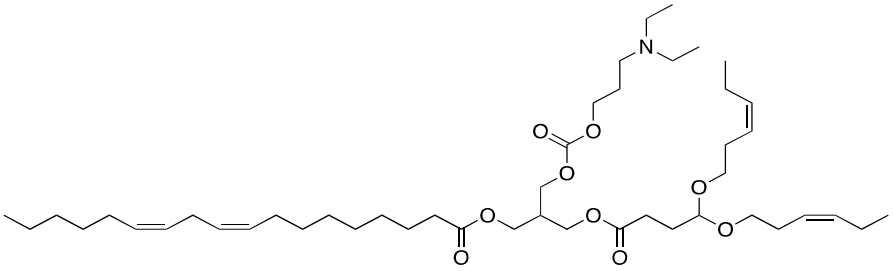
Example 98

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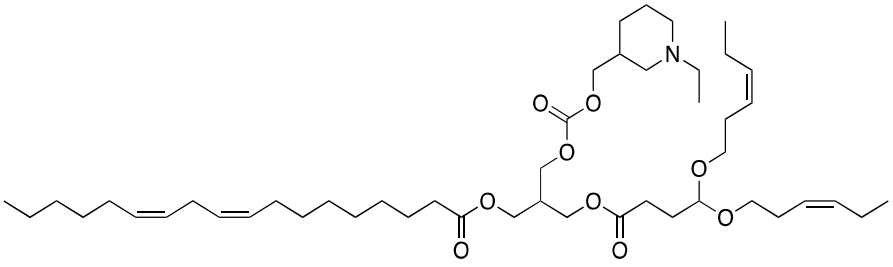
Example 99

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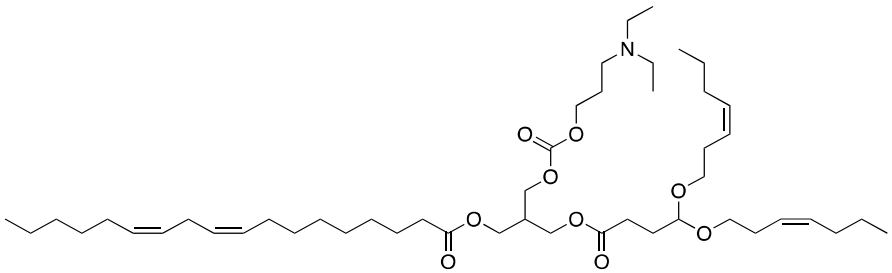
Example 100

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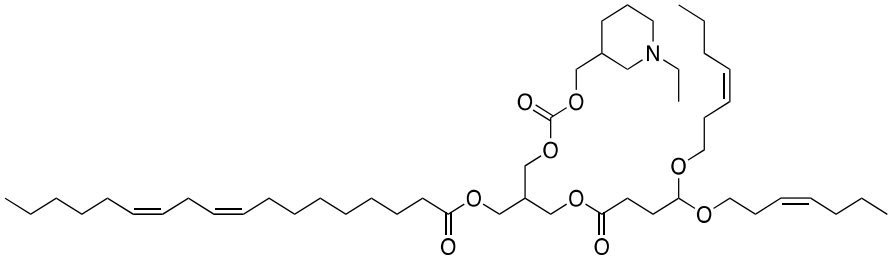
Example 101

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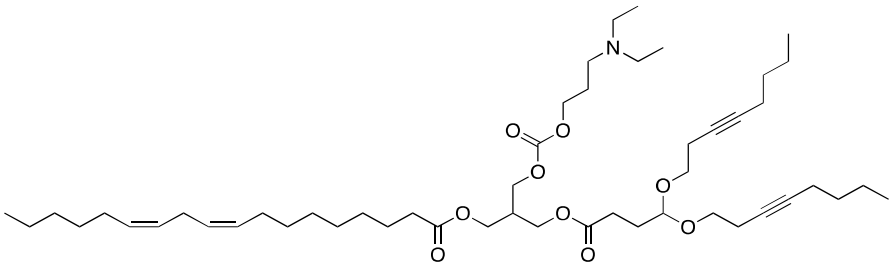
Example 102

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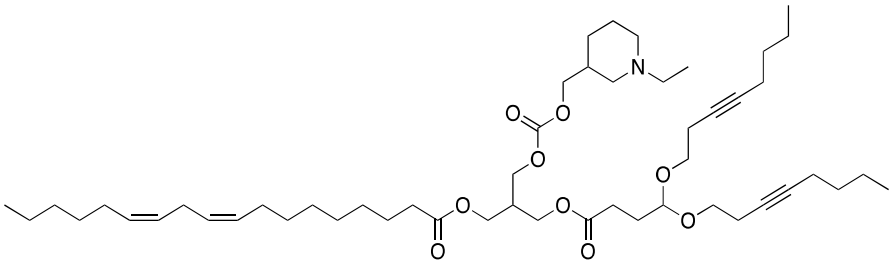
Example 103

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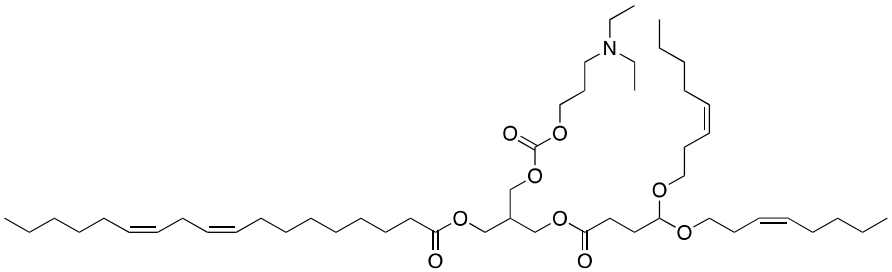
Example 104

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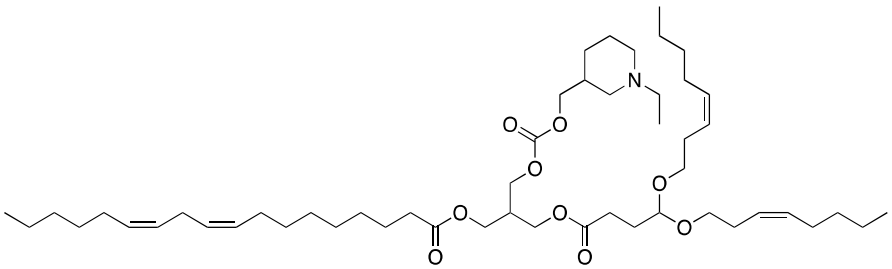
Example 105

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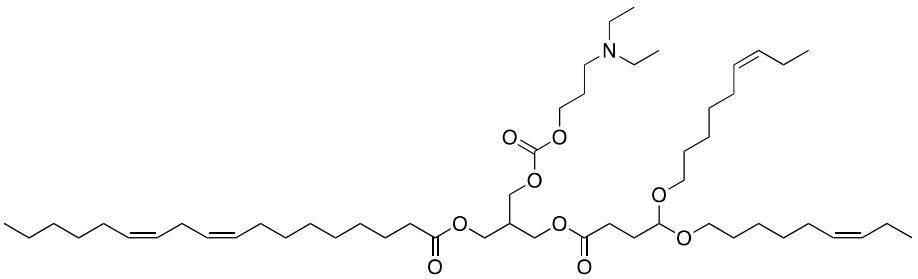
Example 106

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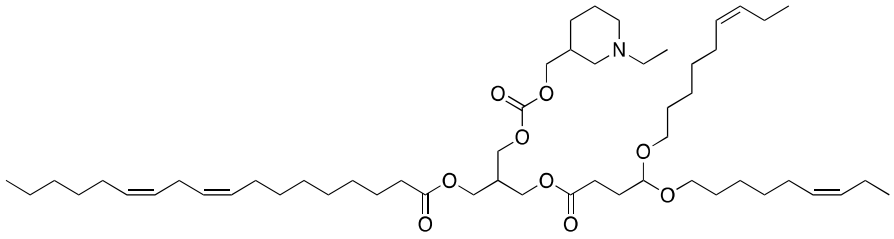
Example 107

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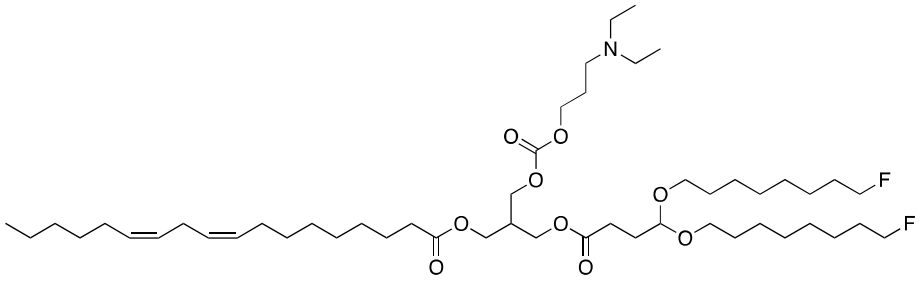
Example 108

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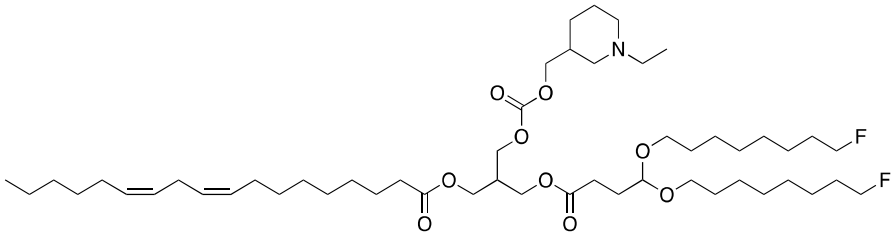
Example 109

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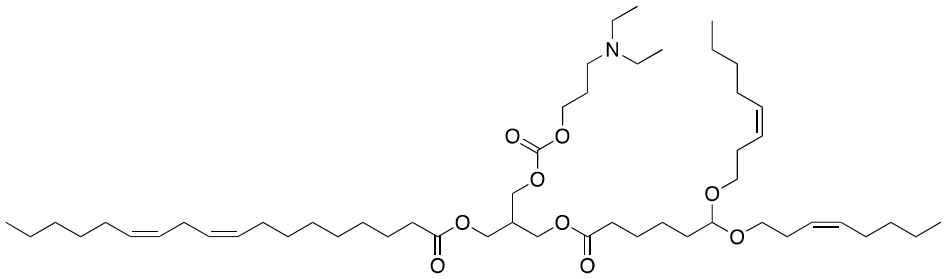
Example 110

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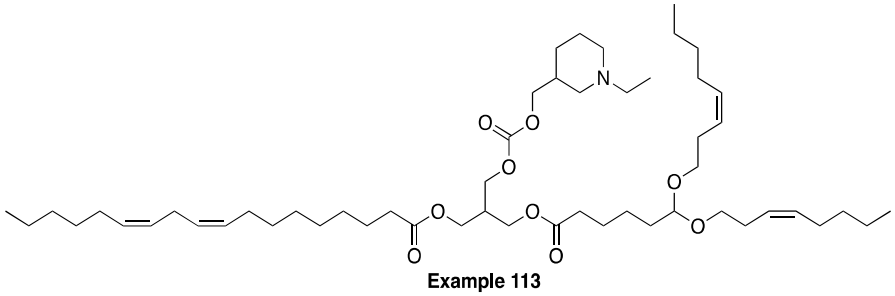
Example 111

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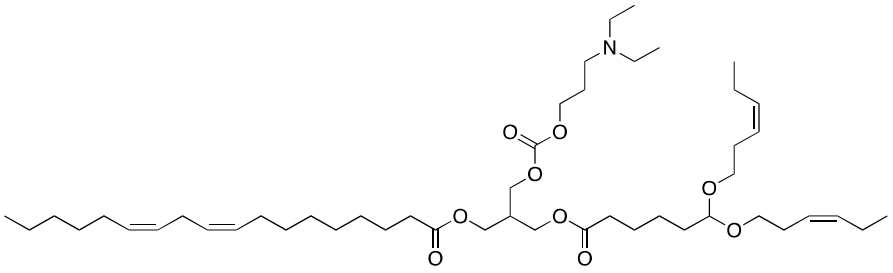
Example 112

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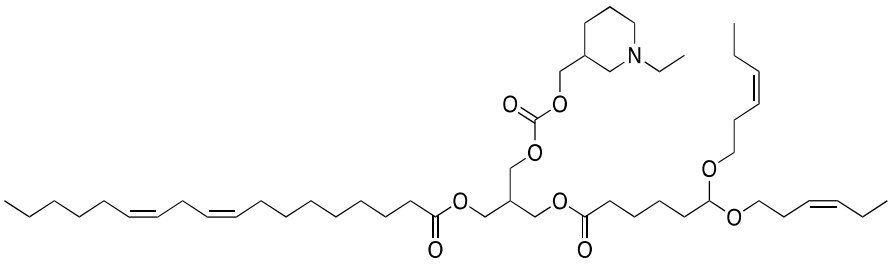
Example 113

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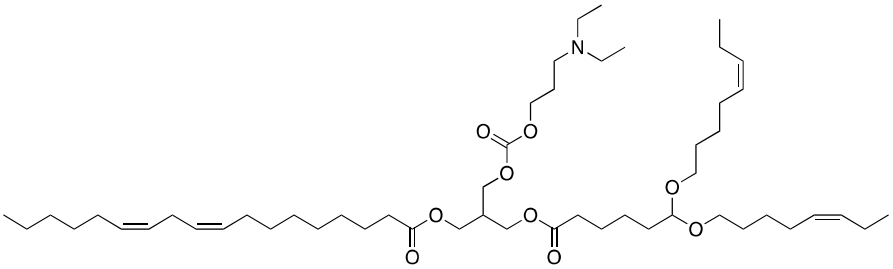
Example 114

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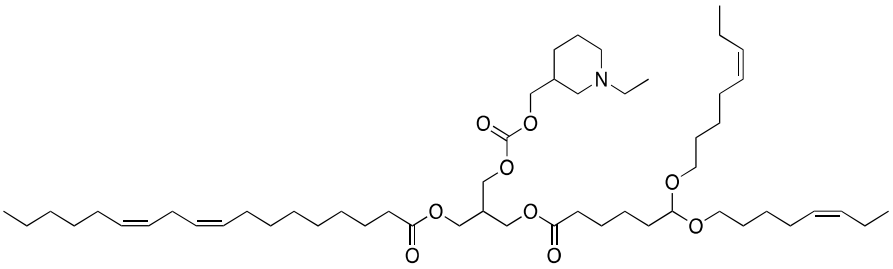
Example 115

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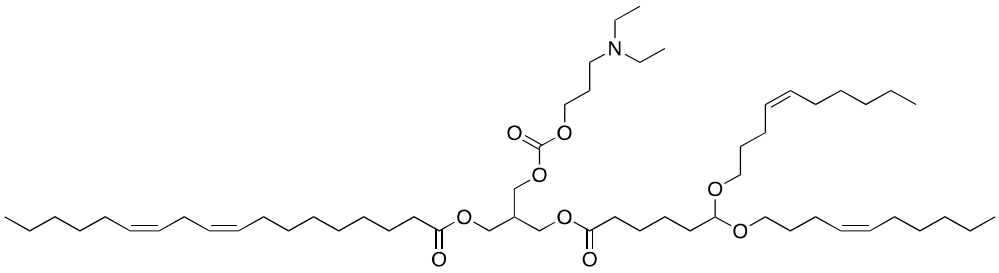
Example 116

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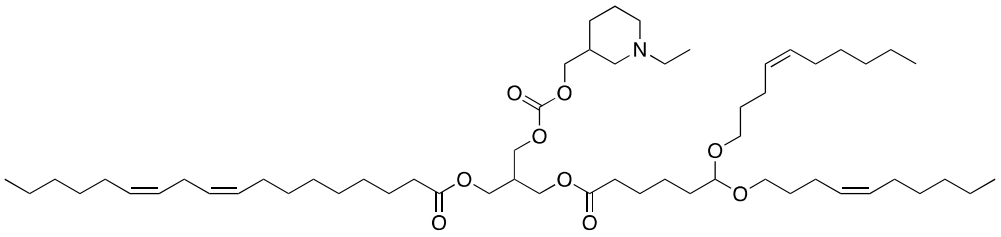
Example 117

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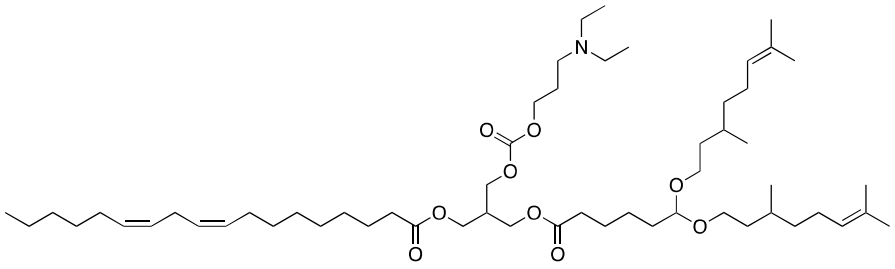
Example 118

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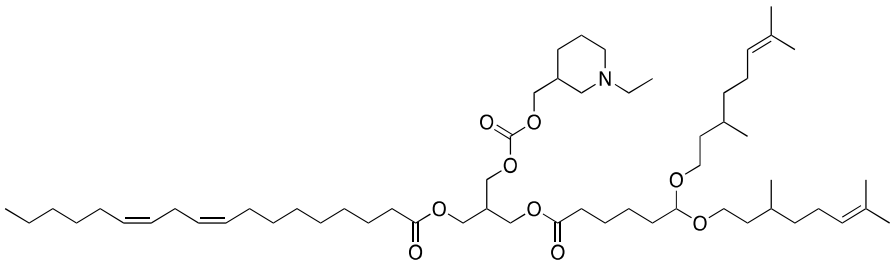
Example 119

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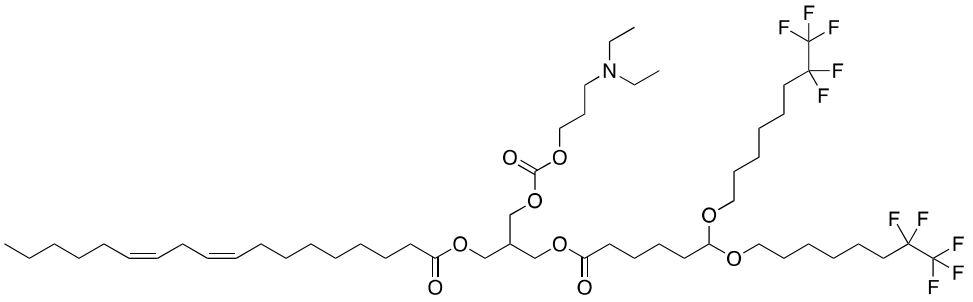
Example 120

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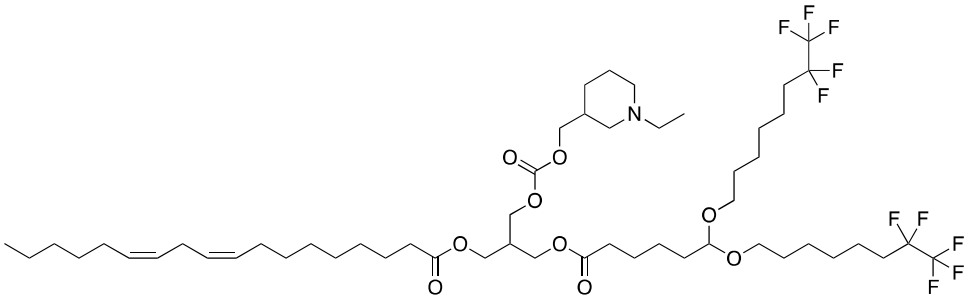
Example 121

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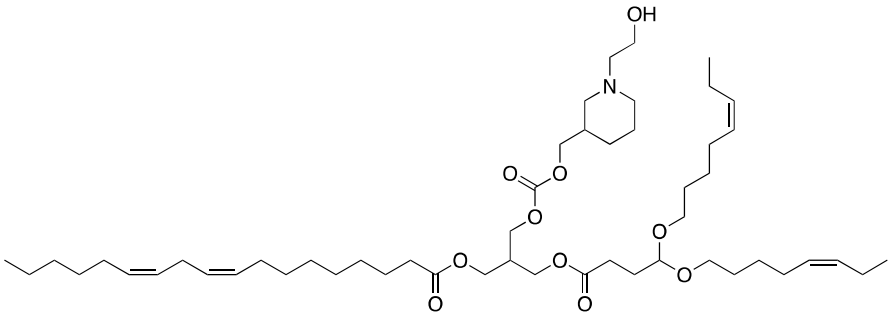
Example 122

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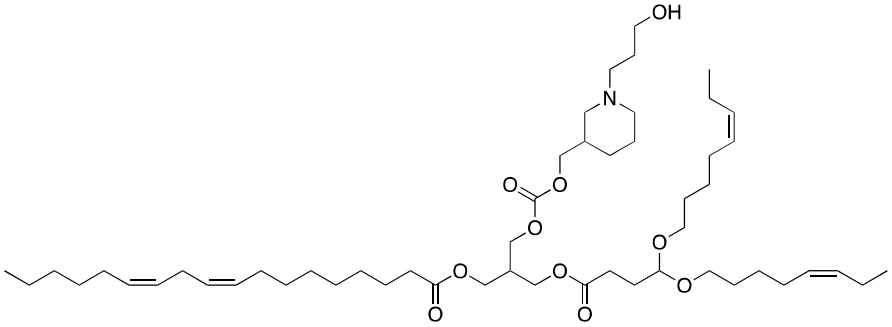
Example 123

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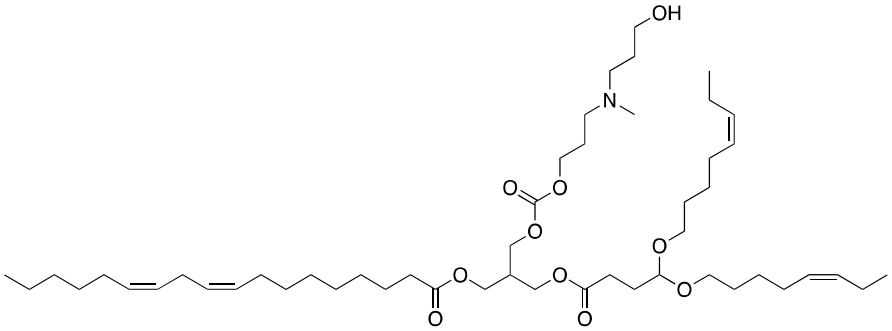
Example 124

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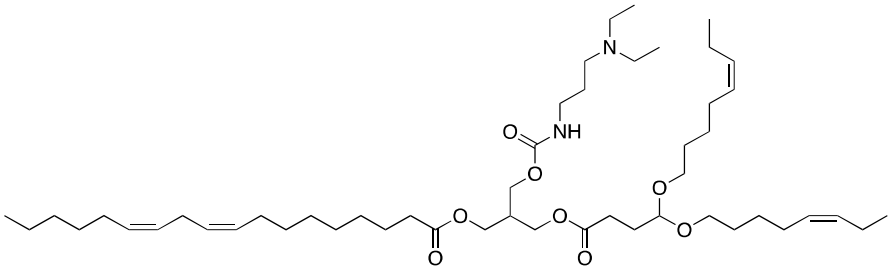
Example 125

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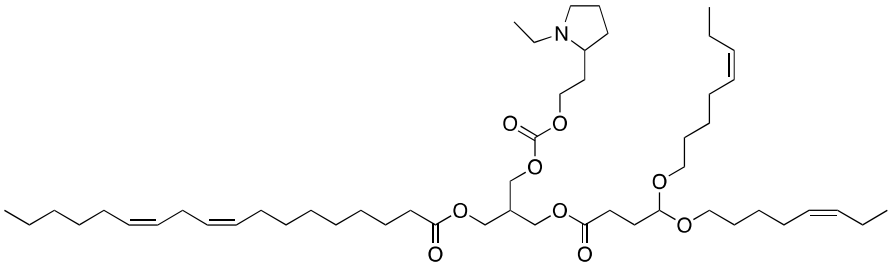
Example 126

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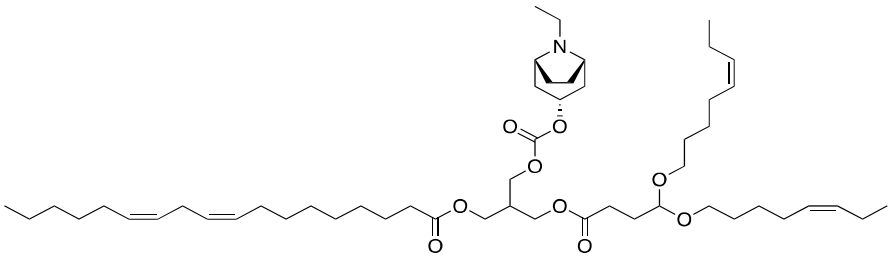
Example 127

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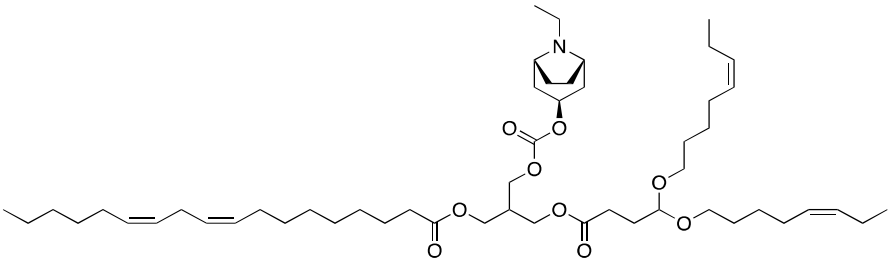
Example 128

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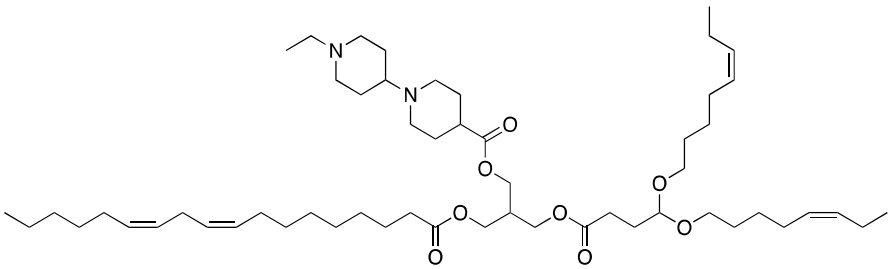
Example 129

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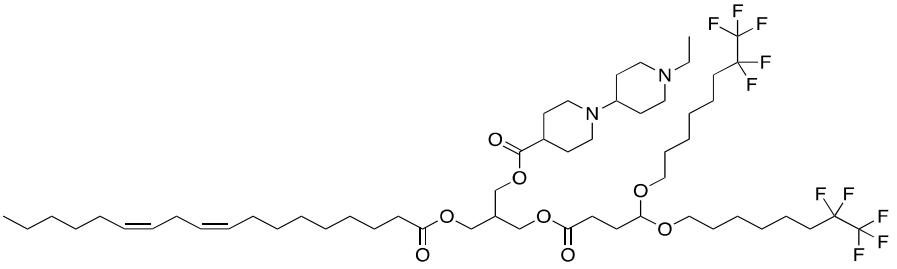
Example 130

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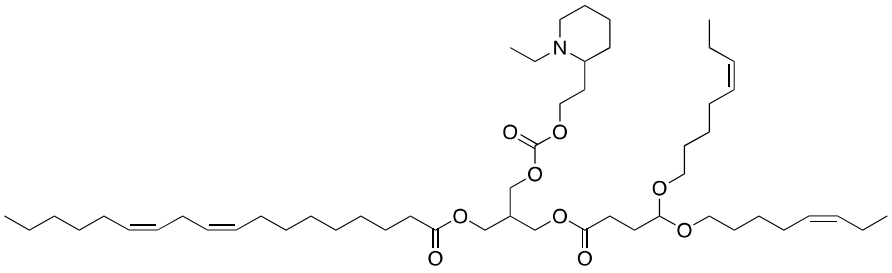
Example 131

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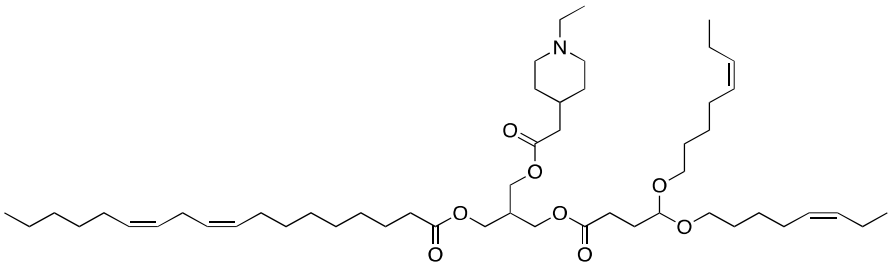
Example 132

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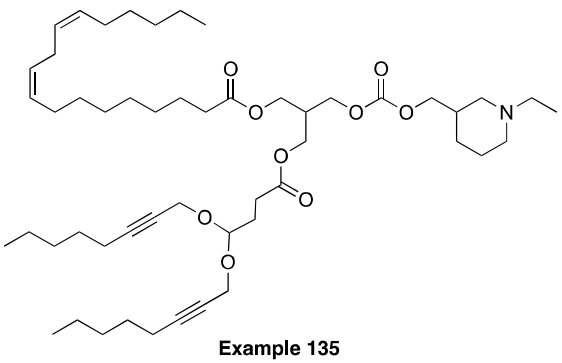
Example 133

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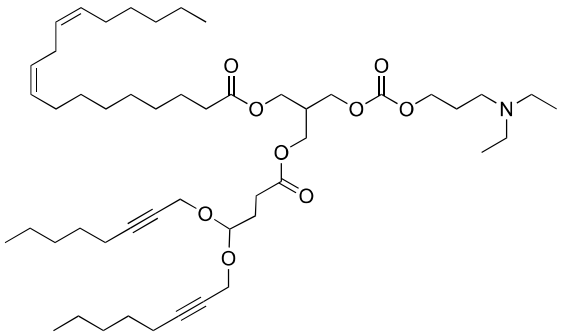
Example 134

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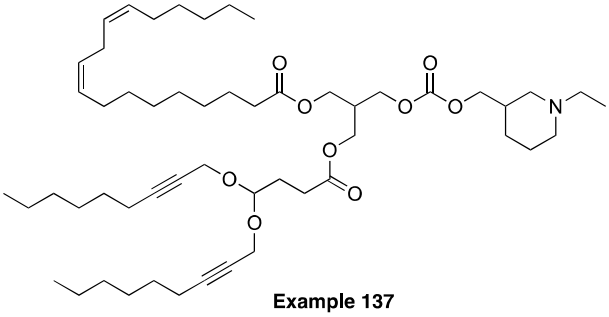
Example 135

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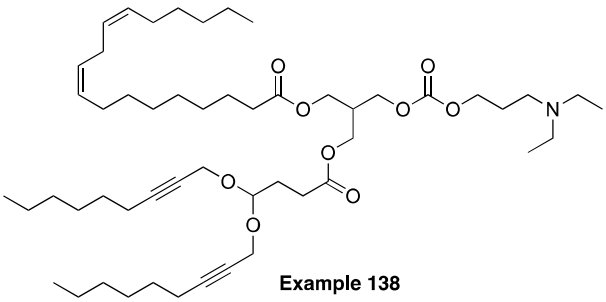
Example 136

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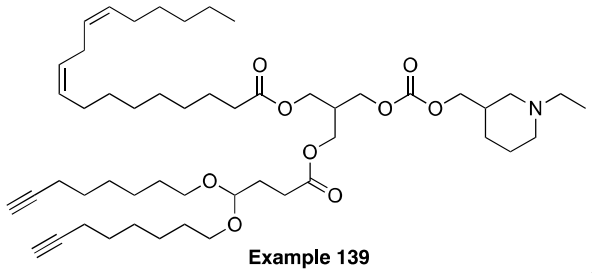
Example 137

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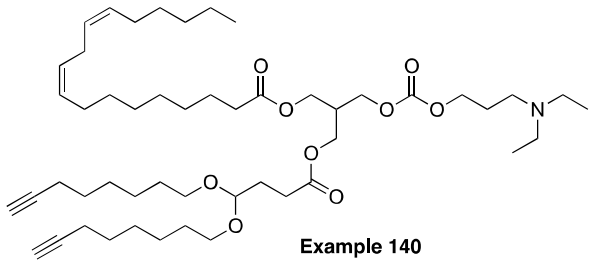
Example 138

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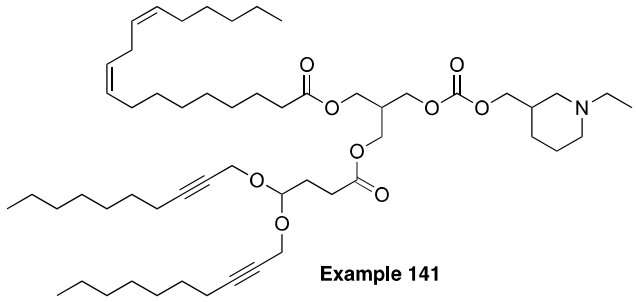
Example 139

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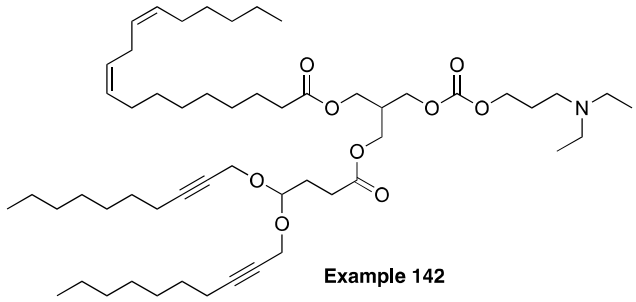
Example 140

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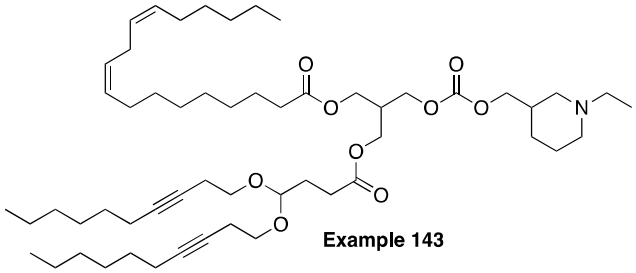
Example 141

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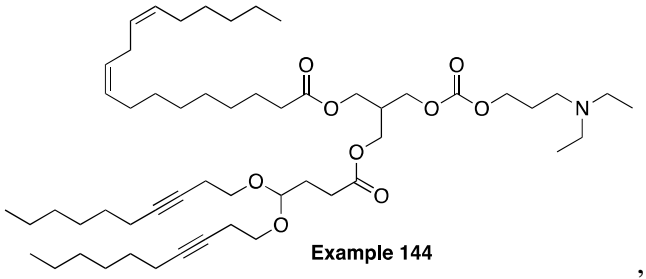
Example 142

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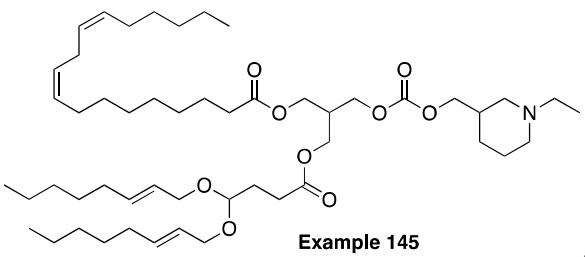


Example 143

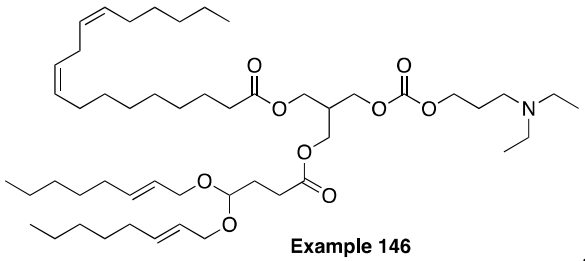
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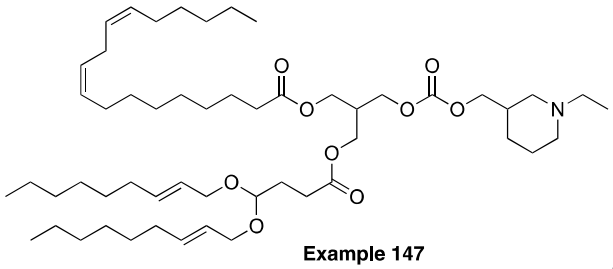
Example 144 ,



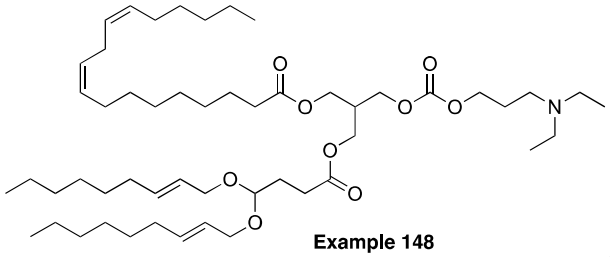
Example 145 ,



Example 146 ,

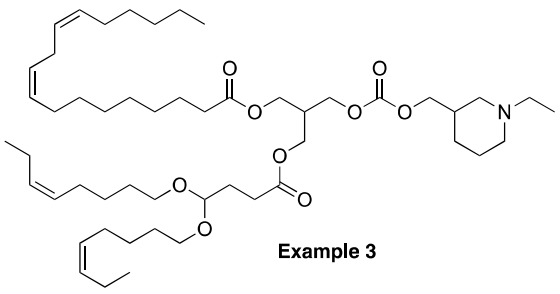


Example 147 ,

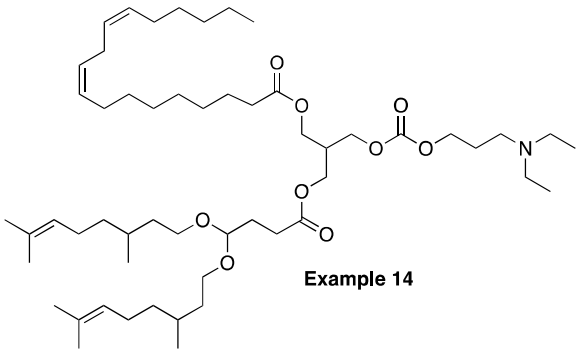


Example 148 .

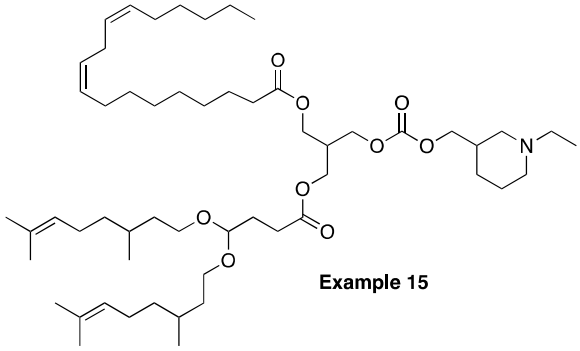
11. The compound of claim 1, wherein the compound is selected from the group consisting of:



Example 3 ,

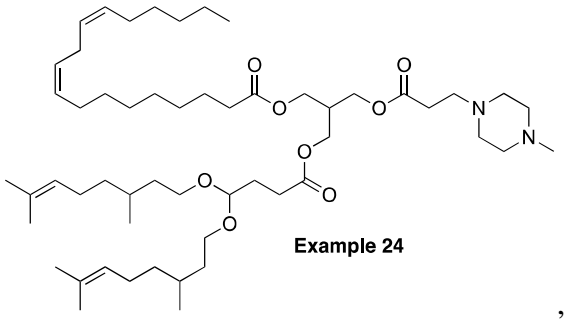


Example 14 ,



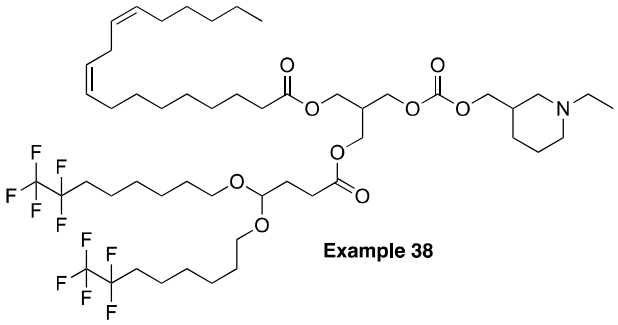
Example 15

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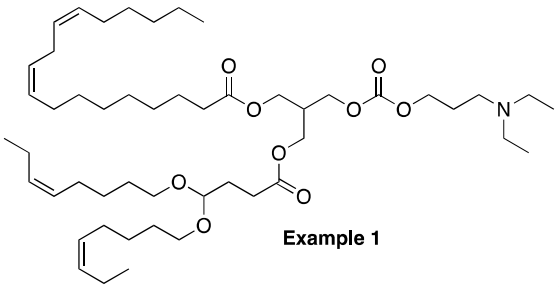
Example 24

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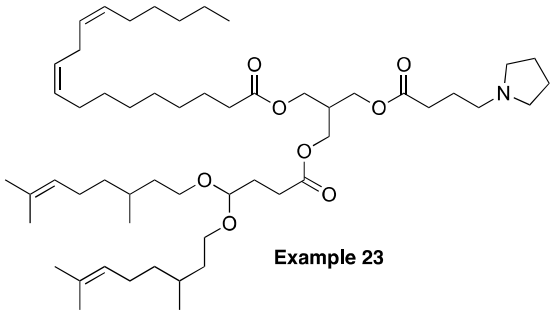
Example 38

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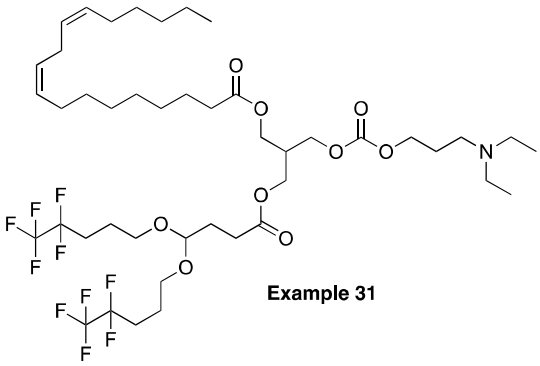
Example 1

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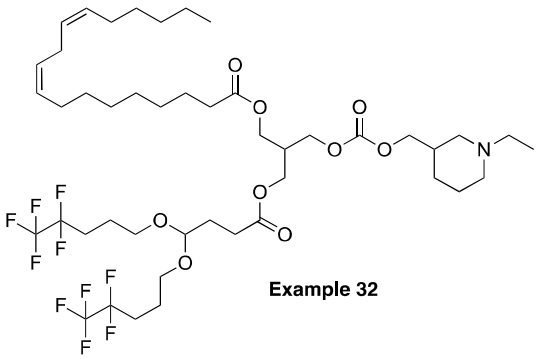
Example 23

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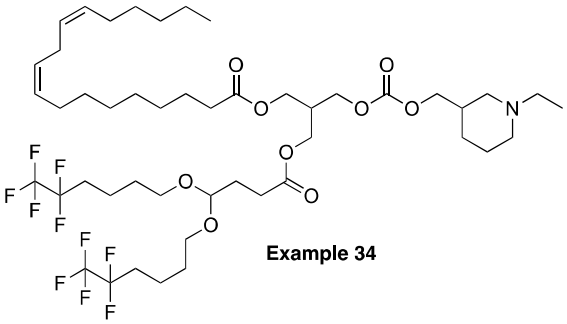
Example 31

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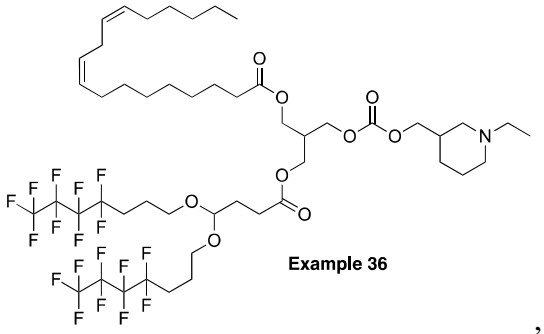
Example 32

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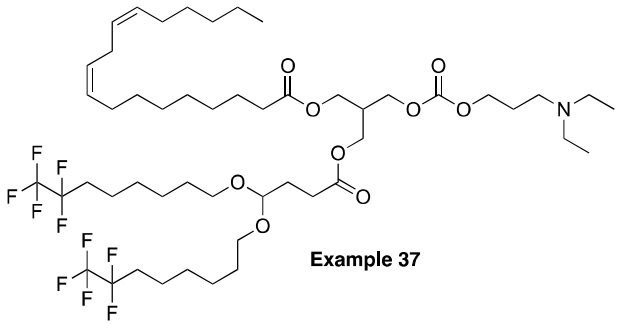


Example 34

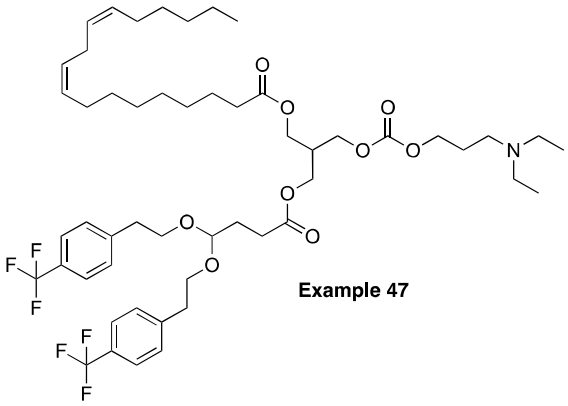
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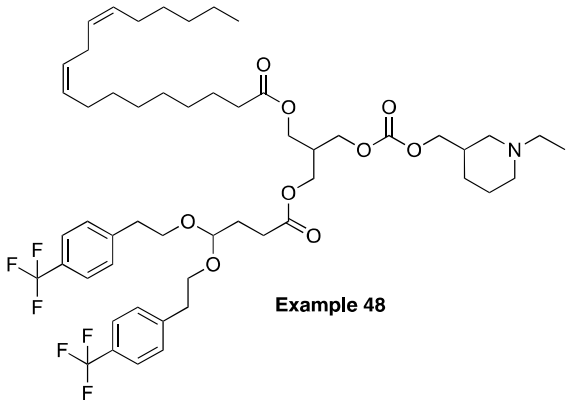
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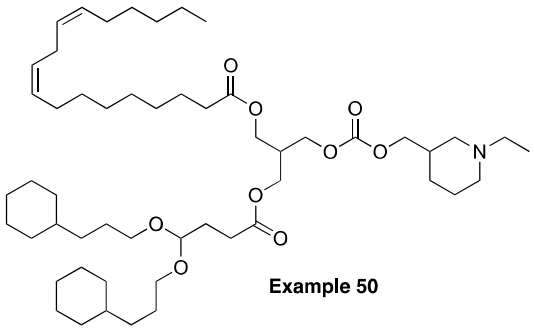
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and .

12. A lipid nanoparticle composition comprising:

An ionizable lipid that comprises a compound of any one of claims 1-11, optionally wherein the amount of the ionizable lipid is present in a range of about 35 to 65 mole percent, based on total moles;

a phospholipid, optionally wherein the phospholipid is DSPC or DMPC;

a polyethylene glycol-lipid;

a cholesterol; and optionally

a nucleic acid.

13. The lipid nanoparticle composition of claim 12, wherein the nucleic acid is siRNA, miRNA, mRNA, expressing DNA, anti-sense oligonucleotide, or immunostimulatory oligonucleotide.

14. The lipid nanoparticle composition of claim 12, wherein the nucleic acid is guide RNA.

15. A method of delivering a nucleic acid to a subject in need thereof, comprising administering to the subject the lipid nanoparticle composition of any one of claims 12-14.