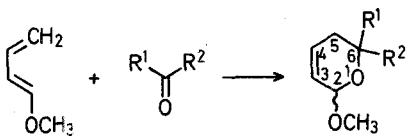
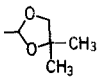


1 2a-g 3a-g

2,3	R^1	R^2
a	H_3C	$-COOCH_3$
b	H	$-CH_2-NH-COOCH_2C_6H_5$
c	H	$-CH(CH_3)-O-Si(CH_3)_2C_4H_9$-t
d	H	
e	H	$-CH_3$
f	H	
g	H	

Organic Syntheses under High Pressure: Lanthanide-Catalysed [4 + 2]Cycloaddition of 1-Methoxybuta-1,3-diene to Carbonyl Compounds

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High-pressure [4 + 2]cycloaddition of 1-methoxybuta-1,3-diene to carbonyl compounds is described. The pressure required is successfully reduced to 10 kbar with the use of a lanthanide catalyst.

We have recently reported on the high-presure (15–25 kbar) [4 + 2]cycloaddition of 1-methoxybuta-1,3-diene (**1**) to simple, representative carbonyl compounds[1] and demonstrated the efficacy of this method in the context of cycloaddition of **1** to 2,3-*O*-isopropylidene-D-glyceraldehyde[2]. Cycloadducts obtained in these reactions are versatile synthons in organic synthesis. For many organic chemists, however, very high-pressure technique is not readily available because of the high cost of the apparatus. This prompted us to check the influence of Lewis acid catalysis[3,4] on the reaction between carbonyl compounds and diene **1**. Unfortunately, diene **1** polymerises immediately even in the presence of traces of Lewis acids such as zinc chloride, boron trifluoride etherate, dialkoxy aluminium chloride etc.

Danishefsky and Bednarski have recently proved[5] that rare-earth cations, suitably complexed with solubilizing ligands e.g. $Eu(fod)_3$, $Yb(fod)_3$, $Eu(hfc)_3$, are very mild Lewis acids and are excellent catalysts for hetero-Diels-Alder reactions. We have now found that polymerisation of diene **1** is negligible in the presence of these catalysts. However, $Eu(fod)_3$-mediated Diels-Alder reactions of **1** with non-activated carbonyl compounds such as simple aldehydes, carried out at atmospheric pressure are much too slow to be observable.

We report here the combination of the two methods – high pressure and use of lanthanide catalyst – for a successful [4 + 2]cycloaddition of diene **1** with non-activated carbonyl compounds **2** (Table) to give the adducts **3**. As expected, the pressure required could be successfully reduced to 10 kbar with the use of a lanthanide catalyst.

High-pressure experiments were performed in a piston-cylinder apparatus for pressures of about 12 kbar. The initial working volume was 10 ml. The details of this apparatus were described earlier[6]. All reactions were carried out during 20 h, in dichloromethane as solvent, under 10 kbar at 50 °C in the presence of 1 mol% $Eu(fod)_3$.

Much better yields were obtained when dienophiles **2a–d**, bearing an α- or β-heterosubstituent with respect to the carbonyl group, were used. This is probably due to the coordination of the europium catalyst to both carbonyl group and heterosubstituent. On the other hand, in the case of **2e–g**, the yields were significantly lower because of the absence of dienophile heterosubstituents. It should be noted that cycloaddition reactions between diene **1** and dienophiles **2** carried out under exactly the same conditions (pressure, temperature, solvent, reaction time), but without catalyst, failed.

cis:*trans*-Isomer ratio of the products obtained in the presence of the catalyst is shifted in favour of the *trans*-adduct as compared with that observed for very high-pressure cycloaddition performed without catalyst[1]. This is due to the slightly acidic equilibration of **3** during the reaction course.

Application of lanthanide catalysts to high-pressure heterodiene synthesis simplifies substantially the method proposed by us earlier[1,2]. The main advantage of this approach is significant drop in the pressure required for cycloaddition reactions and consequently the high-pressure apparatus can be simpler and cheaper.

6-Benzyloxycarbonylaminomethyl-2-methoxy-5,6-dihydro-2*H*-pyran (3b); Typical Procedure:

The high-pressure apparatus[6] is charged with aldehyde **2b**[7] (1.93 g, 0.01 mol), 1-methoxybuta-1,3-diene (**1**; 1.66 g, 0.02 mol), dichloromethane (6 ml), and $Eu(fod)_3$ (0.104 g, 0.1 mmol). After closing the vessel with the mobile piston, the apparatus is placed between the pistons of a hydraulic press and the pressure is raised to 10 kbar. After stabilization of the pressure, the heater is switched on, whereupon the temperature is raised to 50 °C. The reaction mixture is kept under these conditions for 20 h, then cooled to room temperature, and decompressed. After decompression, the solvent is evaporated under reduced pressure and the residue is chromatographed on silica gel (Merck Kieselgel 60, 230–400 mesh) using hexane/ethyl acetate (6:4) as eluent. The solvent is evaporated and the residue is dried under reduced pressure to provide chromatographically pure adduct **3b** as an oil; yield: 1.39 (50%).

Table. Cycloadditions of 1-Methoxy-1,3-diene (**1**) to Dienophiles **2** under 10 kbar at 50 °C in the presence of 1 mol% $Eu(fod)_3$[a,b]

Adduct	Yield[c] [%]	b.p. [°C]/torr	Isomer ratio[d] *cis* : *trans*	Molecular formula[e] or Lit. b.p. [°C]/torr	^{1}H-N.M.R. ($CDCl_3$)[f] δ [ppm]
3a	81	89–90°/20	1:1	81–82°/1.2[1]	See Ref.[1]
3b	50	148–150°/0.05	1:1	$C_{15}H_{19}NO_4$ (277.3)	2.05 (m, 2H, H-5,5'); 3.45, 3.58 (2s, 3H, OCH_3); 3.3–4.3 (m, 3H, H-6 + CH_2—N); 4.92, 5.20 (2 br.s, 1H, H-2); 5.24 (s, 2H, CH_2—C_6H_5); 5.50 (br.s, 1H, NH); 5.4–6.3 (m, 2H, H-3 + H-4); 7.50 (s, 5H, C_6H_5)
3c	35	40–41°/2.0	6:4	$C_{14}H_{28}O_3Si$ (272.4)	0.08 [s, 6H, $Si(CH_3)_2$]; 0.90 [s, 9H, $C(CH_3)_3$]; 1.18 (d, 3H, J = 6.6 Hz, C—CH_3); 2.11 (m, 2H, H-5,5'); 3,43, 3.47 (2s, 3H, OCH_3); 3.58 (m, 1H, CH—O); 3.83 (m, 1H, H-6); 4.88, 5.05 (2 br.s, 1H, H-2); 5.65 (m, 1H, H-3); 6.01 (m, 1H, H-4)
3d	53	70–71°/0.05	1:1	$C_{11}H_{18}O_4$ (214.3)	1.32, 1.42 (2s, 6H, H_3C—C—CH_3); 2.0–2.4 (m, 2H, H-5,5'); 3.48 (s, 3H, OCH_3); 3.6–4.4 (m, 4H, H-6 + O—CH—CH_2—O); 4.90, 5.02 (2 br.s, 1H, H-2); 5.6–6.2 (m, 2H, H-3 + H-4)
3e	15	57–58°/30	3:7	48–50°/22[1]	See Ref.[1]
3f	12	107–108°/0.8	1:1	119–120°/1.2[1]	See Ref.[1]
3g	17	96–97°/0.8	4:6	106–108°/1.2[1]	See Ref.[1]

[a] The pressure was measured by manganin coil (accuracy: ± 0.5 kbar).

[b] The temperature was measured by thermocouple (accuracy: ± 1 °C).

[c] Yield of isolated product.

[d] *cis* : *trans*-Ratios calculated from the ^{1}H-N.M.R. spectra by integration of H-2 (*cis*/*trans*) signals.

[e] All products gave satisfactory microanalyses (C ± 0.41%, H ± 0.43%).

[f] ^{1}H-N.M.R. spectra were recorded on a Jeol JNM-100 (100 MHz) spectrometer.

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