

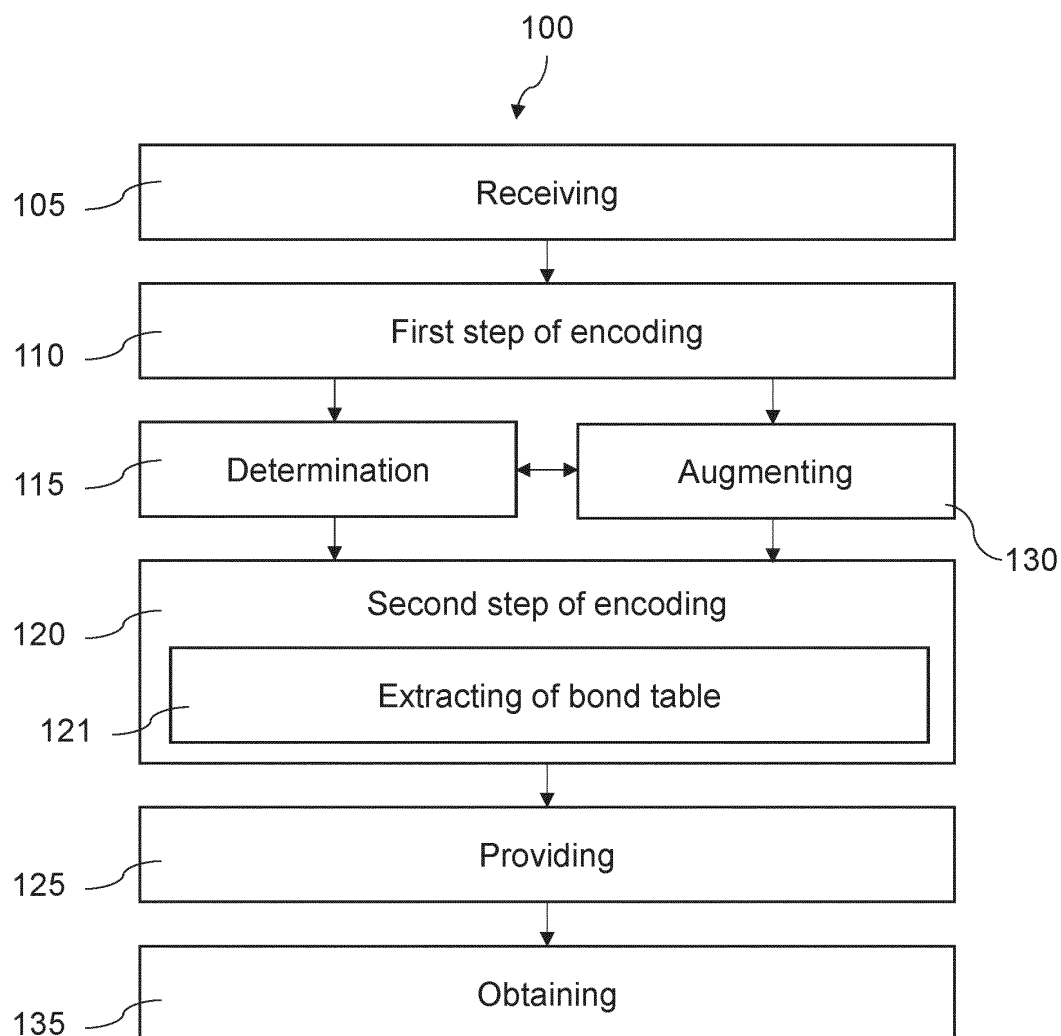


Figure 1

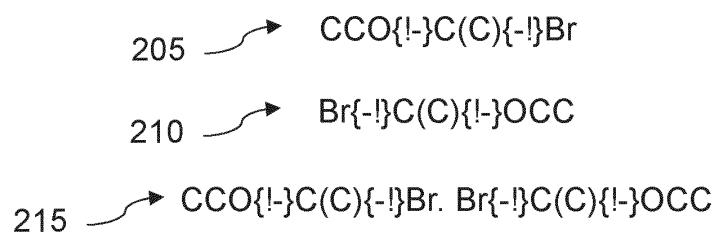


Figure 2

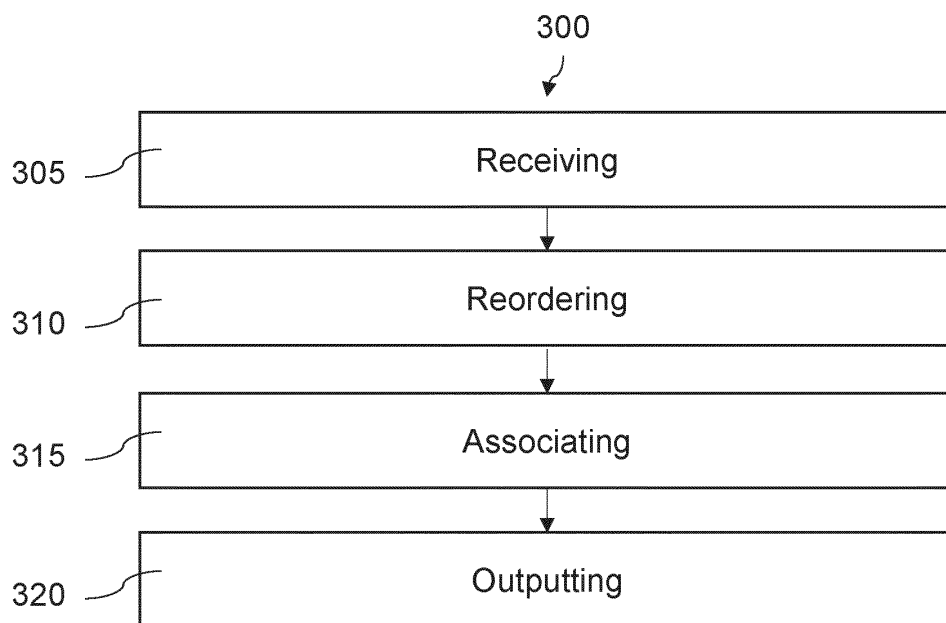


Figure 3

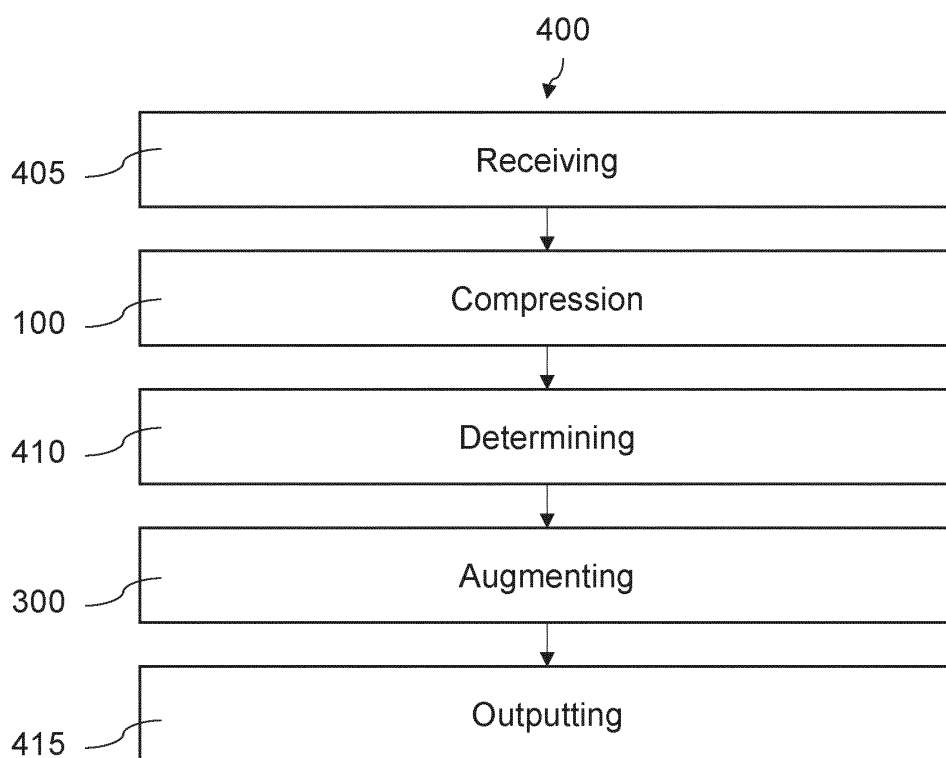


Figure 4

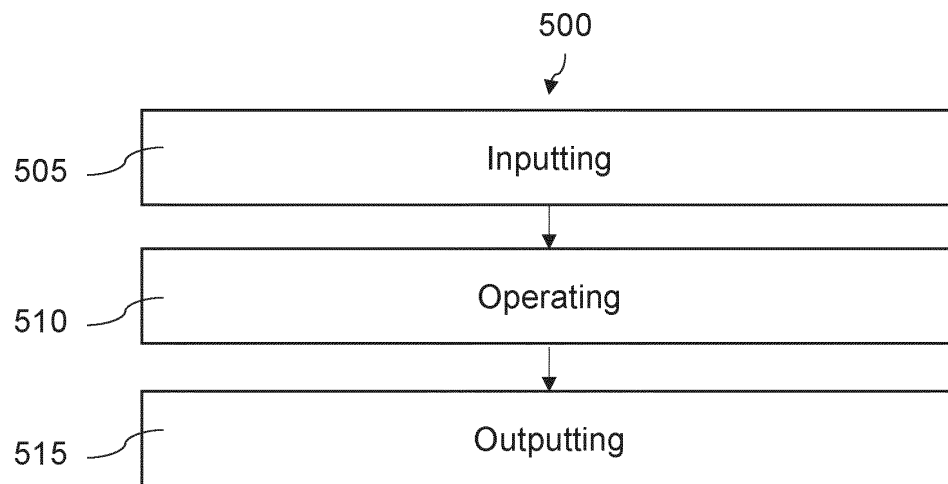


Figure 5

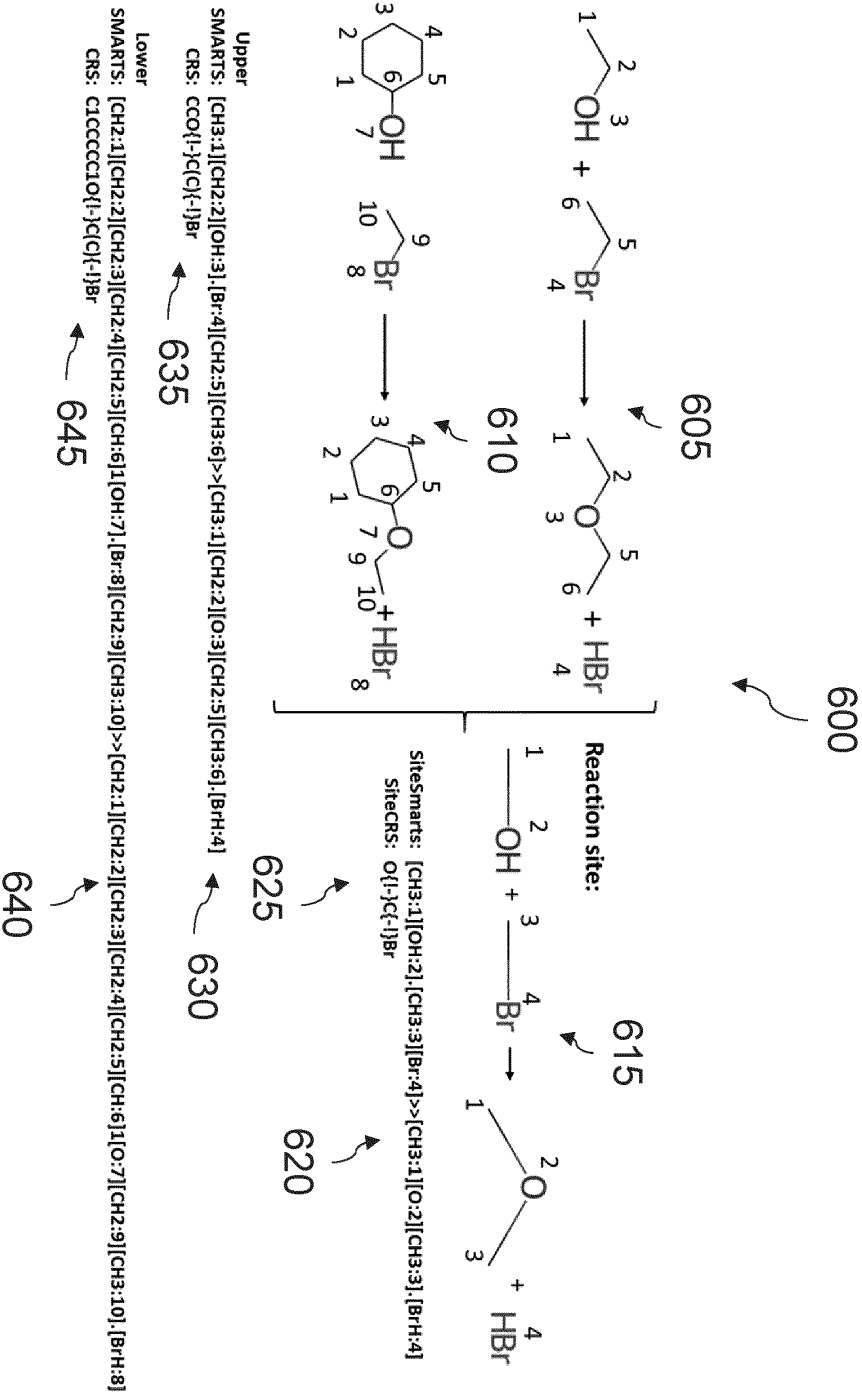


Figure 6

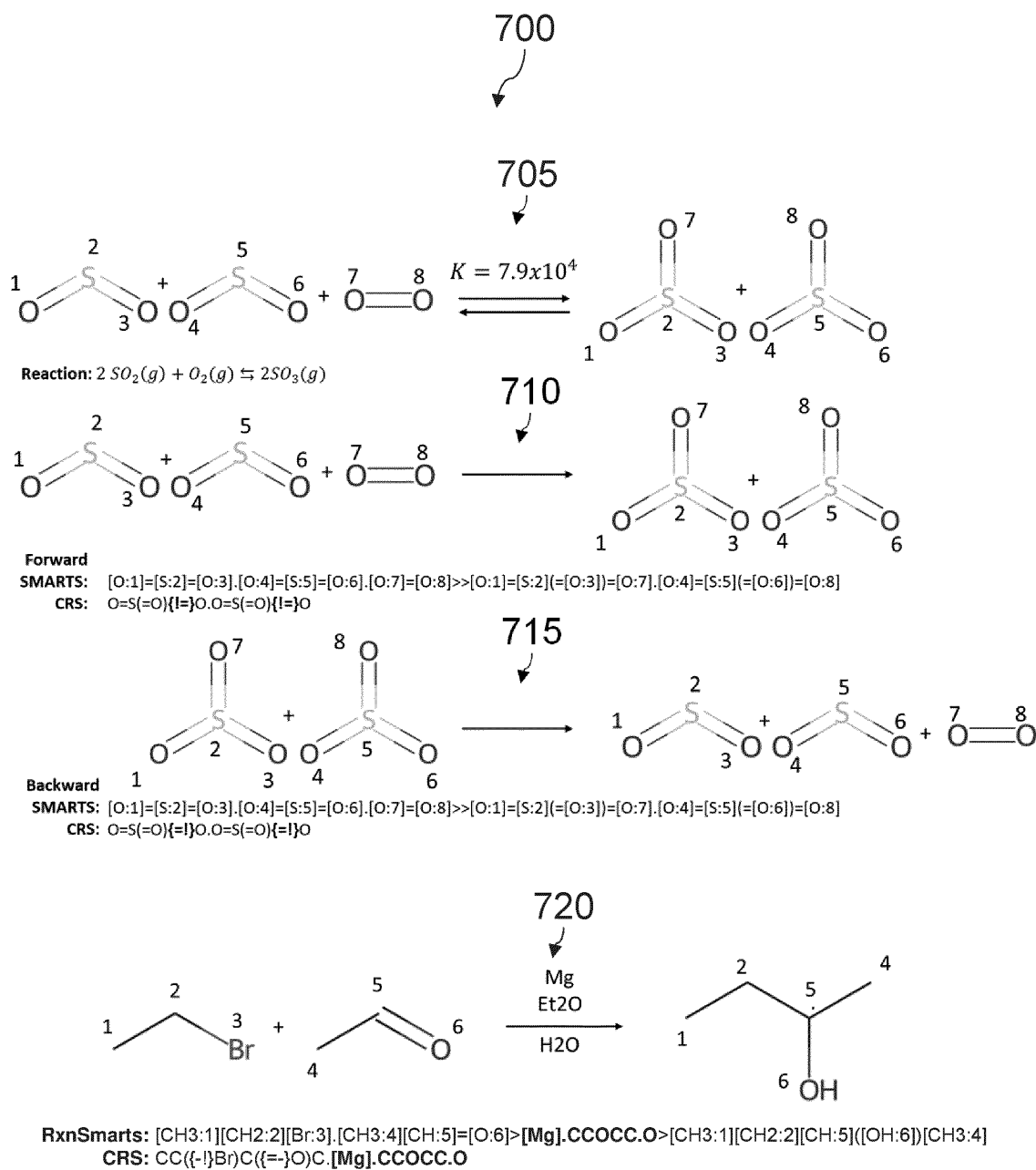


Figure 7

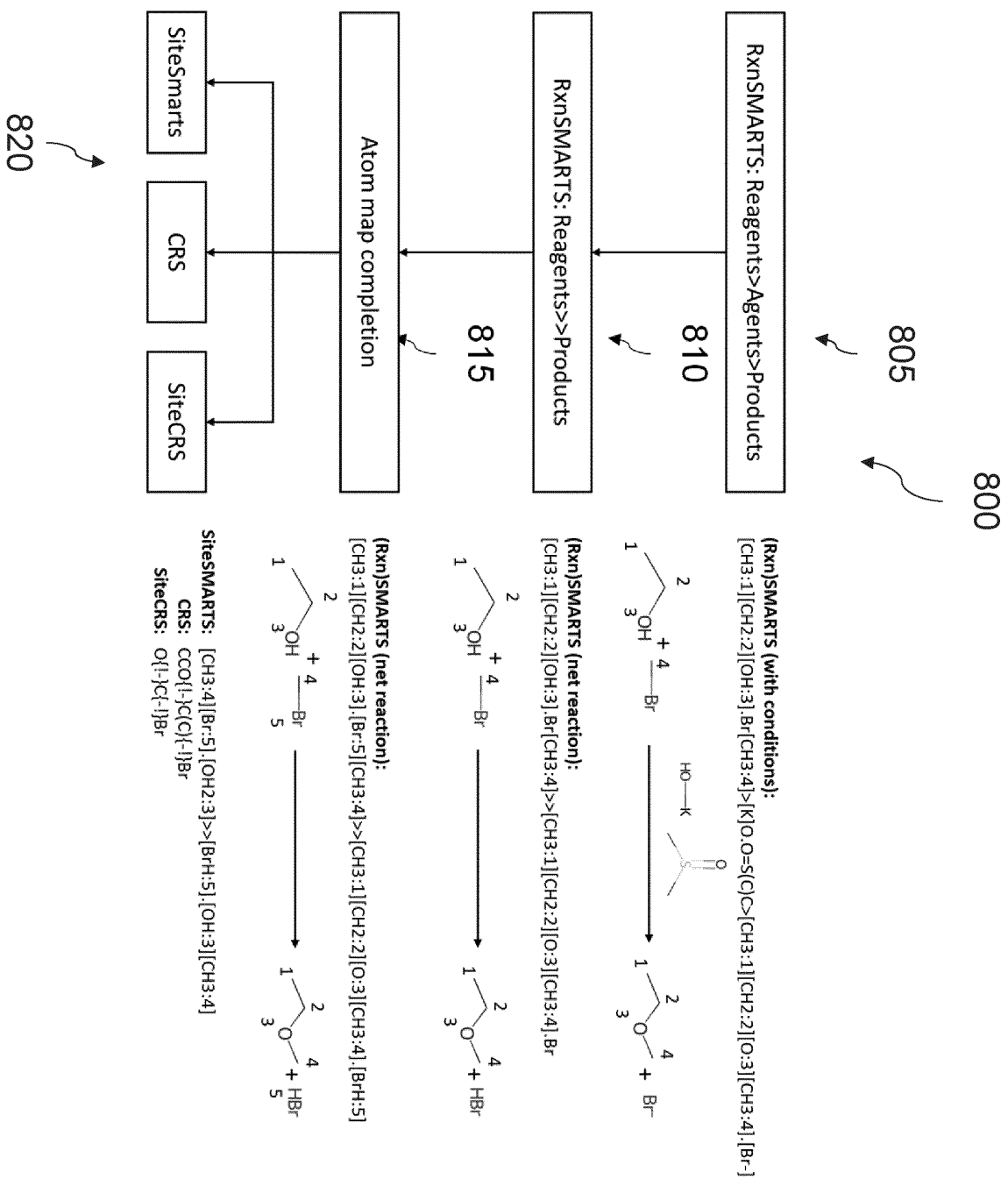


Figure 8

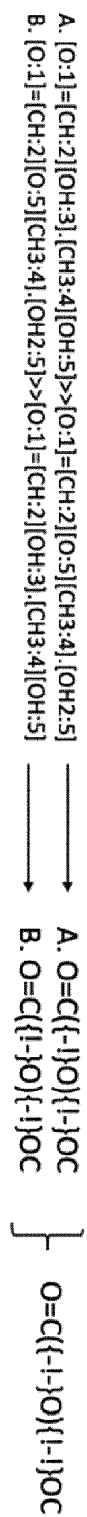
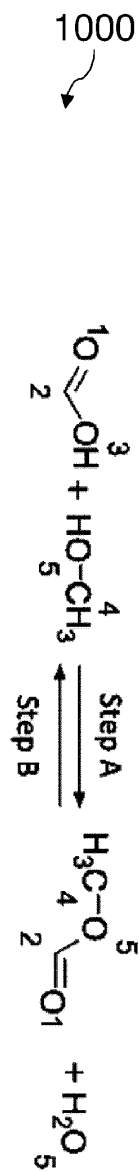
one-step
CRSequilibrium
CRS A+B

Figure 10

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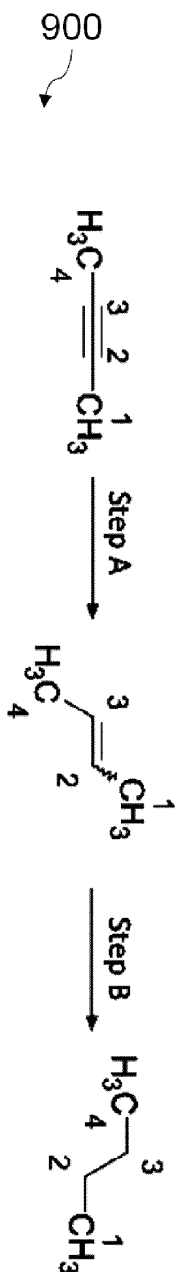
one-step
CRSmulti-step
CRS A+B

Figure 9

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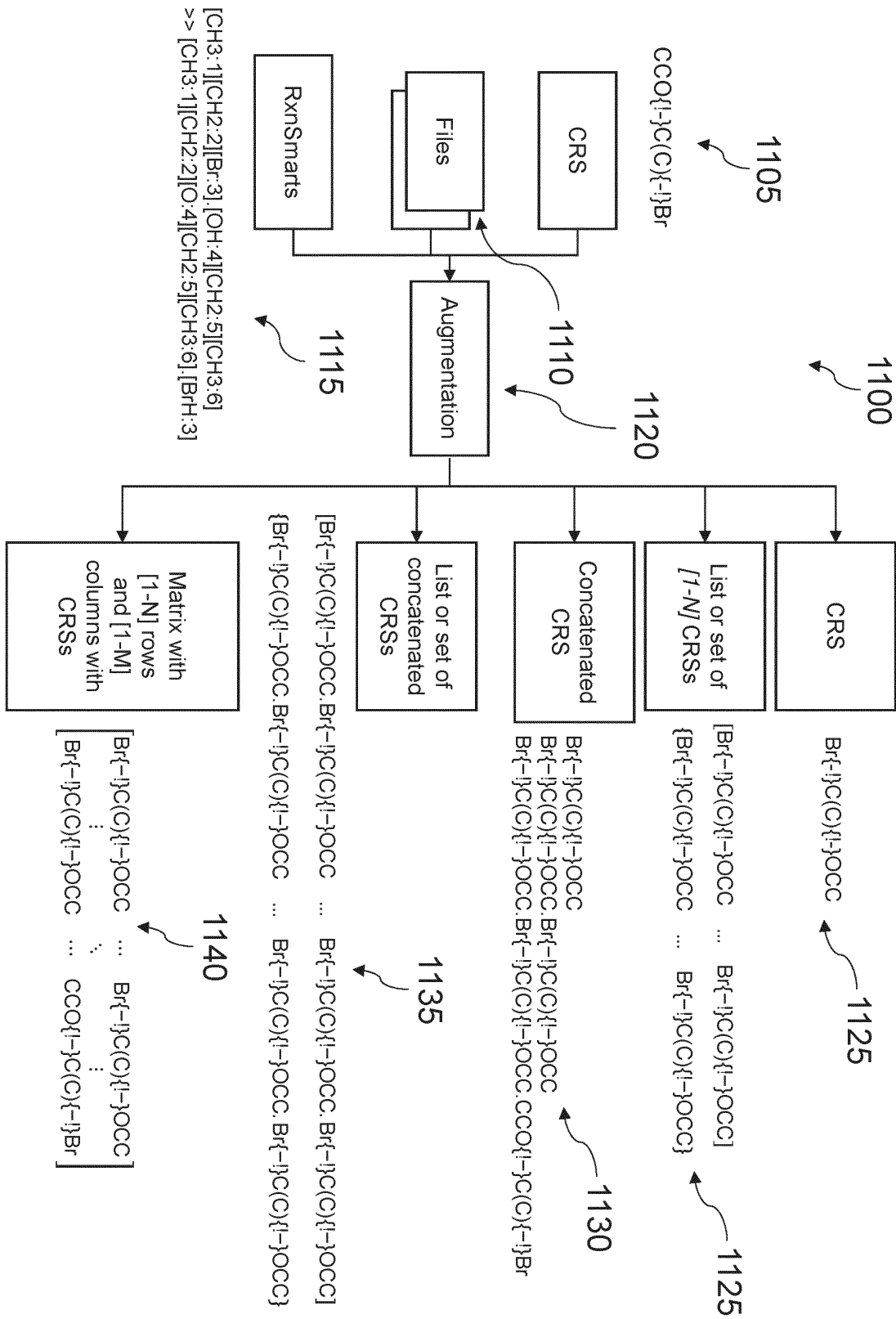


Figure 11

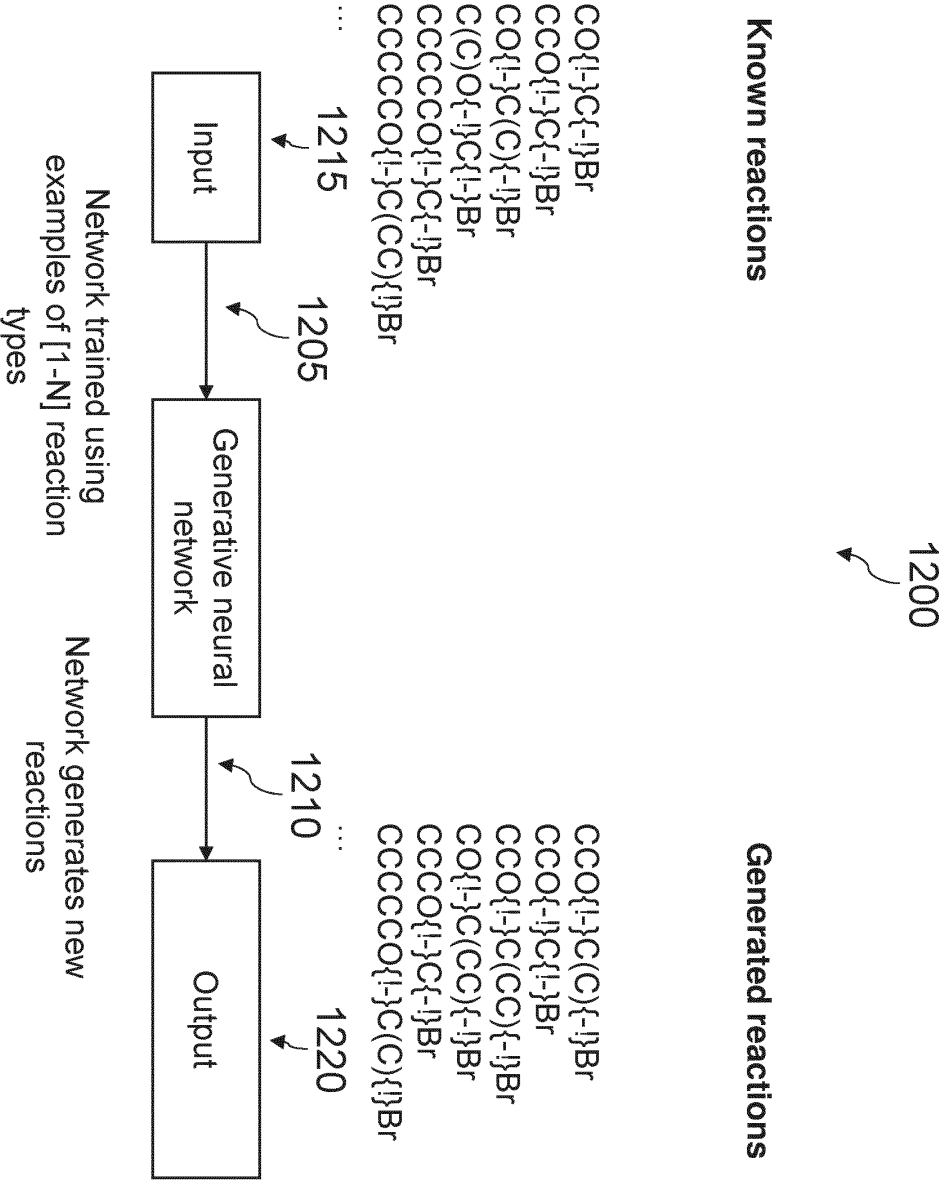


Figure 12

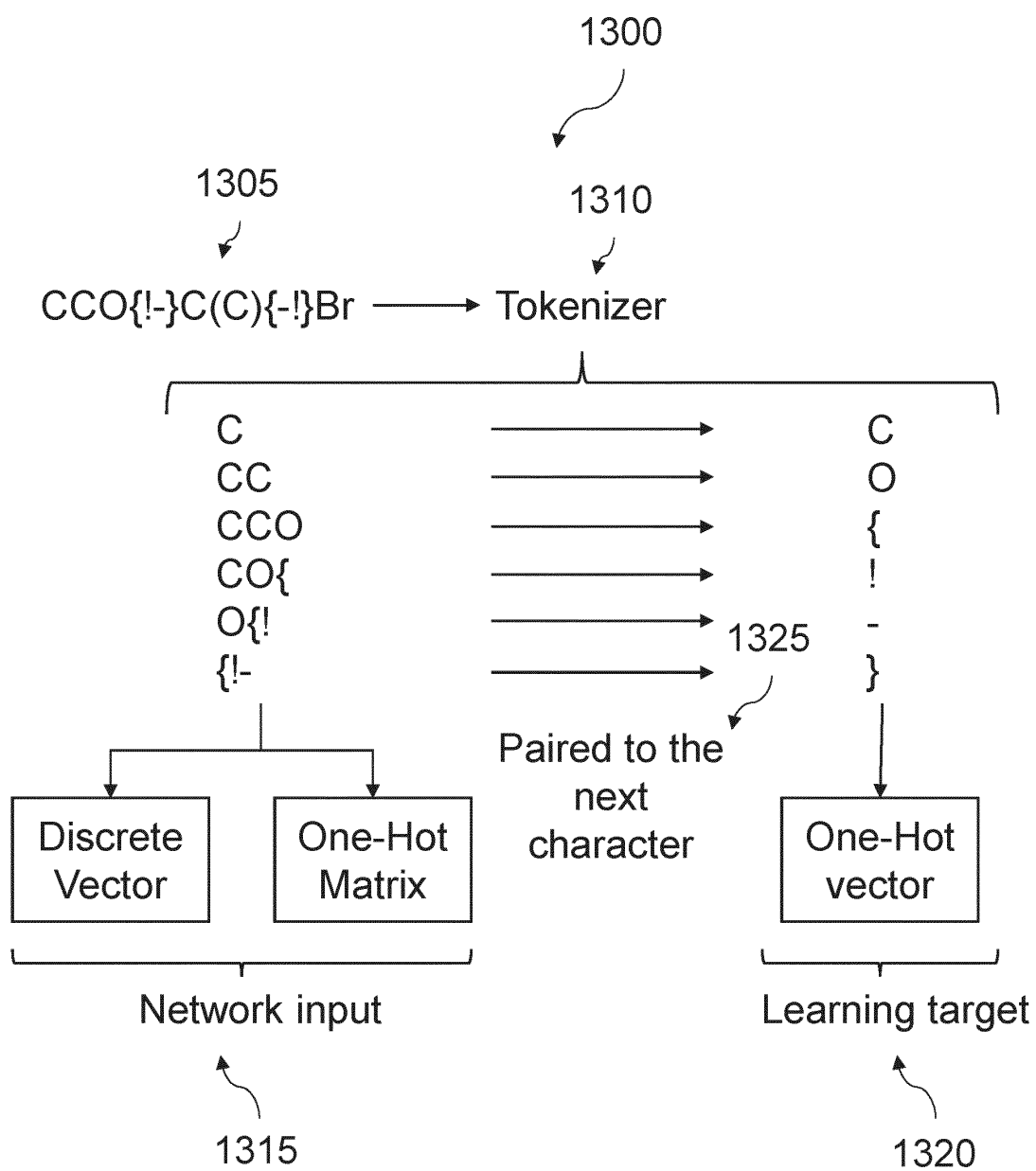


Figure 13

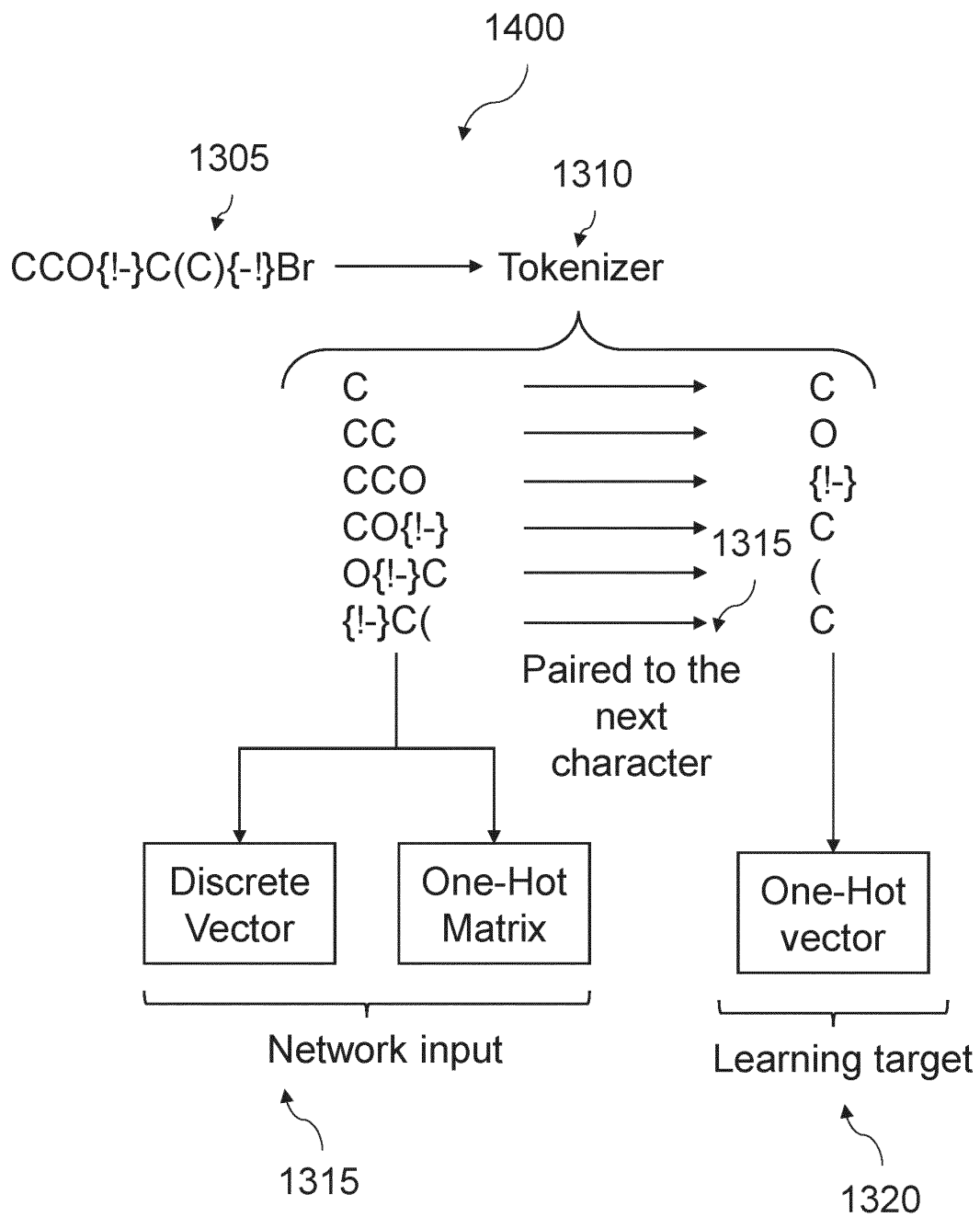


Figure 14

1500



SiteCRS	Description	Number	Density
Br{!-}c{-!}I	Aromatic substitution iodine to bromine	1073	15.2%
Br{!-}C{-!}I	Aliphatic substitution iodine to bromine	1108	15.7%
O{!-}c{-!}I	Aromatic substitution iodine to hydroxy	579	8.2%
Cl{!-}c{-!}I	Aromatic substitution iodine to chlorine	1098	15.6%
Cl{!-}C{-!}I	Aliphatic substitution iodine to chlorine	1126	16.0%
N{!-}c{-!}I	Aromatic substitution iodine to primary amine	105	1.5%
N{!-}C{-!}I	Aliphatic substitution iodine to primary amine	1181	16.7%
O{!-}C{-!}I	Aliphatic substitution iodine to hydroxy	783	11.1%

Figure 15

1600



SiteCRS	Description	Number	Density
C{#=-}C	Hydrogenation of alkyne to alkene to alkane	6255	50%
C{-=#}C	Dehydrogenation of alkane to alkene and alkane	6255	50%

Figure 16

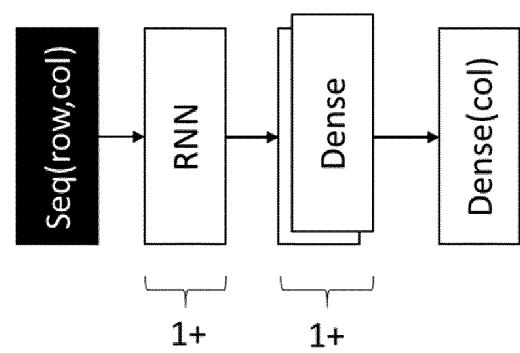


Figure 17

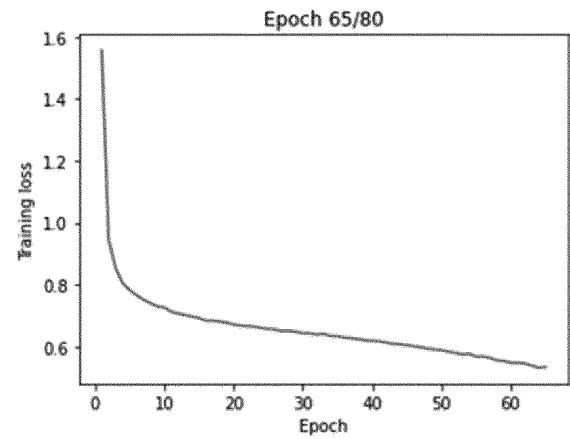


Figure 18

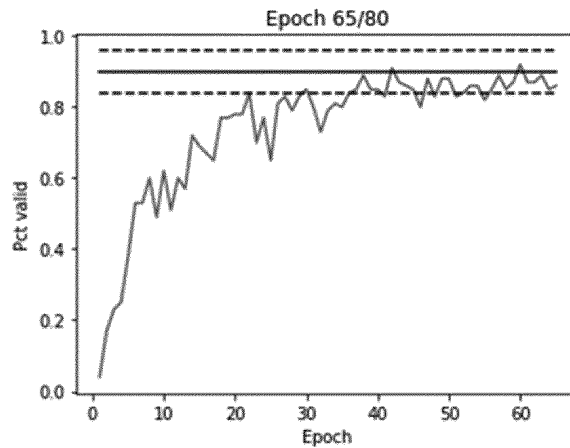


Figure 19

Rxn	Description	Valid chemistry	Input	180 run 1:	180 run 2:	180 run 3:	1800 run 1:	1800 run 2:	1800 run 3:
Cl(-)-C(-)-I)	Aliphatic iodine to chlorine substitution	Yes	1190	20	7	15	128	154	176
N(-)-C(-)-I)	Aliphatic iodine to amine substitution	Yes	1138	26	21	18	232	226	218
Br(-)-C(-)-I)	Aliphatic iodine to bromine substitution	Yes	1123	9	9	15	113	93	100
Br(-)-C(-)-I)	Aromatic iodine to bromine substitution	Yes	1093	12	6	11	120	111	104
N(-)-C(-)-I)	Aromatic iodine to amine substitution	Yes	1083	17	13	16	165	196	184
Cl(-)-C(-)-I)	Aromatic iodine to chlorine substitution	Yes	1082	20	19	13	144	156	149
O(-)-C(-)-I)	Aliphatic iodine to hydroxy substitution	Yes	744	6	9	5	60	59	38
O(-)-C(-)-I)	Aromatic iodine to hydroxy substitution	Yes	547	2	9	8	43	41	50
Cl(-)-I)	Dehalogenation of iodine.	Known.	0	2	1	0	7	6	3
N(-)-C(-)-I), Cl(-)-C(-)-I)	Substitution of I to Cl and I to N	No	0	1	1	1	3	1	1
Cl(-)-C(-)-I)	Substitution of I by a carbanion	Known.	0	1	0	0	0	3	4
N(-)-CC(-)-I)	Elimination-addition reaction	Possible, 2 step	0	0	1	0	2	1	1
O(-)-C(-)-I), N(-)-C(-)-I)	Aromatic I2 elimination and alkoxylation	Possible	0	0	1	0	0	0	0
Cl(-)-C(-)-I), N(-)-C(-)-I), n(-)-I)	Substitution of I to Cl and I to N	No	0	0	1	0	0	0	0
N(-)-C(-)-I), Cl(-)-I)	I to N substitution and ether formation	No	0	0	0	1	0	0	1
Br(-)-C(-)-I), O(-)-I)	I to Br substitution and hydroperoxide formation	Possible, 2 step	0	0	0	0	1	0	0
Cl(-)-CC(-)-I)	Elimination-addition reaction	Possible, 2 step	0	0	0	0	1	0	0
Br(-)-C(-)-I), Cl(-)-C(-)-I)	I-Cl and I-Br substitution.	Possible, one-pot	0	0	0	0	1	0	0
Cl(-)-N(-)-I)	I-Cl substitution on amine nitrogen.	Known.	0	0	0	0	1	0	2
Br(-)-C(-)-I), N(-)-C(-)-I)	Aromatic I-Br and I-N substitution.	Possible, 2 step	0	0	0	0	1	0	1
F(-)-C(-)-I)	Aromatic I-F substitution	Possible	0	0	0	0	1	0	0
O(-)-N(-)-I)	Hydroxyamino formation from iodo-amine	No	0	0	0	0	1	0	0
Br(-)-C(-)-I), N(-)-C(-)-I)	Aliphatic I-Br and aromatic I-N substitution	Possible, 2 step	0	0	0	0	1	0	0
Br(-)-C(-)-I), O(-)-C(-)-I)	Aliphatic ether formation and aromatic I-Br substitution	Possible, 2 step	0	0	0	0	1	0	0
Br(-)-CC(-)-I)	Elimination-addition reaction	Possible, 2 step	0	0	0	0	1	1	1
N(-)-O(-)-I)	#	No	0	0	0	0	1	1	0
O(-)-C(-)-I), Cl(-)-C(-)-I)	Aliphatic ether formation and aromatic I-Cl substitution	Possible, 2 step	0	0	0	0	1	0	0
Br(-)-N(-)-I)	Bromoalkaneamine formation	No	0	0	0	0	1	0	0
O(-)-C(-)-I), N(-)-C(-)-I)	#	No	0	0	0	0	1	0	0
N(-)-n(-)-I)	N-iodopyrrole to N-aminopyrrole substitution.	Known.	0	0	0	0	1	1	0
N(-)-C(-)-I), N(-)-O	I to amine substitution and hydroxyamino formation.	Possible, 2 step	0	0	0	0	1	0	0
Cl(-)-CC(-)-I)	#	No	0	0	0	0	1	0	1
I(-)-Cl(-)-I), CCOC(=O)C1	Cyclization by substitution.	Possible	0	0	0	0	1	0	0
N(-)-C(-)-I), C(-)-N(-)-I)	Double aromatic I-N substitution (ortho).	Possible	0	0	0	0	1	0	0
N(-)-C(-)-I), C(-)-I)	Aromatic I-N substitution and alkoxylation.	Possible, 2 step	0	0	0	0	1	0	0

Figure 20

$\text{Cl}(\text{I})\text{-}\text{CCl}(\text{I})$	#	No	0	0	0	0	1	0	1
$\text{I}(\text{I})\text{Cl}(\text{I})\text{-}\text{CCCCCCCC1}$	Cyclization by substitution.	Possible	0	0	0	0	1	0	0
$\text{N}(\text{I})\text{-}\text{C}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{N}(\text{I})\text{-}\text{I})$	Double aromatic I-N substitution (ortho).	Possible	0	0	0	0	1	0	0
$\text{N}(\text{I})\text{-}\text{C}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{O}$	Aromatic I-N substitution and alkoxylation.	Possible, 2 step	0	0	0	0	1	0	0
$\text{O}(\text{I})$	I-O bond breaking.	No	0	0	0	0	1	0	0
$\text{Br}(\text{I})\text{-}\text{OC}(\text{I})$	#	No	0	0	0	0	1	0	0
$\text{Cl}(\text{I})\text{-}\text{I})\text{N}(\text{I})\text{-}\text{Cl}(\text{I})$	I-N substitution and dehalogenation.	Possible, 2 step	0	0	0	0	1	0	0
$\text{N}(\text{I})\text{-}\text{I})\text{CC}(\text{I})\text{-}\text{O}(\text{I})\text{-}\text{I})\text{-}\text{I})$	Aliphatic ether formation plus I-N substitution.	Unknown	0	0	0	0	1	0	0
$\text{Cl}(\text{I})\text{-}\text{N}$	Amination of alkanes.	Known.	0	0	0	0	0	0	0
$\text{N}(\text{I})\text{-}\text{C}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{O}$	I-N substitution and oxidative alkoxylation	Possible, 2 step	0	0	0	0	2	0	0
$\text{N}(\text{I})\text{-}\text{I})\text{CC}(\text{I})\text{-}\text{O}(\text{I})\text{-}\text{I})\text{-}\text{I})\text{C}(\text{I})$	^	No	0	0	0	0	1	0	0
$\text{O}(\text{I})\text{-}\text{I})\text{CC}(\text{I})\text{-}\text{O}(\text{I})\text{-}\text{I})$	Elimination-ether formation.	Possible, 2-3 step	0	0	0	0	1	0	0
$\text{O}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{O}$	Oxidation alkoxylation plus williamson-type ether formation.	Possible, 2 step	0	0	0	0	1	0	0
$\text{O}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{Cl}\text{N}(\text{I})\text{-}\text{C}(\text{I})$	#	No	0	0	0	0	0	1	0
$\text{Cl}(\text{I})\text{-}\text{C}(\text{I})$	Aromatic alkylation.	Known.	0	0	0	0	0	1	1
$\text{Br}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{Br}(\text{I})\text{-}\text{C}(\text{I})$	Aromatic and aliphatic I-Br substitution.	Known.	0	0	0	0	0	1	0
$\text{Cl}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{N}(\text{I})\text{-}\text{C}(\text{I})$	Aromatic I-N and I-Cl substitution.	Unknown	0	0	0	0	0	1	0
$\text{Cl}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{O}$	Carbanion I-C substitution and aromatic alkoxylation.	Possible, 2 step	0	0	0	0	0	1	0
$\text{O}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{-}\text{I})$	Aliphatic I-Cl and I-O substitution	Unknown	0	0	0	0	0	1	0
$\text{Br}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{N}(\text{I})\text{-}\text{C}(\text{I})$	Aliphatic I-Br and I-N substitution	Unknown	0	0	0	0	0	2	0
$\text{Cl}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})$	Double aliphatic I-Cl substitution	Known.	0	0	0	0	0	1	0
$\text{O}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{O}$	I-alkoxy substitution and aromatic alkoxylation	Possible, 2 step	0	0	0	0	0	1	1
$\text{Br}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{N}(\text{I})\text{-}\text{C}(\text{I})$	Aromatic I-Br and aliphatic I-N substitution	Known.	0	0	0	0	0	1	1
$\text{O}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})$	Aromatic I-Cl and I-alkoxy substitution	Unknown	0	0	0	0	0	1	0
$\text{O}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{C}(\text{I})$	Aromatic I-N substitution and Williamson ether formation	Known.	0	0	0	0	0	1	0
$\text{O}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{N}(\text{I})\text{-}\text{C}(\text{I})$	Aromatic I-Br substitution and oxidative alkane alkoxylation	Possible, 2 step	0	0	0	0	0	1	0
$\text{Br}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{O}$	Elimination to alkene plus aminohydroxylation	Known.	0	0	0	0	0	1	0
$\text{N}(\text{I})\text{-}\text{I})\text{CC}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{O}$	Aliphatic + aromatic to I-Br substitutions.	Known.	0	0	0	0	0	1	1
$\text{Cl}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})$	Double aliphatic to I-Br substitutions.	Known.	0	0	0	0	0	1	0
$\text{Br}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{Br}(\text{I})\text{-}\text{I})\text{C}(\text{I})$	Aliphatic I-Br substitution plus oxidative alkoxylation	Possible, 2 step	0	0	0	0	0	1	0
$\text{O}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{Br}(\text{I})\text{-}\text{I})$	Double aliphatic I-Amine substitution.	Known.	0	0	0	0	0	1	0
$\text{N}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{N}(\text{I})\text{-}\text{C}(\text{I})$	Aliphatic I-Cl and S-I to S-Cl substitution.	No	0	0	0	0	0	1	0
$\text{Cl}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{S}(\text{I})$	Iodoamine to hydrazine substitution	Unknown	0	0	0	0	0	0	1
$\text{N}(\text{I})\text{-}\text{I})\text{N}(\text{I})$	Three-site substitutions with 3 groups	No	0	0	0	0	0	0	1
$\text{O}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{N}(\text{I})\text{-}\text{I})\text{C}(\text{I})$	N-iodopyrrole to N-bromopyrrole substitution	Known.	0	0	0	0	0	0	1
$\text{Br}(\text{I})\text{-}\text{I})\text{N}(\text{I})$	Aromatic + aliphatic I-N substitution	Known.	0	0	0	0	0	0	1
$\text{N}(\text{I})\text{-}\text{I})\text{C}(\text{I})\text{-}\text{I})\text{N}(\text{I})\text{-}\text{I})\text{C}(\text{I})$									

Figure 21

N(-)-C(-)-I), N(-)-C(-)-I)	Aromatic + aliphatic I-N substitution	Known.	0	0	0	0	0	0	1
N(-)-C(-)-I), C(-)-C(-)-I)	Aromatic I-Cl + aliphatic I-N substitution	Possible, 2 step	0	0	0	0	0	0	2
C(-)-C(-)-I), C(-)-I)O	Aromatic I-Cl + oxidative ether formation	No	0	0	0	0	0	0	1
N(-)-CN(-)-I)	#	No	0	0	0	0	0	0	1
C(-)-O, N(-)-C(-)-I)	Aliphatic I-N substitution + oxidative alkane alkoxylation	Possible, 2 step	0	0	0	0	0	0	1
Br(-)-C(-)-I), Br(-)-C(-)-I)	Double aromatic I-Br substitution	Known.	0	0	0	0	0	0	1
C(-)-C(-)-I), N(-)-C(-)-I)	Aliphatic I-Cl and I-N substitution	Unlikely	0	0	0	0	0	0	1
invalid			0	63	81	77	752	730	751

Figure 22

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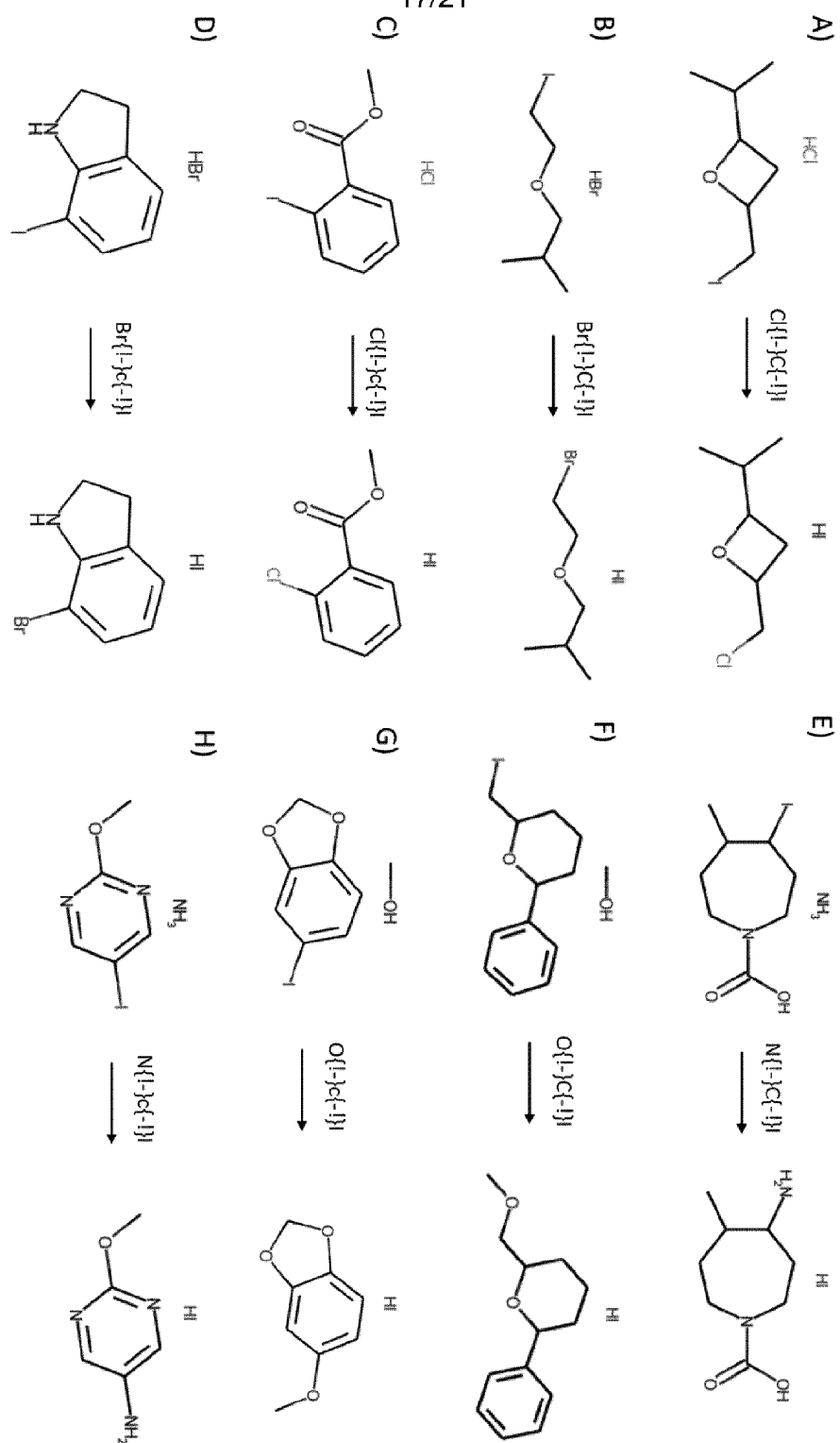


Figure 23

SUBSTITUTE SHEET (RULE 26)

Rxn	Description	Input	Valid chemistry	180 run 1:	180 run 2:	180 run 3:	1800 run 1:	1800 run 2:	1800 run 3:
C(=#)C	Hydrogenation alkyne > alkene > alkane	6255	Yes	76	71	77	794	792	741
C(-=#)C	Dehydrogenation alkane > alkene > alkyne	6255	Yes	87	87	86	849	832	860
C(=#)C.C(-=#)C	Mixed dehydrogenation and hydrogenation	0	No	0	0	0	2	3	2
C(-=#)C	Equilibrium: Alkane <> alkene	0	Yes	0	0	1	2	3	3
C(=#)C.C(=#)C	Two site hydrogenation	0	Yes	0	0	0	2	1	2
C(=#)C	Equilibrium: Alkyne <> alkene	0	Yes	0	0	0	0	2	0
C(-=#)C.C(-=#)C	Two site dehydrogenation	0	Yes	0	0	0	0	0	1
invalid	Invalid reactions	0	No	17	22	16	151	167	191

Figure 24

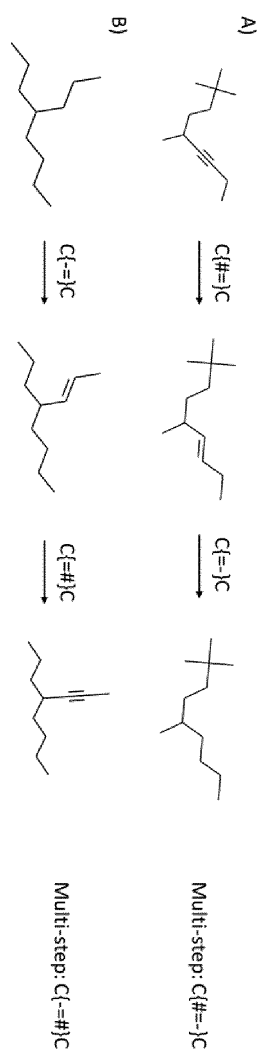


Figure 25

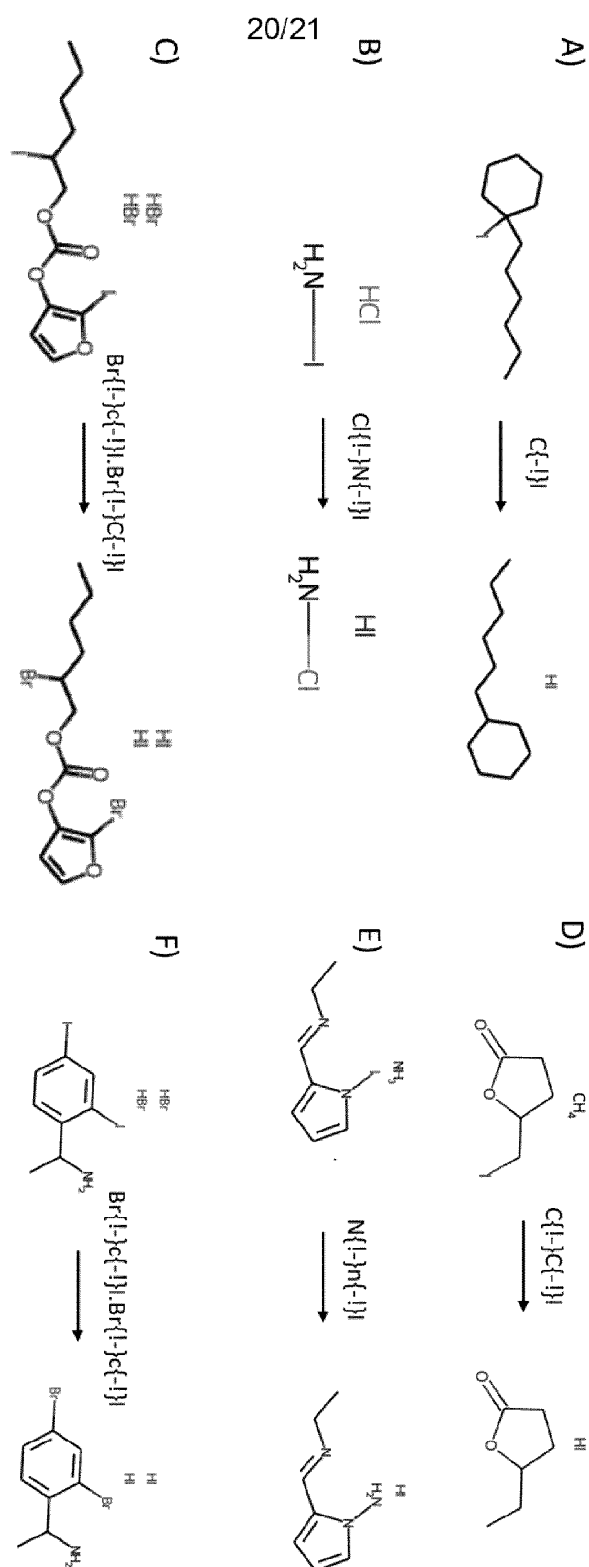


Figure 26
SUBSTITUTE SHEET (RULE 26)

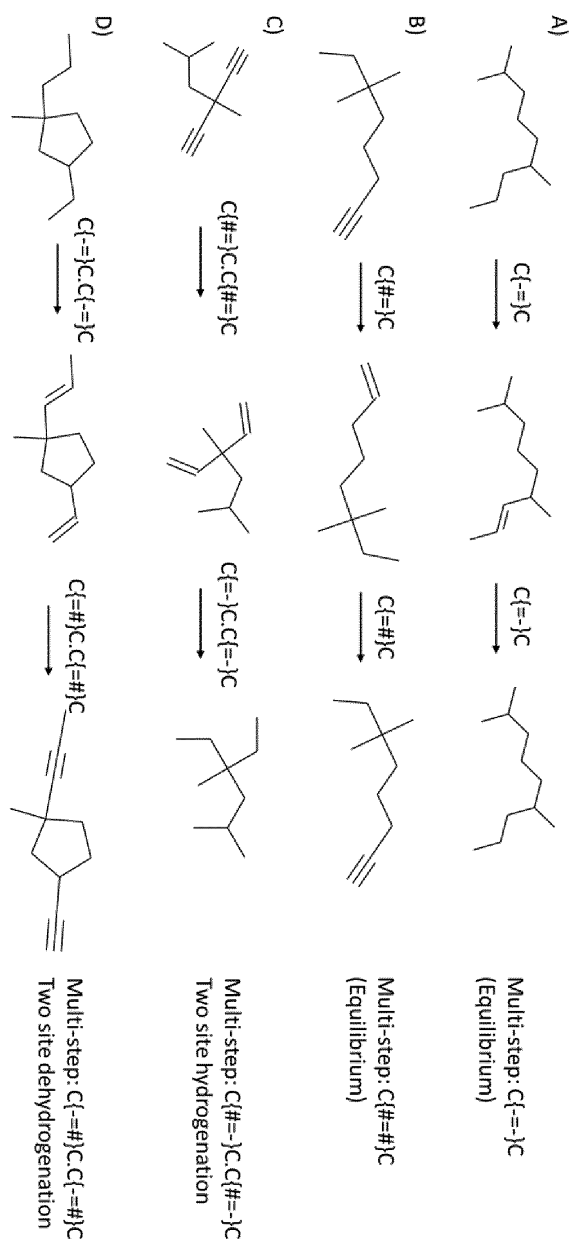


Figure 27