Electronic Supplementary Material (ESI) for Catalysis Science & Technology.

Supplementary Information

Computational Design of Transition Metal Catalysts for Hydrodefluorination of Trifluoromethylarenes using Hydrosilane

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Table S1 Relative free energies of **TS1′** and **TS1′′** with respect to $[NiL_2]_2$(COD) (in kcal/mol).

L	ΔG (kcal/mol)	
	TS1′	TS1′′
CAAC0	45.08	53.53
CAAC1	52.15	44.27
CAAC2	45.64	47.11
CBA0	28.74	39.49
CBA1	36.45	31.33
CBA2	21.69	25.55
CSO0	57.23	53.04
CSO1	52.19	51.00
NHC0	39.04	45.86
NHC1	35.17	45.95
NHC2	N/A	33.54
NHC3	32.59	45.80
NHC4	35.57	48.96
NHC5	59.81	34.49
NHC6	34.58	45.64
NHC7	49.01	47.90
NHC8	61.23	43.66
NHC9	49.20	45.34
P0	50.79	44.97
P1	47.07	47.24
P2	51.88	42.25
P3	55.44	45.48
P4	49.25	49.13
P5	52.48	49.78
P6	55.83	49.66
P7	56.69	52.64
aNHC0	38.52	41.57
aNHC1	35.79	39.11
aNHC2	32.81	35.82
aNHC3	28.21	41.30

Table S2 Relative free energies of **TS2′** and $\boldsymbol{TS2''}$ with respect to $[NiL_2]_2$(COD) (in kcal/mol).

L	ΔG (kcal/mol)	
	TS2′	TS2″
CAAC0	14.50	31.47
CAAC1	23.53	25.50
CAAC2	13.83	27.61
CBA0	-8.13	1.59
CBA1	-10.86	-8.76
CBA2	-11.15	-10.12
CSO0	26.59	28.52
CSO1	25.35	27.15
NHC0	-1.82	21.26
NHC1	1.55	20.35
NHC2	12.08	-12.33
NHC3	-0.81	2.56
NHC4	7.84	11.31
NHC5	31.56	2.36
NHC6	-1.15	14.16
NHC7	14.94	20.10
NHC8	34.98	19.54
NHC9	17.57	20.09
P0	38.96	24.70
P1	26.38	19.78
P2	40.41	15.90
P3	33.61	15.74
P4	40.29	23.71
P5	39.50	27.04
P6	52.62	36.99
P7	55.56	34.88
aNHC0	6.14	20.89
aNHC1	4.22	17.64
aNHC2	-5.84	11.65
aNHC3	-6.50	16.02

Table S3 Relative free energies (ΔG_{ref}) of NiL_2 with respect to $[NiL_2]_2$(COD) (in kcal/mol) according to the chemical equation: (1/2) $[NiL_2]_2$(COD) → NiL_2 + (1/2)COD.

L	ΔG_{ref}
CAAC0	8.92
CAAC1	-2.39
CAAC2	7.32
CBA0	4.21
CBA1	4.13
CBA2	-2.65
CSO0	10.93
CSO1	5.44
NHC0	6.41
NHC1	6.18
NHC2	-14.87
NHC3	-2.39
NHC4	4.29
NHC5	-10.04
NHC6	7.04
NHC7	6.99
NHC8	8.34
NHC9	5.92
P0	12.12
P1	12.95
P2	10.80
P3	9.95
P4	17.62
P5	14.85
P6	12.61
P7	12.42
aNHC0	5.43
aNHC1	-12.71
aNHC2	0.87
aNHC3	3.91

Table S4 Relative free energies (in kcal/mol) of intermediates and transition states in the Ni-catalyzed hydrodefluorination of trifluoromethylarene with $SiMe_2Ph$-H without CsF, using $[NiL_2]_2$(COD) as the reference state.

L	**INT2**	**TS1**	**INT3**	**INT4**	**TS2**	**INT5**	**INT6**	**TS3**
CAAC0	6.64	45.08	-15.23	-15.93	14.50	-34.17	-31.32	-6.89
CAAC1	11.58	44.27	-0.54	-13.94	23.53	-28.55	-22.37	-9.75
CAAC2	7.72	45.64	-14.01	-17.91	13.83	-33.89	-21.80	-8.70
CBA0	-2.13	28.74	-29.32	-30.44	-8.13	-40.62	-44.46	-11.53
CBA1	1.12	31.33	-29.55	-35.60	-10.86	-43.95	-43.58	-10.72
CBA2	-1.59	21.69	-31.93	-35.82	-11.15	-46.99	-43.53	-11.04
CSO0	11.62	53.04	3.49	-1.35	26.59	-22.11	-18.43	-4.06
CSO1	11.43	51.00	0.79	1.45	25.35	-20.01	-17.24	-3.58
NHC0	5.54	39.04	-16.56	-18.61	-1.82	-36.69	-34.82	-9.33
NHC1	2.09	35.17	-18.01	-23.02	1.55	-36.32	-36.90	-9.70
NHC2	6.33	33.54	-13.18	-24.79	-12.33	-39.83	-34.98	-13.22
NHC3	2.47	32.59	-15.19	-25.90	-0.81	-40.30	-34.37	-11.61
NHC4	5.85	35.57	-15.78	-18.07	7.84	-36.93	-32.60	-12.26
NHC5	10.18	34.49	-7.36	-29.99	2.36	-42.38	-29.53	-15.37
NHC6	0.81	34.58	-18.66	-24.12	-1.15	-38.54	-38.22	-10.53
NHC7	8.73	47.90	-6.91	-11.28	14.94	-29.26	-25.48	-6.25
NHC8	11.26	43.66	-2.05	-6.02	19.54	-25.18	-21.91	-6.02
NHC9	8.44	45.34	-4.57	-9.51	17.57	-25.74	-24.13	-6.62
P0	11.41	44.97	7.54	3.29	24.70	-16.56	-15.68	-2.34
P1	9.27	47.07	0.78	-3.66	19.78	-22.57	-19.84	-9.28
P2	10.12	42.25	4.09	-7.59	15.90	-23.52	-16.73	-7.41
P3	15.52	45.48	10.17	-1.44	15.74	-27.24	-15.51	-5.71
P4	11.93	49.13	7.70	10.80	23.71	-16.61	-11.92	-2.12
P5	15.51	49.78	8.64	7.61	27.04	-12.31	-13.73	-1.44
P6	15.59	49.66	30.09	26.90	36.99	3.13	-0.24*	1.69*
P7	15.95	52.64	22.43	28.18	34.88	0.81	-2.95*	2.85*
aNHC0	3.22	38.52	-17.51	-21.64	6.14	-36.59	-35.75	-9.97
aNHC1	1.13	35.79	-16.18	-27.37	4.22	-37.84	-33.68	-12.69
aNHC2	-1.20	32.81	-24.57	-27.75	-5.84	-41.36	-36.10	-10.65
aNHC3	-1.34	28.21	-27.47	-29.25	-6.50	-38.94	-38.61	-9.76

*The iterative imputer method was used to determine these relative energies.

Table S5 Relative free energies (in kcal/mol) of intermediates and transition states in the Ni-catalyzed hydrodefluorination of trifluoromethylarene with $SiMe_2Ph$-H without CsF, using NiL_2 as the reference state.

L	**INT2**	**TS1**	**INT3**	**INT4**	**TS2**	**INT5**	**INT6**	**TS3**
CAAC0	-2.28	36.16	-24.15	-24.85	-5.64	-43.09	-40.24	-15.81
CAAC1	13.96	46.65	1.84	-11.55	13.41	-26.17	-19.99	-7.37
CAAC2	0.40	38.32	-21.33	-25.23	6.51	-41.22	-29.13	-16.02
CBA0	-6.35	24.53	-33.53	-34.65	-12.34	-44.84	-48.67	-15.74
CBA1	-3.01	27.21	-33.68	-39.72	-14.98	-48.07	-47.71	-14.84
CBA2	1.06	24.33	-29.28	-33.17	-8.50	-44.35	-40.88	-8.39
CSO0	0.69	42.12	-7.43	-12.28	15.67	-33.04	-29.36	-14.99
CSO1	6.00	45.57	-4.64	-3.99	19.92	-25.45	-22.67	-9.01
NHC0	-0.87	32.63	-22.97	-25.02	-8.23	-43.11	-41.23	-15.74
NHC1	-4.09	28.99	-24.19	-29.21	-4.63	-42.51	-43.09	-15.88
NHC2	21.20	48.41	1.70	-9.92	2.55	-24.96	-20.11	1.65
NHC3	4.86	34.97	-12.81	-23.52	1.57	-37.92	-31.99	-9.23
NHC4	1.57	31.29	-20.06	-22.35	3.56	-41.22	-36.88	-16.54
NHC5	20.22	44.53	2.68	-19.95	12.40	-32.35	-19.49	-5.34
NHC6	-6.22	27.55	-25.70	-31.15	-8.18	-45.58	-45.25	-17.57
NHC7	1.74	40.91	-13.90	-18.27	7.96	-36.25	-32.47	-13.24
NHC8	2.91	35.31	-10.39	-14.36	11.20	-33.52	-30.25	-14.36
NHC9	2.53	39.42	-10.48	-15.42	11.66	-31.65	-30.05	-12.53
P0	-0.70	32.86	-4.57	-8.83	12.59	-28.67	-27.80	-14.45
P1	-3.68	34.12	-12.17	-16.61	6.83	-35.52	-32.79	-22.23
P2	-0.67	31.46	-6.71	-18.38	5.11	-34.32	-27.53	-18.20
P3	5.58	35.54	0.23	-11.38	5.80	-37.19	-25.45	-15.65
P4	-5.70	31.51	-9.92	-6.82	6.09	-34.23	-29.54	-19.74
P5	0.66	34.93	-6.21	-7.24	12.19	-27.16	-28.58	-16.29
P6	2.99	37.06	17.49	14.30	24.82	-9.48	-11.99*	-13.76*
P7	3.53	40.22	10.01	15.76	22.46	-11.61	-13.53*	-11.74*
aNHC0	-2.20	33.09	-22.94	-27.06	-2.66	-42.02	-41.18	-15.40
aNHC1	13.84	48.50	-3.47	-14.66	16.93	-25.13	-20.97	0.01
aNHC2	-2.06	31.94	-25.43	-28.61	-6.70	-42.23	-36.97	-11.52
aNHC3	-5.25	24.31	-31.38	-33.15	-10.40	-42.85	-42.52	-13.67

*The iterative imputer method was used to determine these relative energies.

Table S6 Relative free energies (in kcal/mol) of intermediates and transition states in the Ni-catalyzed hydrodefluorination of trifluoromethylarene with $SiMe_2Ph$-H in the presence of CsF, using $[NiL_2]_2$(COD) as the reference state.

L	**INT2**	**TS1**	**INT3**	**INT4**	**TS2**	**INT5**	**INT6**	**TS3**
CAAC0	6.64	42.90	-23.11	-20.15	-2.19	-32.66	-29.81	-5.38
CBA0	4.37	21.53	-41.61	-42.68	-16.36	-36.96	-42.95	-10.02
NHC0	5.54	34.46	-20.54	-22.98	-6.31	-35.18	-33.31	-7.82
NHC1	2.09	29.72	-26.55	-27.61	-8.68	-34.81	-35.39	-8.19
NHC3	2.47	28.35	-26.73	-29.70	2.22	-38.79	-32.86	-10.10
NHC9	8.44	45.79	-7.70	-8.61	14.60	-24.23	-22.62	-5.11
P1	9.27	41.56	-3.05	-5.95	16.04	-21.06	-18.33	-7.77
P4	11.93	41.48	3.55	-5.94	14.69	-15.10	-10.40	-0.61
P5	15.51	43.94	1.15	4.72	23.53	-10.80	-12.22	0.07
P7	15.95	39.60	-2.41	-0.14	23.73	2.32	-11.18*	-0.89*

*The iterative imputer method was used to determine these relative energies.

Table S7 Correlation (R^2) and mean absolute error (MAE) metrics of ΔG_{RRS}(**INT3**) and ΔG_{RRS}(**INT4**) as descriptor variables with ΔG_{RRS}(**TS1**) and ΔG_{RRS}(**TS3**) under $[NiL_2]_2$(COD) (REF1) and NiL_2 (REF2) reference states.

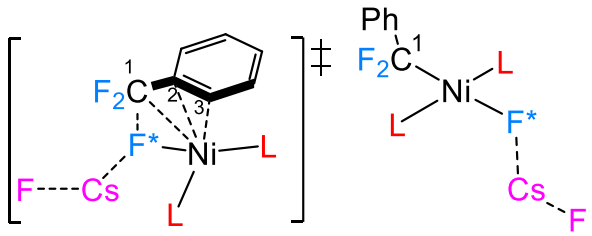
Descriptor:			**INT3**	**INT4**
$[NiL_2]_2$(COD) (REF1)	**TS1**	R^2	0.71	0.74
		MAE (kcal/mol)	3.49	3.18
	TS3	R^2	0.66	0.86
		MAE (kcal/mol)	2.04	1.28
NiL_2 (REF2) (L = carbene)	**TS1**	R^2	0.87	0.79
		MAE (kcal/mol)	2.43	3.00
	TS3	R^2	0.47	0.25
		MAE (kcal/mol)	3.09	3.76

Table S8 Correlations (R^2) between the energy descriptors and the electronic/steric variables obtained for $NiL(CO)_3$ (L = carbene and phosphine) using ωB97XD/def2-TZVP//ωB97XD/def2-SVP.

	$\Delta G_{RRS,[NiL_2]_2(COD)}$(INT4)	$\Delta G_{RRS,NiL_2}$(INT3)	ΔG_{ref}
[a]**Electronic variables**			
q_{Ni}	0.714	0.315	0.412
WBI_{avg}(C-O)	0.914	0.587	0.303
WBI_{max}(Ni-CO)	0.823	0.619	0.200
Steric variables			
[b]V_b	0.274	0.012	0.347
[c]B5	0.457	0.178	0.230
[c]B1	0.108	0.000	0.116

[a]The natural population analysis (NPA) charge on Ni (q_{Ni}) and Wiberg bond index (WBI) were obtained from natural bond orbital (NBO)[1] calculation of $NiL(CO)_3$.
[b]Buried volume[2] (V_b) was calculated with Ni as the center of the sphere with Ni-L as the z-axis. The sphere radius used to calculate buried volume is 3.5 Å.
[c]Sterimol steric parameters:[3-5] (i) B1 is the minimum distance perpendicular to the primary axis of Ni-L, indicating the shortest distance of a substituent on L and (ii) B5 represents the maximum distance perpendicular to the primary axis, signifying the farthest distance of a substituent on L. The Ni-L is chosen as the primary axis.

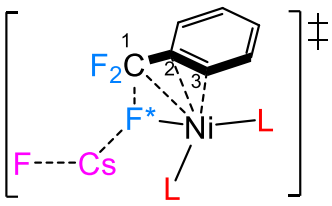
Table S9 Wiberg bond index (WBI) as a measure of bond covalency for the selected pair of atoms in the nickel catalyzed hydrodefluorination of trifluoromethylarene with $SiMe_2Ph$-H in the absence and the presence of CsF (L = NHC0).



TS1$_{CsF}$ **INT4$_{CsF}$**

WBI	**Ni-F***	**C1-F***	**Ni-C1**	**C1-C2**	**C2-C3**	**Ni-C2**	**Ni-C3**	**Cs-F***
$PhCF_3$	-	0.908	-	0.964	1.417	-	-	-
INT2	-	0.875	0.021	0.989	1.174	0.322	0.360	-
TS1	0.053	0.154	0.183	1.312	1.118	0.146	0.399	-
TS1$_{CsF}$	0.055	0.221	0.094	1.409	1.084	0.087	0.448	0.015
INT4	0.232	-	0.582	1.005	1.403	-	-	-
INT4$_{CsF}$	0.188	-	0.616	1.003	1.406	-	-	0.012

Table S10 NPA charge (q) on selected chemical species in the nickel catalyzed hydrodefluorination of trifluoromethylarene with $SiMe_2Ph$-H in the absence and the presence of CsF (L = NHC0).



$TS1_{CsF}$

q	**Ni**	**F***	**C1**	**C2**	**C3**	**Cs**
CsF	-	-	-			0.939
$PhCF_3$	-	-0.318	0.959	-0.146	-0.185	-
INT2	0.407	-0.346	0.971	-0.356	-0.415	-
TS1	0.632	-0.790	0.952	-0.377	-0.411	-
$TS1_{CsF}$	0.626	-0.764	0.934	-0.388	-0.452	0.969

Table S11 Calculated buried volume (V_b) and Wiberg bond index (WBI) of C-O for $NiL(CO)_3$ using ωB97XD/def2-TZVP//ωB97XD/def2-SVP.

L	V_b	WBI_{avg}(C-O)
CAAC0	0.291	2.064
CAAC1	0.358	2.068
CAAC2	0.312	2.061
CBA0	0.260	2.030
CBA1	0.307	2.039
CBA2	0.310	2.028
CSO0	0.206	2.092
CSO1	0.234	2.094
NHC0	0.263	2.061
NHC1	0.282	2.060
NHC2	0.357	2.067
NHC3	0.306	2.058
NHC4	0.319	2.064
NHC5	0.357	2.060
NHC6	0.282	2.058
NHC7	0.269	2.077
NHC8	0.330	2.089
NHC9	0.237	2.084
P0	0.180	2.099
P1	0.237	2.079
P2	0.308	2.073
P3	0.319	2.073
P4	0.299	2.090
P5	0.266	2.100
P6	0.244	2.142
P7	0.218	2.139
aNHC0	0.285	2.048
aNHC1	0.303	2.044
aNHC2	0.303	2.045
aNHC3	0.310	2.049

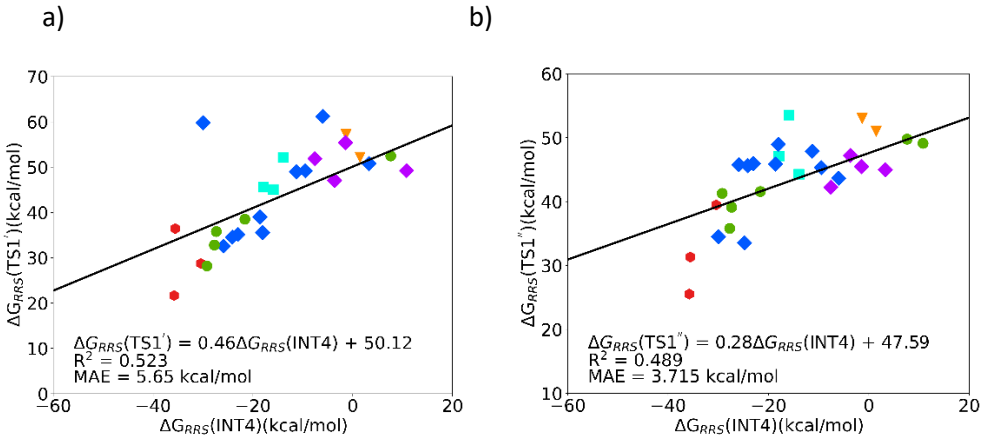


Fig. S1 (a) Linear free energy scaling relationship between ΔG_{RRS}(**INT4**) and $\Delta G_{RRS}(\boldsymbol{TS1'})$. (b) Linear free energy scaling relationship between ΔG_{RRS}(**INT4**) and $\Delta G_{RRS}(\boldsymbol{TS1''})$. $[NiL_2]_2COD$ is the reference state.

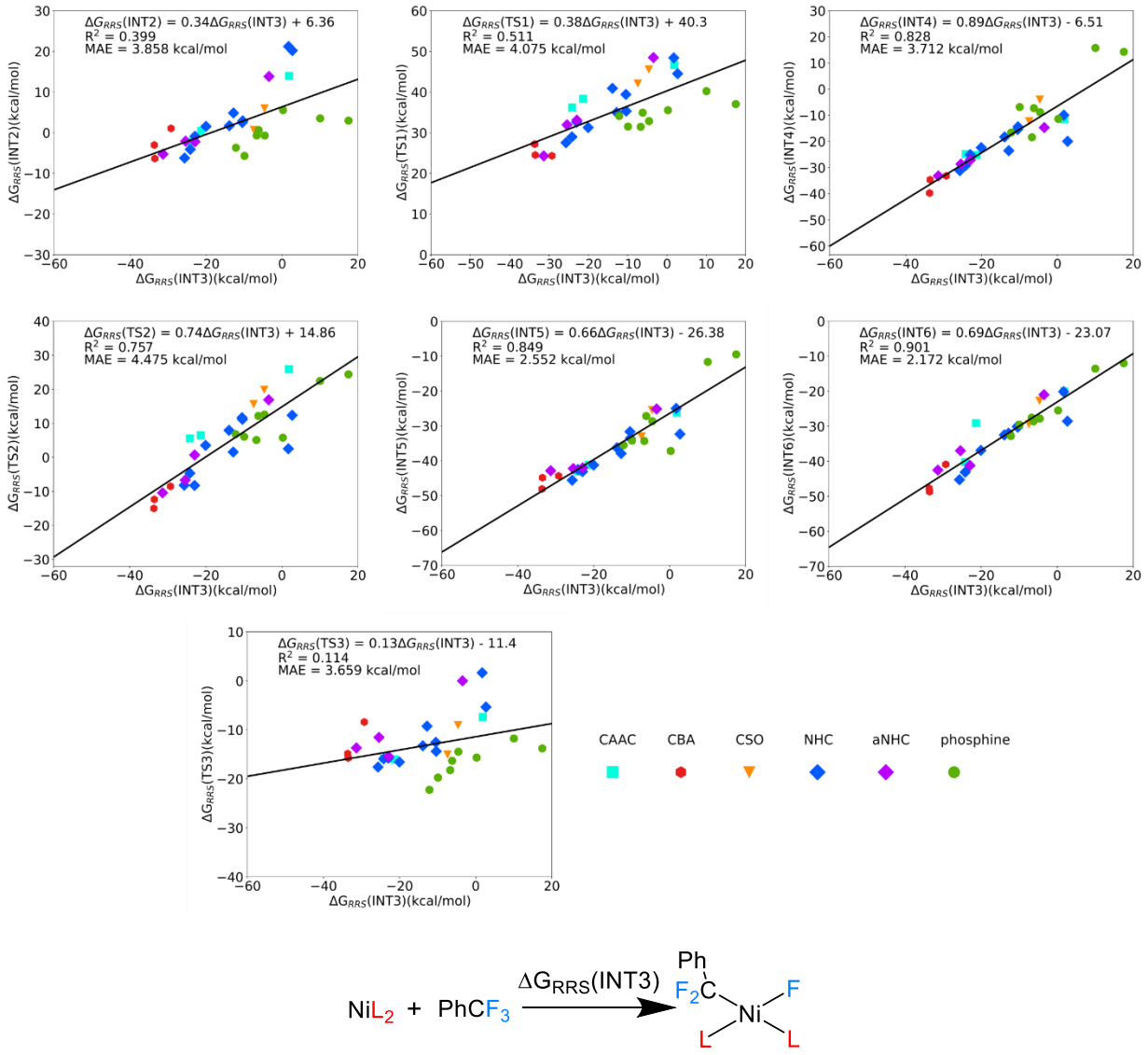


Fig. S2 Linear free energy scaling relationships between $\Delta G_{RRS,REF2}$(**INT3**) and relative energies of other intermediates and transition states in the absence of CsF, using NiL_2 (L = carbene and phosphine) as the reference state for nickel catalyzed hydrodefluorination of trifluoromethylarene.

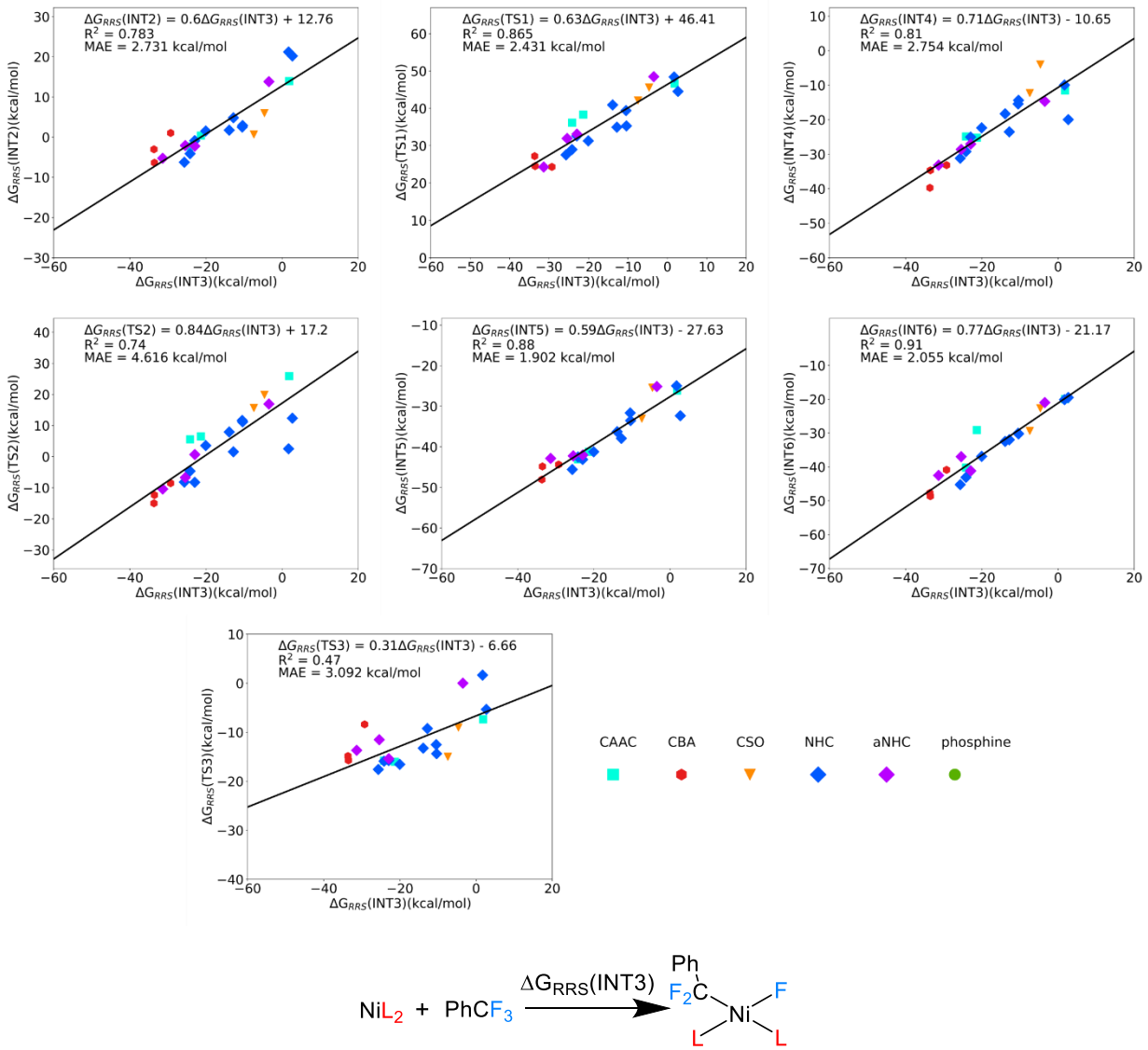


Fig. S3 Linear free energy scaling relationships between $\Delta G_{RRS,REF2}$(**INT3**) and relative energies of other intermediates and transition states in the absence of CsF using NiL_2 (L = carbene) as the reference state for nickel catalyzed hydrodefluorination of trifluoromethylarene.

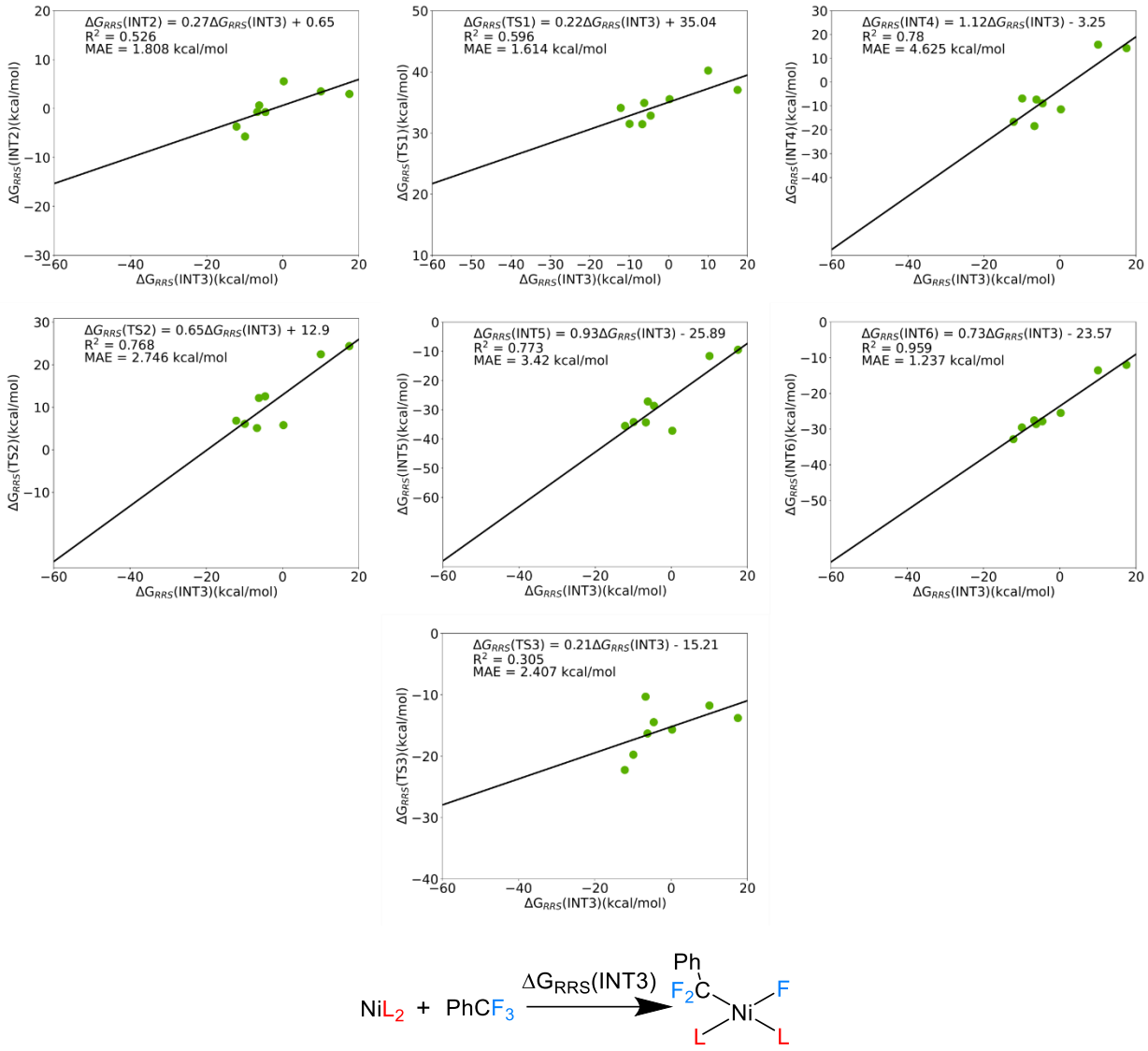


Fig. S4 Linear free energy scaling relationships between $\Delta G_{RRS,REF2}$(**INT3**) and relative energies of other intermediates and transition states in the absence of CsF under NiL_2 (L = phosphine) as the reference state for nickel catalyzed hydrodefluorination of trifluoromethylarene.

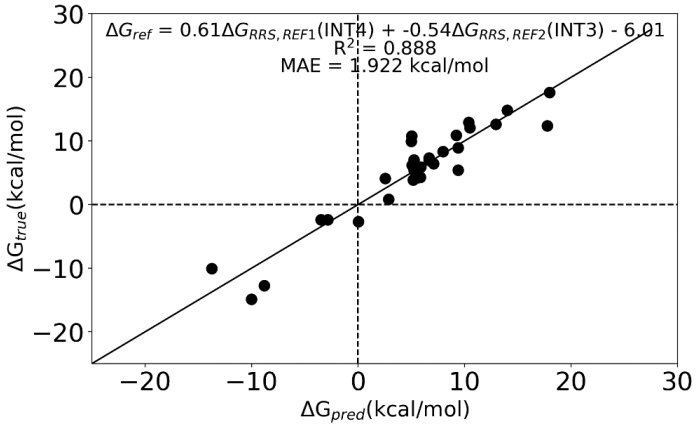


Fig. S5 Multivariate linear regression model for the relative stability of $[NiL_2]_2$(COD) with respect to NiL_2 (ΔG_{ref}) using $\Delta G_{RRS,REF1}$(**INT4**) and $\Delta G_{RRS,REF2}$(**INT3**) as variables. REF1 refers to $[NiL_2]_2$(COD) and REF2 refers to NiL_2 as the reference state.

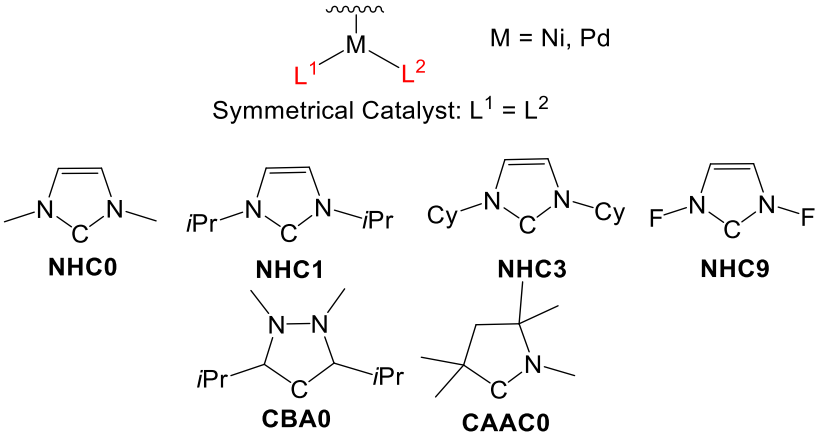


Fig. S6 Ligands on the metal center used to establish Ni/Pd LFESRs.

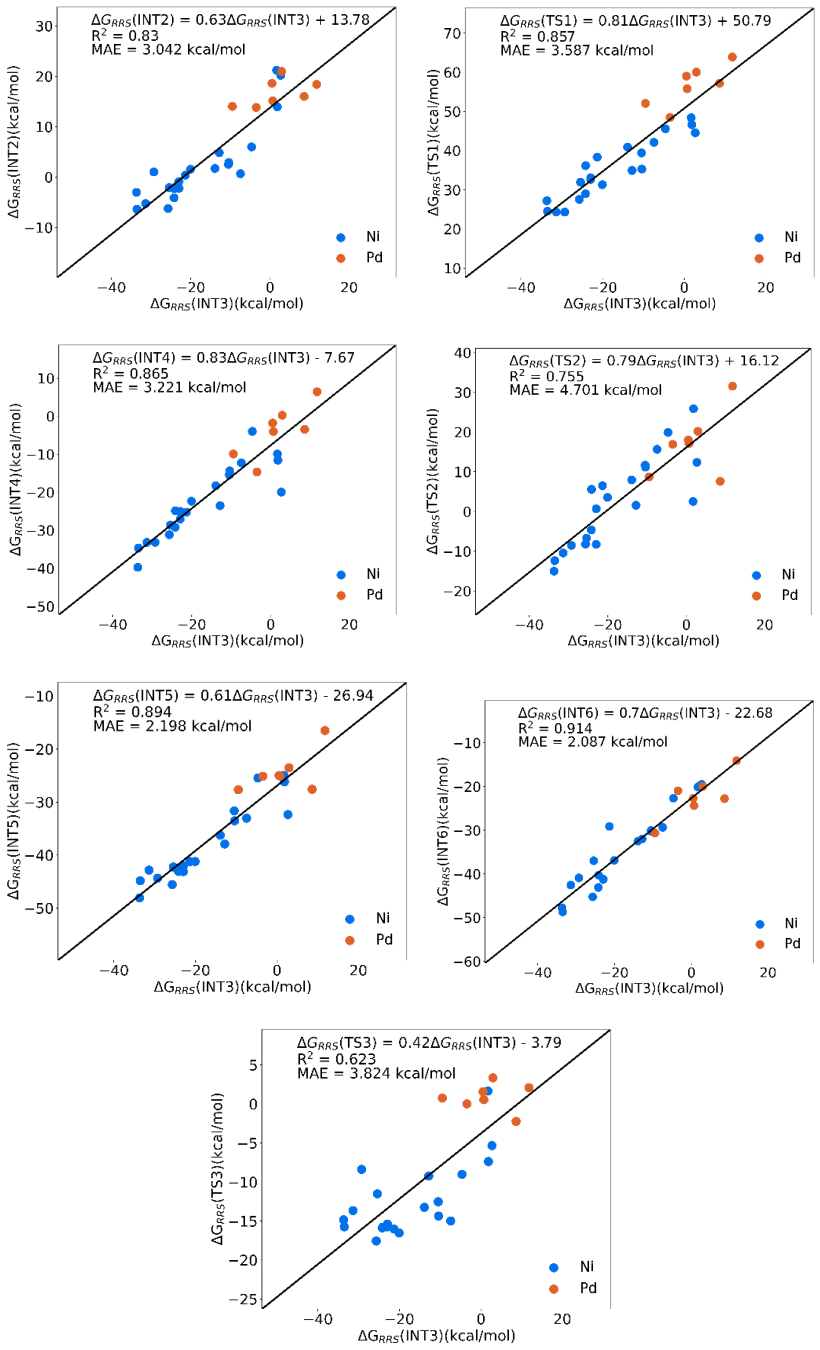


Fig. S7 Linear free energy scaling relationships for the catalytic hydrodefluorination of trifluoromethylarene with $SiMe_2Ph$-H in the absence of CsF, using ML_2 as the reference state (M = Ni, Pd).

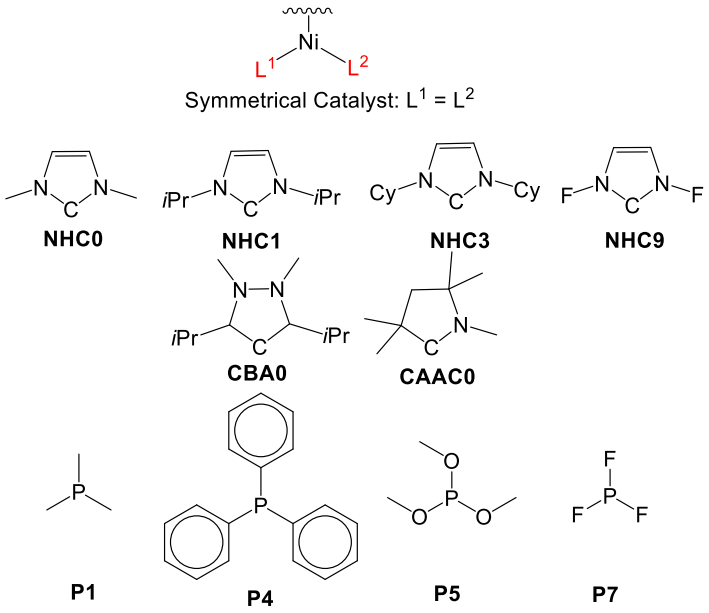


Fig. S8 Ligands on the Ni center used to establish LFESRs for the Ni-catalyzed hydrodefluorination of trifluoromethylarene with $SiMe_2Ph$-H in the presence of CsF, using $[NiL_2]_2(COD)$ as the reference state.

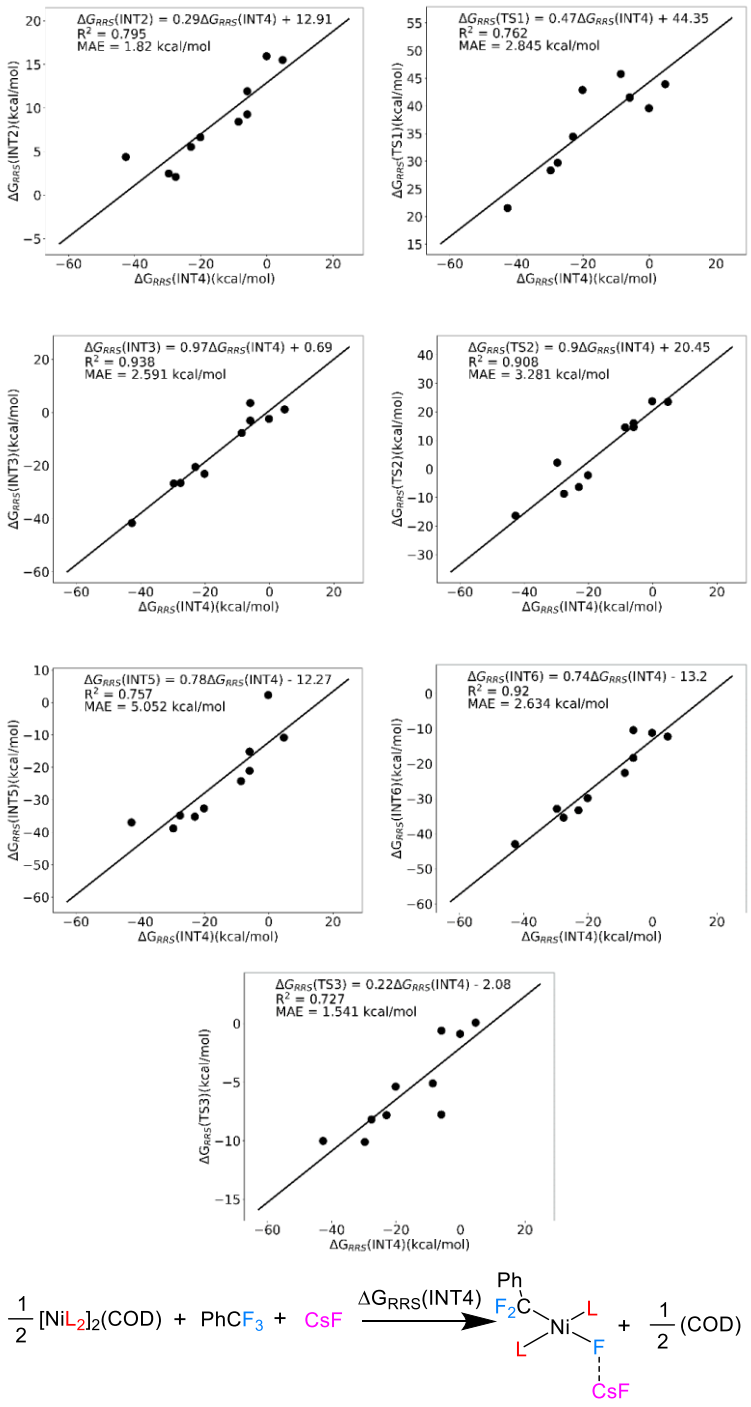


Fig. S9 Linear free energy scaling relationships for the Ni-catalyzed hydrodefluorination of trifluoromethylarene with $SiMe_2Ph$-H in the presence of CsF, using $[NiL_2]_2(COD)$ as the reference state.

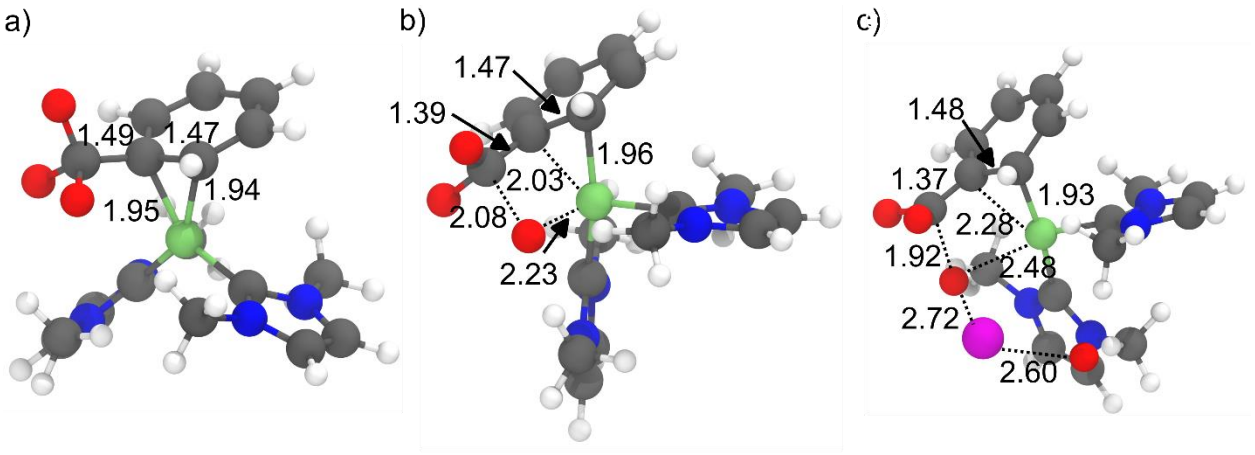


Fig. S10 Optimized structures of (a) **INT2**, (b) **TS1**, and (c) **TS1$_{CsF}$** with NHC0 as a ligand.

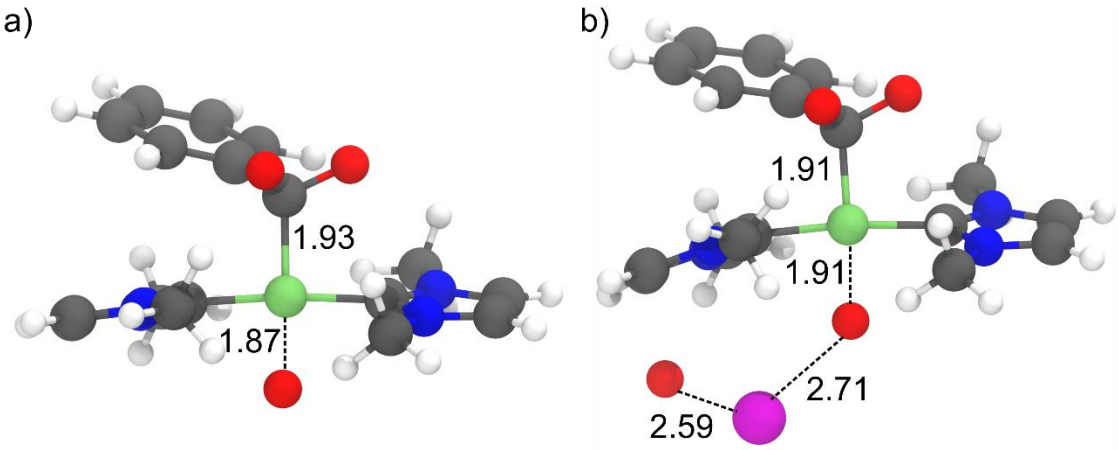


Fig. S11 Optimized structure of (a) **INT4** and (b) **INT4$_{CsF}$** with NHC0 as a ligand.

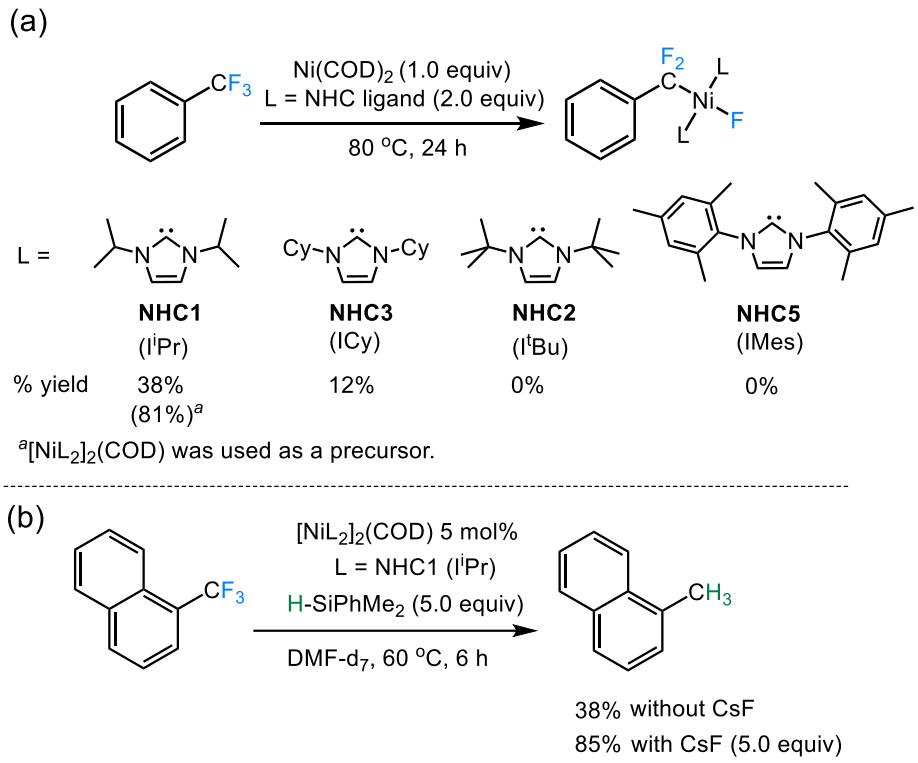


Fig. S12 (a) The C-F activation of $PhCF_3$ by Ni complexes with N-heterocyclic carbene (NHC) ligands and (b) nickel catalyzed hydrodefluorination of $ArCF_3$ with $HSiPhMe_2$ using **NHC1** (I^iPr) ligand (J. Am. Chem. Soc. 2020, 142, 19360).[6]

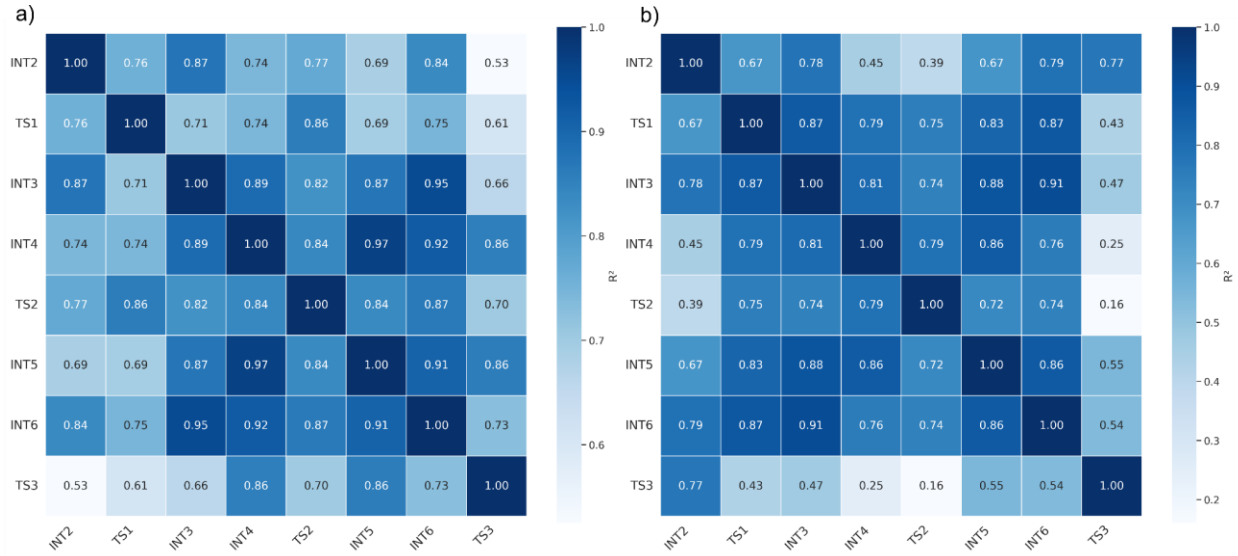


Fig. S13 Correlation matrix from the linear scaling relationships between relative free energies of all species in the catalytic hydrodefluorination of trifluoromethylarene: (a) $\Delta G_{RRS,REF1}$ for $[NiL_2]_2(COD)$ as a reference state (REF1) (L = carbene and phosphine) and (b) $\Delta G_{RRS,REF2}$ for NiL_2 as a reference state (REF2) (L = carbene).

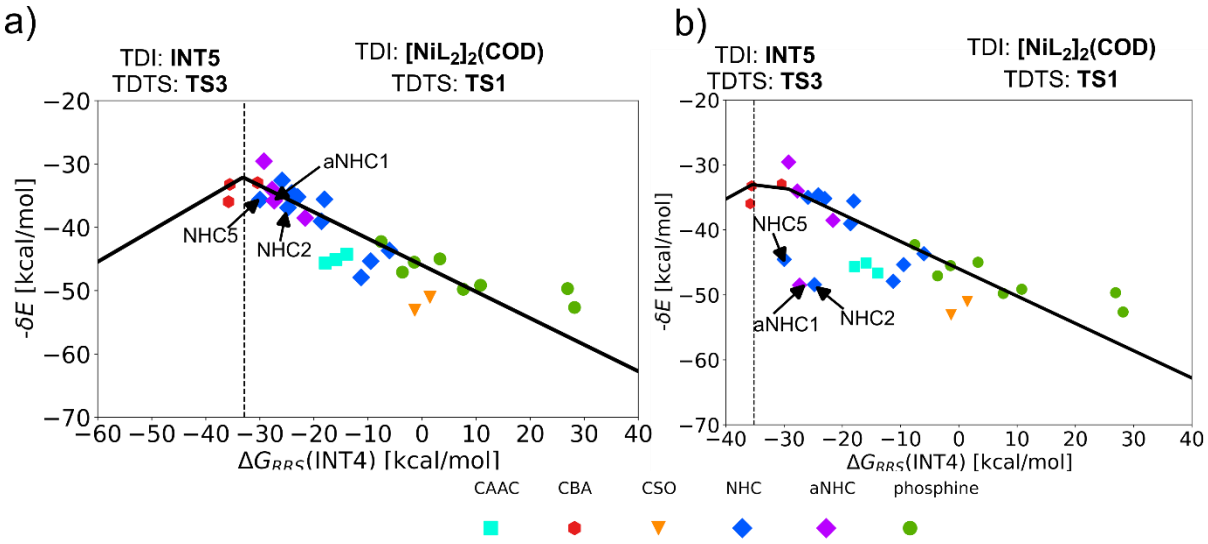


Fig. S14 Energetic span volcano plot with $[NiL_2]_2$(COD) as a reference state for the catalytic hydrodefluorination of trifluoromethylarene in the absence of CsF (L = carbene and phosphine). (a) Equilibrium between $[NiL_2]_2$(COD) and NiL_2 was not included. (b) Equilibrium between $[NiL_2]_2$(COD) and NiL_2 was considered in the catalytic cycle.

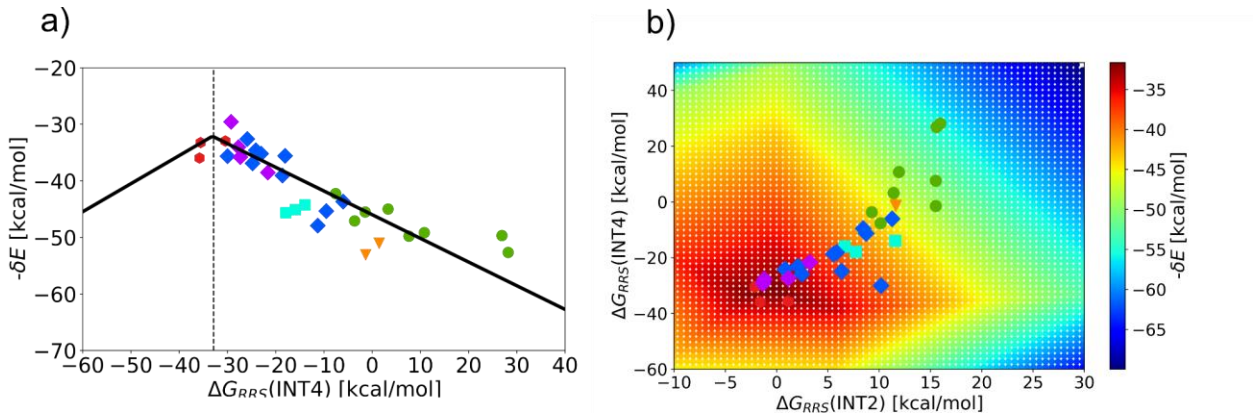


Fig. S15 (a) Energetic span volcano plot with $\Delta G_{RRS,REF1}$(INT4) as a descriptor and (b) activity map with $\Delta G_{RRS,REF1}$(INT4) and $\Delta G_{RRS,REF1}$(INT2) as descriptors. The $[NiL_2]_2$(COD) (L = carbene and phosphine) was considered as a reference state for the catalytic hydrodefluorination of trifluoromethylarene in the absence of CsF (L = carbene and phosphine).

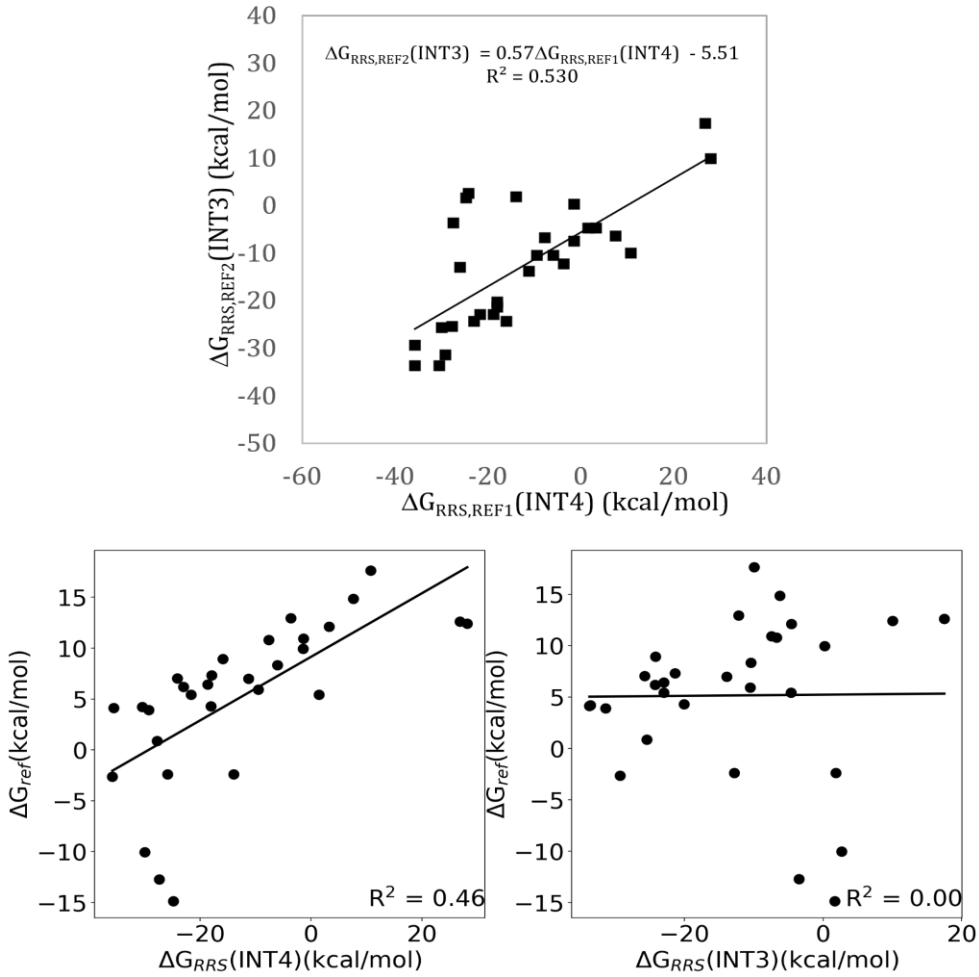


Fig. S16 Linear free energy scaling relationships between (a) $\Delta G_{RRS,REF1}$(**INT4)** and $\Delta G_{RRS,REF2}$(**INT3)**, (b) $\Delta G_{RRS,REF1}$(**INT4)** and ΔG_{ref}, and (c) $\Delta G_{RRS,REF2}$(**INT3**) and ΔG_{Ref}.

Fig. S17 Correlation matrix between the electronic/steric variables obtained for $NiL(CO)_3$ (L = carbene and phosphine) and the relative energies of all species in the catalytic hydrodefluorination of trifluoromethylarene with $[NiL_2]_2$(COD) as a reference state.

[a]The natural population analysis (NPA) charge on Ni (q_{Ni}) and Wiberg bond index (WBI) were obtained from natural bond orbital (NBO) calculation of $NiL(CO)_3$.

[b]Buried volume (V_b) was calculated with Ni as the center of the sphere with Ni-L as the z-axis. The sphere radius used to calculate buried volume is 3.5 Å.

[c]Sterimol steric parameters: (i) B1 is the minimum distance perpendicular to the primary axis of Ni-L, indicating the shortest distance of a substituent on L and (ii) B5 represents the maximum distance perpendicular to the primary axis, signifying the farthest distance of a substituent on L. The Ni-L is chosen as the primary axis. (iii) L is the length of the substituent along the axis that passes through the point of attachment

[d]d_Ni-C is the Ni-CO distance of $NiL(CO)_3$ in Å.

Example for molecular volcano plot derivation

As an example, we considered constructing an energetic-span volcano plot for Ni-catalyzed hydrodefluorination of trifluoromethylarene without CsF, using $[NiL_2]_2$(COD) as the reference state. Overall, ΔG_{RRS}(**INT4**) provides the best linear correlation with other relative free energies of intermediates and transition states in the profile. The LFESRs are given as below.

$$\Delta G_{RRS}(\mathbf{INT2}) = 0.29\Delta G_{RRS}(\mathbf{INT4}) + 0.85 \text{ kcal/mol} \quad (1)$$

$$\Delta G_{RRS}(\mathbf{TS1}) = 0.42\Delta G_{RRS}(\mathbf{INT4}) + 45.99 \text{ kcal/mol} \quad (2)$$

$$\Delta G_{RRS}(\mathbf{INT3}) = 0.86\Delta G_{RRS}(\mathbf{INT4}) + 3.36 \text{ kcal/mol} \quad (3)$$

$$\Delta G_{RRS}(\mathbf{TS2}) = 0.78(\mathbf{INT4}) + 20.53 \text{ kcal/mol} \quad (4)$$

$$\Delta G_{RRS}(\mathbf{INT5}) = 0.73\Delta G_{RRS}(\mathbf{INT4}) - 20.37 \text{ kcal/mol} \quad (5)$$

$$\Delta G_{RRS}(\mathbf{INT6}) = 0.67\Delta G_{RRS}(\mathbf{INT4}) - 18.03 \text{ kcal/mol} \quad (6)$$

$$\Delta G_{RRS}(\mathbf{TS3}) = 0.24\Delta G_{RRS}(\mathbf{INT4}) - 4.69 \text{ kcal/mol} \quad (7)$$

$$\Delta G_{rxn} = -140.17 \text{ kcal/mol} \quad (8)$$

The negative of energetic span (-δE) is used to describe the catalytic activity.

$$\delta E = \max_{i,j}(T_i - I_j + \delta G_{ij})$$
$$\delta G'_{ij} = \begin{cases} \Delta G_r & \text{if } i > j \\ 0 & \text{if } i \leq j \end{cases} \quad 9$$

TDI: INT5/ TDTS: TS3

$$\Delta G_{RRS}(\mathbf{TS3}) - \Delta G_{RRS}(\mathbf{INT5}) = -0.66\Delta G_{RRS}(\mathbf{INT4}) + 15.62 \text{ kcal/mol} \quad 10$$

TDI: $[NiL_2]_2$(COD)/ TDTS: TS1

$$\Delta G_{RRS}(\mathbf{TS1}) - \Delta G_{RRS} = \Delta G_{RRS}(\mathbf{TS1}) = 0.42\Delta G_{RRS}(\mathbf{INT4}) + 45.99 \text{ kcal/mol} \quad 11$$

Multivariate linear regression analysis

$NiL(CO)_3$ with each individual ligand L was initially represented by SMILES strings. Then, OpenBabel[7, 8] was used to convert SMILES into a 3D structure and MMFF94[7] force field was used to perform geometry optimization and conformation search. The 3D structure from Openbabel was further optimized using ωB97XD[9]/def2-SVP[10] in gas phase. Based on the DFT-optimized structures, Morfeus was used to measure the steric descriptors V_b. Based on the ωB97XD/def2-TZVP single-point energy calculation in gas phase, natural bond orbital (NBO)[1] calculations were carried out to obtain electronic variables, i.e., Wiberg bond index (WBI)[11] and natural population analysis (NPA) charge. These non-energetic descriptors were then chosen as molecular features to perform regression analysis based on the multivariate linear regression model.

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