Structural assignments and compositional analyses of the components were made by inspection of increasing and decreasing nmr signals in spectra obtained from different column chromatography fractions. The nmr structural assignments[14] were verified by double irradiation experiments. Initial fractions contained a mixture of dimethyl phthalate (**3**) and dimethyl cycloheptatriene-1,2-dicarboxylate (**6**): $\delta_{TMS}^{CDCl_3}$ 2.52 (d, 2 H, J = 7.0 Hz, C-7 protons), 3.79 (s, 3 H, CO_2Me), 3.81 (s, 3 H, CO_2Me), 5.48 (dt, 1 H, J = 8.8, 7.0 Hz, C-6 proton), 6.33 (dt, 1 H, J = 8.8, 3.0 Hz, C-5 proton), 6.82 (br d, 2 H, J = 3.0 Hz, C-3 and C-4 protons). Subsequent fractions provided increasing amounts of dimethyl cycloheptatriene-1,7-dicarboxylate (**7**) [$\delta_{TMS}^{CDCl_3}$ 3.61 (s, 3 H, CO_2Me), 3.81 (s, 3 H, COOMe), 4.18 (d, 1 H, J = 8.0 Hz, C-7 proton), 5.91 (br dd, 1 H, J = 8.0, 10 Hz, C-6 proton), 6.42 (br dd, 1 H, J = 10, 6 Hz, C-5 proton), 6.64 (br dd, 1 H, J = 10, 6.0 Hz, C-3 proton), 6.84 (dd, 1 H, J = 10, 6 Hz, C-4 proton), 7.38 (br d, 1 H, J = 6.0 Hz, C-2 proton)] and dimethyl cycloheptatriene-2,3-dicarboxylate (**8**) [$\delta_{TMS}^{CDCl_3}$ 2.45 (dd, 2 H, J = 6.5, 7.5 Hz, C-7 protons), 3.74 (s, 3 H, CO_2Me), 3.82 (s, 3 H, CO_2Me), 5.86 (dt, 1 H, J = 9.5, 7 Hz, C-6 proton), 6.35 (dd, 1 H, J = 9.5, 5.5 Hz, C-5 proton), 6.52 (t, 1 H, J = 7.5 Hz, C-1 proton), 7.65 (d, 1 H, J = 5.5 Hz, C-4 proton)]. The fourth possible isomer, dimethyl cycloheptatriene-3,4-dicarboxylate,[12] was not detected. Integration of the carbomethoxy region in the nmr spectrum of the crude thermolysis mixture of **2** showed the following composition: **3** (24%), **6** (18%), **7** (27%), and **8** (31%). Thermolysis of a mixture of **3** (28%), **6** (33%), **7** (29%), and **8** (10%) at 220–225° for 1 hr resulted in an increase of **8** (33%) at the expense of compound **6** (7%) whereas the amount of **7** (30%) and **3** (30%) remained practically constant. Heating of a mixture of **3** (11%), **6** (19%), **7** (29%), and **8** (44%) gave a similar relative ratio of cycloheptatriene derivatives as in the previous reaction, indicating that the **6**, **7**, and **8** readily interconvert at 220°. In all cases, equilibrium was already established after 20 min at 220°.

The formation of compounds **3**, **6**, **7**, and **8** from **2** is of considerable mechanistic interest. A possible formation of the cycloheptatriene derivatives **6**–**8** from **2** could proceed under extrustion of sulfur dioxide to give first diradical **9** followed by a collapse to the norcaradiene derivatives **4** and **5**. The reaction could also involve initial formation of dimethyl norborna-2,5-diene-2,3-dicarboxylate. When the latter was thermolyzed under the same conditions as described for **2**, the starting material was recovered exclusively, thus excluding dimethyl norborna-2,5-diene-2,3-dicarboxylate as an intermediate in the formation of compounds **6** to **8**. Another attractive mechanism would be a linear [$_\pi2_a + {}_\sigma2_a + {}_\sigma2_s$] or nonlinear [$_\pi2_s + {}_\sigma2_a + {}_\sigma2_a$] cheletropic sulfur dioxide extrusion–rearrangement reaction (shown for conversion of **2** to **5**) also leading to the norcaradiene intermediates **4** and **5**. From the latter, cycloheptatriene derivatives **6** and **8** would be derived by skeletal rearrangements followed by [1,5]-hydrogen shifts to give **7**.

The formation of **3** may be formulated either as a sulfene extrusion reaction from **2** or possibly as a carbene extrusion reaction of intermediates **4** and **5**. Examples for the loss of carbene from cycloheptatriene derivatives *via* norcaradienes have been described in the literature.[15] Thermolysis of **2** in the presence of cyclododecene as a carbene acceptor as well as prolonged heating of a mixture of **3**, **6**, **7**, and **8** did not result in an increase of **3**. Thus, formation of **3** from intermediates **4** and **5** by a carbene transfer reaction seems to be an unlikely route. The experimental data indicate that in the thermolysis of **2** two independent processes are competing: sulfur dioxide extrusion leading to cycloheptatrienes **6**, **7**, and **8** represents the predominant route, whereas retro Diels–Alder reaction which liberates sulfene from **2** is energetically less favored at 220°. The presence of a phenyl group at C-4 in the thermolysis of the bicyclic sulfone can essentially suppress norcaradiene formation and force the reaction to proceed *via* the sulfene route exclusively.[8] The fate of methylene fragments, possibly derived from sulfene, is not clear. Minor nmr signals typical for cyclopropane ring protons at about δ 0.5 were observed in a short-time thermolysis of **2** at 220°, but were not detected in the 10-min reactions. These signals could be due to thermally labile, sulfene-derived, methylene transfer products. Present investigations are oriented toward the study of the electronic and/or steric influence of different substituents on the two competing processes as well as synthetic aspects of the previously described sulfur dioxide extrustion–rearrangement reaction.

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(14) The chemical shifts for compounds **7** and **8** which were determined in $CDCl_3$ differ by 0.05 to 0.15 ppm from the reported parameters[12] which were obtained in CCl_4.

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(16) Detailed experimental data on the synthesis of α-thiopyran 1,1-dioxide will be described in a coauthored full paper.

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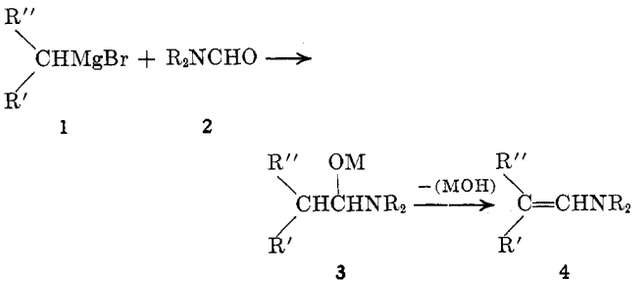
The Preparation of Enamines by Addition of Grignard Reagents to *N*,*N*-Dialkylformamides

Summary: The reaction of *N*,*N*-dialkylformamides with alkylmagnesium bromides, unlike the corresponding reaction with lithium alkyls, gives a primary addition product which undergoes spontaneous elimination forming an enamine in preparatively useful yield.

Sir: We have found that the reaction of Grignard reagents with readily available *N*,*N*-dialkylformamides affords a method of wide applicability for the preparation of aldehyde enamines (Scheme I). The reaction is particularly suited for the preparation of enamines **4** where R′ = alkyl, R″ = H, and R is a bulky substituent such as secondary alkyl. Enamines of this

SCHEME I



type may be of value as synthetic intermediates, as indicated by promising alkylations of enamines prepared from *N*-butylisobutylamine,[1] but they are not readily synthesized by direct condensation of aldehydes with hindered secondary amines.[2,3] A similar addition of Grignard reagents to N-alkylated five- and six-ring lactams has previously been used to prepare heterocyclic enamines.[4]

When primary alkylmagnesium bromides (ether solution) are added to tertiary formamides in tetrahydrofuran (THF) at −15° and the mixture is allowed to reach room temperature, the reaction solution soon shows the characteristic downfield vinyl proton signal (δ 5.5–6.5 ppm) of an enamine. No spectral evidence was found for the accumulation in significant quantities of α-amino alcoholates of type **3** which are presumed to be intermediates in the Bouveault and similar aldehyde syntheses. Pure enamines can be isolated by precipitating inorganic material with hexane and distilling the supernatant (Table I). These sterically

TABLE I

ENAMINES (4) FROM TERTIARY FORMAMIDES (2, 1.3 MOL) AND GRIGNARD REAGENTS (1, 1.0 MOL) IN THF–Et_2O[a]

R′	R″	R	Yield, %[b]
Me	H	*sec*-Bu	63
1-Pr	H	*sec*-Bu	62
1-Pentyl	H	*sec*-Bu	63
1-$C_{11}H_{23}$	H	*sec*-Bu	52
Ph	H	*sec*-Bu	59
CH_2=CH	H	*sec*-Bu	30
1-Pr	H	*n*-Bu	80
1-Pr	H	*i*-Bu	62
1-Pentyl	H	*sec*-Bu	55[c]
1-Pentyl	H	Me	81[c]
Cyclohexyl		Me	66
Cyclohexyl		*sec*-Bu	22[d]

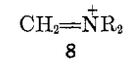
[a] Satisfactory analytical data (±0.4% for C, H, and N) were reported for all new compounds listed unless otherwise stated. [b] Distilled product. Yields were based upon 1. [c] Solvent: pure Et_2O. [d] See footnote *b*, Scheme II.

hindered enamines may be alkylated, *e.g.*, with ethyl iodide in acetonitrile, in high yield without prior isolation of the enamine.

Preliminary experiments had indicated that yields were generally better and the work-up more convenient using THF–Et_2O as solvent instead of pure Et_2O, which is less basic (see Table I). It was found essential to employ a moderate excess of the formamide but the mode of addition and the reaction temperature were less critical. Inverse addition of the Grignard reagent at a low temperature was found to be favorable. It is of interest in this connection that the yield of aldehyde in the related Bouveault syntheses has very recently been reported to be significantly improved when the reaction is run in an ether–hexamethylphosphoric triamide solvent.[5]

Not unexpectedly, reactions with secondary alkyl Grignard reagents were quite sensitive to the steric bulk of the formamide component, particularly in the addition step. With increasing bulk the yields of enamines were lower and the side reactions more pronounced. The reaction of cyclohexylmagnesium bromide with *N*,*N*-dimethylformamide (DMF) and *N*,*N*-di-*sec*-butylformamide was investigated in some detail to obtain information about the major side reactions (Scheme II). After adding the Grignard reagent as before, the temperature was allowed to rise to 25° over ~4 hr and held there for the remainder of the experiment. The reaction was monitored by nmr spectra, vpc, and vpc–ms of the reaction mixture and of samples quenched with water. With R = Me, the by-products cyclohexane and cyclohexene were formed at about the same rate during the first phase of the reaction. After 4 hr their concentrations were constant (quenched samples) indicating that all Grignard reagent had been consumed. Enamine formation progressed much more slowly with secondary Grignard reagents than with primary and was complete only after ~120 hr. No nitrogenous products which could be associated with hydrocarbon formation were identified.

Cyclohexylmagnesium bromide and **2** (R = *sec*-butyl) gave cyclohexane and cyclohexene as before, but in larger quantities (Scheme II). Consumption of the Grignard reagent was complete only after ~40 hr when the enamine signals (δ 5.5 ppm) had just begun to appear. Enamine formation was complete after a further 120 hr, but the yield was low. Our present results indicate that cyclohexene and **6** (R = *sec*-Bu) are formed mainly in a reduction of the formamide **2** by the Grignard reagent with subsequent elimination to form an electrophile, such as **8**, which then adds



8

Grignard reagent. (Similar reductions of carboxamides[6] and immonium salts[7] have been observed before.) Cyclohexane and the glyoxylic amide **7** (R = *sec*-Bu) are presumably formed by abstraction of a proton from the formamide **2** by the Grignard reagent. The resulting carbamoylmagnesium intermediate either adds to a second molecule of **2** or dimerizes like a carbene. No evolution of carbon monoxide could be

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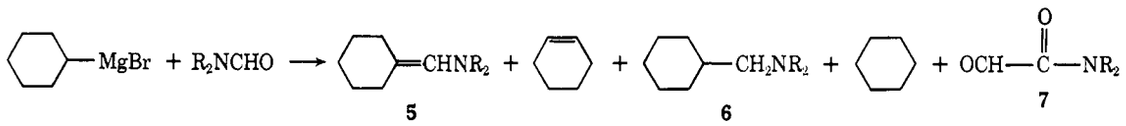
SCHEME II[a]



	5		6		7
R = Me	66%	5%[c]	Not found	7%[c]	Not found
R = *sec*-Bu	22%[b]	28%[c]	27%[b]	24%[c]	10% (2, 4-DNP)

[a] Yields were based on cyclohexylmagnesium bromide. [b] **5** and **6** (R = *sec*-Bu) were isolated by distillation as a mixture and analyzed by vapor phase chromatography (vpc)–mass spectrometry (ms). Hydrolysis afforded pure **6** and cyclohexanecarboxaldehyde. [c] By vpc of the reaction mixture.

detected by vpc. Analogous cases have been reported.[8,9]

When alkyllithium reagents in hexane were added to *N*,*N*-dialkylformamides, the amino alcoholates **3** (M = Li) formed rapidly but did not undergo spontaneous elimination to form enamines. The product **3** (M = Li; R = methyl; R′ = *n*-propyl; R″ = H) was isolated in an amorphous but reasonably pure state by stripping the solvent (30° at 0.3 mm). It was surprisingly soluble in nonpolar solvents but gave consistent ^1H ($CDCl_3$) and ^{13}C (C_6D_6) nmr spectra. Elimination forming an enamine occurred readily when the amino alcoholate **3** was treated *in situ* with Lewis acids ($MgBr_2$, BF_3, and $AlCl_3$) or with alkylating or acylating reagents (MeI, Ac_2O, and also Me_3SiCl). However, the overall yields were lower (40–50%) than with the procedure employing Grignard reagents.

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