The chemistry of Fischer carbene complexes: Discovery of a new rearrangement reaction*

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Fischer carbene complexes have emerged as an important organometallic intermediate for the synthesis of a wide variety of target organic molecules. The reactivities of these complexes do not always follow a predictable pattern. An unprecedented rearrangement of these complexes discussed herein is triggered by an apparently minor structural variation.

Background

SINCE their discovery by E. O. Fischer in 1964, the rich and varied chemistry of Fischer carbene complexes has been extensively explored[1]. This led to their utilization as useful intermediates for the synthesis of numerous complex carbocyclic and heterocyclic molecules of biological interest.

The reactivity pattern of the Fischer carbene complexes can be rationalized in terms of its structure (Figure 1). The octahedral complex contains five carbon monoxide ligands around the metal. The sixth ligand is a substituted alkoxymethylene group, where bonding to the metal occurs via the non-bonding electron pair on the methylene carbon. Five strong π- acceptor CO ligands deplete the electron density on the metal and consequently the methylene carbon is rendered electrophilic. This centre is, therefore, susceptible to nucleophilic attack. As a result of electrophilicity of the carbene carbon, on the other hand, the proton on the α-carbon is rendered acidic ($pK_a > 8$), and carbanion chemistry becomes accessible. In addition, the $M(CO)_5$ fragment can undergo ligand substitution and open up other reaction pathways.

The characteristic spectral features of Fischer carbene complexes are also consistent with its structure and symmetry. For instance, except for the CO group *trans* to the carbene ligand, four other CO ligands are equivalent by symmetry. Thus, the CO stretch in IR spectrum displays two distinct peaks at 2050 (s) and 1970 (vs) cm^{-1}, while the ^{13}C NMR spectrum displays two signals in the range 200 to 230 ppm in the ratio 1:4. The electrophilic carbene carbon signal appears at 340 to

$Cr = C$ 2·04 Å ($Cr - C$ ơ bond 2·21 Å)

$OR'/NR'_2/SR'$

$C - O$ 1·33 Å
Ether 1·43 Å
Acetone 1·23 Å
(High rotation barrier)

^{13}C : ~350 ppm (Carbocations)

Abstraction by base

Nucleophilic attack

Electrophilic attack
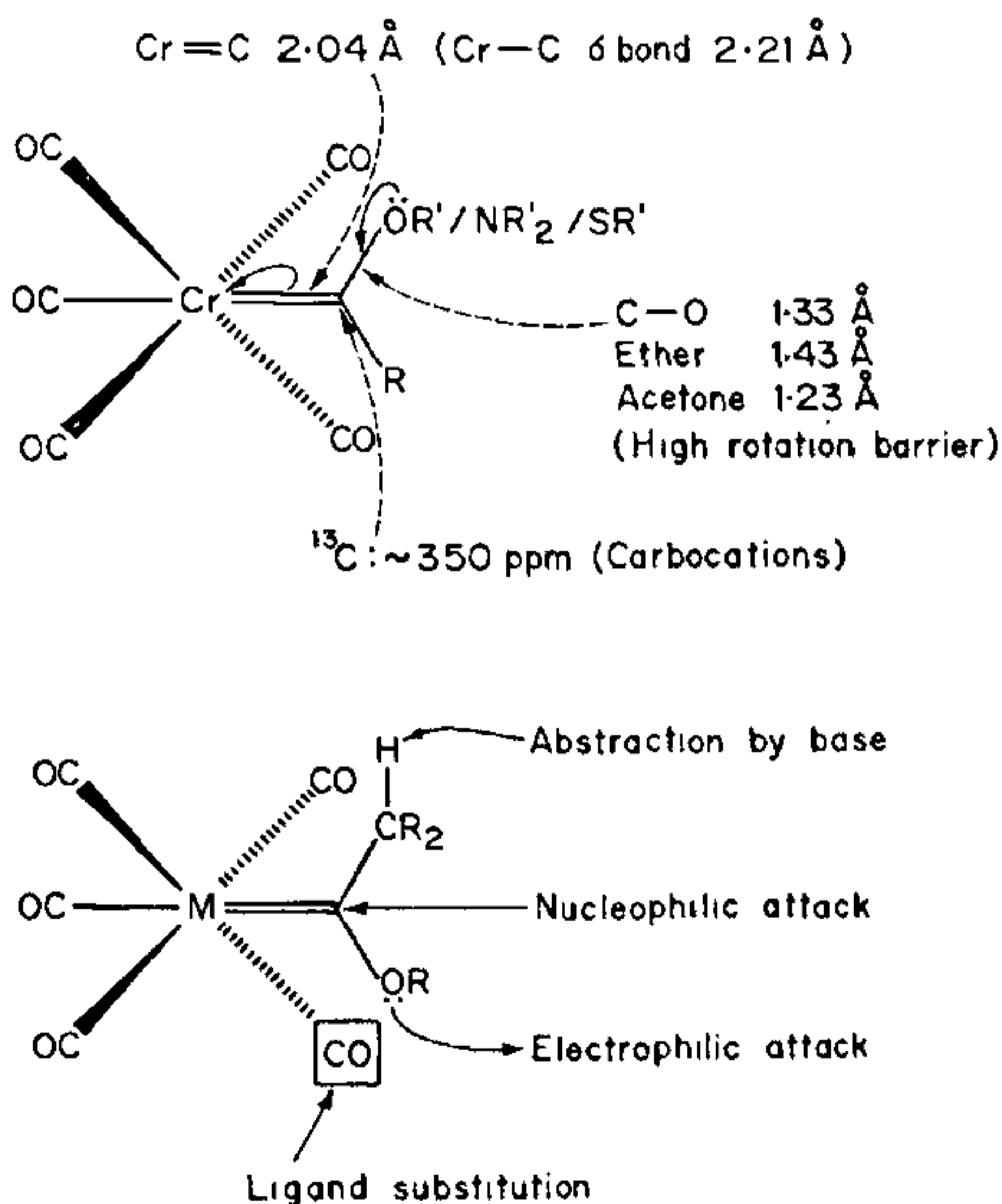
Ligand substitution

Figure 1.

360 ppm. Such diagnostic spectral features are extremely useful for straightforward identification of these complexes.

An interesting stereochemical feature of $(CO)_5M = C(OR)(Ar)$ complexes is that the aryl ring is oriented orthogonal (*out of conjugation!*) to the metal- carbene π-plane in the solid state, as shown by X-ray crystallography. Such preference may be countered to an extent

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by electron-releasing OR or NR$_2$ group in the *para* position. Such orientation is not imposed by crystal packing forces. We have now obtained clear ^{1}H NMR evidence that the orthogonal orientation of the aryl ring can be attained at a low enough temperature in solution. For example, in the low temperature spectrum shown in Figure 2, two sets of benzyl signals are observed for the carbene complex. The broad singlet appears close to the normal position. The doublet of doublet is shielded considerably by the aromatic ring anisotropy. Since the aromatic ring is unsymmetrically substituted, the two benzyl protons are rendered non-equivalent.

Among the several synthetically useful reactions of Fischer carbene complexes, the benzannulation reaction discovered by Dotz[1e] is the most exploited. An aryl, heteroaryl or alkenyl chromium alkoxycarbene complex reacts with acetylenes under thermal conditions to generate a new aromatic ring as shown in Scheme 1. This reaction has been applied to the synthesis of several biologically important molecules such as Daunomycinone, Deoxyfrenolicin, Nanaomycin, Khellin, Sphondin,
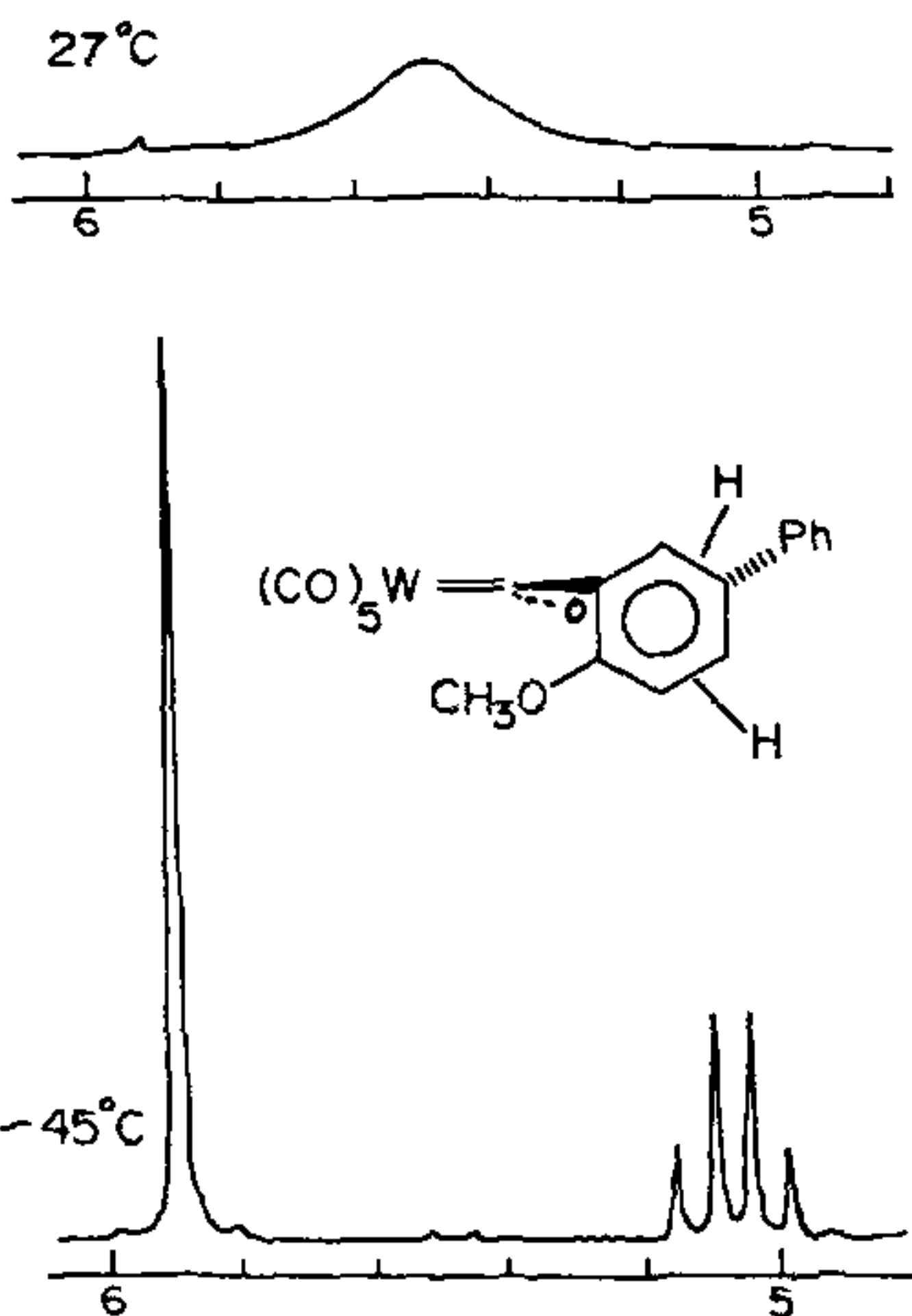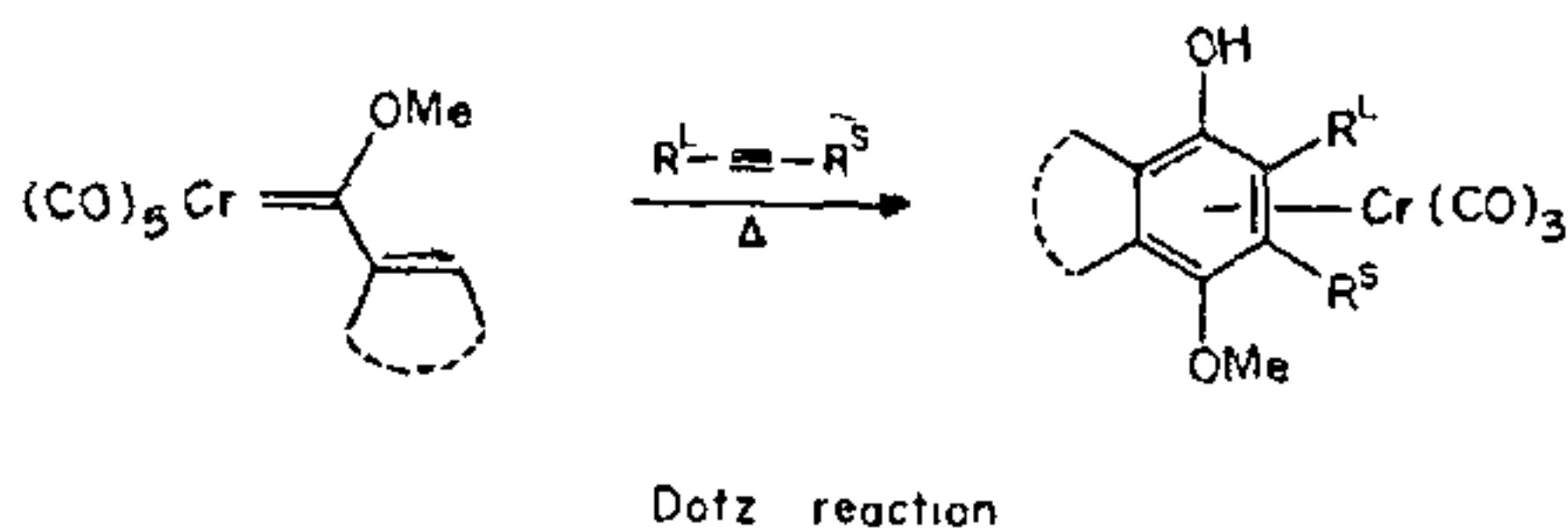
Thiosphondin, Vitamin E and several compounds in Vitamin K series (Chart 1).

Daunomycinone

Deoxyfrenolicin (R = n-Pr) Sphondin (X = O)
Nanaomycin (R = Me) Thiosphondin (X = S)
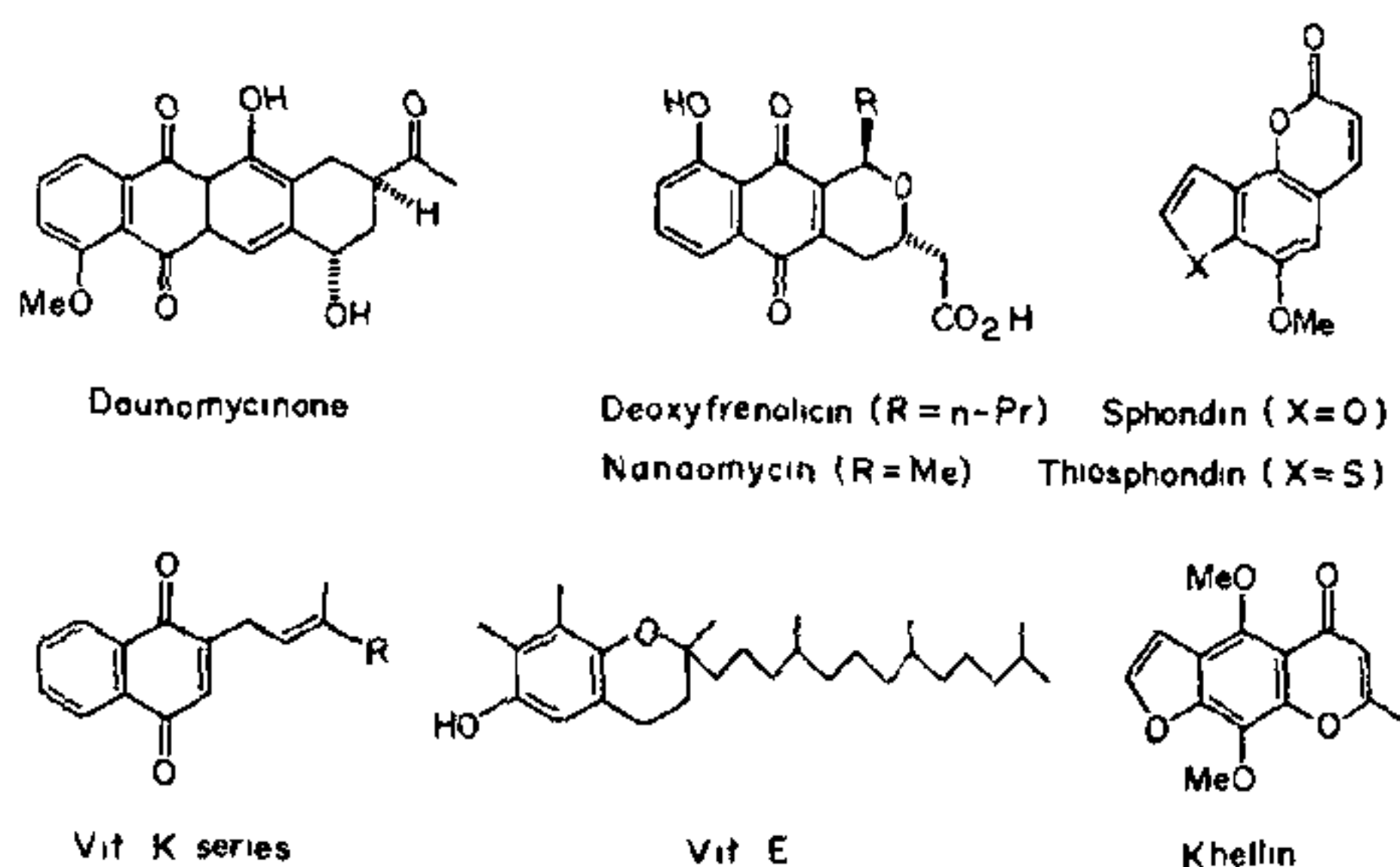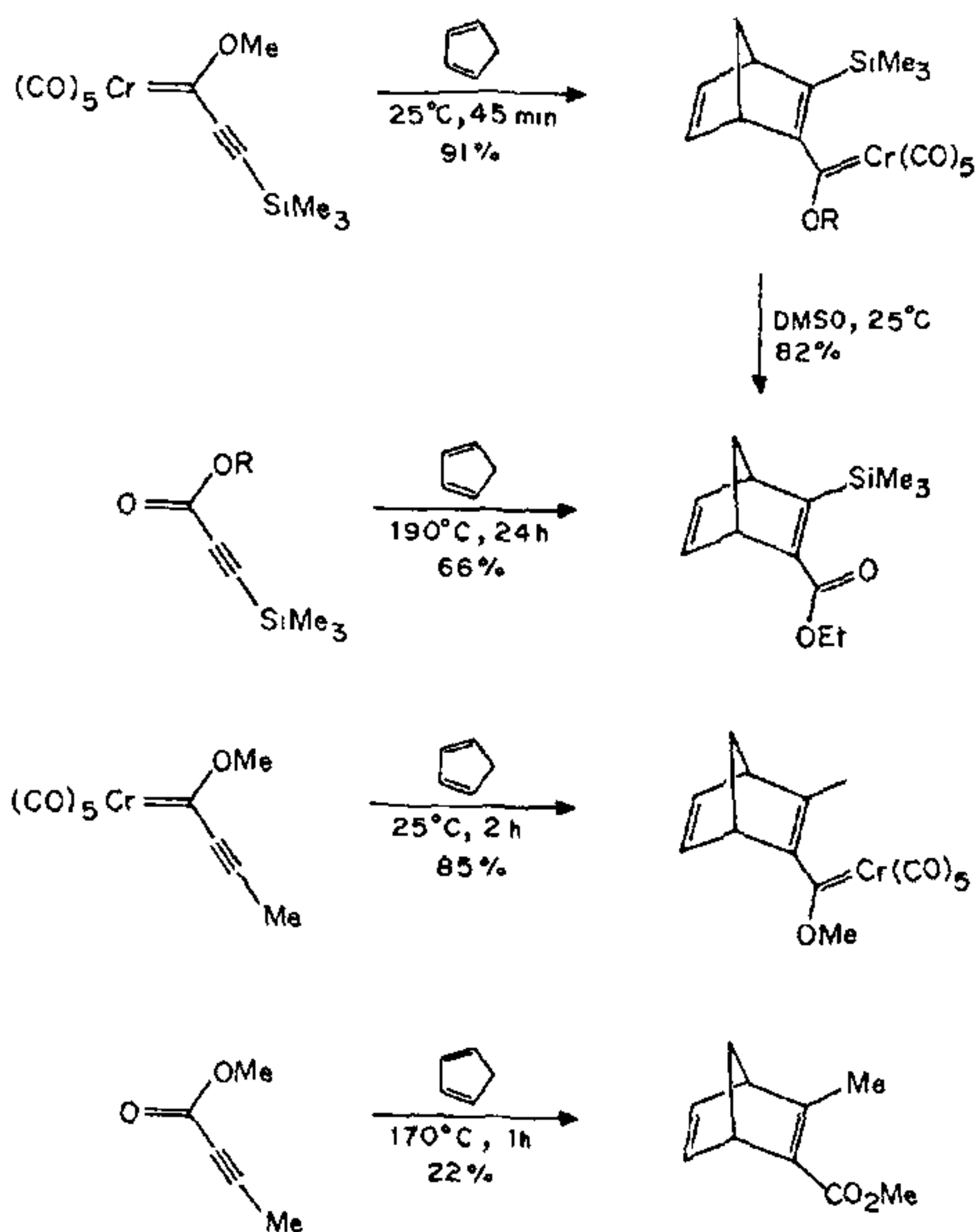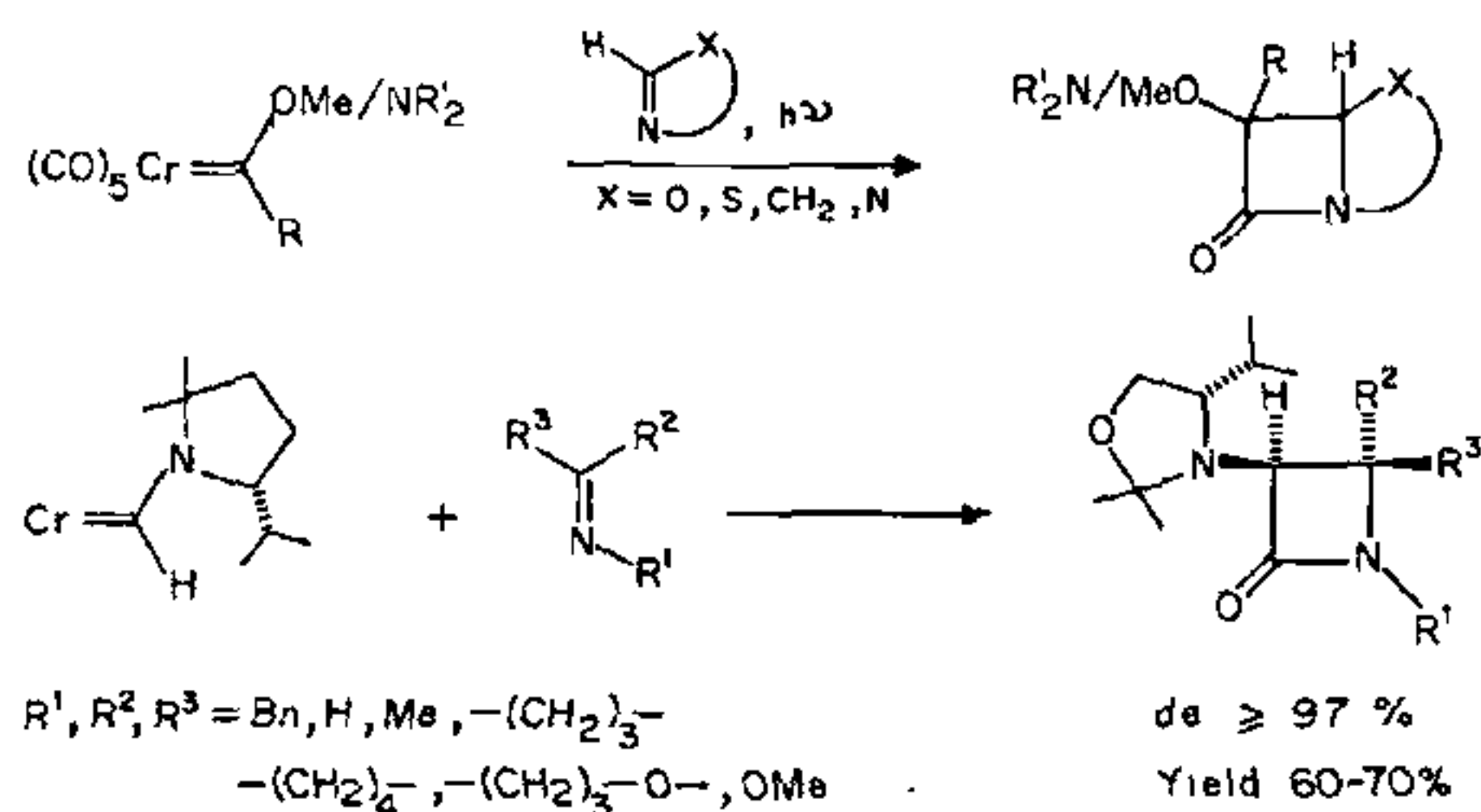
Vit K series   Vit E   Khellin

Chart 1.

Diels–Alder reactions of α,β- unsaturated alkoxycarbene complexes with dienes proceed with much greater facility than observed with corresponding esters (Scheme 2), reminiscent of Lewis acid catalysis in such reactions.

Under photochemical conditions, Fischer carbene complexes of chromium react with Schiff bases to afford β-lactams[2] (Scheme 3). The reaction is believed to

27°C

−45°C

6   5

Figure 2.

Dotz reaction

Scheme 1.

Scheme 2.

a number of alkenes revealed that activated olefins (electron- rich or electron-deficient) provided cyclopropanes on heating at temperatures greater than 90°C although intramolecular cyclopropanations are much more facile and requires no such activation (Scheme 5).
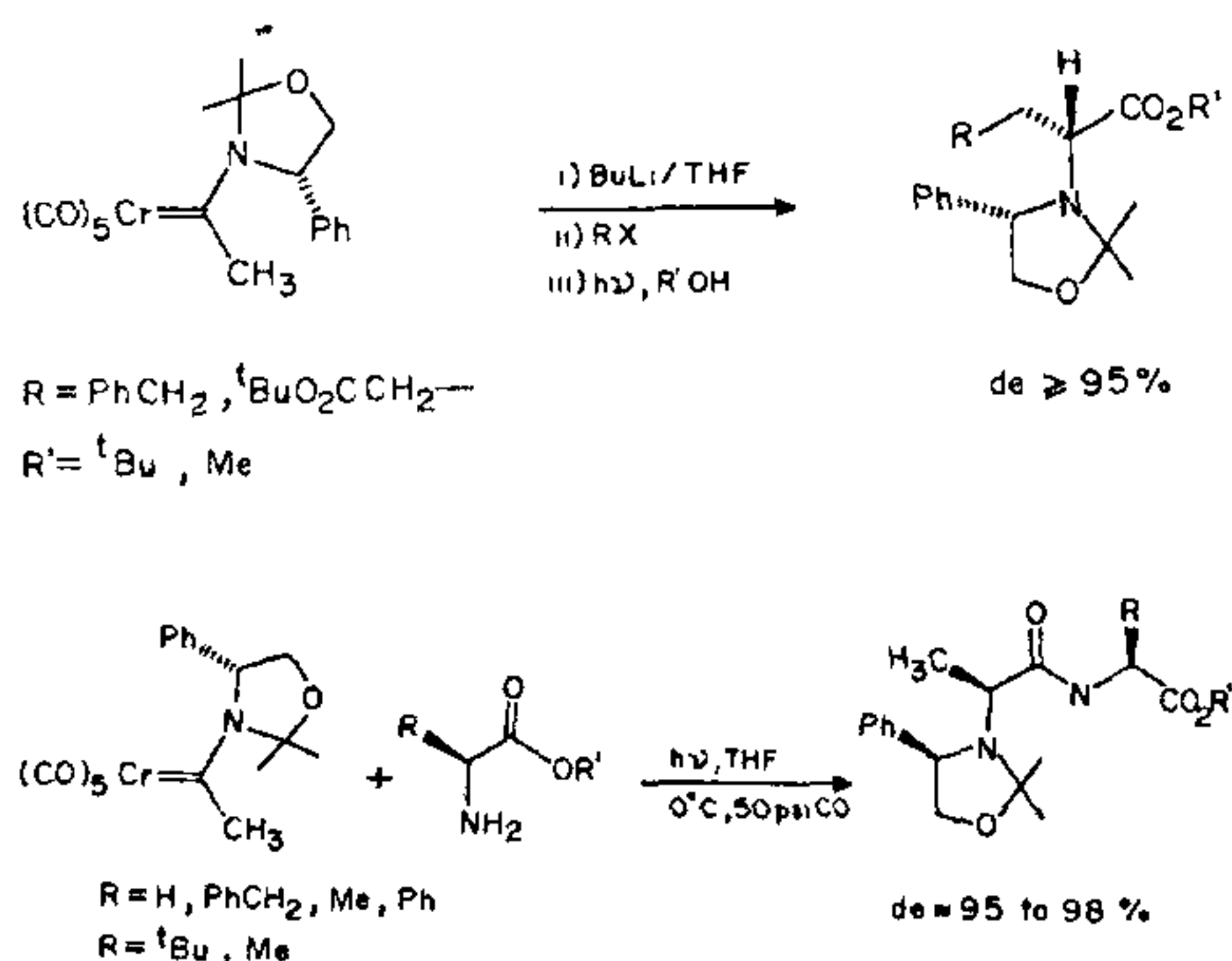
Scheme 3.

proceed *via* a ketene complex which undergoes [2 + 2] cycloaddition with the Schiff base. Excellent stereocontrol has been achieved in this reaction, and it has been possible to synthesize a variety of optically active β-lactams by this method. When the reaction is carried out under CO pressure, $Cr(CO)_6$ precipitates out of the reaction mixture and it can be recycled.
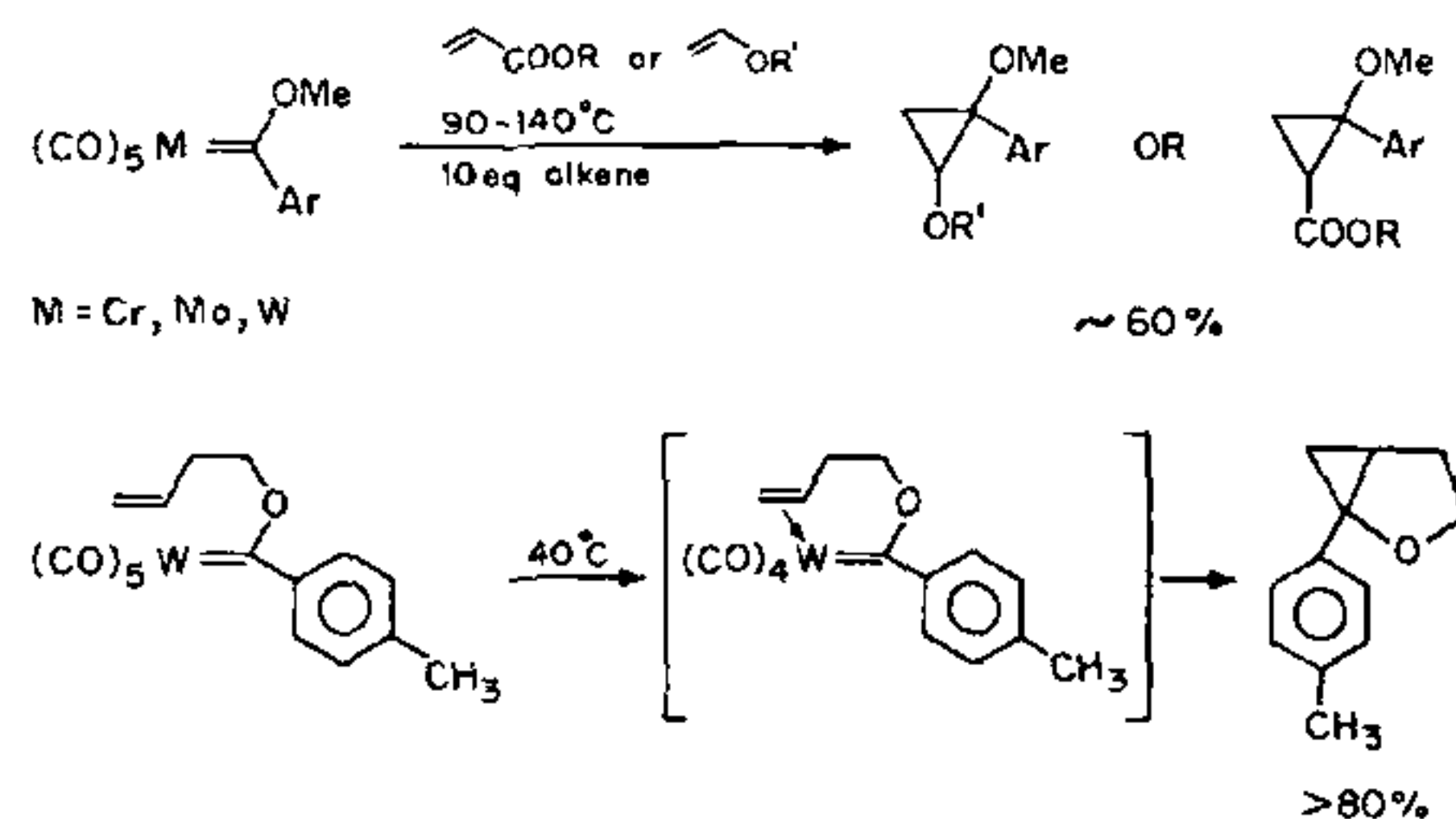
Alternatively, the metal-ketene complex can be solvolyzed *in situ* to obtain N-protected amino acid or esters[3] (Scheme 4). The extent of chiral induction was high with carbene complexes derived from chiral amines. Recently dipeptides have been synthesized with high diastereoselectivity using this method.

Scheme 5.

There has been an increasing trend in recent years to explore new reaction pathways in the chemistry of Fischer carbene complexes, by making structural changes in the carbene ligand. For example, it has been shown that the reactions of an acylmetallate salt with alkynes result in the formation of butenolides in good yields (Scheme 6) while benzannulation is not observed[4].
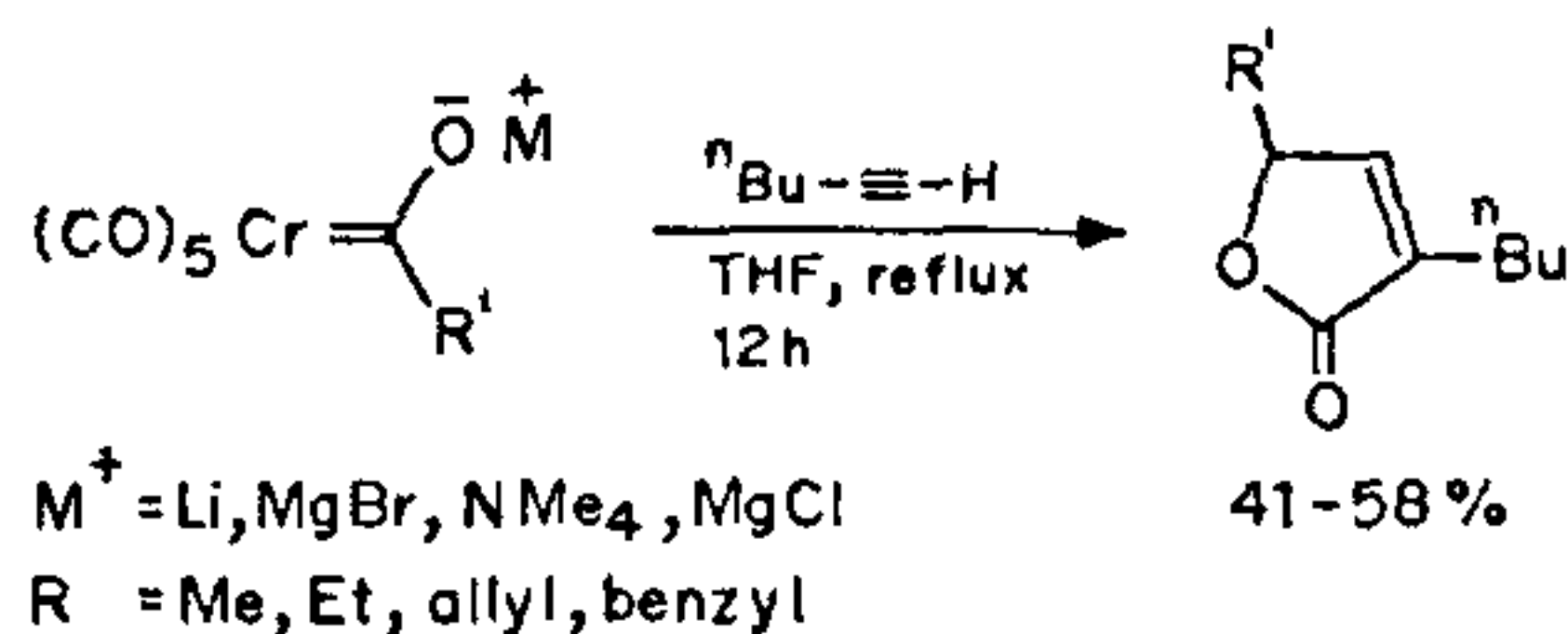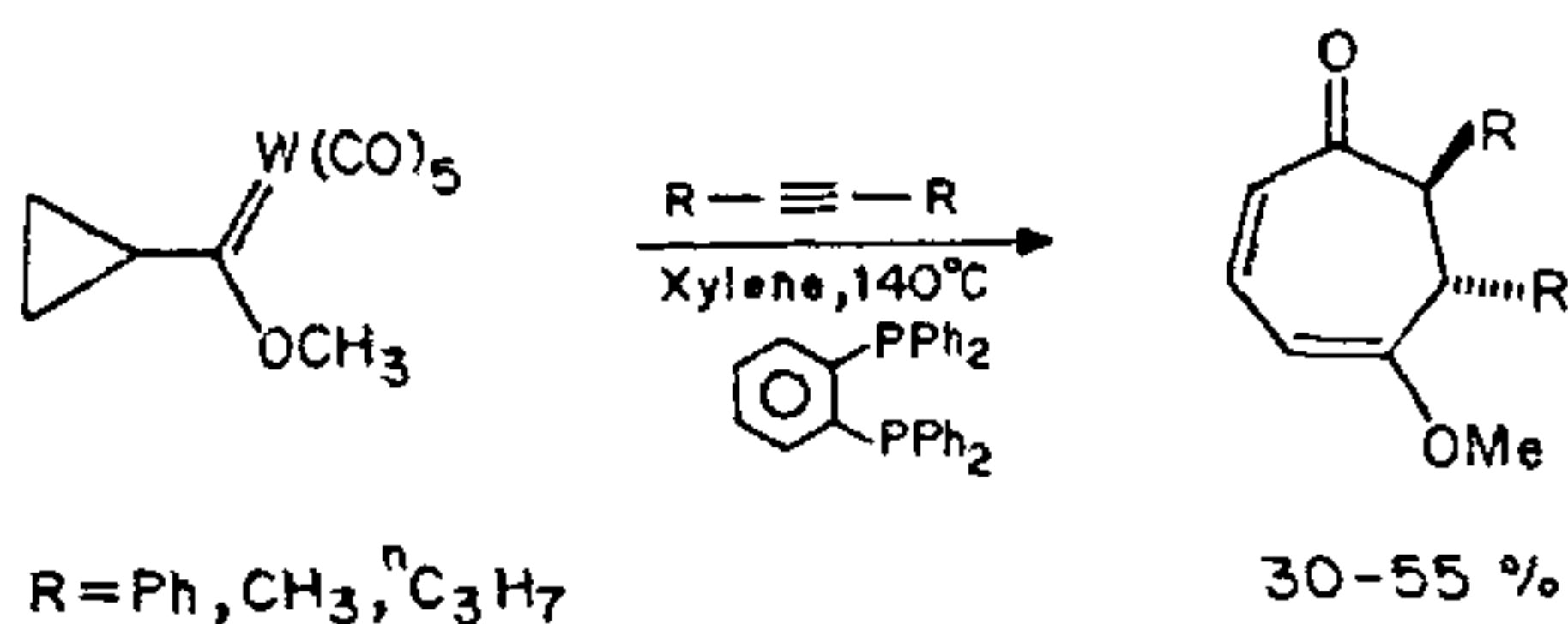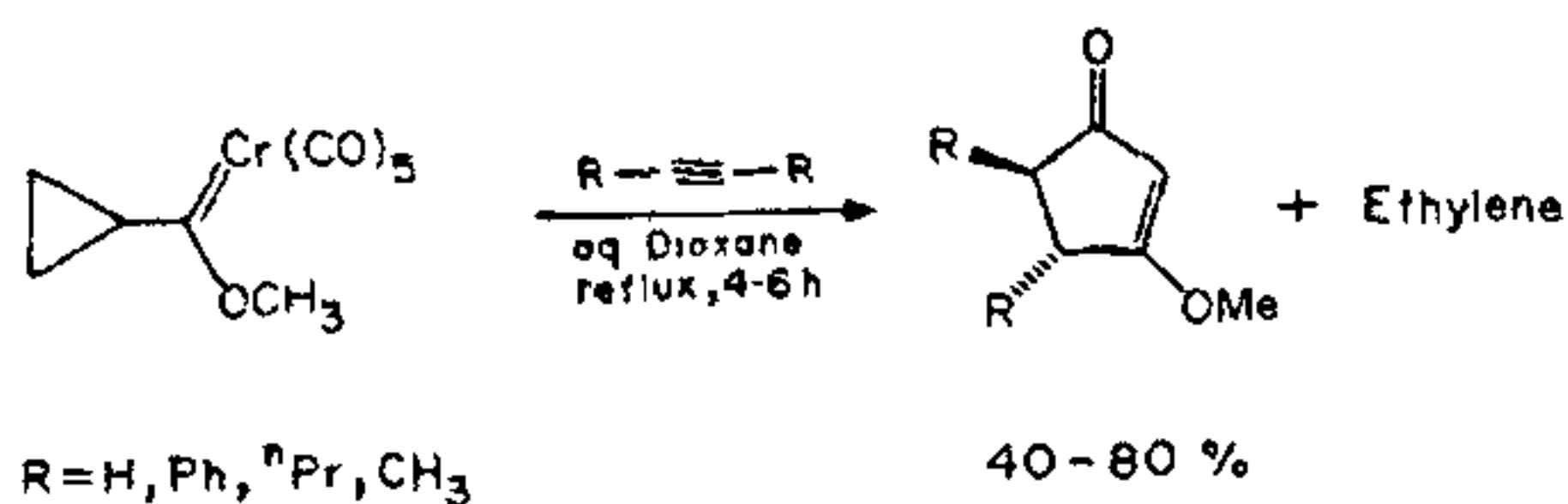
Scheme 4.

Much of the early work was directed towards release of the carbene ligand and observation of reactions typical of free carbenes, e.g. cyclopropanation. Reaction with
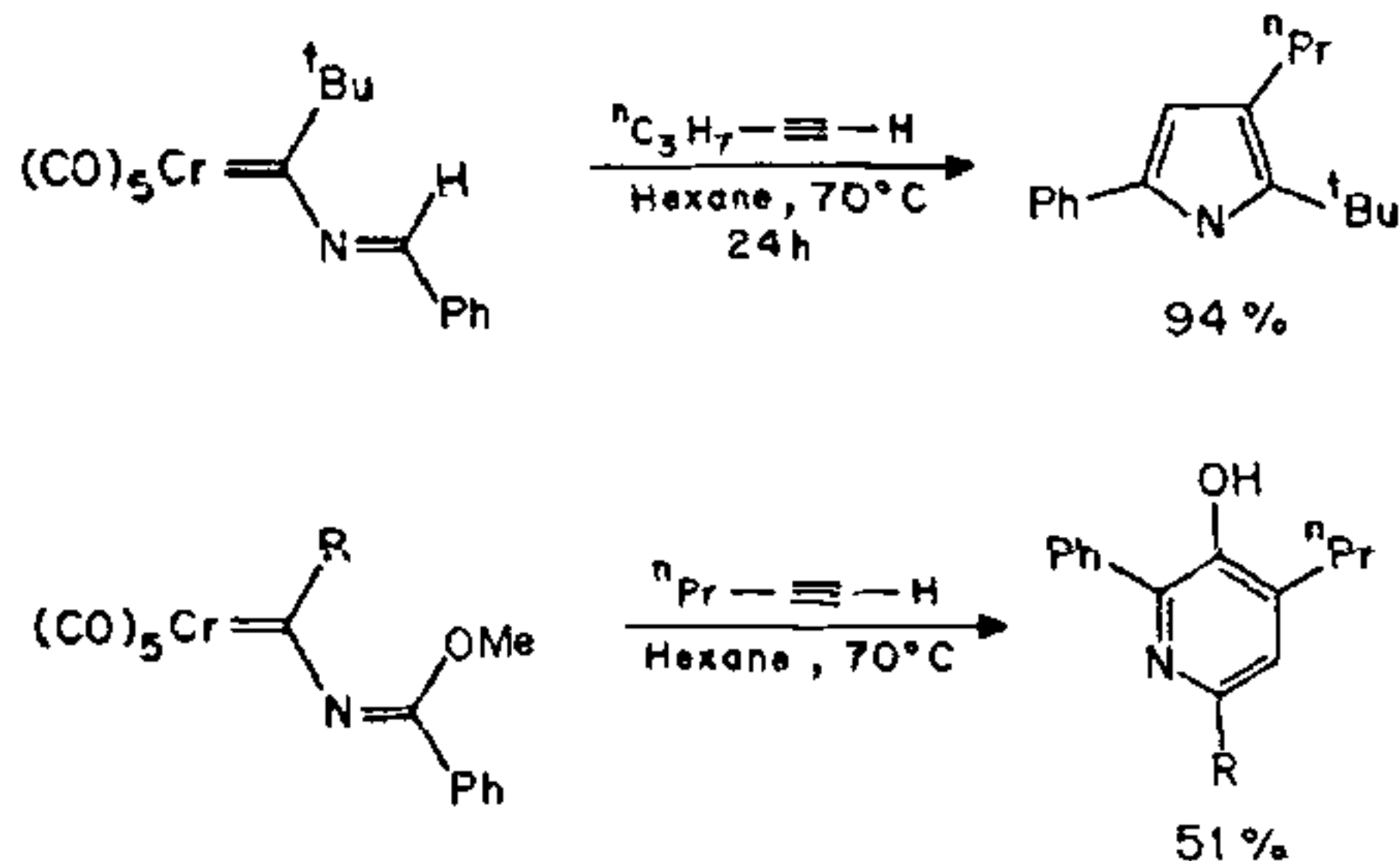
Scheme 6.

Cyclopropyl methoxycarbene complex of chromium reacts with alkynes to afford cyclopentenones. But the corresponding tungsten complex reacts with alkynes *via* a different pathway to provide cycloheptadienones[5] (Scheme 7).

With appropriately substituted carbene derivatives one can devise useful reactions to obtain heterocycles[6] (Scheme 8).

R = H, Ph, ^{n}Pr, CH$_3$

40-80 %

Scheme 9.

R = Ph, CH$_3$, ^{n}C$_3$H$_7$

30-55 %

Scheme 7.

the CO by chelation, but would not compete with incoming ligands for coordination with the metal. From a report by Dotz in 1987 which showed (Scheme 10) that a methoxy group preferentially complexed with the metal than the competing furan moiety, it appeared that furan as a poor donor might meet the above criteria.

94 %

51 %

Scheme 8.

Scheme 10.

The phenyl furfuryloxy carbene complex of tungsten was prepared by the conventional route (Scheme 11) and purified by column chromatography to furnish a red, crystalline, moderately air-stable solid.
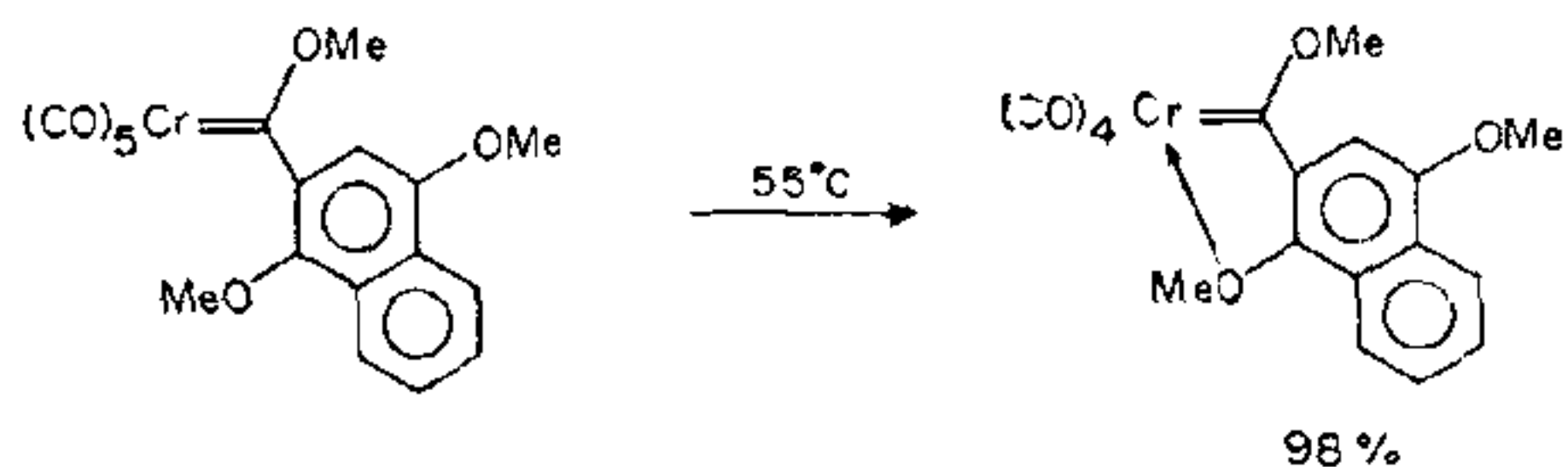
In our work, we discovered a new pathway in thermolysis of Fischer carbene complexes caused by an apparently minor variation in the oxygen substituent.
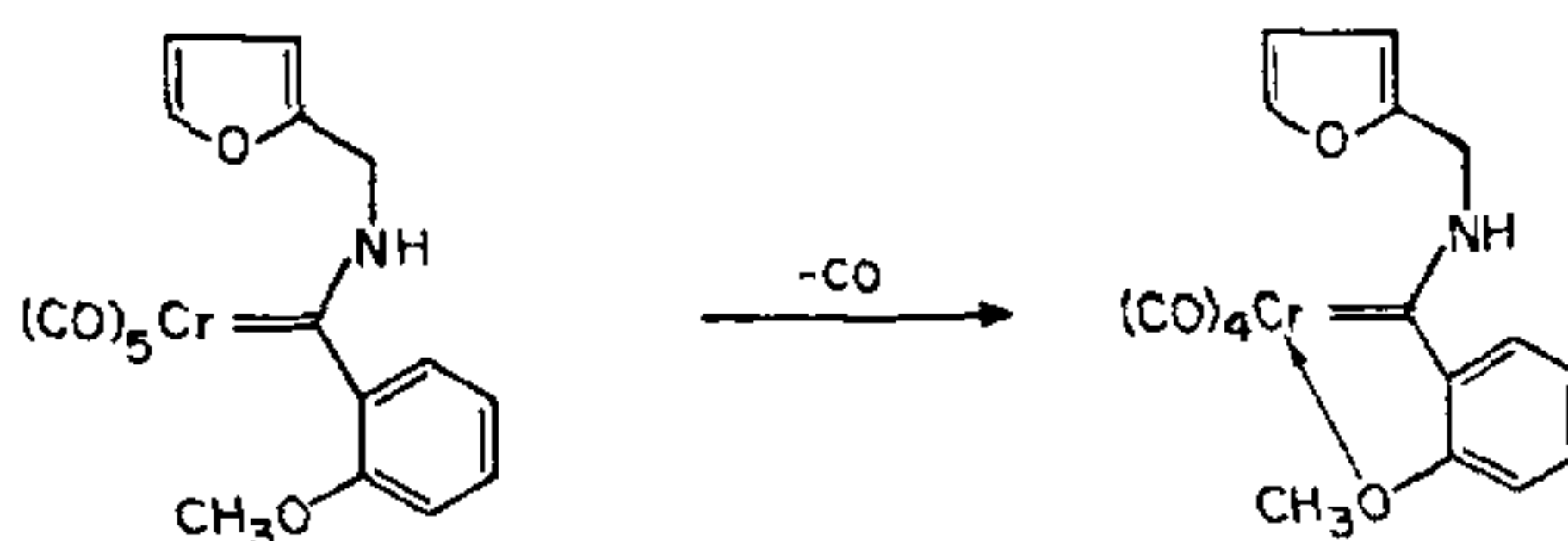
Present work

Although Dotz reaction has found extensive use in organic synthesis, the reaction is successful only with chromium carbene complexes. The tungsten carbene complexes, which are generally stable crystalline solids, lend themselves to easier manipulation but do not undergo benzannulation reaction. The higher W–CO bond strength retards both the initial decarbonylation to create a vacant coordination site and the CO insertion necessary at a later stage. Intramolecular chelation was shown to accelerate dissociation of a CO ligand in the case of chromium and tungsten carbene complexes (Scheme 9). We thought it would be desirable to have a weakly coordinating group which could intramolecularly labilize
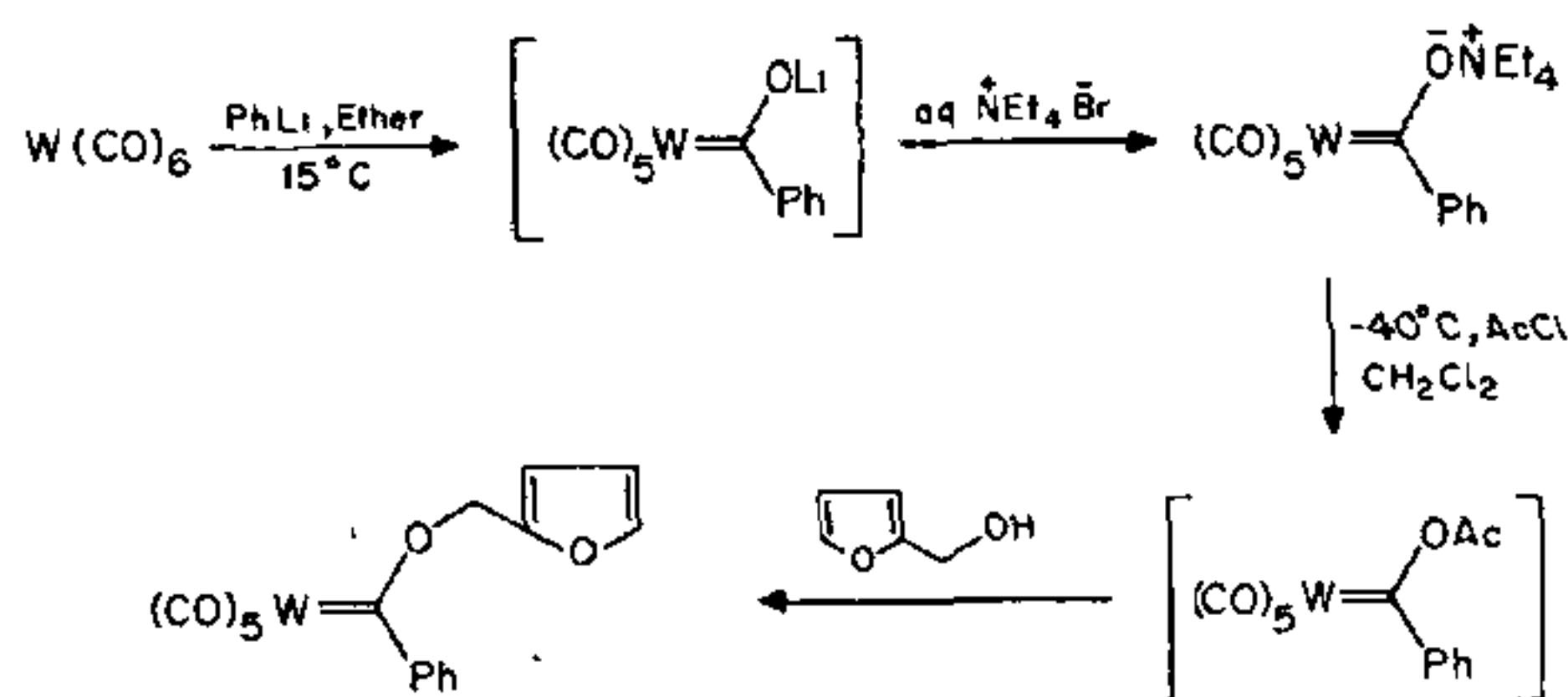

Scheme 11.

Thermolysis of this complex in benzene produced a complete surprise. The starting material was consumed and no new carbene complex was obtained. The only product isolated after chromatography was a ketone as shown in Scheme 12, in 90% yield. The ketone was derived from an unprecedented rearrangement of the carbene complex!

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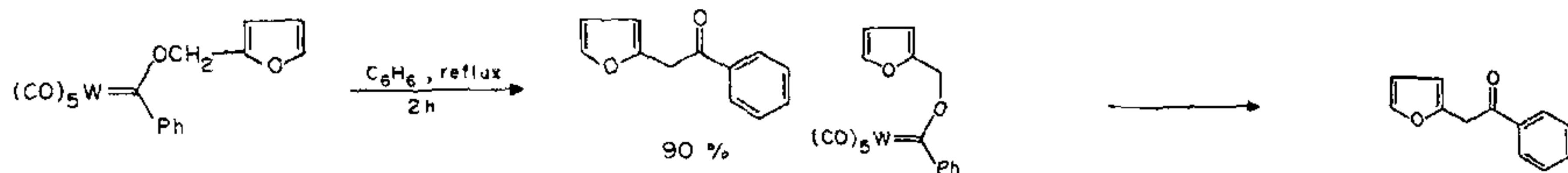
Scheme 12.

Scheme 13.

Preliminary experiments quickly identified at least two essential structural criteria that must be met for the rearrangement to occur: the oxygen must be connected to a benzylic centre, and, an aromatic ring must be attached to the carbene carbon. The results are summarized[7] in Table 1.

The rearrangement of the free carbene derived from the organic ligand could lead, in principle, to the same product. This possibility was discounted on the ground that generation of free carbene from a Fischer carbene complex has never been observed before. A few experiments were carried out to unravel the salient mechanistic features of this reaction.

Photolysis of the carbene complex 1c in benzene at room temperature afforded the ketone in 60% yield suggesting that initial CO decomposition is probably the rate-determining step. This is further supported by the observation that furfuryloxy carbene complexes underwent rearrangement in refluxing benzene while other benzyloxy complexes reacted better in refluxing toluene.
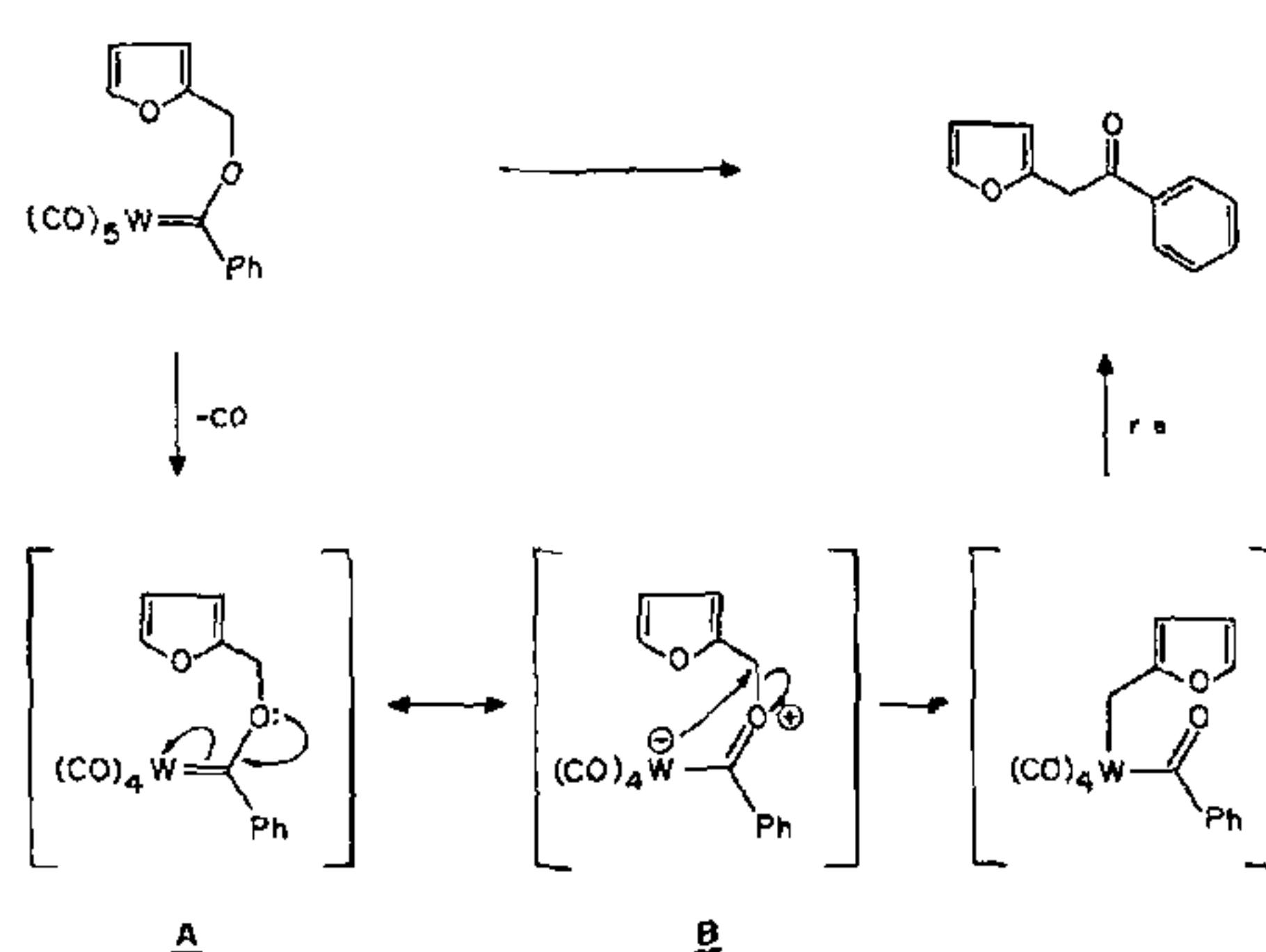
The p-methoxybenzyloxy carbene complex 1b reacted faster (16 h in benzene) than the benzyloxy carbene complex 1a (> 44 h in benzene) indicating the importance of stabilizing an incipient carbonium ion adjacent to the oxygen. Also, a p-OMe substituent on the aromatic ring connected to the carbene carbon (as in 1e) appeared to impair the efficiency of the reaction.

A mechanistic scheme was proposed (Scheme 13), which accommodated these observations. Initial CO loss from the carbene complex generates a 16e intermediate A. The electronic polarization of A generates B, which undergoes cleavage of the carbon-oxygen bond to produce an acylmetal intermediate. This furnishes the product ketone by a facile reductive elimination.

The structurally similar Fischer carbene complexes of chromium also underwent such thermal rearrangement to afford arene-chromium complexes (Table 2). The

yields were moderate to good, partial decomplexation being unavoidable under the present reaction condition. The $Cr(CO)_3$ fragment was found to be appended to the more electron-rich aryl ring exclusively.

The diastereoselectivity of this rearrangement could be probed by the use of o-methoxyphenethyl alkoxy group. The product would have two chiral centres: one at the benzyl carbon and the other due to the metal complexation to an unsymmetrical aromatic ring. The carbene complex 2d provided a single diastereomer of the product complex on heating at 80°. No diastereomeric mixture could be detected by 200 MHz ^{1}H NMR or analytical HPLC with UV detector. Such high diastereoselectivity is suggestive of a high degree of organization in the transition state. The diastereoselectivity was lower if the bath temperature was raised (> 90°). Epimerization of the product could be effected by base. It was established that the diastereomer obtained in the rearrangement was the kinetic product. The structure of this complex was confirmed by X-ray diffraction (Figure 3).

However, further experiments revealed that diastereoselectivity in the reaction is probably of steric origin. The o-methyl phenethyl alkoxycarbene proved to be less

Table 1. $(CO)_5W = C(R)(OCH_2Ar) \xrightarrow{\Delta} R\text{-CO-CH}_2Ar$

No	R	Ar	Solvent	Time (h)	Yield (%)
1a	Ph	Ph	Toluene	2	56
1b	Ph	p-OMe-C$_6$H$_4$	Benzene	16	56
1c	Ph	2-Furyl	"	2	90
1d	p-Me-C$_6$H$_4$	"	"	35	65
1e	p-OMe-C$_6$H$_4$	"	"	10	36
1e	p-OMe-C$_6$H$_4$	"	Toluene	1.5	50
1f	Me	"	Benzene	3	—

Table 2. $(CO)_5Cr = C(R)(OCHR^1\text{-Ar}) \xrightarrow[\text{Benzene}]{\Delta} (CO)_3Cr\text{-Ar-}CHR^1\text{-CO-R}$

No.	Ar	R	R^1	Yield* (%)
2a	Ph	Ph	H	68
2b	p-OMe-C$_6$H$_4$	Ph	H	77
2c	Ph	Ph	Me	43
2d	o-OMe-C$_6$H$_4$	Ph	Me	47
2e	o-OMe-C$_6$H$_4$	Ph	H	48
2f	Ph	Me	H	—

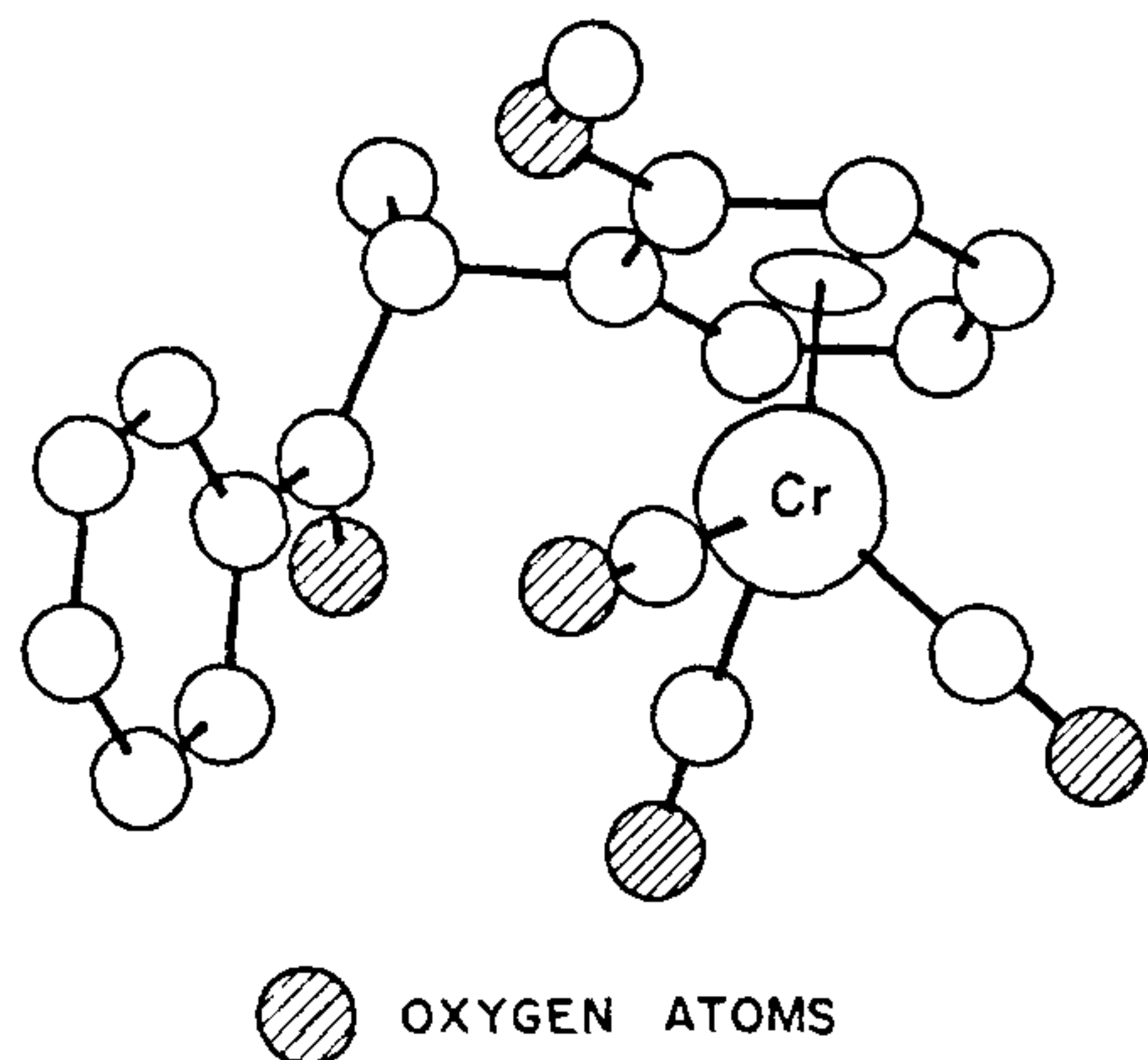*Total yield of decomplexed ketone is about 15-20% higher in all cases.

OXYGEN ATOMS

Figure 3.

diastereoselective and *m*-substituted benzyloxy carbene complexes were not selective at all.

In summary, we have described an unusual rearrangement reaction of arylmethyloxy aryl carbene complexes of tungsten and chromium, which was observed as a fortunate accident. But this also reminds us of the complexity of diverse reactivity patterns such organometallic compounds display, in order to challenge the wits of practising chemists.

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Synthesis and properties of novel π-electron donors—Variants of tetrathiafulvalene*†

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The remarkable one-dimensional conductivity exhibited by the charge transfer complex formed from tetrathiafulvalene (FFT) and tetracyanoquinodimethane has sparked attempts to synthesize related organic metals. In particular, the possibility of utilizing alternative π-donors has attracted considerable attention. In this article, the synthesis and electrochemical characterization of a number of TTF analogues with different olefinic and heterocyclic spacer groups are described.

ORGANIC synthesis continues to play an increasingly important role in modern technology as we approach the twenty- first century. Almost everyone is familiar with liquid crystal displays in electronic equipment, watches and novelty devices. It is anticipated that organic synthesis will lead to synthetic materials with metallic properties, conductors, superconductors, ferromagnets, NLO materials, photoconductors, etc. Synthetic metals are bound to find applications in electronics, plastic batteries etc. Photoconductors, semiconductors and superconductors have applications in photocopiers, solar cells, computer logic gates, etc.[1].

The focus of this article is limited to the synthesis and properties of compounds which may be important in the design of organic conductors or superconductors.

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