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Acylation-Cyclization of Allenes Using Acyltetracarbonylcobalt Complexes.

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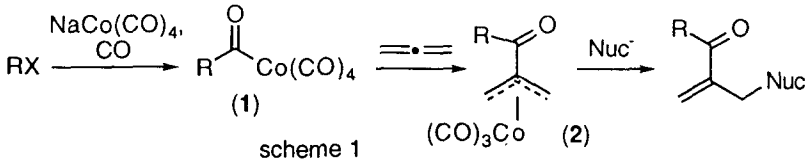
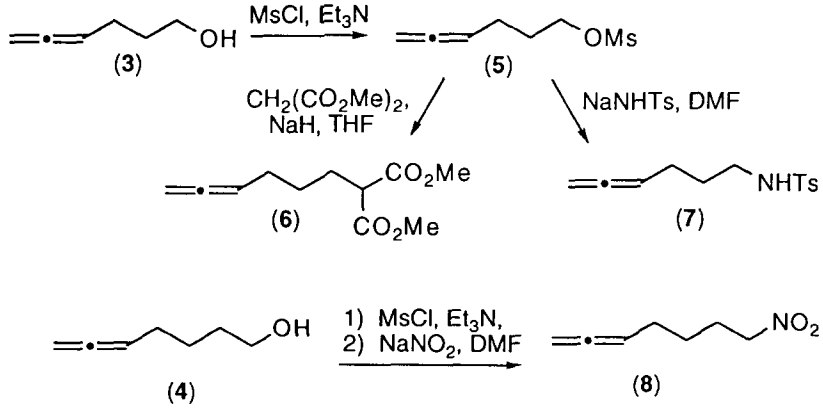
Abstract: Allenes bearing tethered nucleophiles undergo acylation-cyclization on treatment with acylcobalt complexes and base.

Sodium tetracarbonylcobaltate can be alkylated by reactive alkyl halides, especially methyl iodide (scheme 1).[1] Subsequent carbon monoxide insertion gives the acyltetracarbonylcobalt complexes (**1**). Both the insertion of allenes giving electrophilic η^3-allylcomplexes (**2**) and intermolecular nucleophilic attack on the resulting allyl complexes have been demonstrated.[2]



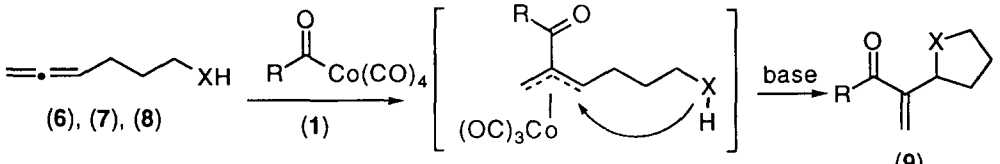
scheme 1

We considered that an intramolecular reaction would provide a useful method for the formation of heterocycles and carbocycles.[3] To test this hypothesis, we synthesized a number of allenes bearing tethered nucleophiles (scheme 2). Starting from either 4,5-hexadien-1-ol (**3**) or 5,6-heptadien-1-ol (**4**) [4], a series of allenes, (**6**) - (**8**), bearing a variety of nucleophilic groups, were prepared.[5]



scheme 2

Treatment of these compounds with acetyltetracarbonylcobalt (**1**, R=CH_3) or benzyloxyacetyl-tetracarbonyl cobalt (**1**, R=$BnOCH_2$) (prepared from methyl iodide and benzylchloromethyl ether respectively) followed by base resulted in smooth cyclization to give the corresponding cyclized compounds (**9**) in moderate to excellent yield (Table) via the intermediate η^3-allyl complex (**10**) (scheme 3).[6] It may be noted that the nitrogen (runs 1,2) and malonate (runs 6 - 9) nucleophiles gave the best results. No products of dialkyation or direct acylation of the nucleophilic group were observed. Optimization showed that much milder bases such as potassium carbonate and tertiary amines, were more efficient (runs 6 - 9).



scheme 3 (**10**) (**9**)

TABLE

run	allene	nucleophile (X)	R	base	yield (%)
1	**7**	NTs	Me	NaH	69
2	**7**	NTs	$BnOCH_2$	NaH	80
3	**3**	O	Me	NaH	30
4	**3**	O	$BnOCH_2$	iPr_2NEt	25
5	**8**	$CHNO_2$	Me	iPr_2NEt	24[7]
6	**6**	$C(CO_2Me)_2$	Me	NaH	49
7	**6**	$C(CO_2Me)_2$	Me	K_2CO_3	78
8	**6**	$C(CO_2Me)_2$	Me	iPr_2NEt_2	92
9	**6**	$C(CO_2Me)_2$	Me	Et_3N	92

The products possessed characteristic ^1H NMR and infra-red spectra.[8] The protons on the double bond appeared in the 200 MHz ^1H NMR spectra between 6 and 6.5 ppm showing characteristically small *gem* and allylic (≤ 2 Hz) coupling. In addition the methyne proton α to nitrogen in the pyrrolidines, (**8**) X = NTs, appeared as a multiplet at *ca* 4.6 ppm. The methylene protons α to nitrogen were non-equivalent and at higher field (3 - 3.6 ppm). The infra-red spectrum showed distinctive absorbances at between 1680 and 1620 cm^{-1} due to the enone.

The acylcobalt based methodology provides a cyclization technique under very mild conditions. A variety of five-membered rings can be formed in modest to excellent yield.

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REFERENCES AND FOOTNOTES

[1] R.F.Heck, D.S.Breslow, *J.Am.Chem.Soc.*, **1963**, *85*, 2779; R.F.Heck, *Adv.Organometal.Chem.*, **1965**, *2*, 157. $NaCo(CO)_4$ is easily prepared as a solution in THF (Edgell, W.F., Lyford IV, J., *Inorg.Chem.*, **1970**, *9*, 1932) which can be gasimetrically titrated (Sternberg, H.W., Wender, I., Orchin, M., *Anal. Chem.*, **1952**, *24*, 175.) and stored for weeks at 0°C under carbon monoxide.

[2] Hegedus, L.S., Inoue, Y., *J.Am.Chem.Soc.*, **1982**, *104*, 4917; Hegedus, L.S., Perry, R.J., *J.Org.Chem.*, **1984**, *49*, 2570; Otsuka, S., Nakamura, A., *Inorg. Chem.* , **1972**, *11*, 644; Alper, H., *Aldrich.Acta*, **1991**, *24*, 3.

[3] For related reactions based on mercury or palladium chemistry, see Walkup, R.D., Kim, S.W., *J.Org.Chem.*, **1994**, *59*, 3433; Davies, I.W., Scopes, D.I.C., Gallagher, T., *Synlett*, **1993**, 85; Walkup, R.D., Guan, L., Mosher, M.D., Kim, S.W., Kim, Y.S., *Synlett*, **1993**, 88; Gallagher, T., Davies, I.W., Jones, S.W., Lathbury, D., Mahon, M.F., Molloy, K.C., Shaw, R.W., Vernon, P., *JCS Perkin I*, **1992**, 433 and references therein; Ma, S., Negishi, E.-i., *J.Org.Chem.*, **1994**, *59*, 4730.

[4] Prepared from the corresponding nor-alkynes: Searles, S., Li, Y., Nassim, B., Robert-Lopes, M.-T., Tran, P.T., Crabbé, P., *JCS Perkin I*, **1984**, 747; Crabbé, P., Nassim, B., Robert-Lopes, M.-T., *Org.Syn.Coll.Vol. VII*, 276.

[5] **Preparation of mesylate (5):** Triethylamine (6.5 mmole) and mesyl chloride (6.5 mmole) were added to a solution of the allenol (**3**) (5 mmole) in dichloromethane (25 ml) at 0°C. The mixture was stirred for 2 hours, diluted with dichloromethane, then washed with saturated sodium bicarbonate solution and brine. The organic layer was dried and concentrated. The crude mesylate was used without further purification.

Preparation of Malonate (**6**): Sodium hydride (6.5 mmole) was added to a solution of dimethyl malonate (13 mmole) in THF (30 ml). The mixture was stirred under nitrogen for 30 minutes, then added via cannula to a solution of the mesylate (5 mmole) in THF (10ml). The mixture was heated at reflux for 18 hours, allowed to cool, quenched with saturated ammonium chloride and extracted with ether. The organic layer was washed with brine, dried, concentrated and purified by flash chromatography (silica gel/ 20% ether-hexane) to give the malonate as an oil: yield 80 %; ^{1}H NMR δ 5.04 (quin., J = 7.1 Hz, 1H, =CH), 4.63 (quin., J = 2.6 Hz, 2H, CH_2=), 3.71 (s, 6H, OCH_3), 3.34 (t, J = 7.8 Hz, 1H, C<u>H</u>$(CO_2CH_3)_2$), 1.97 (m, 4H, =CHC<u>H</u>$_2$; C<u>H</u>$_2$CH), 1.41 (quin., J = 7.2 Hz, 2H, CH_2); ^{13}C NMR δ 208.9 (=C=), 170.2 (C=O), 89.6, 75.5 (<u>C</u>=C=<u>C</u>), 52.9, 51.9, 28.7, 28.2, 27.1, ir (neat) 2959, 2874, 1956 (=C=), 1738 (C=O), 1443, 1346, 1152, 1069, 851 cm^{-1}.

Sulfonamide (7): Sodium hydride (6.5 mmole of a 60% suspension) was added to a solution of *p*-toluenesulfonamide (5 mmole) in DMF (10 ml) at 0°C. After stirring at room temperature for 30 min, a solution of the mesylate (5 mmole) in DMF (10 ml) was added at room temperature. The mixture was heated at 140°C under nitrogen for 18 hours, then cooled and quenched with saturated ammonium chloride solution. The DMF was removed by simple distillation. The residue was taken up in ether, washed with brine, dried, concentrated, and purified by flash chromatography (silica gel/ 30 % ether-hexane) to give the sulfonamide as an oil: 80 % yield; ^{1}H NMR δ 7.75 (d, J = 8.3 Hz, 2H, Ar), 5.02 (m, 2H, =CH; NH), 4.99 (quin., J = 6.6 Hz, 2H, CH_2=), 4.61 (q, J = 3.3 Hz, 2H, CHC$\underline{H}_2$), 2.42 (s, 3H, CH_3), 1.98 (m, 2H, CH_2N), 1.57 (quin., J = 7.3 Hz, 2H, CH_2); ^{13}C NMR δ 208.9 (=C=), 143.8, 137.4, 130.2, 127.6 (Ar), 89.3, 75.8 ($\underline{C}$=C=$\underline{C}$), 43.0, 29.2, 25.5, 22.0; ir (neat) 3289 (NH), 2940, 2876, 1958 (=C=), 1605, 1443, 1327, 1155, 1086, 823 cm^{-1}.

[6] **General procedure for allene acylation-cyclization:** The alkyl halide (1 eq) was added to a stirred solution of sodium tetracarbonyl cobaltate (ca 0.1 M) in THF at 0°C under an atmosphere of carbon monoxide.The mixture was stirred at room temperature for 30 min (methyl iodide) or for 60 min (BOMCl). The allene (1 eq) in THF (0.1 M) was added via cannula at 0°C, under an atmosphere of nitrogen. Stirring was continued for 3 to 4 hours. The base (1 eq) was added and the reaction mixture was stirred under carbon monoxide for 18 hours (if the base is diisopropylethylamine) or for 1 hour (sodium hydride). Residual cobalt carbonyl complexes were decomposed by addition of ethereal iodine until the color of iodine became permanent and no further gas evolution was observed. The reaction mixture was diluted with ether, washed with aqueous ammonium chloride solution, aqueous sodium thiosulfate solution and brine. The organic layer was dried and concentrated. The residue was purified by flash chromatography (silica gel, 20 - 30% ether-hexane) to afford the cyclized products.

[7] The product was isolated as a single diastereomer, presumed to be *trans*.

[8] Ketone (**9**), R = CH_3, X = C(CO_2Me)$_2$:^{1}H NMR δ 6.05 (s, 1H, CH_2=), 5.75 (s, 1H, CH_2=), 3.95 (t, J = 8.9 Hz, 1H, CH), 3.55 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 2.51 (m, 1H, $CH_2C\underline{H}$), 2.31 (s, 3H, $COCH_3$), 2.14 (m, 1H, $CH_2C\underline{H}$), 1.58-2.01 (m, 4H, CH_2CH_2); ^{13}C NMR δ 199.8 ($\underline{C}OCH_3$), 172.9, 171.5 ($\underline{C}O_2CH_3$), 149.9 (CH_2=$\underline{C}$CO), 125.2 (CH_2=), 64.6 ($\underline{C}$(CO_2CH_3)$_2$), 53.1, 52.5 , 45.3 (CO$\underline{C}H_3$), 35.5, 32.1, 26.7, 23.7 ; ir (neat) 2959, 2888, 1726 (C=O), 1680-1630 (C=O, C=C), 1443, 1371, 1271, 1159, 935 cm^{-1}; m/z: 254 (M$^+$), 211 (M$^+$ - Ac), 165 (M$^+$ - $CH_2CHCOCH_3$); Anal: calc C 61.41, H 7.13, found C 61.23, H 6.92.

Ketone (**9**), R = CH_3, X = NTs: ^{1}H NMR δ 7.69 (d, J = 8.2 Hz, 2H, Ar), 7.31 (d, J= 8.2 Hz, 2H, Ar), 6.27 (d, J = 1.5 Hz, 1H, =CH), 6.24 (s, 1H, =CH), 4.60 (m, 1H, CHN), 3.55 (m, 1H, CH_2N), 3.13 (m, 1H, CH_2N), 2.42 (s, 3H, $COCH_3$), 2.36 (s, 3H, $PhCH_3$), 1.42-1.78 (m, 4H, CH_2CH_2); ^{13}C NMR δ 199.4 (CO), 149.7 144.0, 134.5, 130.2, 128.1, 127.1 (Ar, vinyl), 59.5, 49.8, 33.3, 26.8, 23.9, 21.9; ir (neat) 2932, 2859, 1670 (C=O), 1630 (C=C),1561, 1454, 1369, 1342,1155, 1084, 1003, 839 cm^{-1}; m/z: 224 ($C_4H_7NTs^+$), 137 (M$^+$ -Ts), 91 ($C_7H_7^+$). Anal: calc C 61.41, H 6.53, found C 61.28, H 6.68.

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