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# Palladium Catalysed Reactions of Allenes, Carbon Monoxide and Nucleophiles.

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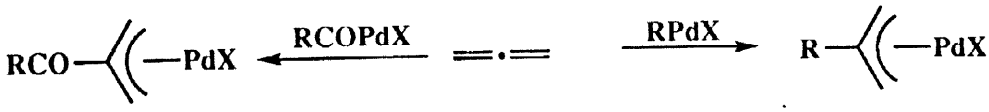
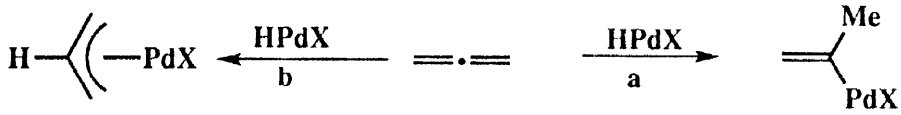
***Abstract.*** Hydridopalladium(II) species generated *in situ* by oxidative addition of Pd(0) to acetic acid or acidic hydroxyl substrates (phenols, oximes) catalyse the termolecular assembly of allenes, CO and amines (primary, secondary) or oxygen nucleophiles to give methacrylamides or methacrylate esters and derivatives thereof in good to excellent yield.


The extraordinary versatility and exquisite selectivity of palladium catalysed reactions continues to foster further innovative developments and application of the metal's salts and complexes. In recent years a range of processes which employ allene and substituted allenes as substrates have been developed.[1-3] These processes have established that both aryl-[4] and acyl-palladium(II)[5] species add the organic moiety to the centre carbon of allene (Scheme 1)[6] forming π-allylpalladium(II) species.




**Scheme 1**

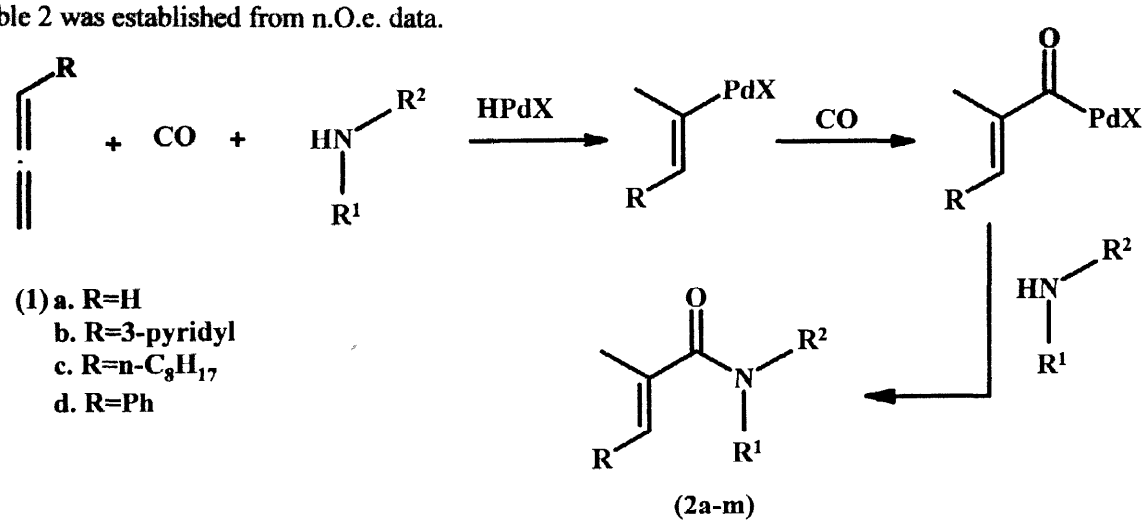
We now report a general process believed to proceed via *in situ* generated HPdX and involving the termolecular assembly of allenes, carbon monoxide and a wide range of nucleophiles. In these processes the hydride formally adds to the terminal position of the allene (Scheme 2, path a) apparently generating a vinylpalladium(II) species rather than the π-allyl pathway (Scheme 2, path b). However, for an alternative interpretation see Scheme 5.




**Scheme 2**


*PII:* S0040-4020(98)00115-X

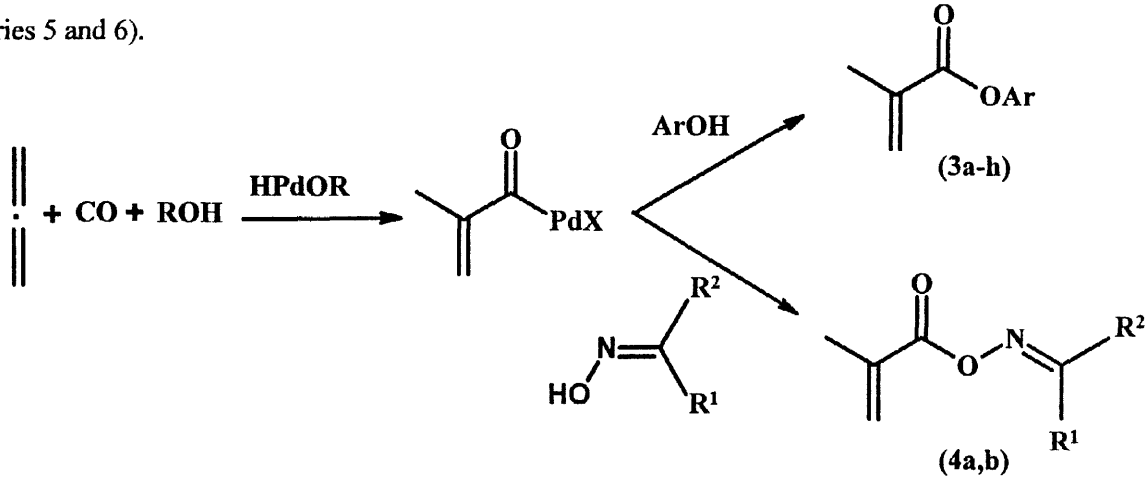
Primary and secondary amines (including indoles) react (THF, 110°C, 1h, Schlenk tube) with carbon monoxide (1 atm) and allene (1 atm) or substituted allenes (1.2 mol eq) **1a-d** to give acrylamides **2a-m** (Scheme 3) in excellent yield (Tables 1 and 2). The catalyst system comprises 5 mol% $Pd(PPh_3)_4$ and 5 mol% acetic acid except for indole where no acetic acid was required. The E-stereochemistry of the products in Table 2 was established from n.O.e. data.




**Scheme 3**

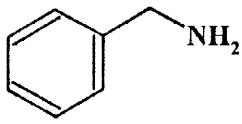
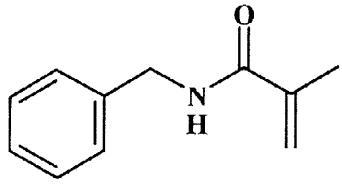
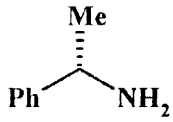
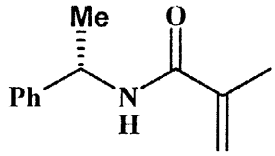
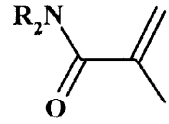
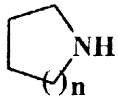
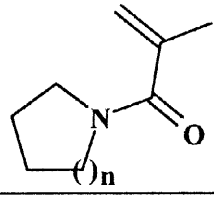
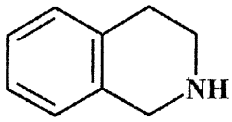
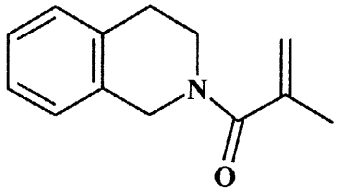
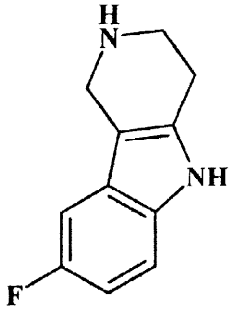
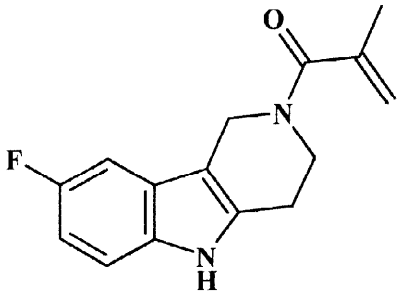
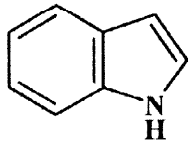
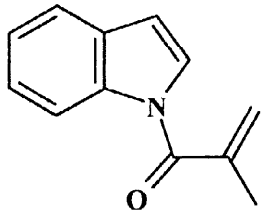
The reaction appears quite general and constitutes a mild non-basic method for N-acylation of indoles as illustrated by Table 1, final entry. The expected greater reactivity of a secondary amine versus the indolic NH group is illustrated by the selective reaction of the former moiety in the formation of **2h** (Table 1). Indole N-acylation requires a considerably longer time than the corresponding reactions of p- or s- amines (16h versus 1h).

An analogous series of reactions (THF, 110°C, 1h) was carried out with phenols and oximes as nucleophiles (Scheme 4) utilising 5 mol% $Pd(PPh_3)_4$ as catalyst. In these cases the pKa of nucleophiles (ca. 10-12) was sufficiently low for there to be no requirement for acetic acid (Table 3). Thus the hydroxylic substrates are presumed to generate HPdX *in situ*. The aryl methacrylates **3a-h** were obtained in 53-68% yield with little variation in yield between o-, m- and p- substituted phenols (Table 3, entries 3 and 4). A patent reports related processes for aliphatic alcohols requiring considerably higher pressures and the addition of a Bronsted acid.[7] Oximes are also converted to their methacryloyl esters under analogous conditions (Table 3, entries 5 and 6).



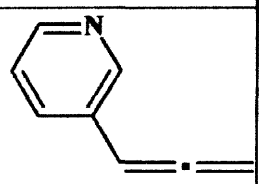
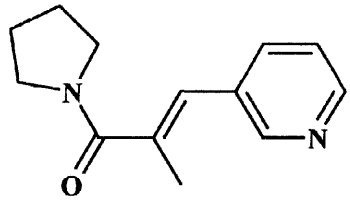
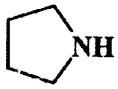
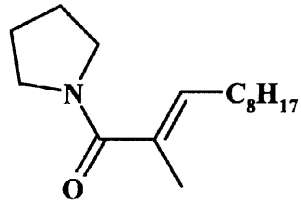
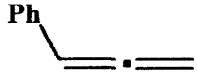
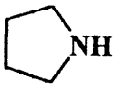
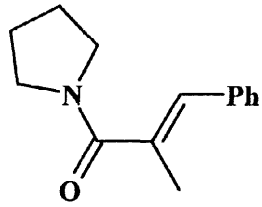
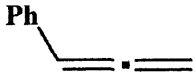
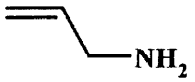
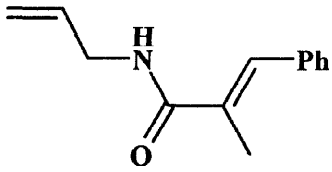

**Scheme 4**

**Table 1**[a]

| Nitrogen nucleophile | Product | | Yield (%)[b] |
|---|---|---|---|
|  |  | (2a) | 80 |
|  |  | (2b) | 83 |
| $HNR_2$ |  | (2c,d) | R=Me 60<br>R=Et 51 |
|  |  | (2e,f) | n=1 80<br>n=2 80 |
|  |  | (2g) | 79 |
|  |  | (2h) | 56 |
|  |  | (2i) | 76[c] |

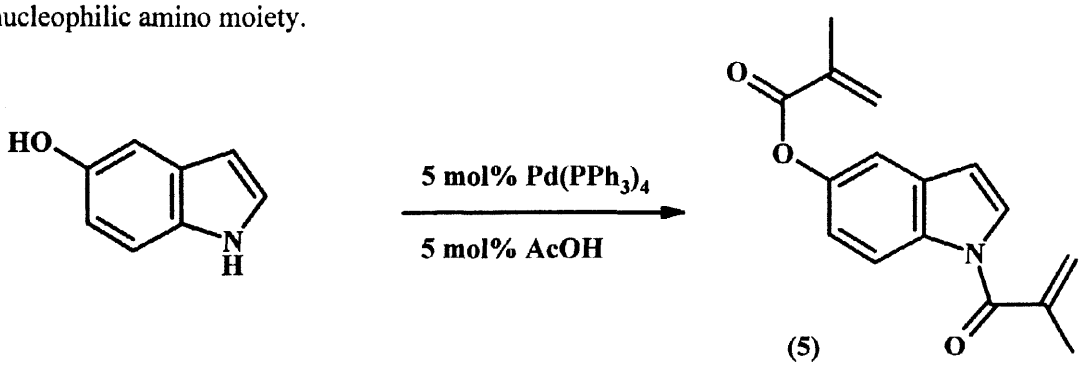
a. All reactions were carried out in a Schlenk tube for 1h with allene (1 atm) and CO (1 atm)
b. Isolated yields
c. Reaction time 16 h, 10 mol% $Pd(PPh_3)_4$, no HOAc added.

**Table 2**[a]

| Allene | Nitrogen nucleophile | Product | | Yield (%)[b] |
|---|---|---|---|---|
|  |  |  | (2j) | 60 |
|  |  |  | (2k) | 64 |
|  |  |  | (2l) | 51 |
|  |  |  | (2m) | 67 |

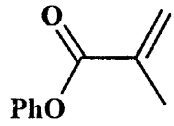
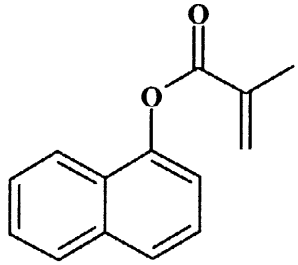
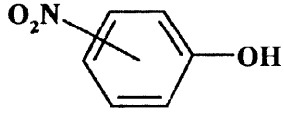
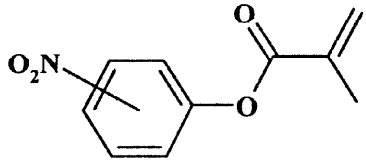
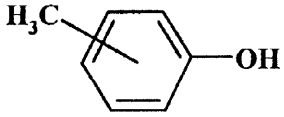
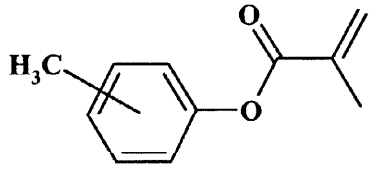
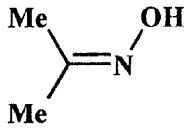
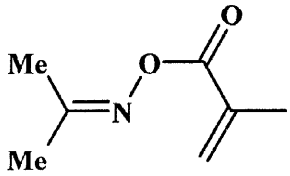
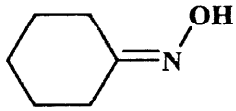
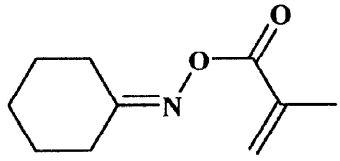
a. All reactions were carried out in a Schlenk tube for 1h with CO (1 atm) and the allene (1.2 eq)
b. Isolated yields

Two examples of N,O-bifunctional nucleophiles have been evaluated. The first of these, 5-hydroxyindole, underwent reaction, under the usual conditions with 5mol% acetic acid, at both the phenolic and indolic sites to afford **5** (47%) after 16h. The reaction of p-aminophenol with allene and CO and no added acid results in selective N-acylation to form **6** in 57% yield after 16h whilst the analogous reaction in the presence of 5mol % acetic acid gives the doubly acylated species **7** (66%) after 16h. If the former case procedes as outlined in Scheme 3 the presumed intermediate **8** undergoes attack by uncomplexed p-aminophenol via the more nucleophilic amino moiety.

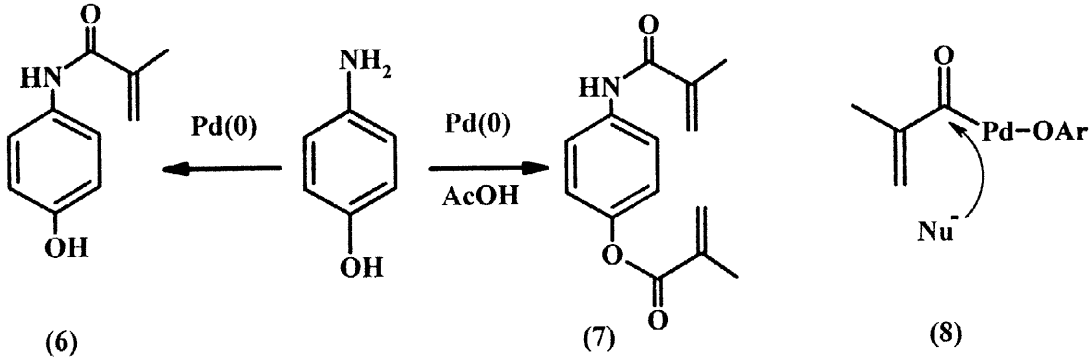



(5)

**Table 3** [a]

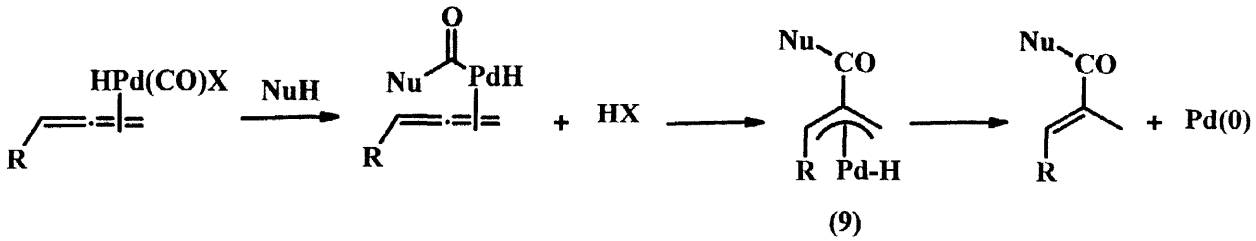
| Nucleophile | Product | | Yield (%)[b] |
|---|---|---|---|
| **PhOH** |  | (3a) | 65 |
| **1-Naphthol** |  | (3b) | 68 |
|  |  | (3c-e) | ortho 55<br>meta 57<br>para 58 |
|  |  | (3f-h) | ortho 65<br>meta 53<br>para 57 |
|  |  | (4a) | 53 |
|  |  | (4b) | 56 |

a. All reactions were carried out in a Schlenk tube with allene (1 atm) and CO (1 atm)
b. Isolated yields




(6) (7) (8)

**Mechanism.** Our results with allenes, CO and amines appear to contrast with those of other groups employing allenes and amines in the absence of CO.[8] These latter processes employed either $Et_3NHI$ or HOAc to generate HPdX and these reactions furnish allylic amines via π-allyl complexes. A π-allyl complex could intervene in the processes described herein as shown in Scheme 5. This would reflect the slow rate of insertion of CO into π-allyl complexes in the presence of phosphine ligands. Some support for Scheme 5 is provided by observations on related processes employing nickel complexes.[9]




(9)

**Scheme 5**

The operation of Scheme 5 would require the *anti*- π-allyl complex **9** as the precursor of **2j - 2m** which would accord with some related observations by Cazes et al.[10]

**Experimental.** General experimental details are as previously noted.[11]

**General procedure for amidation of amines.** Amine (2mmol), $Pd(PPh_3)_4$ (5 mol%) and acetic acid (5 mol%) were mixed in dry THF (10ml). The solution was degassed before addition of allene (1 bar, or 1.2 eq of substituted allene) and CO (1 bar). The reaction mixture was heated to 110°C for one hour, during which time the pressure rose to 5 bar, then concentrated *in vacuo* and the residue purified by column chromatography.

**N-Benzylmethacrylamide (2a).** Column chromatography eluting with 7:5 v/v petroleum ether - ethyl acetate afforded the product in 80% yield which crystallised from petroleum ether - ethyl acetate as colourless needles, m.p. 82-83°C (Found: C, 75.45; H, 7.45; N, 7.8. $C_{11}H_{13}NO$ requires: C, 75.45; H, 7.45; N, 8.0%); $\delta_H$ 7.22-7.4(m, 5H, ArH), 6.55(bs, 1H, NH), 5.7 and 5.35(2xs, 2x1H, $C=CH_2$), 4.5(d, 2H, J5.7Hz, $NCH_2$) and 1.98(s, 3H, $CH_3$); m/z(%): 175($M^+$,100), 174(38), 160(13), 131(26), 91(82); 77(20), 69(45) and 41(65).

**(S)-N-(Methylbenzyl)-methacrylamide (2b).** Column chromatography eluting with 1:3 v/v petroleum ether - ether afforded the product (83%) which crystallised from ether as colourless needles, m.p. 90°C (Found: C, 76.0; H, 7.9; N, 7.35. $C_{12}H_{15}NO$ requires: C, 75.2; H, 7.9; N, 7.4%); $\delta_H$ 7.22-7.48(m, 5H, ArH), 6.05(bs, 1H, NH), 5.67 and 5.32(2xs, 2x1H, $C=CH_2$), 5.17(m, 1H, CH), 1.97(s, 3H, $=C-CH_3$) and 1.52(d, 3H, $CH_3$); m/z(%): 189($M^+$, 100), 174(64), 145(30), 120(25), 105(52); 104(44), 77(42), 69(89), 51(16) and 41(87).

**N,N-Dimethylmethacrylamide (2c).**[12] Column chromatography eluting with 1:2 v/v petroleum ether- ether afforded the product (60%) as a pale yellow oil. $\delta_H$ 5.17 and 5.0(2xs, 2x1H, $C=CH_2$), 3.0(m, 6H, $N(CH_3)_2$) and 1.97(s, 3H, $CH_3$); m/z(%): 113($M^+$,52), 112(56), 98(14), 72(73), 69(57), 58(30); 44(29) and 41(100).

**N,N-Diethylmethacrylamide (2d).**[13] Column chromatography eluting with 7:5 v/v petroleum ether - ethyl acetate afforded the product (51%) as a colourless oil. $\delta_H$ 5.1 and 5.0(2xs, 2x1H, $C=CH_2$), 3.39(m, 4H,

$N(CH_2)_2$), 1.96(s, 3H, $CH_3$) and 1.17-1.13(t, 6H, $(CH_3)_2$); m/z(%): 141($M^+$,66), 140(31), 126(58), 72(25), 69(100) and 41(57).

**N-Methacryloylpyrrolidine (2e).**[14] Column chromatography eluting with 7:5 v/v petroleum ether - ethyl acetate afforded the product (80%) as a pale yellow oil. $\delta_H$ 5.1 and 5.2(2xs, 2x1H, C=$CH_2$), 3.45(bm, 4H, $N(CH_2)_2$), 2.0(s, 3H, $CH_3$) and 1.8-2.0(m, 4H, $(CH_2)_2$); m/z (%): 139($M^+$,17), 138(45), 69(79), 56(21) and 41(100).

**N-Methacryloylpiperidine (2f).** Column chromatography eluting with 7:5 v/v petroleum ether - ethyl acetate afforded the product (80%) as a pale yellow oil. (Found: C, 70.4; H, 9.85; N, 8.85 $C_9H_{15}NO$ requires: C, 70.6; H, 9.8; N, 9.15%); $\delta_H$ 5.15 and 5(2xs, 2x1H, C=$CH_2$), 3.4-3.65(bm, 4H, $N(CH_2)_2$), 1.95(s, 3H, $CH_3$), and 1.5-1.7(m, 6H, $(CH_2)_3$); m/z(%): 153($M^+$,82), 152(100), 138(32), 69(56), 56(12) and 41(57).

**N-Methacryloyl-1,2,3,4-tetrahydroisoquinoline (2g).**[15] Column chromatography eluting with 7:5 v/v petroleum ether - ethyl acetate afforded the product (80%) as a pale yellow oil. $\delta_H$ 7-7.2(m, 4H, ArH), 5.0 and 5.25(2xs, 2x1H, C=$CH_2$), 4.7(bs, 2H, $NCH_2Ph$), 3.8(bs, 2H, $N(CH_2)$), 2.9(t, 2H, ($CH_2Ph$) and 2.0 (s, 3H, $CH_3$); m/z(%): 201($M^+$,100), 200(75), 186(21), 132(20), 117(27), 104(34), 77(16),69(32) and 41(42).

**$N^2$-Methacryloyl-8-fluoro-1,2,3,4-tetrahydropyrido[4,3-b]indole (2h).** Column chromatography eluting with 1:2 v/v petroleum ether-ethyl acetate followed by crystallisation from ether afforded the product (56%) as a colourless amorphous powder, m.p. 194°C (Found: C, 69.65; H, 5.85; N, 10.65; F, 7.65; $C_{15}H_{15}FN_2O$ requires: C, 69.75; H, 5.8; N, 10.85; F, 7.35%); $\delta_H$ 8.26-8.2(bs, 1H, NH), 7.25(m, 1H, ArH), 7.1(s, 1H, ArH), 6.9(m, 1H, ArH), 5.25 and 5.1(2xs, 2x1H, C=$CH_2$), 4.75(m, 1H, $NCH_2Ar$), 3.9-4.0(m, 2H, $ACH_2$), 1.8(m, 2H, $CH_2Ar$) and 2.0(s, 3H, $CH_3$); m/z(%): 258($M^+$,100), 257(41), 189(27), 174(28), 161(84), 133(14), 69(24) and 41(35).

**N-Methacryloylindole (2i).** Column chromatography eluting with 18:1 v/v petroleum ether - ether afforded the product (76%) as a light yellow oil. (Found: C, 77.7; H, 6.2; N, 7.35. $C_{12}H_{11}NO$ requires: C, 77.85; H, 5.95; N, 7.65%); $\delta_H$ 8.4(d, 1H,, J7.9Hz, ArH), 7.6(d, 1H, J7.5Hz, ArH), 7.5(d, 1H, J3.75Hz, ArH), 7.4-7.25(m, 1H, ArH), 6.6(d, 1H, J3.75Hz, ArH), 5.7 and 5.5(2xs, 2x1H, C=$CH_2$) and 2.15(s, 3H, $CH_3$); m/z(%): 185$M^+$,59), 157(48), 117(19.5), 116(18.5), 89(33), 69(100), 63(21) and 51(5).

**(E)-N-[2-Methyl-3-($3^1$-pyridyl)acryloyl]-pyrrolidine (2j).** Column chromatography eluting with 9:1 v/v ether- methanol afforded the product (60% yield) as a colourless oil. (Found: C, 72.0; H, 7.2; N, 12.75. $C_{13}H_{16}N_2O$ requires: C, 72.2; H, 7.4; N, 12.95%); $\delta_H$ 8.6(s, 1H, ArH), 8.5 and 7.6(2xd, 2x1H, ArH), 7.3(m, 1H, ArH), 6.6(s, 1H, C=CH), 3.55(m, 4H, $N(CH_2)_2$), 2.1(s, 3H, $CH_3$) and 1.95(m, 4H, $(CH_2)_2$) m/z(%): 217 ($M^+$+1, 15), 216($M^+$,41), 215(11), 201(12), 147(100), 146 (63); 118(75), 117(68), 91(31) and 41(24).

**(E)-N-(2-Methyl-3-undecylacryloyl)-pyrrolidine (2k).** Column chromatography eluting with 7:5 v/v petroleum ether - ethyl acetate afforded the product (64%) as a pale yellow oil. (Found: C, 76.4; H, 11.8; N, 5.35. $C_{16}H_{29}NO$ requires: C, 76.5; H, 11.5; N, 5.6%); $\delta_H$ 5.65(t, 1H, C=CH) 3.45(bs, 4H, $N(CH_2)_2$), 2.1(q, 2H, J7.Hz, C=C-$CH_2$), 1.9(bs, 4H, $(CH_2)_2$), 1.8(s, 3H, =C-$CH_3$), 1.2-1.45(bm, 12H, $(CH_2)_6$) and 0.86(t, 3H, $CH_3$); m/z(%): 251($M^+$,33), 181(53), 166(62), 138(100), 98(19); 69(49), 55(86) and 41.

**(E)-N-(2-Methyl-3-phenylacryloyl)-pyrrolidine (2l).** Column chromatography eluting with 7:5 v/v petroleum ether - ethyl acetate afforded the product (51%) as a colourless oil. (Found: C, 77.9; H, 7.65; N, 6.5. $C_{14}H_{17}NO$ requires: C, 78.15; H, 7.9; N, 6.5%); $\delta_H$ 7.45-7.25(m, 5H, ArH), 6.65(s, 1H, C=CH), 3.57(bs, 4H, $N(CH_2)_2$), 2.12(s, 3H, $CH_3$) and 1.92(bs, 4H, $(CH_2)_2$); m/z(%): 215($M^+$,72), 200(22), 145(86), 138(26); 117(100), 91(36) and 70(37).

**(E)-N-Allyl-2-methyl-3-phenylacrylamide (2m).** Column chromatography eluting with 1:2 v/v petroleum ether - ether followed by crystallisation from petroleum-ether afforded the product (67%) as colourless needles, m.p. 67-68°C (Found: C, 77.5; H, 7.65; N, 6.9. $C_{13}H_{16}NO$ requires: C, 77.25; H, 7.9; N, 6.95%); $\delta_H$ 7.27-7.41(m, 6H, ArH and C=CH), 6.0(bs, 1H, NH), 5.9 and 6.0(m, 1H, C=CH-Ph), 5.17-5.28(2xd, J16.5Hz, J23.5Hz, 2x1H, $C=CH_2$), 4.0(t, 2H, $NCH_2$) and 2.1(s, 3H, $CH_3$); m/z(%): 202($M^+$,5), 201(34), 145(99.5), 117(100), 91(44) and 41(20.

**General procedure for esterification of oxygen nucleophiles in the presence of CO and allene.** Nucleophile (2mmol) and $Pd(PPh_3)_4$, (5 mol%) were mixed in dry THF (10ml) and the solution was degassed before addition of allene (1 bar) and CO (1 bar). The reaction mixture was heated to 100°C for 16h during which time the pressure rose to 5 bar After cooling the mixture was concentrated under reduced pressure and the residue purified by column chromatography.

**Phenyl methacrylate (3a).**[16] Column chromatography eluting with 9:1 v/v petroleum ether - ether afforded the product (55%) as a colourless oil. $\delta_H$ 7.1-7.4(m, 5H, ArH), 6.35 and 5.75(2xs, 2x1H, $C=CH_2$) and 2.05(s, 3H, $CH_3$); m/z(%): 162($M^+$,19), 94(27), 69(100) and 41(86).

**1-Naphthyl methacrylate (3b).** Column chromatography eluting with 9:1 v/v petroleum ether - ether afforded the product (68%) as a colourless oil. (Found: C, 79.15; H, 5.95. $C_{14}H_{12}O_2$ requires: C,79.2; H, 5.7%); $\delta_H$ 7.85(m, 2H, ArH), 7.7(d, 1H, J8.1Hz, ArH), 7.45-7.5(m, 3H, ArH), 7.3(d, 1H, J8Hz, ArH), 6.5 and 5.9(2xs, 2x1H, $C=CH_2$) and 2.15(s, 3H, $CH_3$); m/z(%): 212($M^+$,26), 115(41), 69(100) and 41(58).

**2-Nitrophenyl methacrylate (3c).** Column chromatography eluting with 9:1 v/v petroleum ether - ether afforded the product (55%) as a light yellow oil. (Found: C, 58.3; H, 4.4; H, 6.7. $C_{10}H_9NO_4$ requires: C, 58.0; H, 4.35; N, 6.75%); $\delta_H$ 8.1(dd, 1H, J1.34Hz, J8.15Hz, ArH), 7.65(ddd, 1H, J7.8, 7.8, 1.4Hz, ArH), 7.4(t, 1H, J7.7Hz, ArH), 7.3(dd, 1H, J1.8.1Hz, ArH), 6.4 and 5.8(2xs, 2x1H, $C=CH_2$) and 2.1(s, 3H, $CH_3$); m/z(%): 207($M^+$,8), 139(6), 69(100) and 41(59).

**3-Nitrophenyl methacrylate (3d).** Column chromatography eluting with 9:1 v/v petroleum ether - ether afforded the product (57%) which crystallised from petroleum ether - ethyl acetate as colourless needles, m.p. 63°C. (Found: C, 58.05; H, 4.5; N, 6.75. $C_{10}H_9NO_4$ requires: C, 58.0; H, 4.35; N, 6.75%); $\delta_H$ 8.15(dd, 1H, J1.6, 8.2Hz, ArH), 8.0(s, 1H, ArH), 7.5-7.6(m, 2H, ArH), 6.4 and 5.8 (2xs, 2x1H, $C=CH_2$) and 2.1(s, 3H, $CH_3$); m/z(%): 207($M^+$,1.5), 139(6), 92(8), 69(100), 63(18) and 41(65).

**4-Nitrophenyl methacrylate (3e).** Column chromatography eluting with 9:1 v/v petroleum ether - ether afforded the product (58%) which crystallised from petroleum ether - ethyl acetate as colourless needles, m.p. 96°C (Found: C, 57.8; H, 4.15; N, 6.5. $C_{10}H_9NO_4$ requires: C, 58.0; H, 4.35; N, 6.75%); $\delta_H$ 8.3(d, 2H, J9.1Hz, ArH), 7.3(d, 2H, J9Hz, ArH), 6.4 and 5.8(2xs, 2x1H, $C=CH_2$) and 2.1(s, 3H, $CH_3$); m/z(%): 207($M^+$, <1), 139(3), 109(8), 69(100), 63(14) and 41(57).

**2-Tolyl methacrylate (3f).** 10 Mol% of palladium tetrakis-triphenylphosphine were used in this experiment. Column chromatography eluting with 9:1 v/v petroleum ether - ether afforded the product (65%) as a colourless oil. (Found: C, 74.95; H, 6.8. $C_{11}H_{12}O_2$ requires: C, 75; H, 6.8%); $\delta_H$ 7.25-7.15(m, 3H, ArH), 7.0(d, 1H, J8Hz, ArH), 6.4 and 5.75(2xs, 2x1H, $C=CH_2$), 2.2(s, 3H, $ArCH_3$) and 2.1(s, 3H, $CH_3$); m/z(%): 176($M^+$,33), 107(11), 91(4), 77(16), 69(100) and 41(63).

**3-Tolyl methacrylate (3g).** Column chromatography eluting with 9:1 v/v petroleum ether - ether afforded the product (53%) as a colourless oil. (Found: C, 74.85; H, 7.05. $C_{11}H_{12}O_2$ requires: C, 75; H, 6.8%); $\delta_H$ 7.25-

7.05(m, 4H, ArH), 6.35 and 5.75(2xs, 2x1H, C=$CH_2$), 2.2(s, 3H, $ArCH_3$) and 2.0(s, 3H, $CH_3$); m/z(%): 176($M^+$,19), 107(10), 91(9), 77(17), 69(100) and 41(72).

**4-Tolyl methacrylate (3h).** 10 Mol% of palladium tetrakis-triphenylphosphine were used in this experiment. Column chromatography eluting with 9:1 v/v petroleum ether - ether afforded the product (57%) as a colourless oil. (Found: C, 75.0; H, 7.05. $C_{11}H_{12}O_2$ requires: C, 75.0; H, 6.8%); $\delta_H$ 7.2(d, 2H, J8.35Hz), 7.0(d, 2H, J8.35Hz, ArH), 6.3 and 5.7(2xs, 2x1H, C=$CH_2$), 2.3(s, 3H, $ArCH_3$) and 2.0(s, 3H, $CH_3$); m/z(%): 176($M^+$,29), 107(18.4), 81(6), 77(19), 69(100) and 51(8).

**O-Methacryloyl acetoxime (4a).** Column chromatography eluting with 2:1 v/v petroleum ether - ether afforded the product (53%) as a colourless oil. (Found: C, 59.3; H, 7.7; N, 9.75. $C_{11}H_{12}O_2$ requires: C, 59.55; H, 7.8; N, 9.95%); $\delta_H$ 6.18 and 5.65(2xs, 2x1H, C=$CH_2$) and 2.15-2.05(3xs, 3x3H, 3x$CH_3$); m/z(%): 141($M^+$,6), 69(100), 56(17) and 41(77).

**O-Methacryloyl cyclohexanone oxime (4b).** Column chromatography eluting with 2:1 v/v petroleum ether - ether afforded the product (56%) as a colourless oil. (Found: C, 66.0; H, 8.35; N, 7.5. $C_{11}H_{12}NO_2$ requires: C, 66.3; H, 8.3; N, 7.7%); $\delta_H$6.15 and 5.6(2xs, 2x1H, C=$CH_2$), 2.6-2.4(2xt, 2x2H, 2x$(CH_2)_2$), 2.0(s, 3H,$CH_3$), and 1.8-1.6(m, 6H, $(CH_2)_3$); m/z(%): 181($M^+$,6), 69(100), 56(17) and 41(77).

**1,5-Bis(methacryloyl)-5-hydroxyindole(5).** Reaction time of 16h. Column chromatography eluting with 3:1 v/v petroleum ether - ether afforded the product (47%) as a colourless oil. (Found: C, 71.65; H, 5.6; N, 5.5. $C_{16}H_{15}NO_3$ requires: C, 71.4; H, 5.6; N, 5.2%); $\delta_H$ 8.0(d, 1H, J8.9Hz, ArH), 7.5(d, 1H, J3.8Hz, ArH), 7.3(d, 1H, J2.3Hz, ArH), 7.1(dd, 1H, J2.3, J8.9Hz, ArH), 6.6(1H, J3.8Hz, ArH), 6.4 and 5.75(2xs, 2x1H, C=$CH_2$ ), 5.7 and 5.45(2xs, 2x1H, C=$CH_2$), 2.15(3xs, 3x3H, 3x$CH_3$) and 2.1(3xs, 3x3H, 3x$CH_3$); m/z(%): 269($M^+$,35), 241(19), 200(6), 69(100) and 41(59).

**4-Hydroxyphenyl methacrylamide (6).** Reaction time 16h. Column chromatography eluting with 4.5:4.5:1 v/v petroleum ether - ether-methanol afforded the product (57%) which crystallised from petroleum ether - ethyl acetate as colourless needles, m.p. 152°C. (lit.[17] m.p. 150.5-151.5 °C). (Found: C, 67.75; H, 6.4; N, 7.7. $C_{10}H_{11}NO_2$ requires: C, 67.8; H, 6.2; N, 7.9%); $\delta_H$ (DMSO.D6): 9.5 and 9.2(2xbr s, 2x1H, NH and OH), 7.4(d, 2H, J9.Hz, ArH), 6.6(d, 2H, J9Hz, ArH), 5.4 and 5.7(2xs, 2x1H, C=$CH_2$) and 1.9(s, 3H $CH_3$); m/z): 177($M^+$,80), 162(5), 122(5), 108(15), 81(12), 69(100) and (86).

**4-Acryloyloxyphenyl methacrylamide (7).** Reaction time 16h. Column chromatography eluting with 1:1 v/v petroleum ether - ether afforded the product (66%) which crystallised from petroleum ether - ethyl acetate as colourless needles, m.p. 123°C (Found: C,68.4; H, 6.25; N, 5.5. $C_{14}H_{15}NO_3$ requires: C, 68.6; H, 6.1; N, 5.7%); $\delta_H$ 7.6(d, 2H, J9Hz, ArH), 7.1(d, 2H, J9Hz, ArH), 6.3 and 5.8(2xs, 2x1H, C=$CH_2$), 5.7 and 5.5(2xs, 2x1H, C=$CH_2$) and 2.0(s, 6H, 2x$CH_3$); m/z(%): 245($M^+$,29), 177(8), 69(100) and 41(66).

Further studies of these and related processes are in hand

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**References.**

1. **For intermolecular processes see:** Besson, L.; Gore, J.; Cazes, B.; *Tetrahedron Lett.*, **1995**, *36*, 3853-3856 and 3857-3860; Yamamoto, Y.; Al-Masum, M.; Fujiwara, N.; *Chem. Commun.*, **1996**, 381-382; Trost, B.M.; Gerusz, V.J.; *J. Am. Chem. Soc.*, **1995**, *117*, 5156-5157. Maguro, M.; Kamijo, S.; Yamamoto, Y.; *ibid*, **1996**, *37*, 7453-7456.

2. **For cyclisation processes see:** Grigg, R.; *J. Heterocyclic Chem.*, **1994**, *31*, 631-639; Negishi, E.; Copéret, C.; Ma, S.; Liou, S.-Y.; Liu, F.; *Chem Rev.*, **1996**, *96*, 365-393; Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R.J.; *Chem. Rev.*, **1996**, *96*, 635-662; Balme, G.; Bouyssi, D.; *Tetrahedron*, **1994**, *50*, 403-414; Davies, I.W.; Scopes, D.I.C.; Gallagher, T., *Synlett.*, **1993**, 85-87; Walkup, R.D.; Guan, L.F.; Kim, Y.S.; Kim, S.W.; *Tetrahedron Lett.*, **1995**, *36*, 3805-3808. **For cyclisation cascades involving allene/nucleophiles see:** Terrier, C.; *Tetrahedron Lett.*, **1996**, *37*, 4221-4224; Grigg, R.; Savic, V.; Grigg, R.; Sridharan, V.; *ibid*, **1996**, *37*, 6565-6568. Grigg, R.; Rasul, R.; Savic, V.; *ibid*, **1997**, *38*, 1825-1828.
3. **For cycloaddition processes see:** O'Connor, J.M.; Stallman, B.J.; Clark, W.G.; Shu, A.Y.L.; Spada, R.E.; Stevenson, T.M.; Dieck, H.A.; *J. Org. Chem.*, **1983**, *48*, 807-809; An, Z.W.; Catellani, M.; Chiusoli, GP.; *J. Organomet. Chem.*, **1990**, *397*, C31-C32; Kalinin, V.N.; Shostakovsky, M.V.; Ponomayov, A.B.; *Tetrahedron Lett.*, **1990**, *31*, 4073-4076. Larock, R.C.; Zenner, J.M.; *J. Org. Chem.*, **1995**, *60*, 482-483; Larock, R.C.; Guo, L.Q..; *Synlett.*, **1995**, 465-466; Larock, R.C.; Yum, E.K.; Doty, M.J.; Sham, K.K.C.; *J. Org. Chem.*, **1995**, *60*, 3270-3271; Chen, C.-Y.; Lieberman, D.R.; Larsen, R.D.; Reamer, R.A.; Verhoeven, T.R.; Reider, P.J.; Cottrell, I.F.; Houghton, P.G.; *Tetrahedron Lett.*, **1994**, *35*, 6981-6984; Larock, R.C.; Doty, M.J.; Cacchi, S.; *J. Org. Chem.*, **1993**, *58*, 4579-4583; Eriksson, A.; Jeschke, T.; Wensbo, D.; Annby, U.; Gronowitz, S.; Cohen, L.A.; *Tetrahedron Lett.*, **1993**, *34*, 2823-2826 and 6471-6474; Grigg, R.; Xu, H.-L.; *Tetrahedron Lett.*, **1996**, *37*, 4251-4254.
4. Cazes, B.; *Pure Appl. Chem.*, **1990**, *62*, 1867-1878.
5. Grigg, R.; Brown, S.; Sridharan, V.; Uttley, M.D., *Tetrahedron Lett.*, **1997**, *38*, 5031-5034; Grigg, R.; Pratt, R.; *ibid*, **1997**, *38*, 4489-4492; Okuro, K.; Alper, H.; *J. Org. Chem.*, **1997**, *62*, 1566-1567.
6. The normal regiochemistry can be perturbed by adverse steric factors e.g. see: Grigg, R.; Rasul, R.; Redpath, J.; Sridharan, V.; Wilson, D., *Tetrahedron Lett.*, **1996**, *37*, 4609-4612; Oppolzer, W.; Pimm, A.; Stammen. B and Hume, W.E., *Helv. Chim. Acta.*, **1997**, *80*, 623-639. **For an alternative strategy for perturbing regiochemistry see:** Grigg, R.; Sansano, J.M.; *Tetrahedron*, **1996**, *52*, 13441-13454.
7. Drent, E.; European Patent, 190473 (1986), through *Chem. Abs.*, **1986**, *105*, 191782a.
8. Besson, L.; Goré, J.; Cazes, B.; *Tetrahedron Lett.*, **1995**, *36*, 3857-3860; Al-Masum, M.; Meguro, M.; Yamamoto, Y.; *ibid*, **1997**, *38*, 6071-6074.
9. Fananas, F.J.; Hoberg, H.; *J. Organomet. Chem.*, **1984**, *274*, 249-256.
10. Friess, B.; Cazes, B.; Goré, J.; *Bull. Soc. Chim. Fr.*, **1992**, *129*, 273-279.
11. Grigg, R.; Loganathan, V.; Sridharan, V.; Stevenson, P.; Sukirthalingam, S.; Worakun, T., *Tetrahedron*, **1996**, *52*, 11479-11502.
12. Montaudo, G. ; Librando, V.; Caccamese, S.; and Maravigna, P., *J. Am. Chem. Soc.*, **1973**, *95*, 6365.
13. Szalontai, G.; Sandor, P.; Bangerter, F.; Kollar, L., *Magnetic Resonance in Chemistry*, **1989**, *27*, 216-222.
14. Steinfels, M.A.; Dreiding, A.S., *Helv. Chim. Acta*, **1972**, *55*, 702-739.
15. Schuyler, P.; Popp, F.D.; Catala Noble, A.; Alwani D.W.; Masters, B.R., *J. Med. Chem.*, **1966**, *9*, 704.
16. Banks, A.R.; Fibiger R.F.; Jones, T., *J. Org. Chem.*, **1977**, *42*, 3965.
17. Panarin, E.F.; Berov, M.B.; *J. Org. Chem.* USSR (Engl.), **1968**, *4*, 802-803.