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Rhodium-catalyzed coupling of *N*-allylamides of organic acids

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Abstract

N-Allylamides of organic acids have been shown to couple with unsaturated diamides under catalysis by a rhodium(I) complex. The synthesis is regioselective and moderately stereoselective, the *Z* diamide being obtained predominantly. A metallacyclic intermediate is suggested.

Introduction

In the preceding paper [1] we described a new reaction of (diphenylmethylene) cyclopropane with *N*-allylamides, which was assumed to occur via a metallacycle. The presence of small amounts of diamides prompted us to study conditions for a coupling reaction with *N*-allylamides.

Results and discussion

We find that *N*-allylamides can couple to 2-methyl-3-ethyl-1-propene-1,3-diamides in a highly regioselective reaction, which takes place to give good yields under mild conditions, according to eq. 1 (R = alkyl, aryl):

$$\underset{\text{(I)}}{2H_2C{=}CHCH_2NHCOR} \xrightarrow{\text{Rh cat.}} \underset{\text{(II)}}{RCONHCH{=}C(CH_3)CH(CH_2CH_3)NHCOR} \qquad (1)$$

The reaction is carried out simply by dissolving the reagents in toluene containing the catalyst $RhCl(PPh_3)_3$, and keeping the solution at 90 °C under nitrogen. Some results are reported in Table 1.

The synthesis is regioselective and moderately stereoselective, the (*Z*)-diamide being mainly obtained, particularly in the case of the *N*-benzoyl substrate (*Z*/*E* ca. 87/13). The structure of the main isomer (*Z*) thus formed has been determined by an X-ray diffraction study for R = Ph [2].

By-products of this reaction are enamides $CH_3CH{=}CHNHCOR$ (III), both *E* and *Z*. Isomerization of *N*-allylamides [3], as well as of allylamines [4,5], had been

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Table 1

Reaction of allylamine *N*-acylderivatives I (2.0 mmol) and $RhCl(PPh_3)_3$ (0.03 mmol) in toluene (3.0 ml) at 90 °C for 60 h [a]

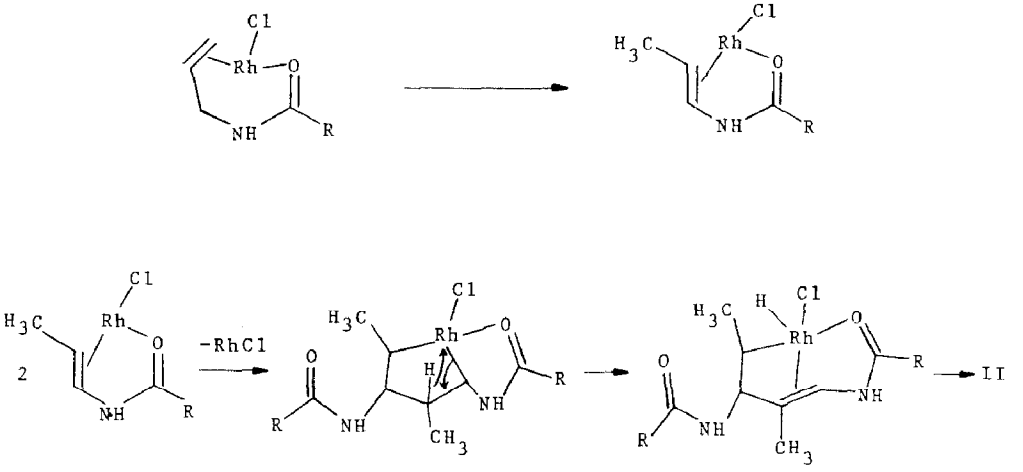
R	Conversion [b] (%)	Product yield [b] (%)			
		II-(*Z*)	II-(*E*)	III-(*Z*)	III-(*E*)
CH_3	88	48	33	5	1
Ph	90	70	11	6	2
OEt	90	54	31	4	1
$CH{=}CHCH_3$-(*E*)	80	43	13	7	2

[a] The time can be substantially shorter, depending on the type of substrate and the concentration, but no optimization was attempted. [b] By GLC, based on substrate I.

described previously. *N*-Allyl-*N*-alkylamides, *N*-allylacrylamides, and *N*-crotylamides do not dimerize under the conditions used.

It has been established that coupling is favoured by prior isomerization to the *E* enamide isomer. The latter couples with itself much faster than the *N*-allylamide or the 1/1 mixture of the *N*-allylamide with the *E* enamide. The *Z* enamide reacts very slowly. Increasing the concentration of the reaction solution results in a remarkable increase of the coupling rate. It is not clear why coupling occurs selectively, with involvement of different positions of the two molecules. It is possible that the sites of attack are determined by the need for forming appropriate rhodacycles. It is of interest in this context to make a comparison with the results obtained by Aresta in the coupling reaction of *N*-allylaniline [4]; the product formed had the same coupling sites as ours, and so the mechanisms are probably similar. We suggest the mechanism shown in Scheme 1 (non reactive ligands are omitted for simplicity).

After isomerization to enamides two molecules must form a rhodacycle, which gives rise to the final product by hydrogen transfer. It is noteworthy that other rhodium(I) complexes with labile ligands can be used to effect the coupling reaction in place of the Wilkinson's catalyst. Amide-containing complexes are currently being studied and will be described in due course.



Scheme 1

Experimental

Products were analyzed and quantitatively determined by GLC on a methylsilicone (OV-101 stationary phase) capillary column by use of an internal standard, and isolated by preparative TLC or flash chromatography.

Compounds were identified by comparison with known samples or by mass, IR and NMR spectroscopy. Mass spectra were obtained with a Finnigan 1020 instrument at 70 eV. IR spectra were recorded on a Perkin–Elmer 298 IR spectrophotometer. ^1H NMR and ^{13}C NMR spectra were recorded with AC100 and CXP200 Bruker spectrometers; chemical shifts are in ppm (δ) from TMS as reference. Melting points were determined with an Electrothermal Apparatus and are uncorrected.

Complexes $RhCl(PPh_3)_3$ [6] and $RhH(PPh_3)_4$ [7], were prepared by published methods. *N*-Allylacetamide was prepared as described in ref. 3 and the other *N*-allylamides and ethyl *N*-allylcarbamate were made by standard methods [8]. All the compounds are colourless liquids.

Crotylamine was made by Gabriel synthesis [9], starting from crotyl bromide and potassium phtalimide. All the substrates used gave correct analytical and spectral data.

Coupling reaction. A mixture of 0.03 g (0.03 mmol) of $RhCl(PPh_3)_3$ and the *N*-allylamide (2.0 mmol) in toluene (3.0 ml) in a Schlenk tube was stirred magnetically at 90 °C for 60 h under nitrogen, then cooled to room temperature and 15 ml of Et_2O were added. The solution was filtered and the solvent was distilled off under vacuum.

Isomerization reaction. A mixture of 0.035 g (0.03 mmol) of $RhH(PPh_3)_4$ and the *N*-allylamide (2.0 mmol) in toluene (5 ml) in a Schlenk tube was stirred magnetically at 90 °C for 60 h under nitrogen. Work-up was as above.

Compounds II and III were isolated by the following chromatographic procedures (eluent composition in parentheses): II and III (R = CH_3): TLC on silica gel (n-hexane/EtOAc 1/1); the II-(*E*) isomer was further purified by TLC on silica gel (EtOAc/MeOH 98/2); II and III (R = Ph): flash chromatography on silica gel (n-hexane/EtOAc 8/2), compound II-(*Z*) was recrystallized from n-hexane/THF solution; II and III (R = OEt): TLC on silica gel (n-hexane/EtOAc 8/2); II and III (R = *E*-CH=CHCH$_3$): flash chromatography on silica gel (n-hexane/EtOAc 1/1).

The structures of products III-(*Z*) and III-(*E*) (R = Me, Ph, OEt and (*E*)-CH=CHCH$_3$) were confirmed by comparison with the enamides obtained from the respective allylamine *N*-derivatives by isomerization with $RhH(PPh_3)_4$ as described by Stille et al. [3].

Enamides III (R = Me) [3], III (R = Ph) [10] and III (R = OEt) [11] had been reported. Enamides III (R = (*E*)-CH=CHCH$_3$) gave by hydrogenation on Pd/C the same saturated product as the starting *N*-allyl-2-butenamide.

Melting points, ^1H NMR, mass and IR spectral data of compounds II and III (NMR spectra were recorded in $CDCl_3$ with TMS as internal reference).

II-(*Z*) (R = CH_3), $\overset{h}{C}H_3CONH\overset{g}{C}H=\overset{e}{C}(\overset{d}{C}H_3)\overset{c}{C}H(\overset{b}{C}H_2\overset{a}{C}H_3)NH\overset{f}{C}O\overset{i}{C}H_3$, m.p. 137–139 °C. MS: (*m/e*): 198 (M^+), 180, 169, 155, 139, 127, 109, 96, 85(100), 81, 58. IR (KBr) cm^{-1}: 3010, 2990, 1650, 1535, 1460, 1390, 1290, 1165, 790. ^1H NMR: δ 0.86, t, 3H, H^a, J_{ab} 7.5 Hz; 1.55, d, 3H, H^d, J_{de} 1.4 Hz; 1.40–1.68, m, 2H, H^b; 1.97, s, 3H, H^i; 2.03, s, 3H, H^h; 4.43, dt, 1H, H^c, J_{cf} 8.0 Hz, J_{cb} 7.5 Hz; 6.44, d, 1H, H^e, J_{eg} 8.9 Hz; 6.61, br s, 1H, H^f; 9.56, br d, 1H, H^g, J_{ge} 8.9 Hz.

II-(*E*) (R = CH_3), $\overset{h}{C}H_3CONH\overset{g}{C}H=\overset{e}{C}(\overset{d}{C}H_3)\overset{c}{C}H(\overset{b}{C}H_2\overset{a}{C}H_3)N\overset{f}{H}C\overset{i}{O}CH_3$, m.p. 166–168 °C. MS: (*m/e*): 198 (M^+), 180, 139, 127, 126, 98, 96, 85(100), 81, 58. IR (KBr) cm^{-1}: 3040, 1630, 1530, 1460, 1400, 1290, 1170, 790. ^1H NMR: δ 0.87, t, 3H, H^a, J_{ab} 7.2 Hz; 1.57, centered m, 2H, H^b; 1.62, d, 3H, H^d, J_{de} 1.35 Hz; 1.99, s, 3H, H^i; 2.07, s, 3H, H^h; 4.23, dt, 1H, H^c, J_{cf} 8.5 Hz; J_{cb} 6.8 Hz; 5.96, br d, 1H, H^f, J_{fc} 8.5 Hz; 6.73, d, 1H, H^e, J_{eg} 10.5 Hz; 7.51, br d, 1H, H^g, J_{ge} 10.5 Hz.

II-(*Z*) (R = Ph), $PhCONH\overset{g}{C}H=\overset{e}{C}(\overset{d}{C}H_3)\overset{c}{C}H(\overset{b}{C}H_2\overset{a}{C}H_3)N\overset{f}{H}COPh$, m.p. 146–147 °C. MS: (*m/e*): 322 (M^+), 304, 217, 199, 188, 171, 160, 105(100), 96, 77, 51. IR (KBr) cm^{-1}: 3280, 3210, 2940, 1630, 1620, 1520, 1480, 1430, 1300, 850, 790, 705, 680. ^1H NMR: δ 0.95, t, 3H, H^a, J_{ab} 7.4 Hz; 1.66, d, 3H, H^d, J_{de} 1.4 Hz; 1.73, dq, 2H, H^b, $J_{ba} = J_{bc}$ 7.4 Hz; 4.80, dt, 1H, H^c, J_{cf} 8.2 Hz, J_{cb} 7.4 Hz; 6.72, d, 1H, H^e, J_{eg} 8.4 Hz; 7.06, d, 1H, H^f, J_{fc} 8.2 Hz; 7.33–8.17 m, 10H, 2Ph; 10.51, d, 1H, H^g, J_{ge} 8.4 Hz.

II-(*E*) (R = Ph), $PhCONH\overset{g}{C}H=\overset{e}{C}(\overset{d}{C}H_3)\overset{c}{C}H(\overset{b}{C}H_2\overset{a}{C}H_3)N\overset{f}{H}COPh$, m.p. 176–178 °C. MS: (*m/e*): 322 (M^+), 304, 217, 201, 188, 172, 105(100), 96, 77, 51. IR (KBr) cm^{-1}: 3240, 2940, 1625, 1570, 1520, 1480, 1285, 865, 790, 700, 685. ^1H NMR: δ 0.96, t, 3H, H^a, J_{ab} 7.4 Hz; 1.74, d, 3H, H^d, J_{de} 1.3 Hz; 1.73, m, 2H, H^b; 4.50, dt, 1H, H^c, J_{cf} 8.2 Hz, J_{cb} 7.2 Hz; 6.36, br d, 1H, H^f, J_{fc} 8.2 Hz; 7.02, d, 1H, H^e, J_{eg} 9.6 Hz; 7.31 –7.82, m, 11H, 2Ph and H^g.

II-(*Z*) (R = OEt), $\overset{h}{C}H_3\overset{i}{C}H_2OCONH\overset{g}{C}H=\overset{e}{C}(\overset{d}{C}H_3)\overset{c}{C}H(\overset{b}{C}H_2\overset{a}{C}H_3)N\overset{f}{H}COO\overset{i'}{C}H_2\overset{h'}{C}H_3$, m.p. 68–70 °C. MS: (*m/e*): 258 (M^+), 230, 229(100), 183, 169, 157, 140, 129, 111, 96, 85, 58. IR (KBr) cm^{-1}: 3350, 3310, 3000, 1690, 1440, 1265, 1075, 790. ^1H NMR: δ 0.87, t, 3H, H^a, J_{ab} 7.5 Hz; 1.21, 1.25, 2t, 6H, H^h and $H^{h'}$, $J_{hi} = J_{h'i'} = 7.1$ Hz; 1.52, dq, 2H, H^b, $J_{ba} = J_{bc} = 7.5$ Hz; 1.54, d, 3H, H^d, J_{de} 1.4 Hz; 3.99–4.25, m, 5H, H^i, $H^{i'}$, H^c; 4.91, br d, 1H, H^f, J_{fc} 7.6 Hz; 6.28, d, 1H, H^e, J_{eg} 8.9 Hz; 7.97, br s, 1H, H^g.

II-(*E*) (R = OEt), $\overset{h}{C}H_3\overset{i}{C}H_2OCONH\overset{g}{C}H=\overset{e}{C}(\overset{d}{C}H_3)\overset{c}{C}H(\overset{b}{C}H_2\overset{a}{C}H_3)N\overset{f}{H}COO\overset{i'}{C}H_2\overset{h'}{C}H_3$, m.p. 104–106 °C. MS: (*m/e*): 258 (M^+), 229(100), 183, 169, 157, 140, 129, 111, 96, 85, 58, 56. IR (KBr) cm^{-1}: 3320, 2990, 1700, 1530, 1420, 1240, 1105, 1070, 790. ^1H NMR: δ 0.80, t, 3H, H^a, J_{ab} 7.3 Hz; 1.16, 1.19, 2t, 6H, H^h and $H^{h'}$, $J_{hi} = J_{h'i'} = 7.1$ Hz; 1.47, dq, 2H, H^b, $J_{ba} = J_{bc} = 7.3$ Hz; 1.47, s, 3H, H^d; 3.85, br s, 1H, H^f; 3.97–4.15, m, 5H, H^i, $H^{i'}$, H^c; 4.87, br s, 1H, H^g; 6.39, d, 1H, H^e, $J_{eg} = 10.9$ Hz.

II-(*E,Z,E*) (R = (*E*)-$\overset{i'}{C}H=\overset{h'}{C}HCH_3$), $\overset{h}{C}H_3\overset{i}{C}H=\overset{l}{C}H\overset{g}{C}ONH\overset{e}{C}H=\overset{c}{C}(\overset{d}{C}H_3)\overset{b}{C}H(\overset{a}{C}H_2CH_3)NHCOCH=CHCH_3$, m.p. 145–147 °C. MS: (*m/e*) 250 (M^+), 232, 221, 181, 165, 153, 152, 136, 113, 96, 85, 69(100), 68. IR (KBr) cm^{-1}: 3300, 2950, 1680, 1650, 1540, 1465, 1360, 1245, 980, 935, 840. ^1H NMR: δ 0.86, t, 3H, H^a, J_{ab} 7.4 Hz; 1.56, d, 3H, H^d, J_{de} 1.4 Hz; 1.57, m, 2H, H^b; 1.81–1.84, 2dd, 6H, H^h and $H^{h'}$, $J_{hi} = J_{h'i'} = 6.8$ Hz, $J_{hl} = J_{h'l'} = 1.6$ Hz; 4.53, dt, 1H, H^c, $J_{cf} = J_{cb} = 7.8$ Hz; 5.86, 5.96, 2dq, 2H, H^l and $H^{l'}$, $J_{li} = J_{l'i'} = 15.2$ Hz, $J_{lh} = J_{l'h'} = 1.6$ Hz; 6.53, d, 1H, H^e, J_{eg} 9.1 Hz; 6.63–7.06, br s, 2dq, 3H, H^f, H^i and $H^{i'}$, $J_{il} = J_{i'l'} = 15.2$ Hz, $J_{ih} = J_{i'h'} = 6.8$ Hz; 9.76, br d, 1H, H^g, J_{ge} 9.1 Hz.

II-(*E,E,E*) (R = (*E*)-$\overset{i'}{C}H=\overset{h'}{C}HCH_3$), $\overset{h}{C}H_3\overset{i}{C}H=\overset{l}{C}H\overset{g}{C}ONH\overset{e}{C}H=\overset{c}{C}(\overset{d}{C}H_3)(\overset{b}{C}H(\overset{a}{C}H_2CH_3)NHCOCH=CHCH_3$, m.p. 189–192 °C. MS: (*m/e*): 250 (M^+), 232, 221, 181, 153, 152, 124, 113, 96, 85, 69(100), 68. IR (KBr) cm^{-1}: 3290, 3000, 1680, 1640, 1545, 1240, 980, 810. ^1H NMR: δ 0.89, t, 3H, H^a, J_{ab} 7.2 Hz; 1.61, m, 2H, H^b; 1.63, s, 3H,H^d; 1.84, 1.88, 2dd, H^h, $H^{h'}$, $J_{hi} = J_{h'i'} = 6.8$ Hz, $J_{hl} = J_{h'l'} = 1.6$ Hz; 4.37, m, 1H, H^c; 5.37, br d, 1H, H^f, J_{fc} 8.6 Hz; 5.79, 5.84, 2dq, 2H, H^l and $H^{l'}$, $J_{li} = J_{l'i'} = 15.1$ Hz, $J_{lh} = J_{l'h'} = 1.6$ Hz; 6.66–7.11, m, 4H, H^i, $H^{i'}$, H^g, H^e.

III-(E,Z) (R = (E)-CH=CHCH$_3$), CH$_3$CH=CHCONHCH=CHCH$_3$. MS: (m/e): 125 (M^+), 110, 98, 97, 83, 69(100), 57, 56.
III-(E,E) (R = (E)-CH=CHCH$_3$), CH$_3$CH=CHCONHCH=CHCH$_3$. MS: (m/e): 125 (M^+), 110, 98, 97, 83, 69(100), 57, 56.

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