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# Assembling monocyclic, spirocyclic and fused carbocycles by ring-closing metathesis on an arene–chromium template

Bikash C. Maity, Vishwanath M. Swamy and Amitabha Sarkar*

*Divisions of Organic Chemistry (Synthesis), National Chemical Laboratory, Pune 411008, India*

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**Abstract**—A variety of diene precursors assembled stereoselectively on an arene–chromium template underwent facile ring-closing metathesis by ruthenium catalysis at ambient temperature to afford cyclic compounds of varying degrees of complexity in high yields. © 2001 Elsevier Science Ltd. All rights reserved.

Ring-closing metathesis (RCM) has become a powerful tool for the ready construction of cyclic structures over the past few years[1] with the availability of structurally defined, mononuclear metal catalysts developed by Schrock[2] [2,6-$i\text{Pr}_2\text{C}_6\text{H}_3\text{NMo}\{\text{OC(CF}_3)_2\text{Me}\}_2\text{CHCMe}_2\text{Ph}$] and Grubbs[3] [$\text{Cl}_2\{(c\text{-C}_6\text{H}_{11})_3\text{P}\}_2\text{RuCHPh}$]. A significant, practical advantage of Grubbs' ruthenium catalyst is derived from its relative stability to air and moisture, in addition to its tolerance of a wide variety of functional groups.

Almost an infinite variety of structures are amenable to RCM. Since an alkene is the product of metathesis, chiral cyclic products are usually synthesized from preassembled chiral dienes,[4] while only a few examples exist in the literature pertaining to chirality originating from RCM.[5]

Arene–chromium complexes provide a ready access to diastereomerically pure compounds of diverse structural types.[6] The present report describes the use of RCM to synthesize a variety of diastereomerically pure carbocyclic as well as heterocyclic products at ambient temperature, from differently substituted diene precursors assembled on arene–tricarbonylchromium templates in high yield. The products are monocyclic, spirocyclic or fused polycyclic compounds depending on the design of the precursors, and feature one to three stereogenic centers. This study complements recent efforts to create stereochemically defined molecular scaffolds[7] and the use of organometallic precursors[8] for this purpose.

The substrates were independently synthesized by appropriate procedures. Complex **1** was synthesized in three steps from an *o*-methylacetophenone–$\text{Cr(CO)}_3$ complex. Claisen–Schmidt condensation with *p*-tolualdehyde was followed by addition of MeLi in ether. The 1,2-adduct was obtained as the major product[9] and as a single diastereomer, which was converted to the allyl ether **1a** by a standard procedure. The stereochemistry of the new stereogenic center was assigned based on an *exo*-selective attack on the sterically preferred *anti* conformer.[10]

The optically pure substrate **2a** was derived from the optically pure *o*-anisaldehyde–$\text{Cr(CO)}_3$ complex,[11] the product resulting from an *exo* addition to the more stable *anti* conformer.[12] The stereochemistry of substrate **3a** was assigned on similar considerations. RCM with Grubbs' ruthenium catalyst at ambient temperature in dichloromethane yielded[13] the corresponding heterocycles in respectable isolated yields (Table 1). Spirocycles **4b** and **5b** were similarly obtained from RCM of relevant substrates **4a** and **5a**, respectively, which in turn were prepared by well-precedented[14] *exo*-selective allyl Grignard addition to 1-tetralone– and 1-indanone–$\text{Cr(CO)}_3$ complexes.

Based on an earlier report[15] from this laboratory, the synthesis of substrates **6a** and **7a** was accomplished according to the reaction sequence depicted in Scheme 1.

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* Corresponding author.

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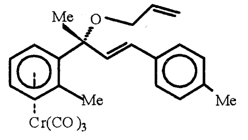
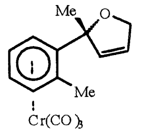
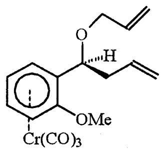
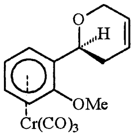
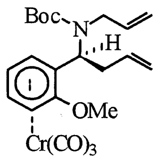
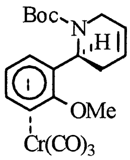
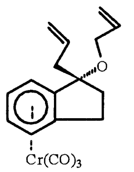
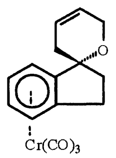
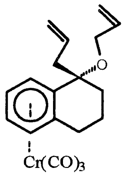
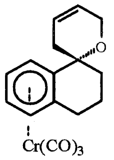
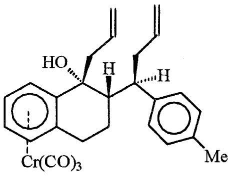
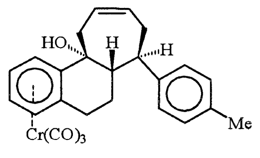
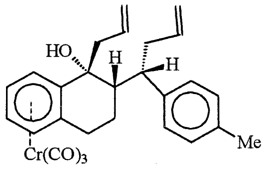
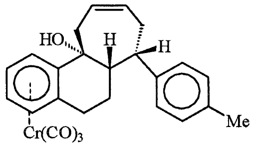
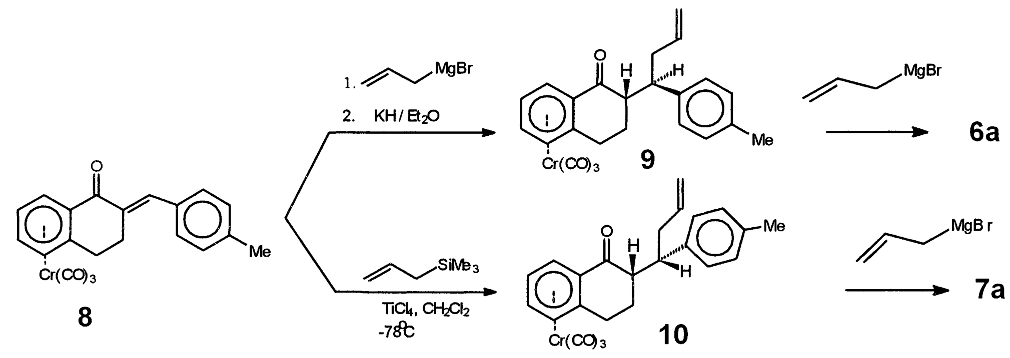
**Table 1.**

| Entry | Substrate | Time (h) | Product | Yield(%) |
|---|---|---|---|---|
| 1 |  **1a** | 3 |  **1b** | 90 |
| 2 |  (+) **2a** | 2.5 |  (+) **2b** | 88 |
| 3 |  **3a** | 3 |  **3b** | 78 |
| 4 |  **4a** | 3 |  **4b** | 86 |
| 5 |  **5a** | 3 |  **5b** | 85 |
| 6 |  **6a** | 3.5 |  **6b** | 80 |
| 7 |  **7a** | 4.0 |  **7b** | 80 |

The last step, Grignard addition to the intermediate ketone complexes,[16] was totally *exo*-selective and afforded the complexes in diastereomerically pure form. RCM afforded a fused tricyclic system whose stereochemical features are well-defined. Remarkably, the reaction itself tolerated the tertiary alcohol function without loss of efficiency.[17]

These reactions establish the feasibility of a flexible synthetic design based on stereoselective functionaliza-



Scheme 1.

tion attainable via arene–$Cr(CO)_3$ complexes. The ease of operation, reasonable reaction times, ambient temperature and low catalyst requirement are indeed attractive features of this strategy, as exemplified by seven substrates leading to monocyclic products, spirocycles and fused polycyclic rings by RCM.

**Typical procedure for the ring closing metathesis reaction**: To a solution of diene (1.5 mmol) in $CH_2Cl_2$ (15 ml) was added $RuCl_2(Pcy_3)_2CHC_6H_5$ (10 mol%) with stirring under an inert atmosphere at rt for 2.5–4 h. The reaction mixture was concentrated in vacuo, and the crude product was purified by column chromatography (pet. ether/EtOAc, 10:1) to provide the desired product as a yellow solid (78–90%).

## Acknowledgements

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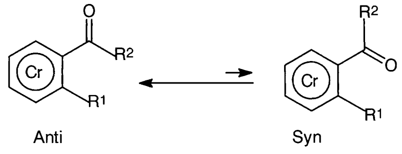

$R^1$ = Me, OMe
$R^2$ = H, Me, Vinyl

The chemical shift of the aromatic proton adjacent to the carbonyl function is a convenient probe for the preferred solution conformation: $\delta$ 6.2 ppm in *anti* conformer and $\delta$ 5.7–5.8 ppm in *syn* conformer are typical.

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