NICKEL-CATALYZED INTRAMOLECULAR ALLYLATION OF ALKENES AND ALKYNES COUPLED WITH β-ELIMINATION OR CARBONYLATION

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Abstract: Intramolecular allylations, combined with either β-eliminations ($\underline{1} \rightarrow \underline{2}$) or carbonylations ($\underline{10} \rightarrow \underline{12} + \underline{13}$, $\underline{14} \rightarrow \underline{16}$ and $\underline{17} \rightarrow \underline{19} + \underline{20}$) were catalyzed by $Pt(PPh_3)_4$, Ni(COD)/dppb, or $Ni(CO)_3PPh_3$, respectively.

Pd[0]-catalyzed conversion of allylic acetates, alcohols and acetals $\underline{A}$, $\underline{B} \rightarrow \underline{F}$ (Scheme 1) exemplifies part of a new stereospecific methodology leading to an array of monocylic or annulated carbo- and heterocyclic systems. The experimental results are consistent with an alkene insertion into a σ-allyl- ($\underline{D} \rightarrow \underline{E}$) or π-allyl-palladium unit ($\underline{C} \rightarrow \underline{E}$) and a subsequent β-elimination which regenerates Pd[0] [1)].

Scheme 1
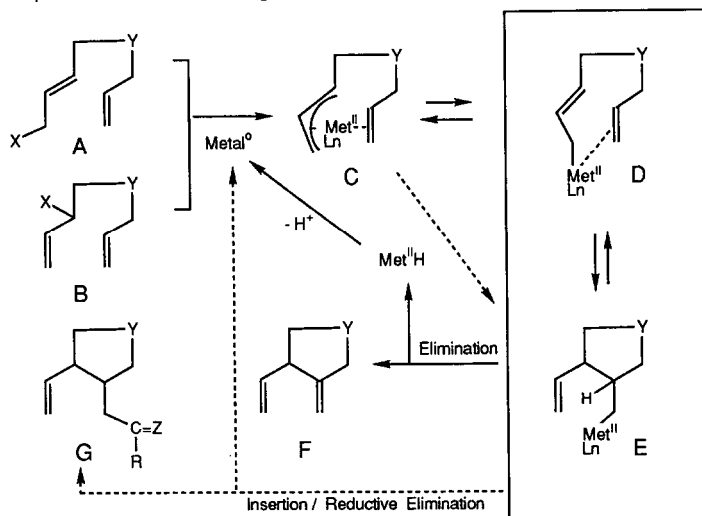
X = OAc , OH , OTHP , Y = C(SO₂Ar)₂ , C(COOMe)₂ , CH₂ (ref 2b) , NR , O

As an extension of this work we envisaged catalysis of these and related cyclizations with other transition metals as well as insertion/reductive elimination reactions $\underline{E} \rightarrow \underline{G}$ to continue the catalytic cycle [1b)] while forming an additional carbon-carbon bond. Indeed, heating dienyl acetate $\underline{1}$, Y = $C(SO_2Ph)_2$ with 3.5 mol% of $Pt(PPh_3)_4$ in acetic acid at 80° for 5 h furnished 1,4-diene $\underline{2}$ in 85% yield [2)].

We then focussed our attention on analogous Ni[0]-catalyzed transformations. Insertion of butadiene into allylnickel species is apparently involved in Ni-catalyzed polymerizations and oligomerizations of 1,3-butadiene [3a)]. This holds particularly for the $Ni(Bu_3P)_2Br_2$/BuLi-catalyzed dimerization of butadiene to give $\underline{F}$, Y = CH_2 (90%) [3b)]. Norbornene undergoes either catalytic or stoichiometric additions of allylnickel complexes followed by rearrangement/elimination [3c)] or *cis*-methoxycarbonylation (CO,MeOH) [3d)]. Addition of transient allylnickel species to alkenes and alkynes in the presence of CO were reported to give cyclopentanones and cyclopentenones, respectively, in variable yields indicating "double" insertions of CO into alkyl(alkenyl)-nickel and olefinic bonds [3e)]. Despite all these encouraging precedents a synthetically useful nickel-catalyzed cyclization $\underline{A}$ or $\underline{B} \rightarrow \underline{F}$ or $\underline{G}$ was not straightforward.

In an exploratory experiment allyl chloride $\underline{A}$, X = Cl, Y = C(SO$_2$Tol)$_2$ was added to Ni(COD)$_2$ (1.2 equiv) in toluene under N$_2$ at +20° giving within 10 min cyclized "dimer" $\underline{3}$ [4] (40%, Scheme 2).

Scheme 2
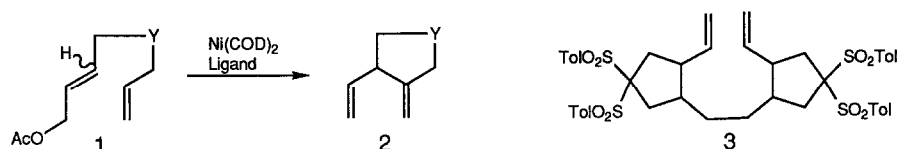
Table 1: Nickel–Catalyzed Intramolecular Alkene Allylation/Eliminations $\underline{1} \rightarrow \underline{2}$, THF, N$_2$, 20°C

| Entry	Bridge Y	Ni(COD)$_2$ [mol%]	Ligand	(mol%)	Reaction Time [h]	Yield [%]
1	C(SO$_2$Tol)$_2$	120	PPh$_3$	(480)	4	62[1]
2	C(SO$_2$Ph)$_2$	20	PPh$_3$	(80)	18	80[1]
3	C(SO$_2$Ph)$_2$	10	PPh$_3$	(40)	18	55[1,2]
4	C(SO$_2$Ph)$_2$	120	P(OiPr)$_3$	(480)	24	74[1]
5	C(SO$_2$Ph)$_2$	10	Ph$_2$P-(CH$_2$)$_4$-PPh$_2$	(10)	3	83
6	NCOOCH$_2$Ph	100	Ph$_2$P-CH$_2$-PPh$_2$	(100)	12	59
7	NCOOCH$_2$Ph	100	Ph$_2$P-(CH$_2$)$_2$-PPh$_2$	(100)	12	36
8	NCOOCH$_2$Ph	100	Ph$_2$P-(CH$_2$)$_3$-PPh$_2$	(100)	12	0[2]
9	NCOOCH$_2$Ph	100	Ph$_2$P-(CH$_2$)$_4$-PPh$_2$	(100)	12	95
10	NCOOCH$_2$Ph	100	Ph$_2$P-(CH$_2$)$_5$-PPh$_2$	(100)	12	81
11	NCOOCH$_2$Ph	100	Ph$_2$P-(CH$_2$)$_6$-PPh$_2$	(100)	12	76
12	NCOOCH$_2$Ph	100	dppf	(100)	12	48
13	NCOOCH$_2$Ph	40	Ph$_2$P-(CH$_2$)$_4$-PPh$_2$	(40)	18	46
14	NSO$_2$-Tol	10	Ph$_2$P-(CH$_2$)$_4$-PPh$_2$	(10)	12	76
15	N-CPh$_3$	10	Ph$_2$P-(CH$_2$)$_4$-PPh$_2$	(10)	0.75	92

[1]$\underline{2}$ contains 6-12% of 5-methyl-3,3-(disulfonylaryl)-1-vinylcyclopentane. [2]Recovered $\underline{1}$: *Entry 3*: 37%; *Entry 8*: 73%.

The effect of coordinating the Ni^0 with various phosphorous ligands was studied in order to impede dimerization (Scheme 2, Table 1). *Entries 1 - 3* show a smooth conversion of $\underline{1}$ [5] to $\underline{2}$, Y = C(SO$_2$Ar)$_2$ on treatment with Ni(COD)$_2$/PPh$_3$ (1:4) in THF at +20° (without formation of $\underline{3}$). However, lowering the amount of the catalyst from 1.2 equiv to 0.1 equiv resulted in longer reaction time and incomplete conversion (*Entry 3*). Tri i-propylphosphite coordinated nickel turned out to be even less efficient (*cf. Entries 4 and 1*). In contrast, 0.1 equiv of a 1:1-mixture of Ni(COD)$_2$ [6] and dppb (Ni(COD)/dppb) promoted complete cyclization of $\underline{1}$, Y = C(SO$_2$Ph)$_2$ within 3 h at +20° to give after isolation, pure $\underline{2}$, Y = C(SO$_2$Ph)$_2$ in 83% yield (*Entry 5*).

Recognizing the importance of bidentate ligands prompted a variation of the chain linking the two phosphorus atoms. The efficiency of their Ni-complexes (1 equiv) to promote the transformation $\underline{1}$ [5] $\rightarrow$ $\underline{2}$, Y = NCOOCH$_2$Ph was compared (*Entries 6 - 12*). Under otherwise identical reaction conditions Ni(COD)/dppb gave the highest yield of $\underline{2}$, Y = NCOOCH$_2$Ph (95%, *Entry 9*). It is worth mentioning that no trace of the cyclization product was formed in the presence of the dppp ligand (*Entry 8*) probably due to its stronger coordination to nickel. Only moderate yields of $\underline{2}$, Y = NCOOCH$_2$Ph were obtained using 1,1'-bis (diphenylphosphino)ferrocene (dppf)-complexed nickel (*Entry 12*) or on decreasing the amount of Ni(COD)/dppb to 0.4 equiv (*Entry 13*). However, on changing the nitrogen substituent of the substrate, 0.1 equiv of Ni(COD)/dppb again induced complete cyclizations of the N-tosyl- and the N-trityl dienyl acetates $\underline{1}$ [4,5], to give pyrrolidines $\underline{2}$ [4] in 76% and 92% yield respectively (*Entries 14,15*).

These reaction conditions can be readily applied to annulations by incorporation of the transient allylnickel unit into a ring.

Scheme 3
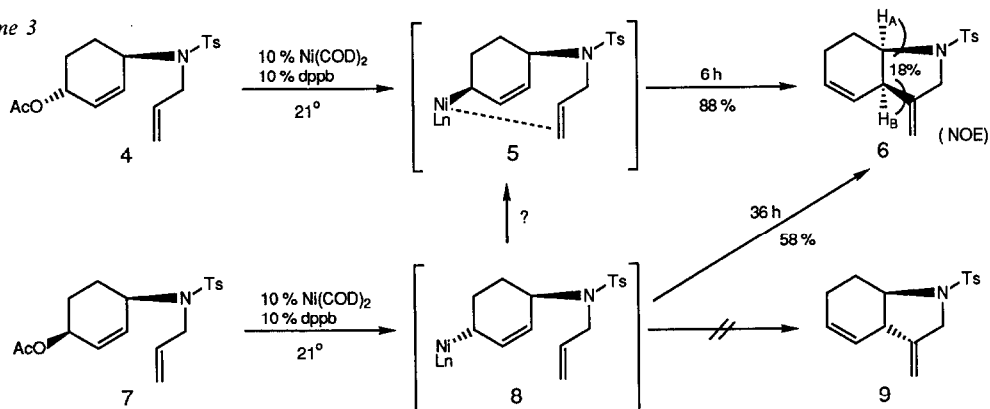
Scheme 3 illustrates the conversion of the easily available *trans*- or *cis*-acetoxydienes 4 [4,5] and 7 [4,5] into the same *cis*-fused 3-methylene-hexahydroindole 6 [4]. However, transformation 4 → 5 → 6 proceeded significantly faster and in higher yield relative to conversion 7 → 8 → 6 which presumably implies a *trans/cis*-isomerization 8 → 5. Inspection of *Dreiding* models shows that in the allylnickel intermediate 8 (resulting initially from 7) coordination of the Ni with the *trans*-disposed terminal alkene is highly unfavorable which seems to prevent its conversion to 9. This result parallels those of closely related palladium catalyzed annulations [1c] indicating a preferred *cis*-allylnickel/olefin insertion *i.e.* within the nickel coordination sphere.

We then reconsidered the prospect of trapping the cyclized alkylnickel intermediate, in particular, by methoxycarbonylation (E → G). Tricarbonyl(triphenylphosphine)nickel [7] (25 mol%), a stable, easy to handle solid (*versus* the highly volatile and toxic $Ni(CO)_4$) smoothly catalyzed the cyclizations/carbonylations depicted in the Schemes 4,5 and in the Table 2.

Scheme 4
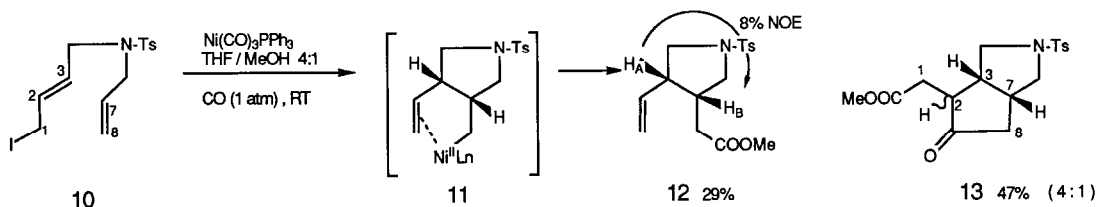
Thus, stirring dienyl iodide 10 [5] with $Ni(CO)_3PPh_3$ (25 mol%) in THF/MeOH (4:1) under CO (1 atm) at RT for 20 h gave monocyclic *cis*-substituted pyrrolidine 12 [4] (29%) and the bicyclic cyclopentanone 13 [4] (47%, 4:1-isomer mixture). Under these conditions, it appears that the cyclization 10 → 11 is stereoselective and that the cyclized acylnickel intermediate G, Z = O, R = NiL_n inserts either methanol (→ 12) or the internal olefinic bond giving after final methoxycarbonylation ketoester 13. Both insertion pathways are preferred over a β-elimination of 11.

Scheme 5
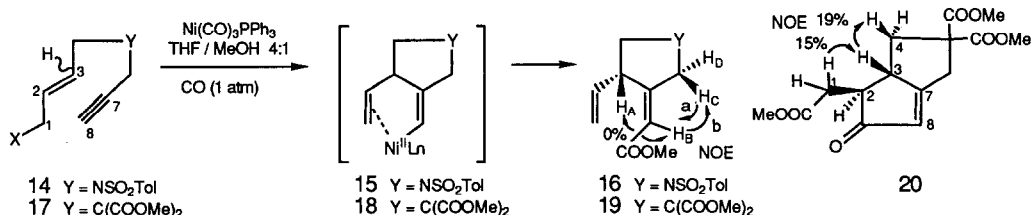
Similar treatment of enyne 14, Y = NSO_2Tol, X = I [5] with $Ni(CO)_3PPh_3$ (25 mol%), CO and MeOH furnished exclusively monocyclized *(Z)*-1,4-diene 16 (69%, Scheme 5, Table 2, *Entry 16*). This new stereocontrolled approach to an exocyclic trisubstituted olefinic bond is consistent with a *cis*-allylnickel/acetylene insertion 14, X = $Ni^{II}L_n$ → 15.

Table 2: Nickel-Catalyzed Intramolecular Allylation/Carbonylation of Alkynes, THF/MeOH(4:1), CO (1 atm)

Entry	Starting Material (E/Z)	Bridge Y	Leaving Group X	Ni(CO)$_x$PPh$_3$ [mol%]	Reaction Temp[°C] Time[h]	Monocyclic Product Yield[%]	Bicyclic Product Yield[%]
16	14 (E)	NSO$_2$Tol	I	25	RT(20)	16 (69)	--[1]
17	17 (E)	C(COOMe)$_2$	I	25	RT(20)	19 (41)	20[2](36)
18	17 (Z)	C(COOMe)$_2$	Br	20[3]	RT(48),50°(12)	19 (14)	20[2](62)

1)No bicyclic product detected. 2)Purity (GC) of 20: *Entry 17*, 94.5%; *Entry 18*, 93%. 3)Prepared *in situ*: Ni(COD)$_2$, CO (1 atm),THF, 0°, 30 min; PPh$_3$ (1 equiv), RT, 30 min.

The analogous malonate *(E)-17*, Y = C(COOMe)$_2$, [5] X = I when subjected to identical cyclization conditions again yielded a *(Z)*-methoxycarbonylmethylene-vinylcyclopentane 19 [4] (41%) accompanied by the bicyclic cyclopentenone 20 [4] (36%, *Entry 17*). Bicyclization (→ 20) becomes more prominent on replacing the allylic iodide by a bromide substituent in the starting enyne [8]. For example, *(Z)-17*, Y = C(COOMe)$_2$, X = Br [5] furnished 19 (14%) and 20 (62%) requiring a higher reaction temperature (50°, 2 h). The major bicyclic isomer 20 was shown by means of NOE evidence to have the depicted relative configuration.

In summary, intramolecular d^{10}-transition metal allylations of alkenes and alkynes may be catalyzed not only by Pd^0 but also by Pt^0 or Ni^0. The latter metal requires an inert atmosphere and a more subtle choice of ligands but provides *cis*-diastereoselectivity in the cyclization step and offers interesting perspectives when combined with CO insertion reactions. Scope, limitations and extensions of this methodology are under investigation.

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3) a) Review: G.Wilke *Angew. Chem.* 1988, 100, 189; *Angew. Chem. Int. Ed. Engl.* 1988, 27, 185; b) J.Kiji, K.Masui, J.Furukawa, *Bull. Chem. Soc. Jpn.*, 1971, 44, 1956; c) M.Catellani, G.P.Chiusoli, E.Dradi, G.Salerno, *J. Organometal. Chem.* 1979, 177, C29; d) M.C.Gallazzi, T.L.Hanlon, G.Vitulli, L.Porri, *ibid.*, 1971, 33, C45; e) G.P.Chiusoli, *Acc. Chem. Res.* 1973, 6, 422.

4) All new compounds were characterized by capillary-GC, IR, ^{1}H-NMR, ^{13}C-NMR and MS. ^{1}H-NMR/NOE-data (δ in ppm, J in Hz) of 6: (CDCl$_3$) H$_B$: 2.76 (*m*); H$_A$: 3.92 (*m*). 12: (CDCl$_3$) H$_B$: 2.56 (*br.quint*, J = 8); H$_A$: 2.85 (*m*). 16: (C$_6$D$_6$) H$_C$+H$_D$: 2.38-2.52; H$_A$: 4.16 (*txq, J* = 6.5, 1.5); H$_B$: 5.44 (*q, J* =1.5); a = b = 3%. 19: (CDCl$_3$) H$_C$: 2.95 (*d, J* = 17); H$_A$: 4.18 (*m*); H$_B$: 5.3 (*m*); a = 15%, b = 10%. 20: (C$_6$D$_6$) C(3)-H: 1.78 (*t, J* = 12.5); C(1)-H$_2$: 2.24-2.41; C(4)-H: 3.02 (*dxd, J* = 12.5, 7.5).

5) Preparation of starting materials: 1, Y = C(SO$_2$Ar)$_2$ ref. 1a); 1, Y = NCOOCH$_2$Ph, Y = NSO$_2$Tol ref 1d); 1 Y = NCPh$_3$: *N*-allyl-*t*-butyloxycarbamate, NaH, DMF, 0, 2h; *(Z)*-1-acetoxy-4-chloro-2-butene, RT, 2h; CF$_3$COOH, MeOH, 0°, 5 min; Ph$_3$CCl, Et$_3$N, DMF, RT, 3h. 4: in analogy to its crotyl homologue ref 1d). 7: *N*-allyltoluenesulfonamide, NaH, THF, RT, 2h; *cis*-1-acetoxy-4-chloro-2-cyclohexene, Pd(PPh$_3$)$_4$ (0.05 equiv), RT, 2 h *cf.* ref 1c). 10: *N*-allyltoluenesulfonamide, NaH, DMF, RT, 2h; *(E)*-1,4-dibromo-2-butene (2 equiv), RT, 3h; NaI (3 equiv), acetone, reflux, 1h. 14, X = I: *N*-2-propynyltoluenesulfonamide, NaH, THF, RT, 1h; *(E)*-1,4-dibromo-2-butene (2 equiv), Pd(PPh$_3$)$_4$ (0.02 equiv) RT, 4h; NaI, acetone, reflux, 0.5h. *(E)-17*, X = I: as 10 but starting with dimethyl 2-propynylmalonate. *(Z)-17*, X = Br: dimethyl *(Z)*-4-(*O*-tetrahydropyranyl)-2-butenylmalonate (P.Deslongchamps, S.Lamothe, H.-S.Lin, *Can. J. Chem.* 1987, 65, 1298), NaH, DMF; 2-propynyl bromide (1.5 equiv), RT, 1 h; Py.TsOH, MeOH, RT, 24 h; NBS, DMS (1.5 equiv), CH$_2$Cl$_2$, 0°, 3h (E.J.Corey, C.U.Kim, M.Takeda, *Tetrahedron Lett.* 1972, 4339).

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8) After we had independently observed carbonylative bicyclizations of 2-nonen-7-ynyl bromides the carbonylative cyclization of 9-methoxy-2-nonen-7ynyl bromides (50% yield), promoted by Ni(CO)$_4$ (200 mol%) was reported: F.Camps, J.Coll, J.M.Moreto, J.Torras, *Tetrahedron Lett.* 1987, 28, 4745.