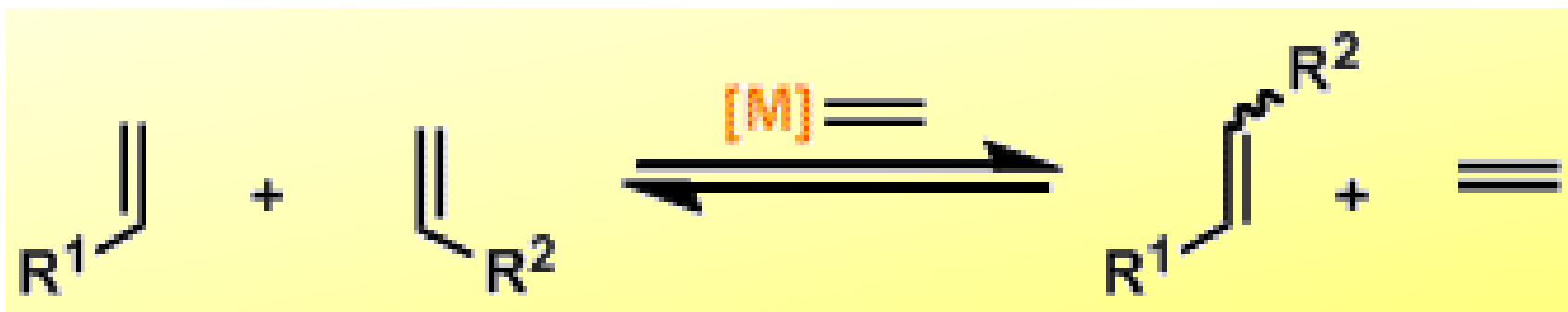


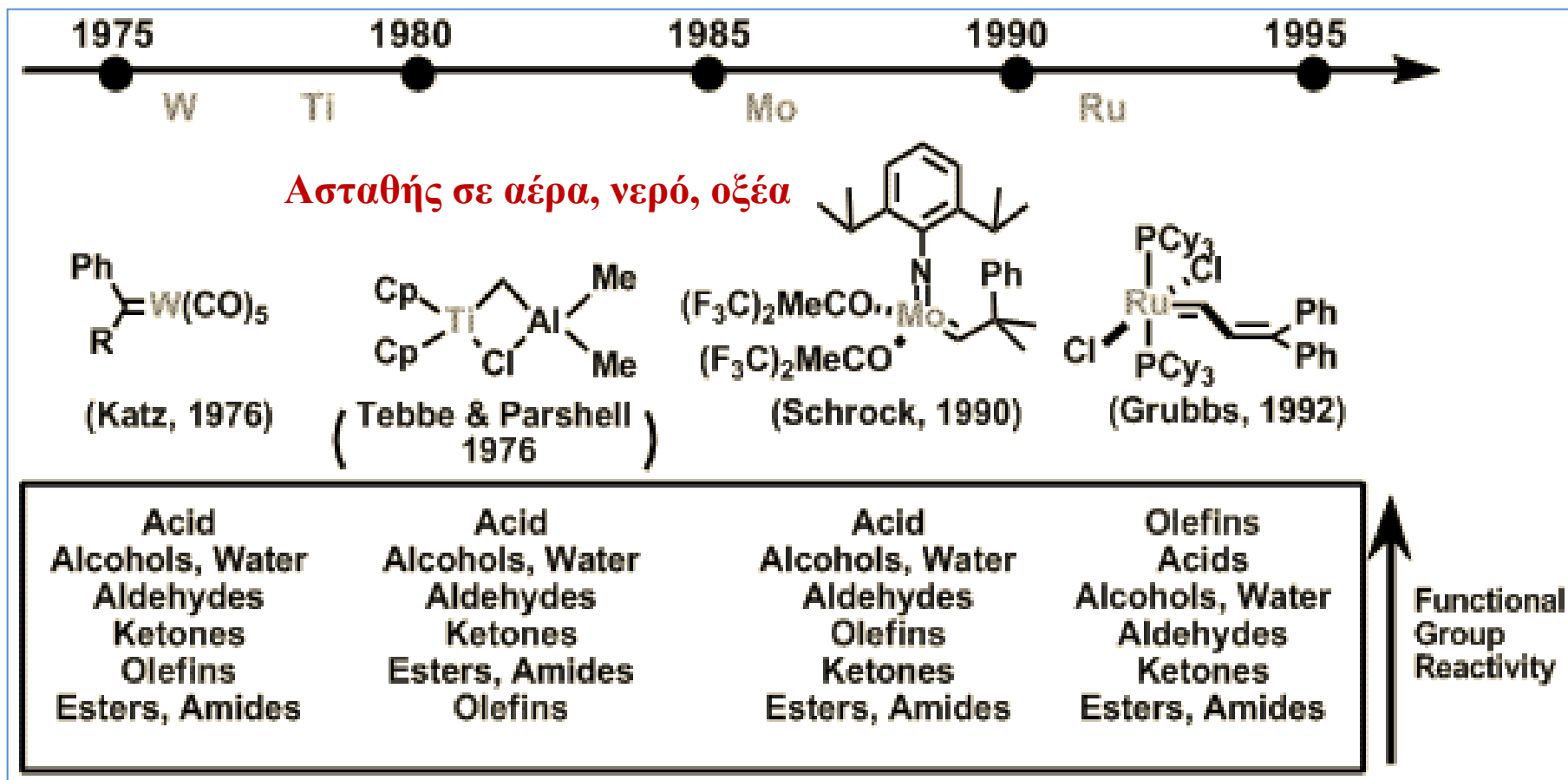
ΜΕΤΑΘΕΣΗ ΟΛΕΦΙΝΗΣ

Είναι η αντίδραση εκείνη, όπου παρουσία κάποιου **μεταλλοακυλίδενο καταλύτη** δύο ολεφίνες ανταλλάσσουν τους υποκαταστάτες τους (**transalkylation**) με αποτέλεσμα το σχηματισμό δύο νέων ολεφινών. Chauvin, Y., Schrock, R. R., Grubbs, R. H. Nobel Χημείας 2005 (Angew. Chem. Int. Ed. 2006, 35, 3740; 3748; 3760; Chem. Rev. 2010, 110, 1746; Tetrahedron 2004, 60, 7117)

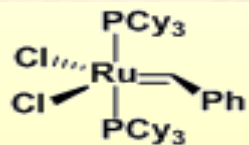
Σύνθεση ολεφινών από το πετρέλαιο (**Shell higher olefin process, SHOP**) αρχικά με καταλύτες του Ni.



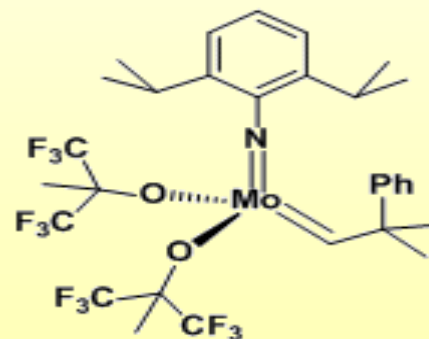
Καταλύτες. Αρχικά καταλύτες με **ασαφή δομή** ($WCl_6-EtOH-EtAlCl_2$ ή $WOCl_4-EtAlCl_2$ ή $Mo(PPh_3)_2Cl_2(NO)_2-Al_2Me_3Cl_3$ -χλωροβενζόλιο ή $PhWCl_3-AlCl_3$)



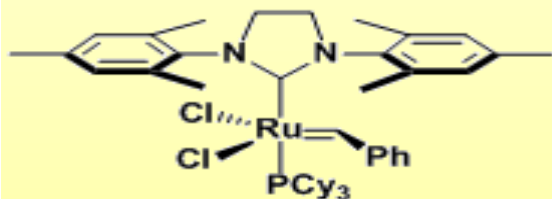
Οι καταλύτες του Grubbs (με Ru) 1^{ης} και 2^{ης} γενιάς είναι πιο εύκολοι στο χειρισμό τους καθώς είναι ανθεκτικοί στην παρουσία πολλών ομάδων. Οι δύο τελευταίοι καταλύτες είναι πιο δραστικοί από τον καταλύτη Grubbs 2^{ης} γενιάς και τον καταλύτη Grubbs-Hoveyda 2^{ης} γενιάς (Angew. Chem. Int. Ed. 2002, 114, 4038).



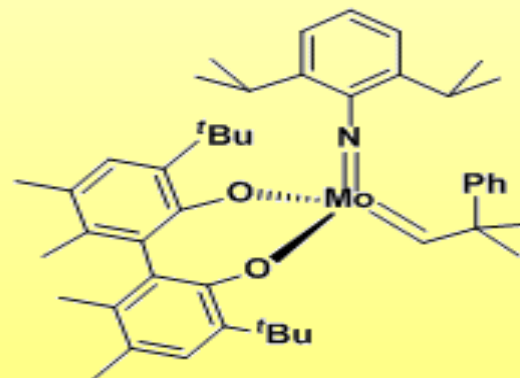
Grubbs 1st-generation catalyst



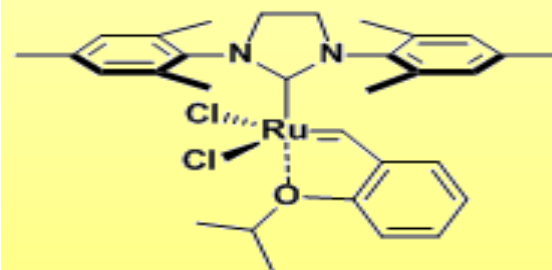
Schrock Catalyst



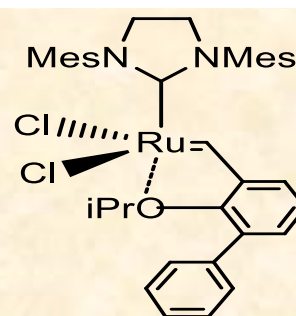
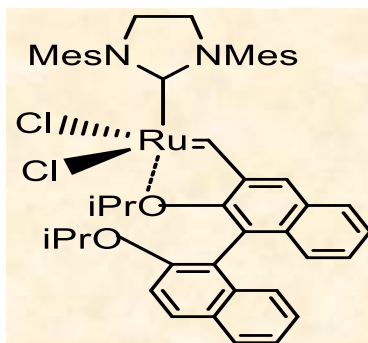
Grubbs 2nd-generation catalyst



Schrock-Hoveyda Catalyst

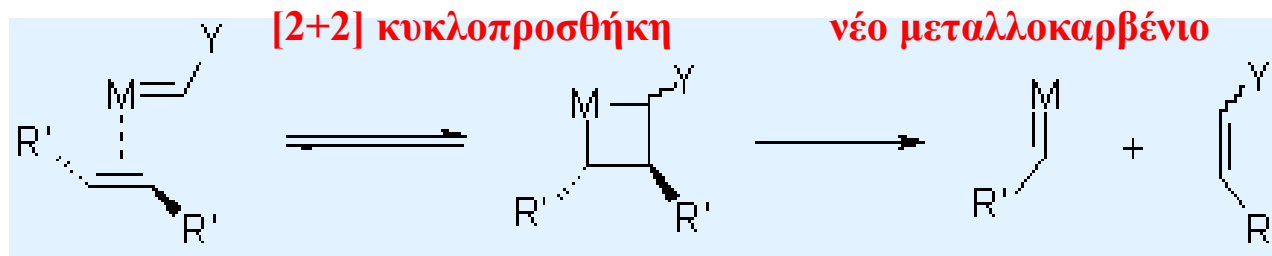


Grubbs-Hoveyda
2nd-generation catalyst

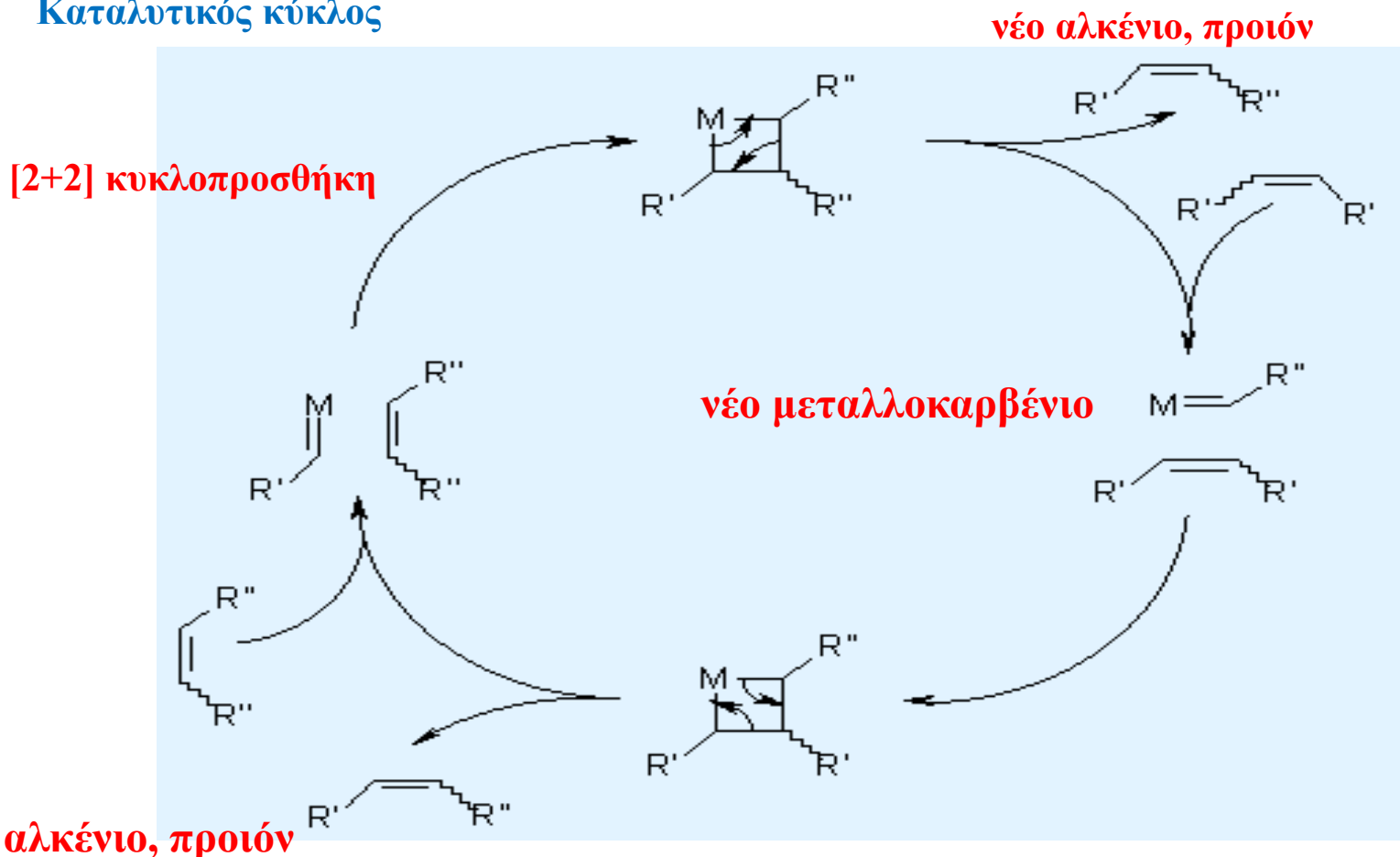


Μηχανισμός. Ο μηχανισμός προτάθηκε από τον **Chauvin (Die Makromol. Chem. 1971, 141, 4038)**

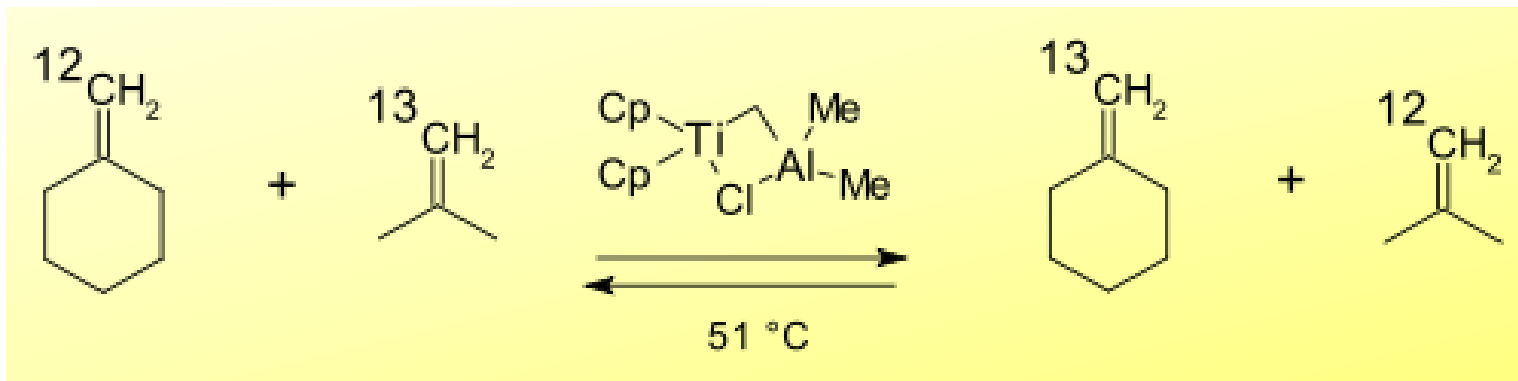
Έναρξη



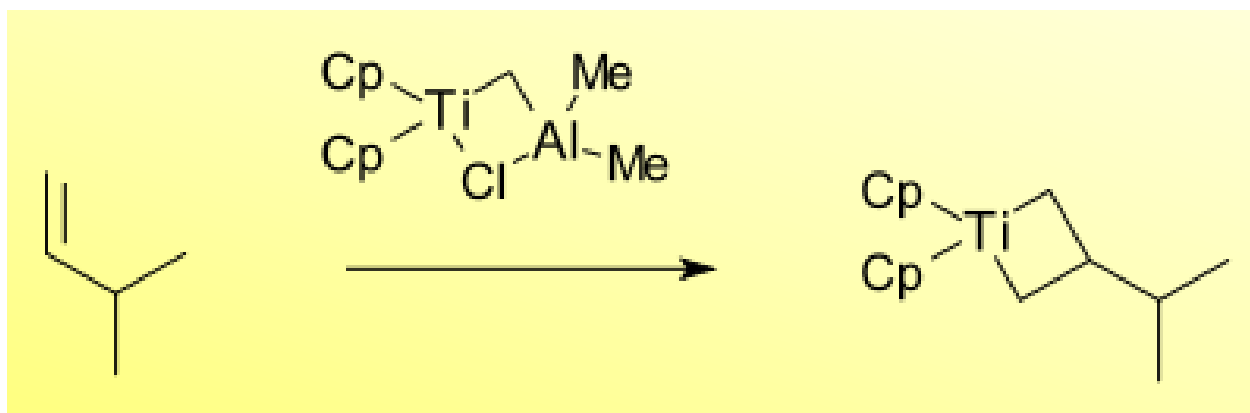
Καταλυτικός κύκλος



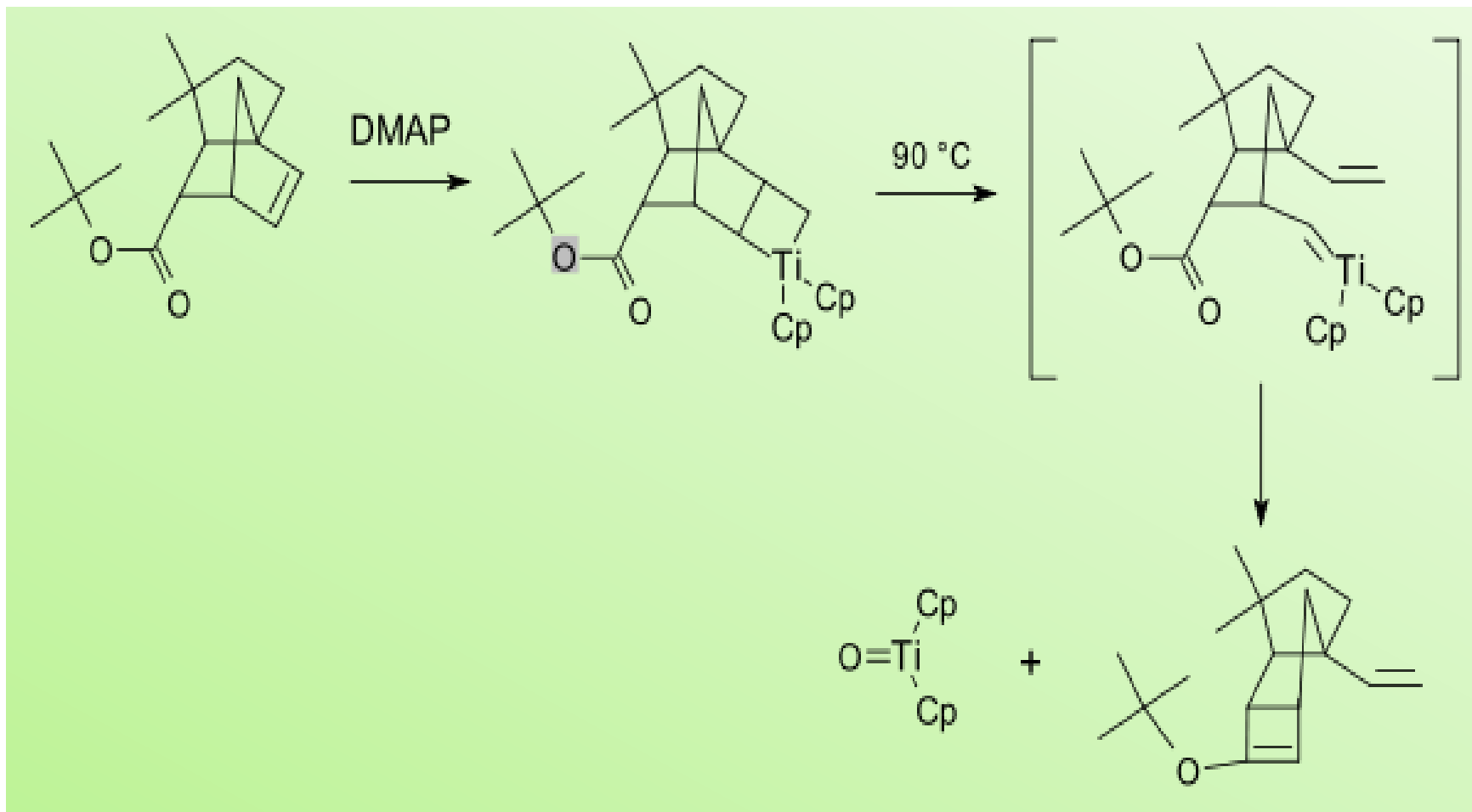
Μετάθεση ολεφίνης με το αντιδραστήριο Tebbe: φαίνεται η ανταλλαγή των αλκυλιδENO-ομάδων (J. Am. Chem. Soc. 1978, 100, 3611)



Απομόνωση τιτανοκυκλοβουτανικού ενδιάμεσου από τον Grubbs (J. Am. Chem. Soc. 1980, 102, 6876).



Απομόνωση ανάλογου ενδιάμεσου και στην ολική σύνθεση του καπνελλενίου (J. Am. Chem. Soc. 1986, 108, 855).



Είδη μετάθεσης ολεφίνης.

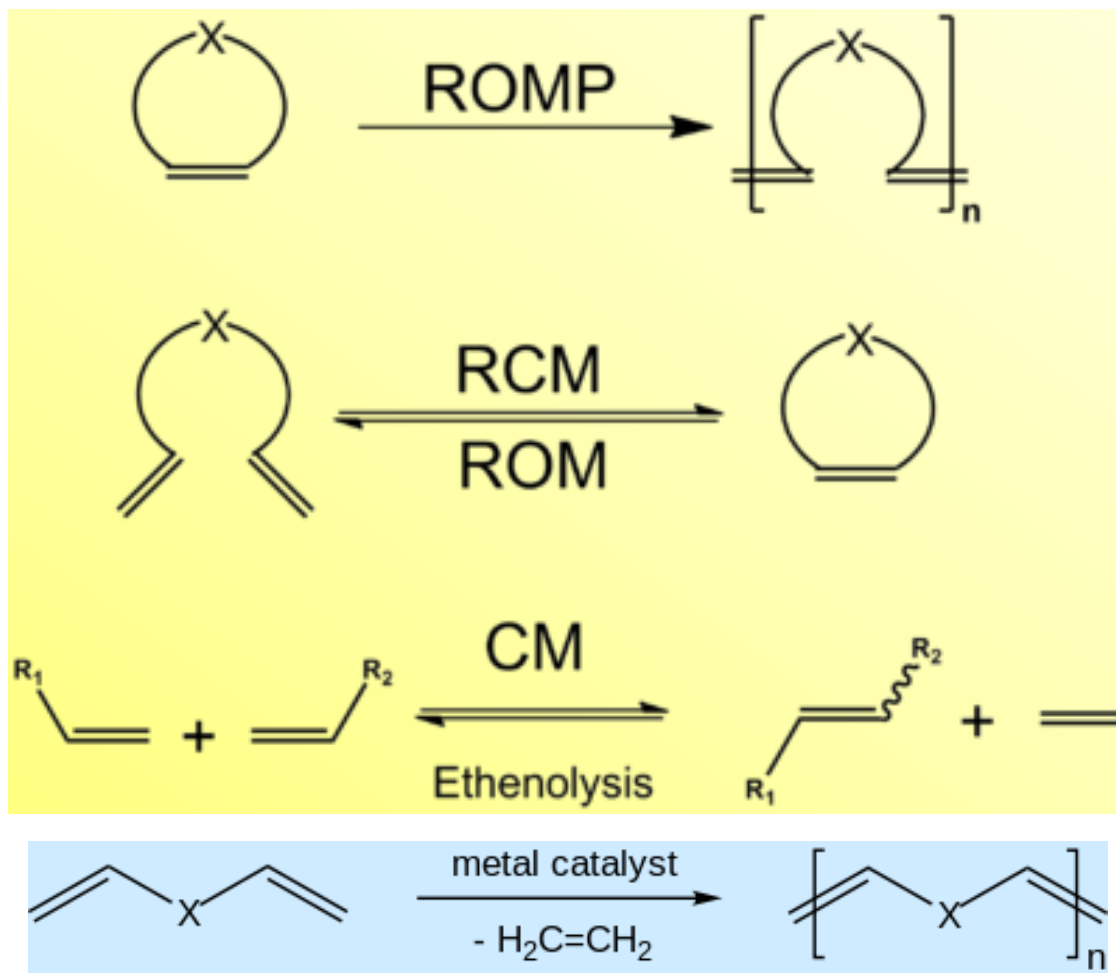
ROMP, Ring Opening Metathesis Polymerization

Μετάθεση με κλείσιμο δακτυλίου (RCM, Ring Closing Metathesis)

Διασταυρούμενη μετάθεση (CM, Cross Metathesis)

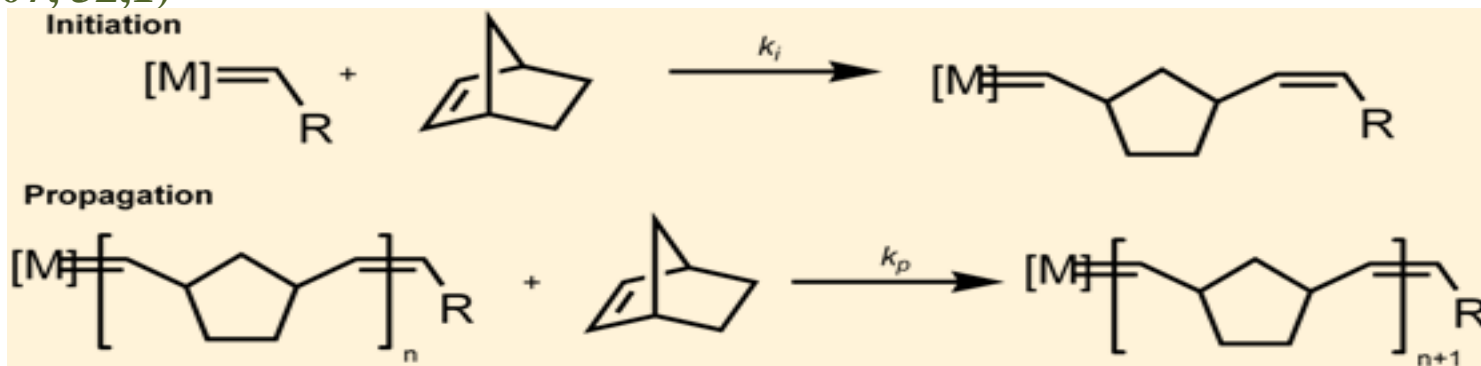
Μετάθεση με άνοιγμα δακτυλίου (ROM, Ring Opening Metathesis)

Μετάθεση άκυκλων διενίων (ADMET, Acyclic Diene Metathesis) (Chem. Soc. Rev. 2011, 40, 1404).

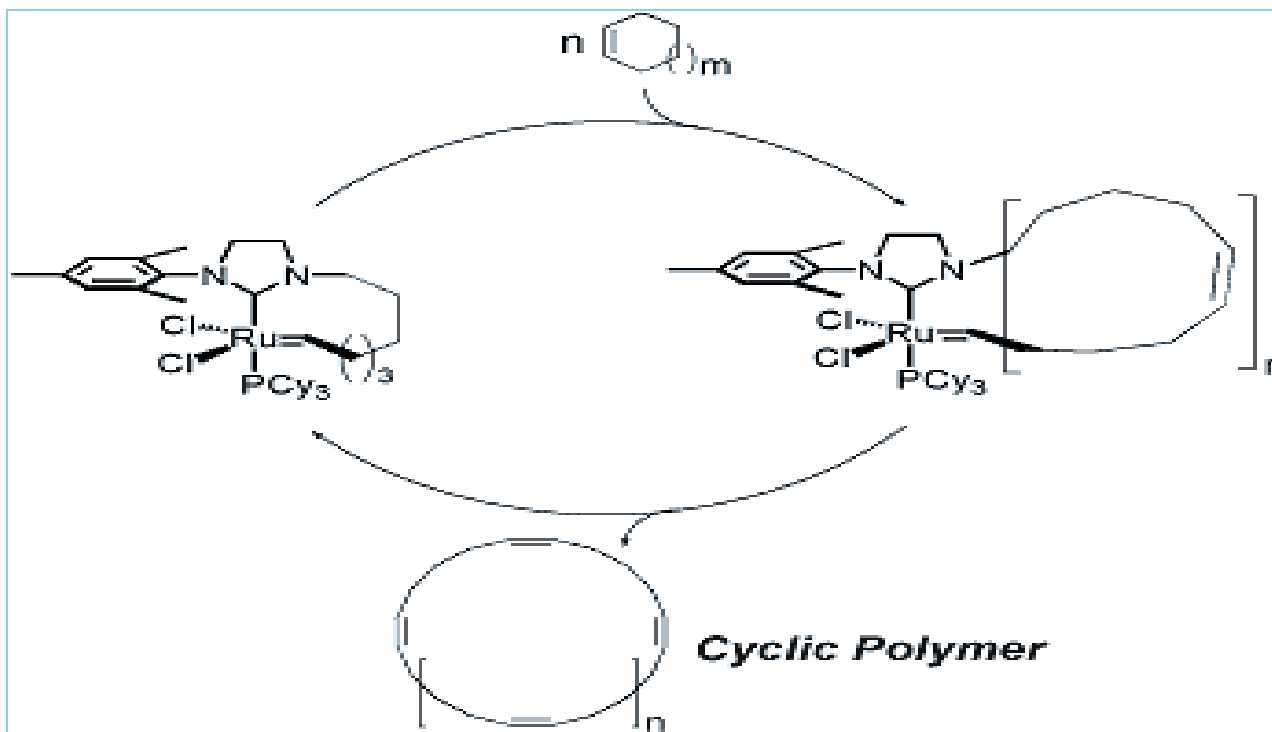


ROMP

Σχηματισμός πολυμερών πολυνορβορνενίων (με μεγάλη οπτική καθαρότητα) με ROMP κατά την επίδραση του καταλύτη Grubbs 1^{ης} γενιάς (Prog. Polym. Sci. 2007, 32,1)



Με τη μέθοδο ROMP σχηματίζονται κυκλικά πολυμερή (Macromol. Rapid Commun. 2004, 25, 1283)

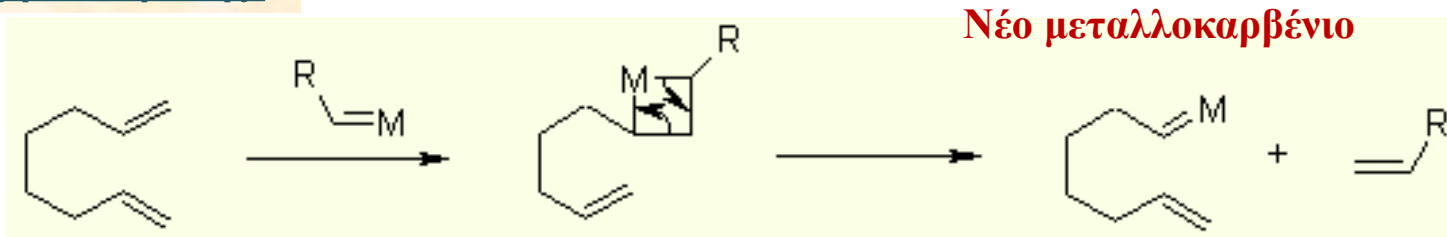


Μετάθεση με κλείσιμο δακτυλίου (RCM):

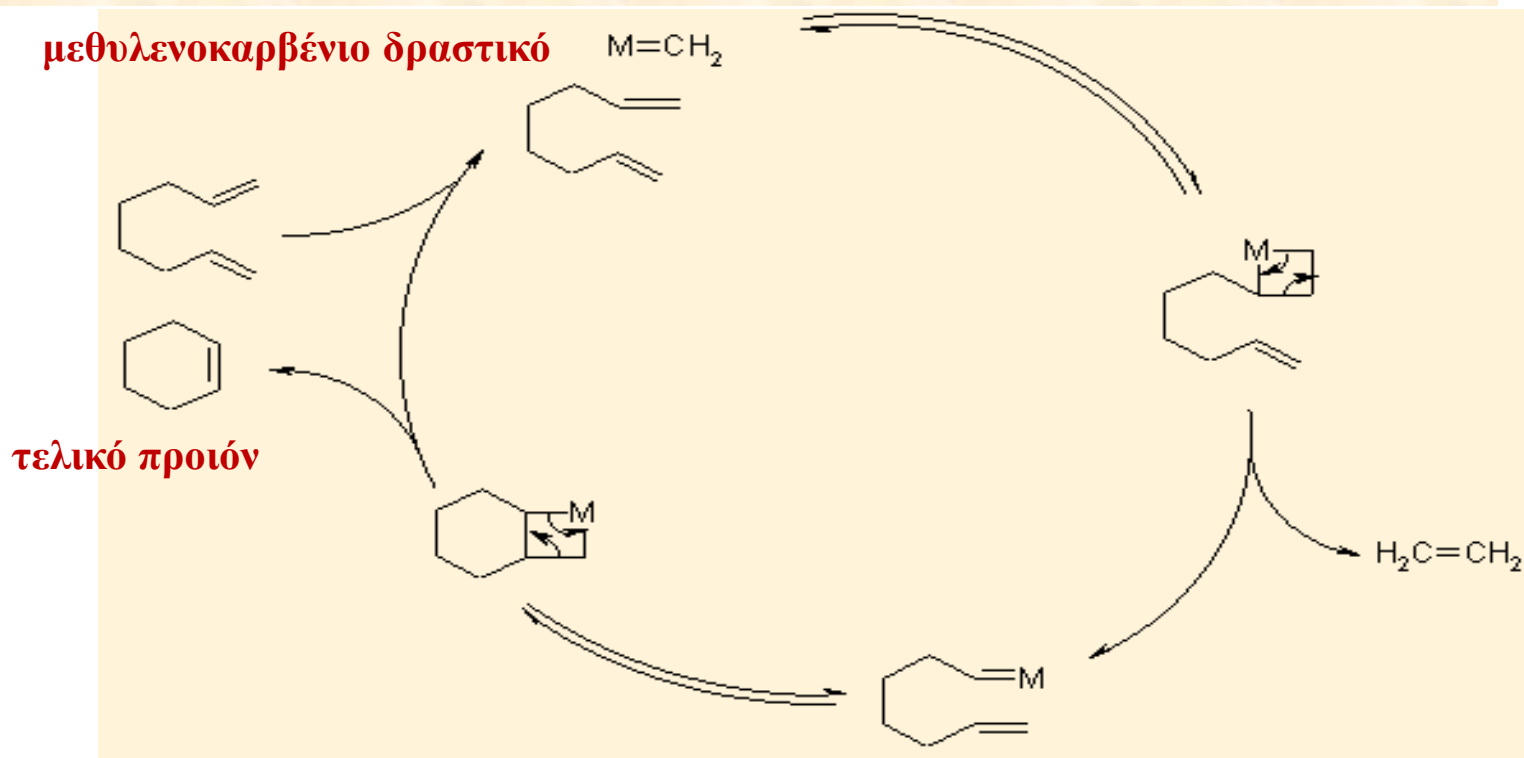
Ενδομοριακή μετάθεση ολεφίνης που οδηγεί σε κυκλοαλκένιο με μέγεθος δακτυλίου από 5 έως 30 μέλη.

Η E-/Z- εκλεκτικότητα εξαρτάται από την τάση του δακτυλίου

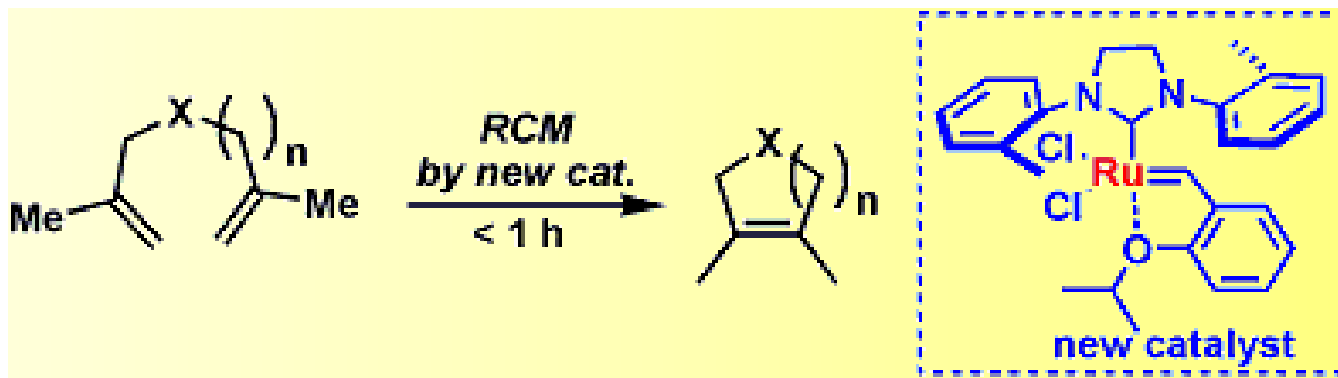
Έναρξη αντίδρασης:



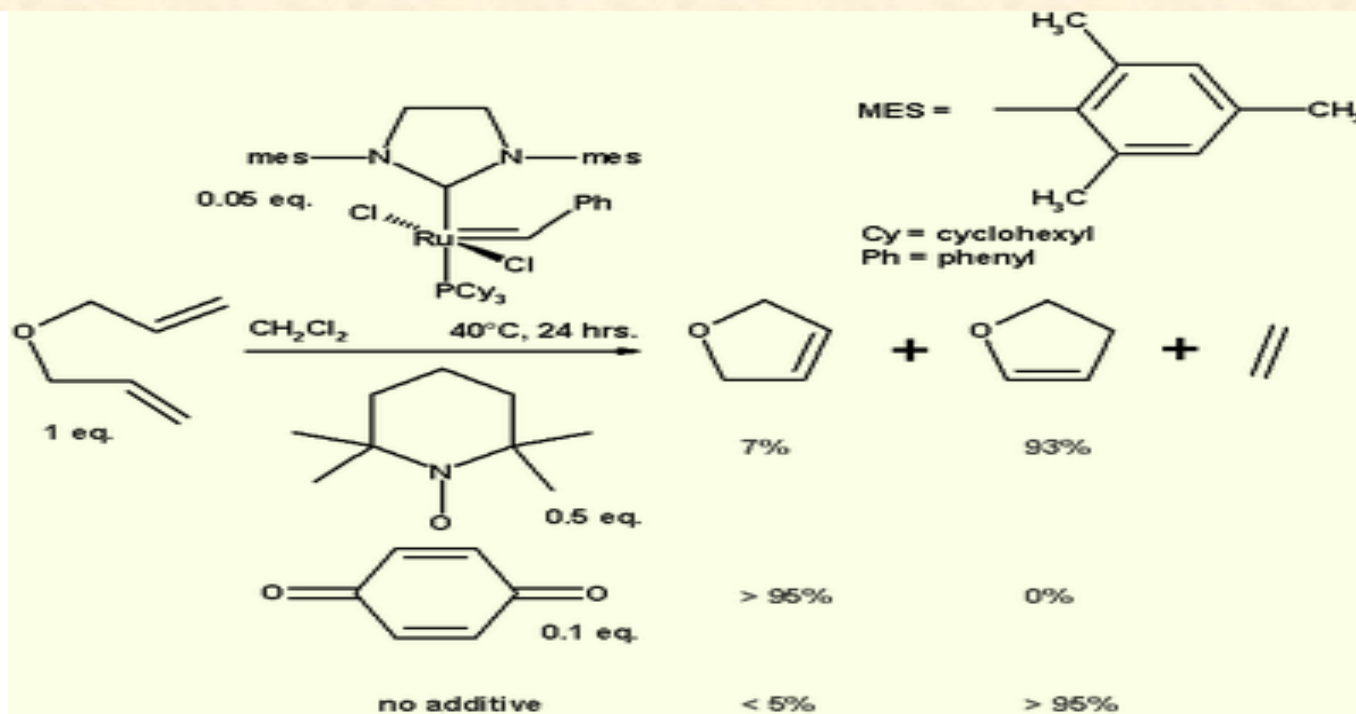
Καταλυτικός κύκλος:



Με τη βοήθεια καταλύτη του τύπου Hoveyda-Grubbs σχηματίζονται τετραυποκατεστημένα κυκλοαλκένια (Org. Lett. 2007, 9, 1589)



Επίδραση της ύπαρξης προσθέτων στην λήψη ισομερών κατά την αντίδραση RCM διαλλυλαιθέρων (J. Am. Chem. Soc. 2005, 127, 17160).



1,2-Διυδρο-1,2-αζαβορίνη. Σταθερή Αρωματική ένωση. Σχηματίζεται με αντίδραση RCM.

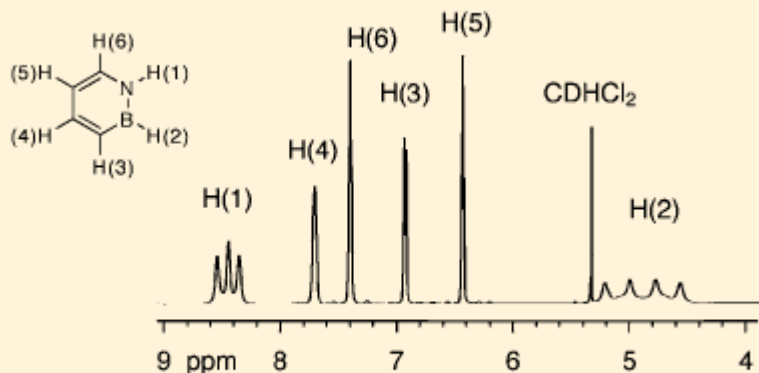
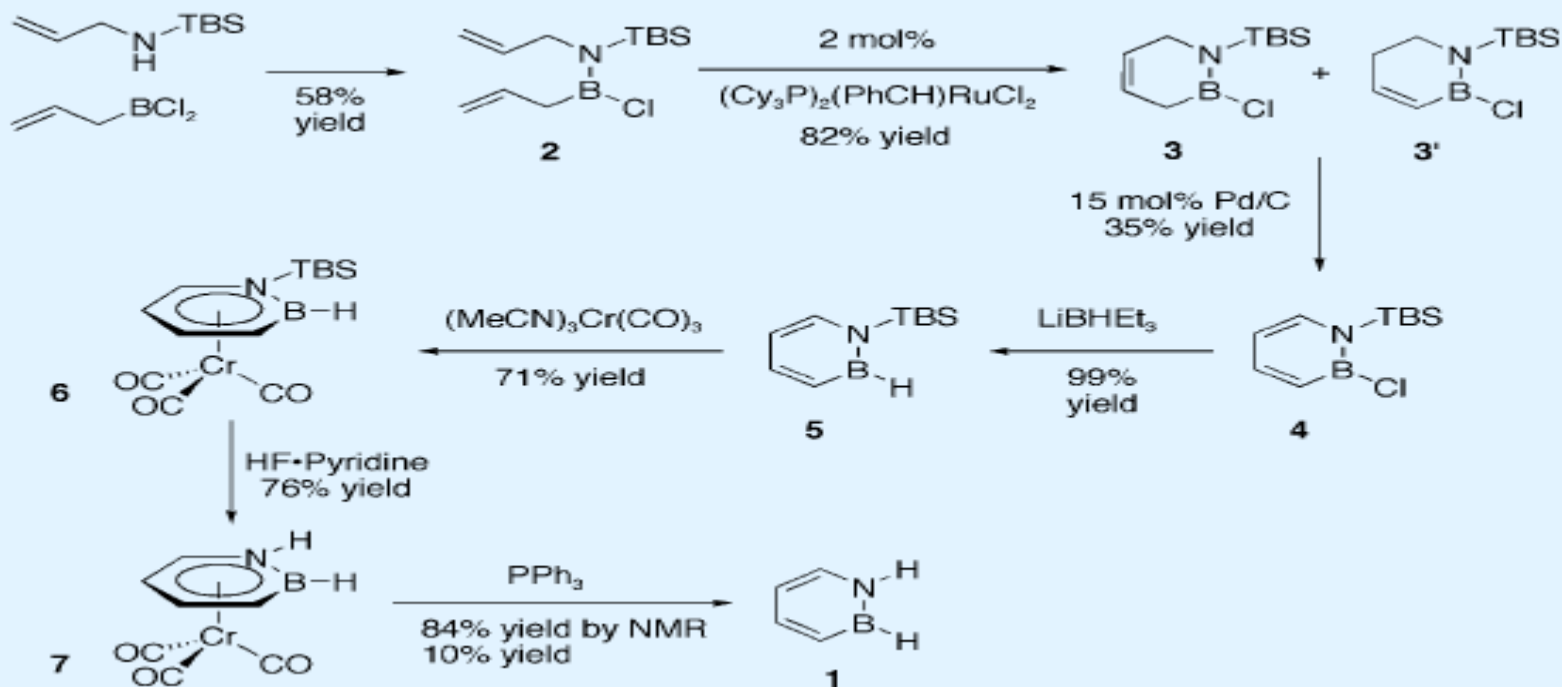


Figure 1. ^1H NMR spectrum of **1** in CD_2Cl_2 .

Ηλεκτρονιόφιλη Αρωματική Υποκατάσταση στις θέσεις 3- και 5-.

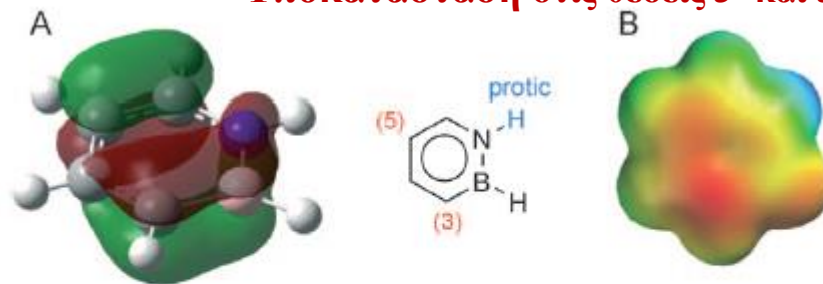
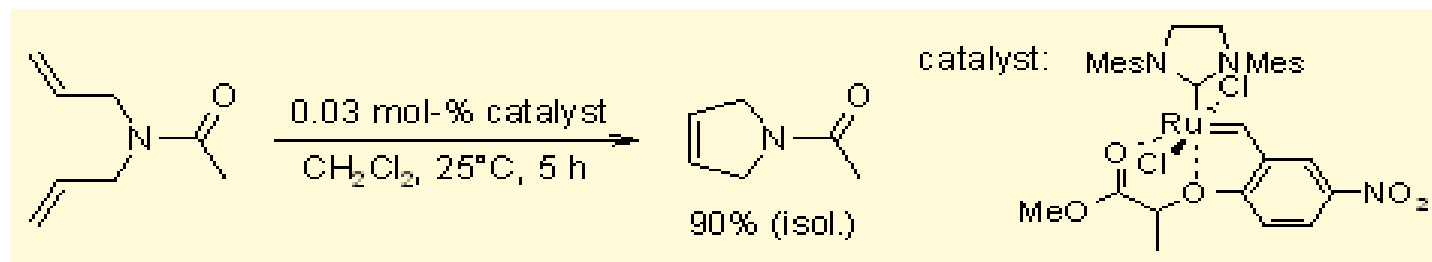
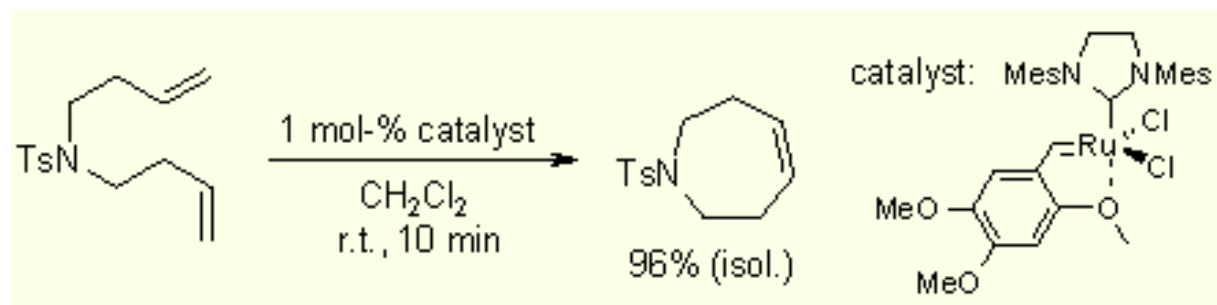
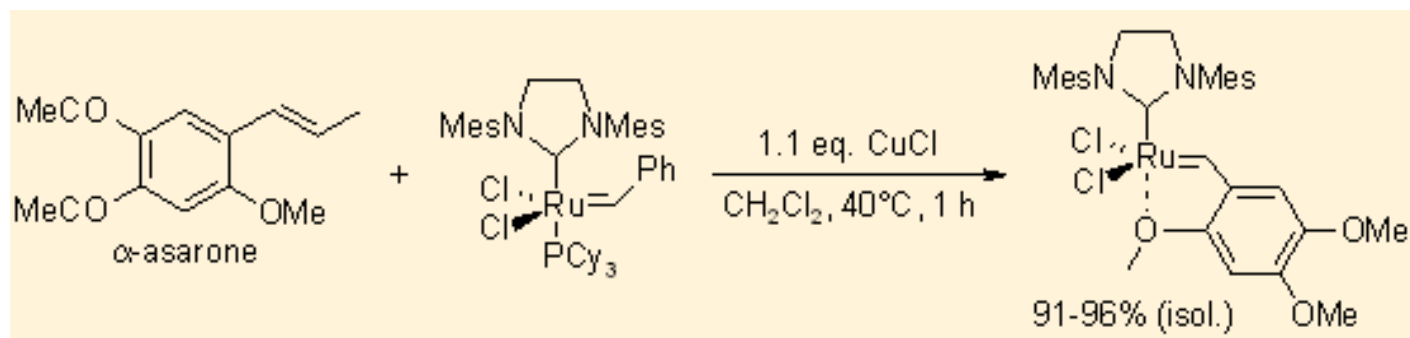


Figure 4. A) HOMO of 1,2-azaborine **1**. B) Electrostatic potential surface of **1** at the 0.002 electron a.u.⁻³ density iso-contour level (-13.6 to 39.9 kcal mol⁻¹).

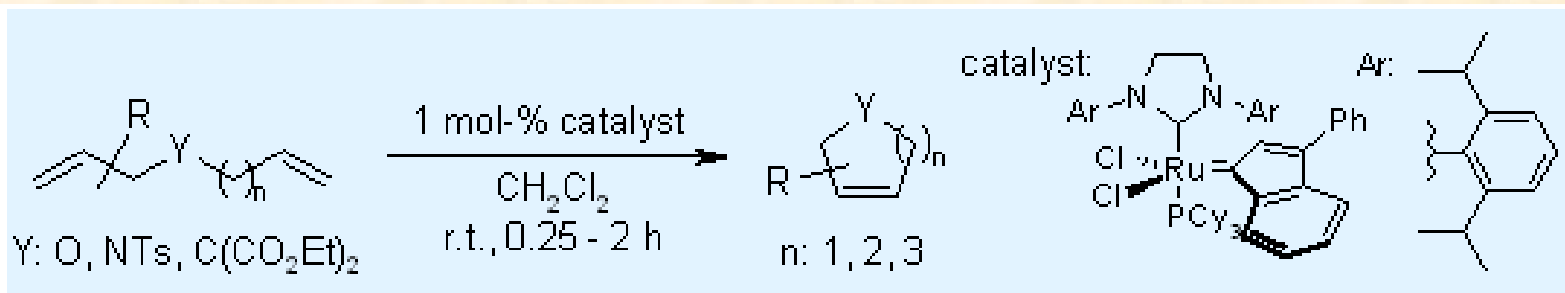
Σύνθεση πυρρολινών μέσω αντίδρασης RCM



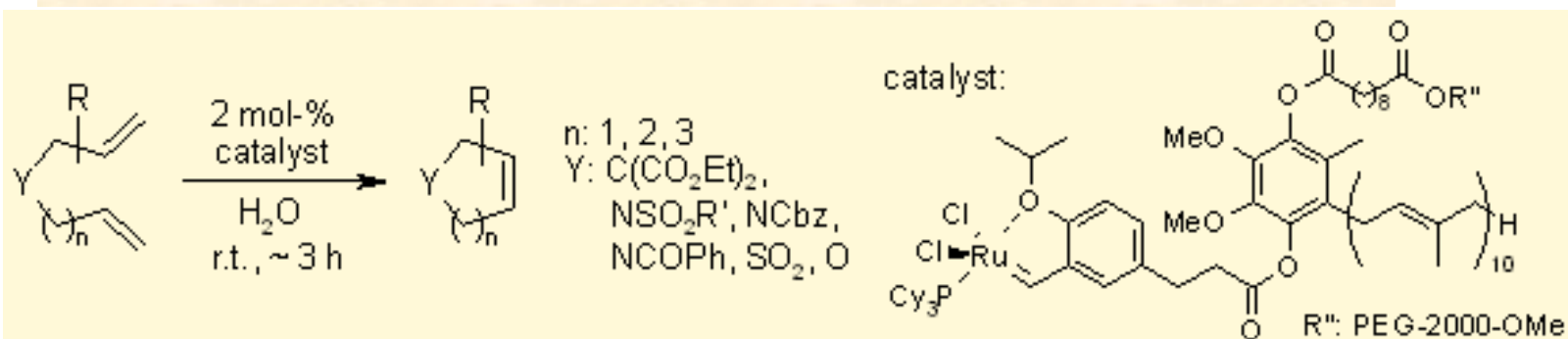
Σύνθεση του καταλύτη του τύπου Hoveyda-Grubbs από μια φθηνή πρώτη ύλη την α -ασαρόνη. Σχηματισμός 7-μελών δακτυλίων μέσω αντίδρασης RCM



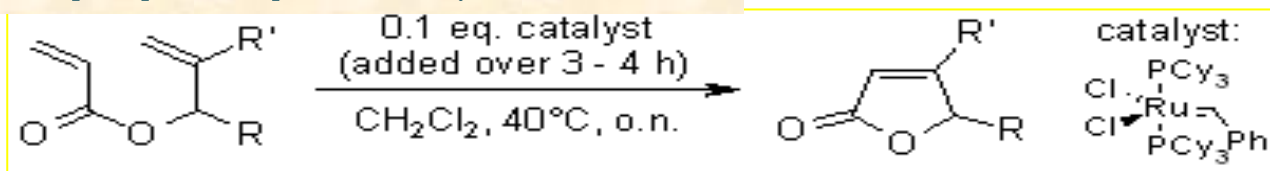
Αντίδραση RCM στη θερμοκρασία δωματίου μέσω του ινδενυλιδενοκαταλύτη του Ru



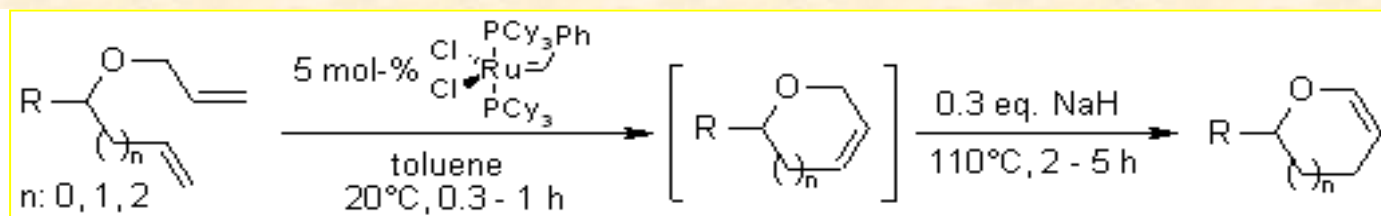
Αντίδραση RCM σε νερό υπό ανακύκλωση του καταλύτη



Σύνθεση α,β-ακορέστων γ-λακτονών



Μετάθεση ολεφίνης και ισομερείωση του διπλού δεσμού



Σύνθεση υποκατεστημένων βενζοφουρανίων μέσω αρχικής ισομερείωσης και αντίδρασης RCM στη συνέχεια

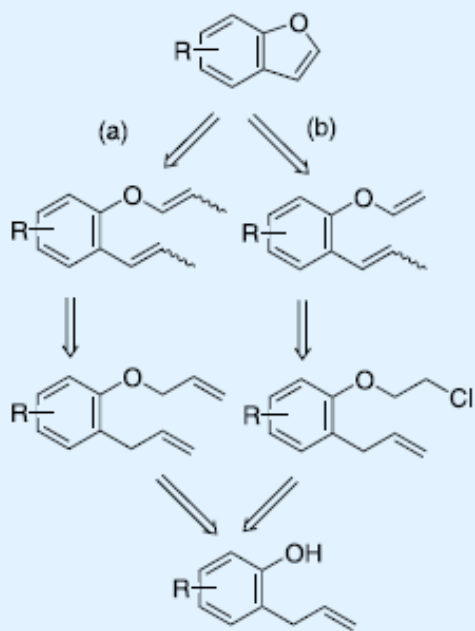


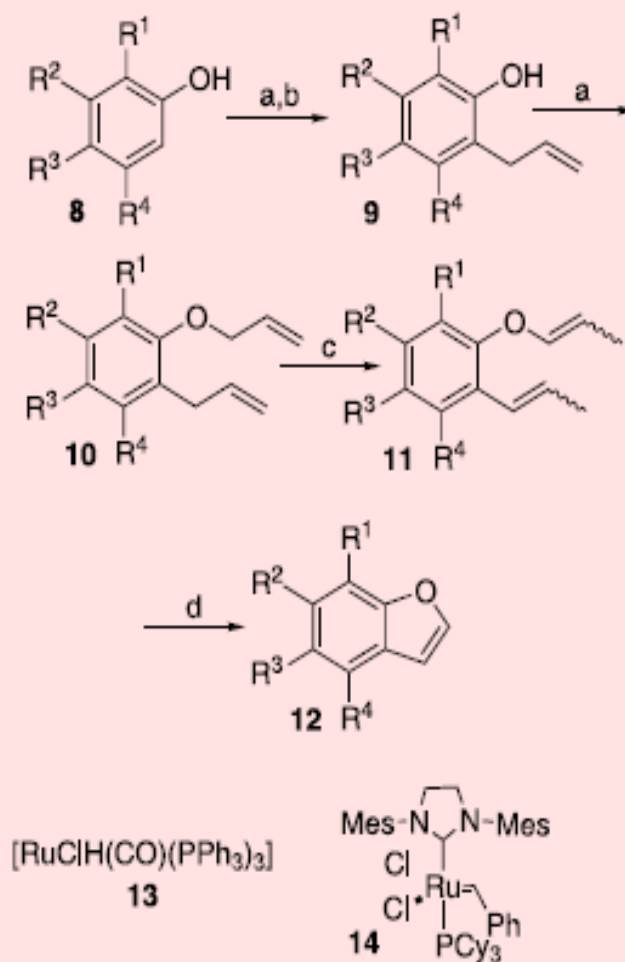
Table 1. Yields for Scheme 1

| | 8 → 10 ^a | 10 → 11 | 11 → 12 |
|--|---------------------|--------------|------------------|
| a R ¹ , R ⁴ = OMe, R ² , R ³ = H | 31% | 99% | 100% |
| b R ¹ , R ³ = OMe, R ² , R ⁴ = H | 61% | 100% | 96% |
| c R ¹ = Ph, R ² , R ³ , R ⁴ = H | 48% | 98% | 63% |
| d R ¹ = CHO, R ² , R ³ , R ⁴ = H | 28% | 57% | 70% |
| e R ¹ , R ² , R ⁴ = H, R ³ = CHO | 36% | 82% | 50% |
| f R ¹ = NO ₂ , R ² , R ³ , R ⁴ = H | 62% | 94% | 82% |
| g R ¹ , R ² , R ⁴ = H, R ³ = NO ₂ | 45% | 85% | 92% |
| h R ¹ = OMe, R ⁴ = CHO, R ² , R ³ = H | 36% | 54% | 50% |
| i R ¹ , R ² , R ⁴ = H, R ³ = <i>t</i> -butyl | 50% | 86% | 70% |
| j R ¹ , R ² , R ⁴ = H, R ³ = Br | 25% | 100% | 20% |
| k R ¹ -R ² = C ₆ H ₄ , R ³ , R ⁴ = H | 85% | 93% | 92% |
| l R ¹ , R ² = H, R ³ -R ⁴ = C ₆ H ₄ | 37% | ^b | 31% ^c |

^a Yield over three steps.

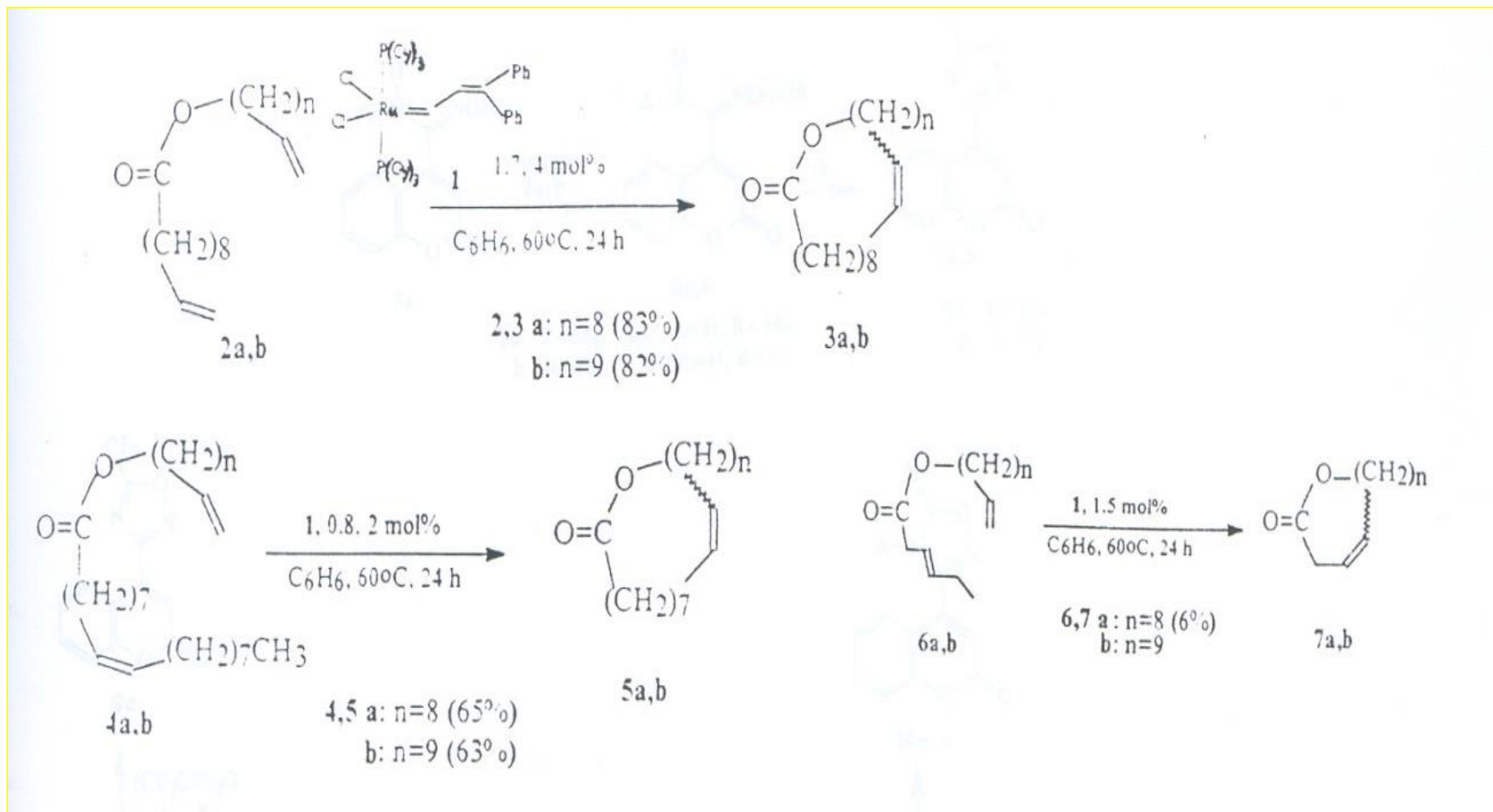
^b Compound not isolated.

^c Yield over two steps.

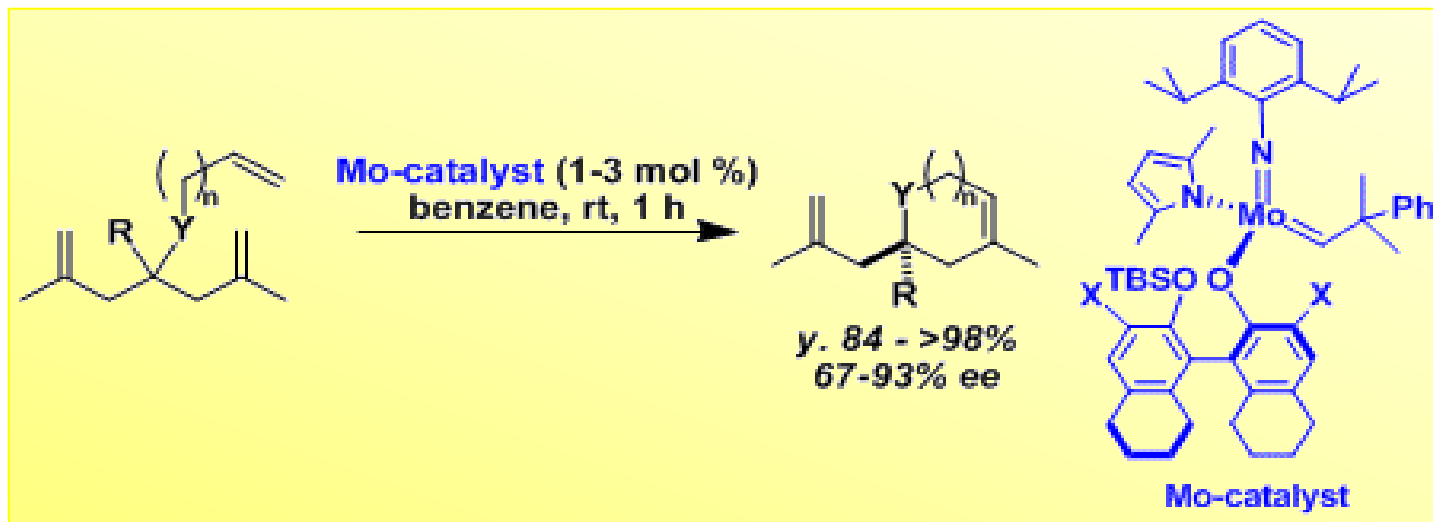


Scheme 1. (a) K₂CO₃, allyl bromide, acetone; (b) microwave irradiation, neat, 100 W, 180–220 °C; (c) 5% catalyst **13**, toluene (or CH₂Cl₂ for **10b**); (d) 5% catalyst **14**, toluene; For yields see Table 1.

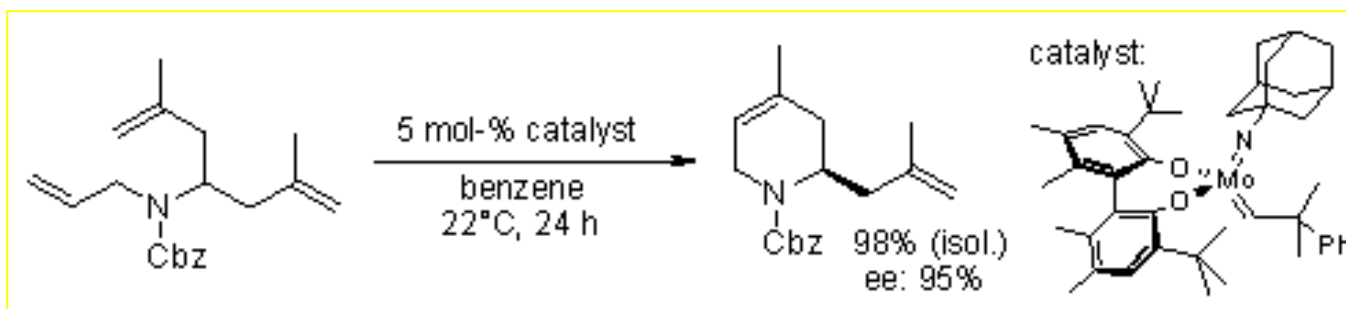
Σχηματισμός μακρολακτονών (13-21 μέλη) μέσω RCM (J. Chem. Soc. Perkin Trans. 1 1997, 2869).



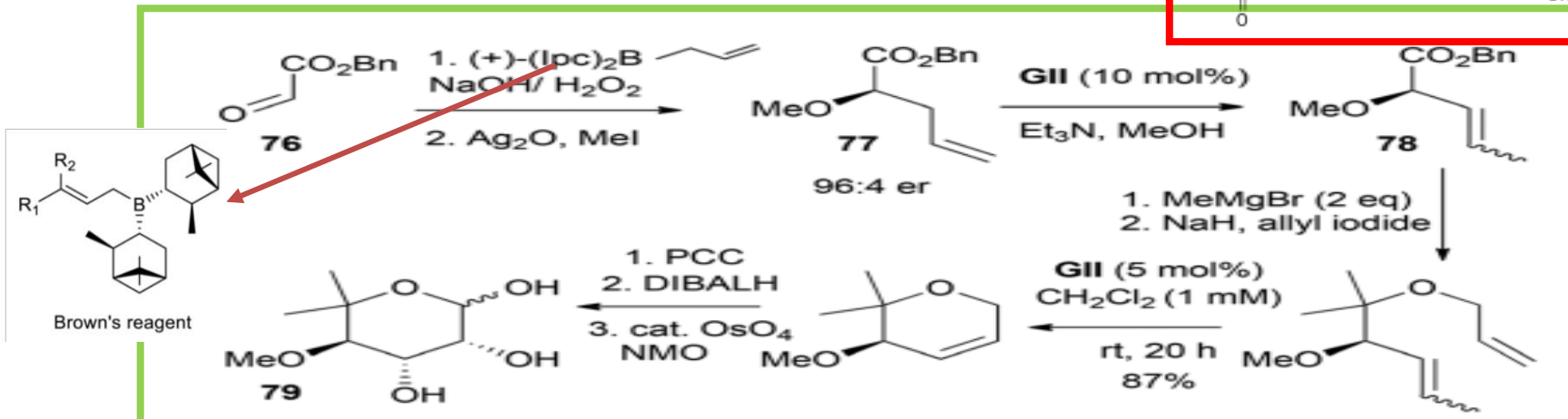
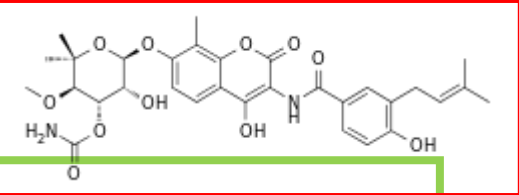
Ασύμμετρη αντίδραση RCM



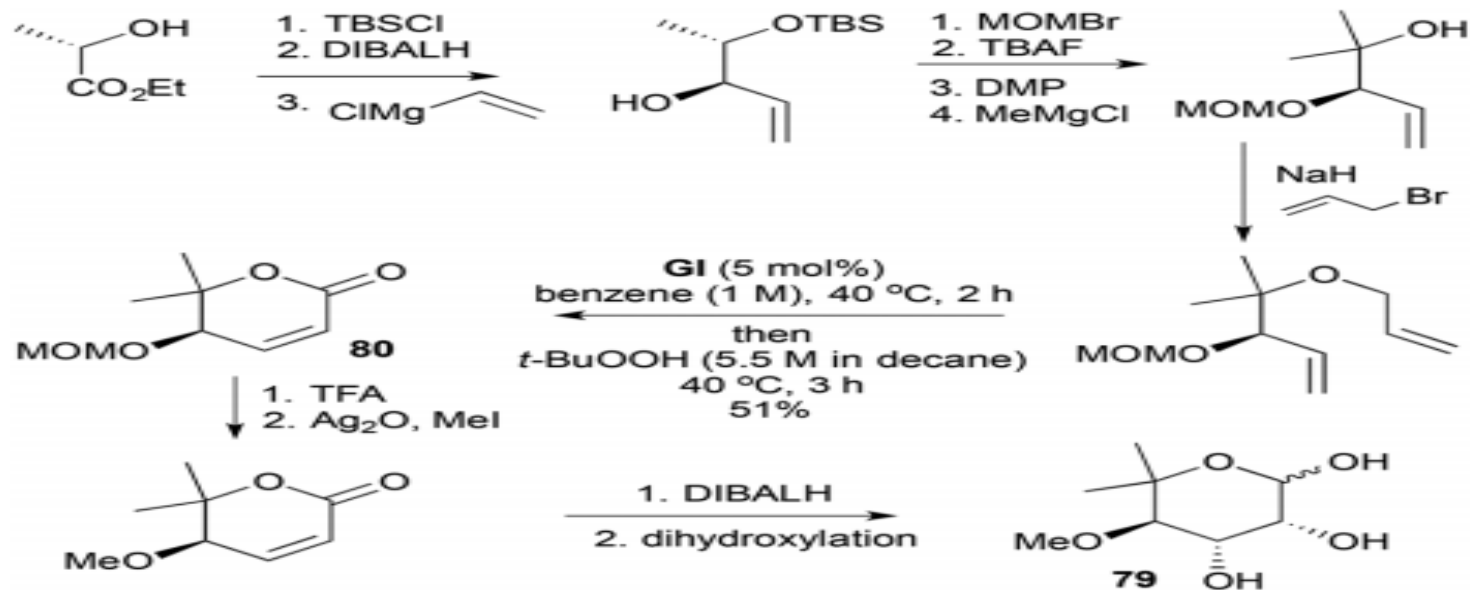
Εναντιοεκλεκτική σύνθεση κυκλικών αμιδίων μέσω ασύμμετρης RCM (J. Am. Chem. Soc. 2005, 127, 8526)



L-(+)-noviose (79), the sugar component of the anticancer agent novobiocin

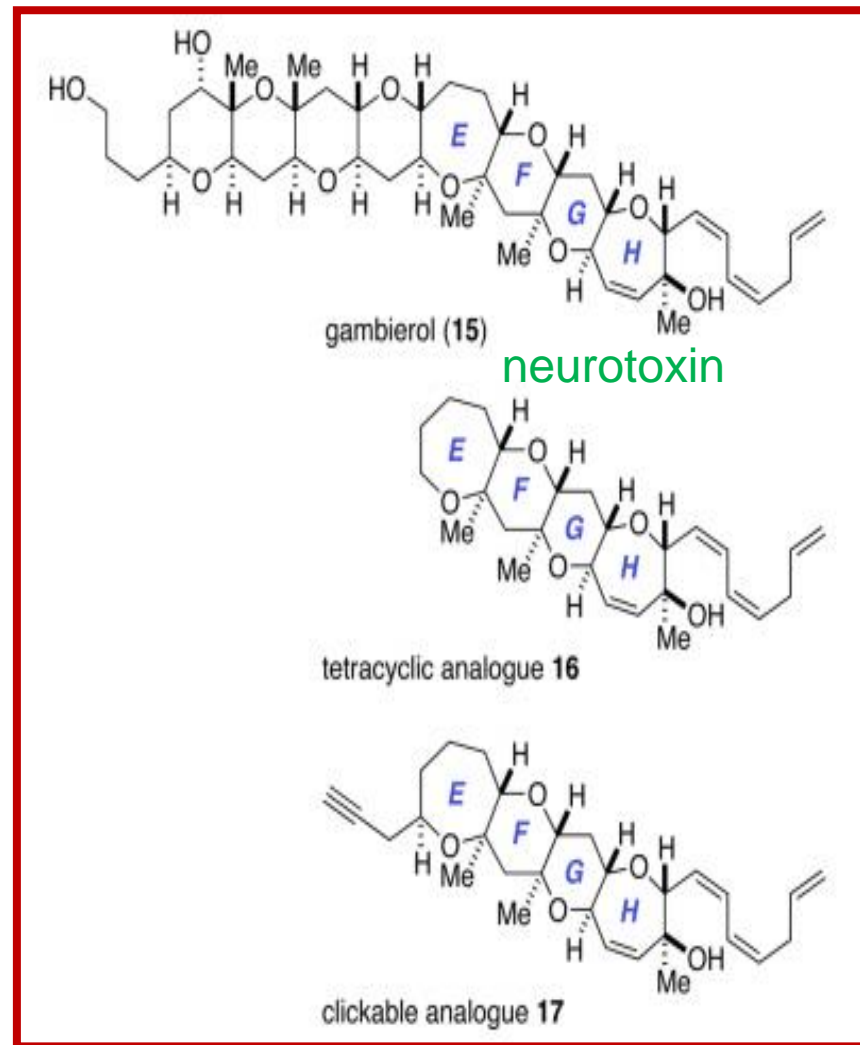
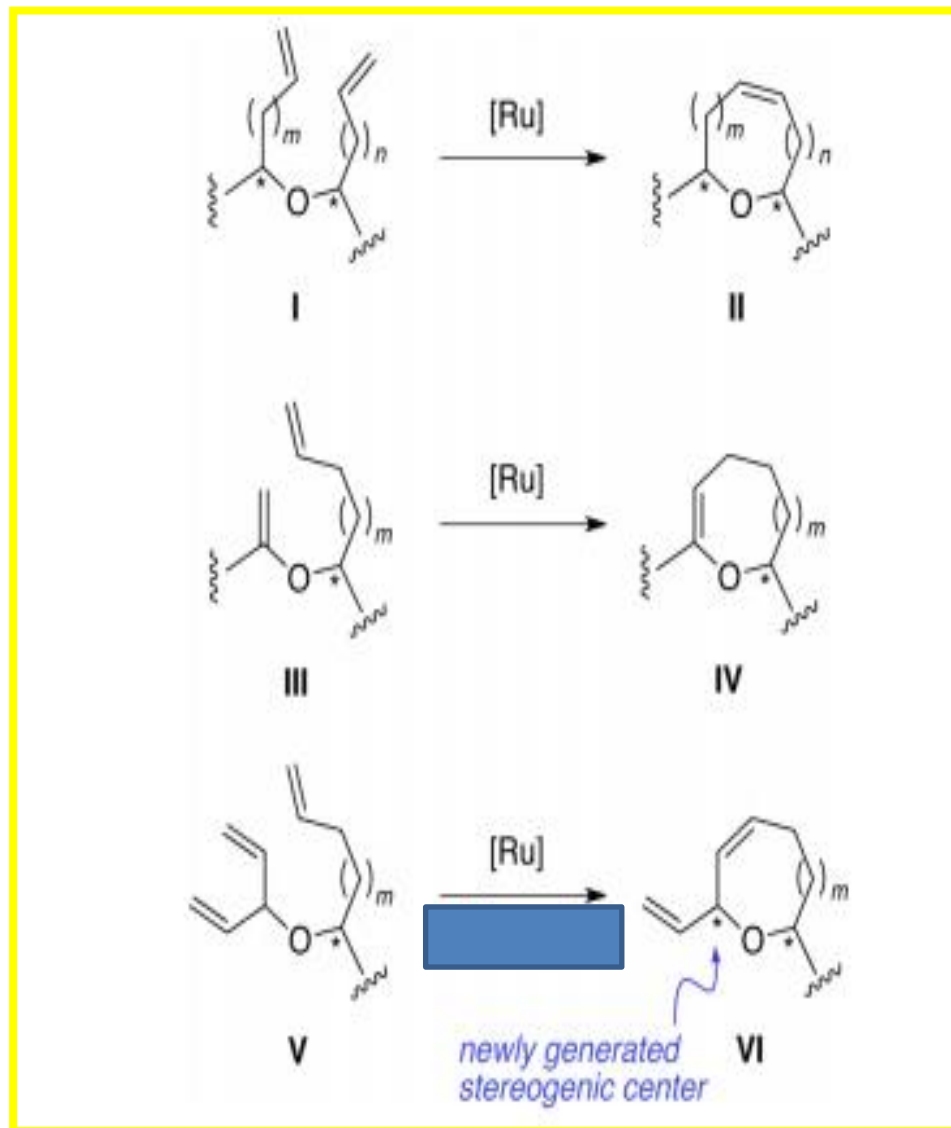


Scheme 21 Synthesis of L-(+)-noviose (79) from benzyl glyoxylate.



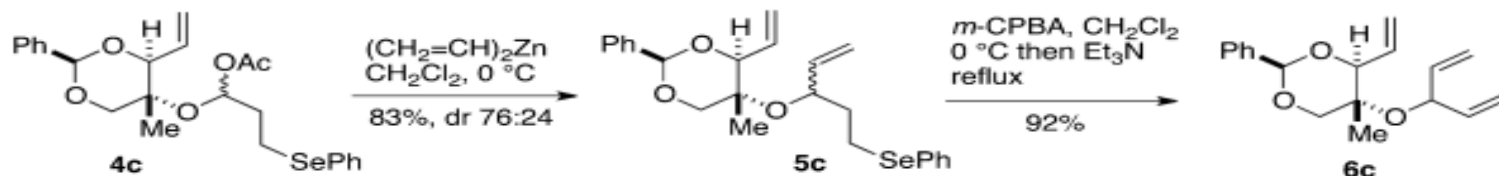
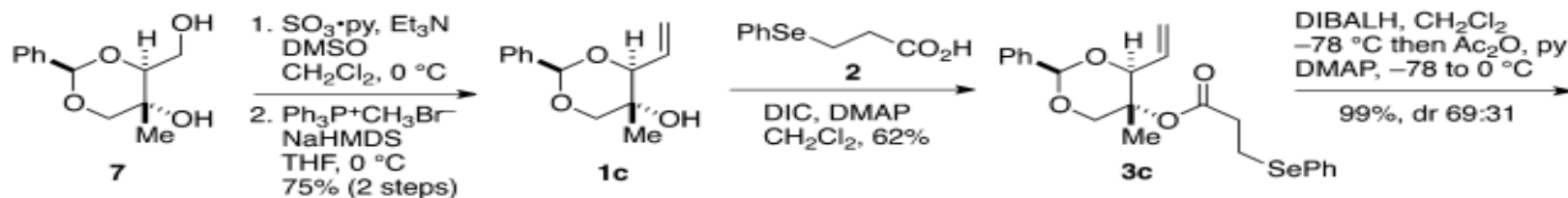
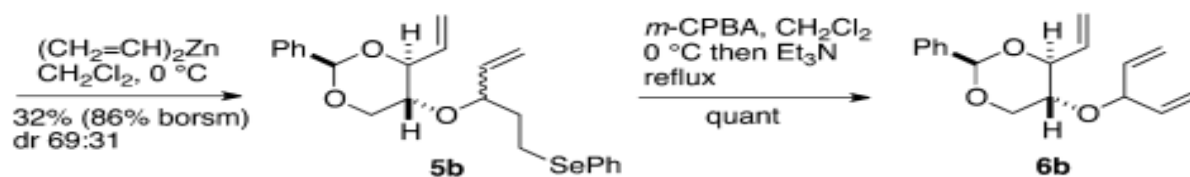
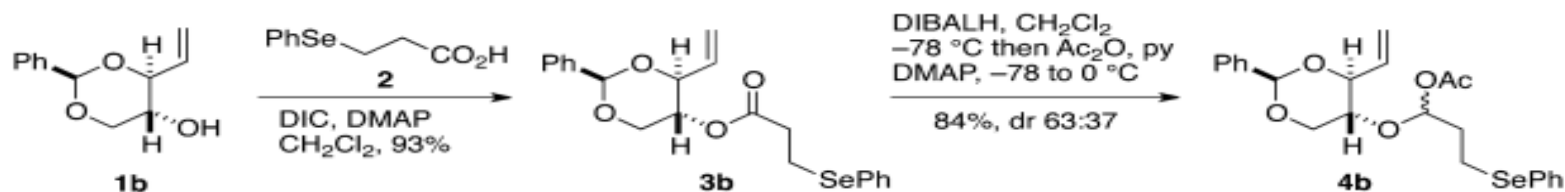
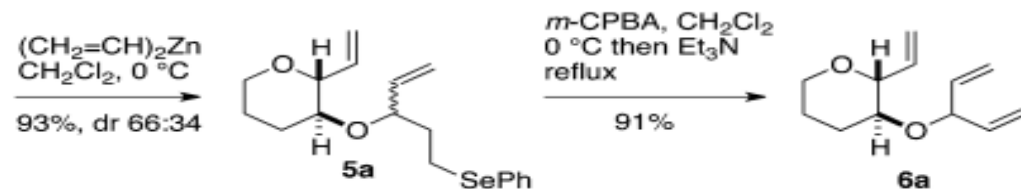
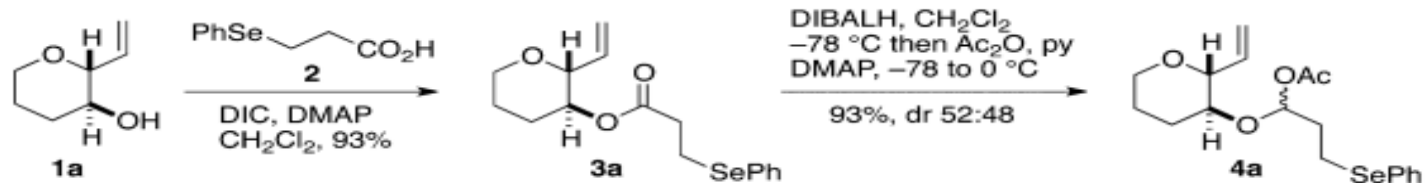
Scheme 22 Synthesis of L-(+)-noviose (79) from ethyl S-lactate.

Diastereoselective Ring-Closing Metathesis as a Means to Construct Medium-Sized Cyclic Ethers: Application to the Synthesis of a Photoactivatable Gambierol Derivative (H. Fuwa et al. J. Org. Chem. 2016, 81, 8234–8252)

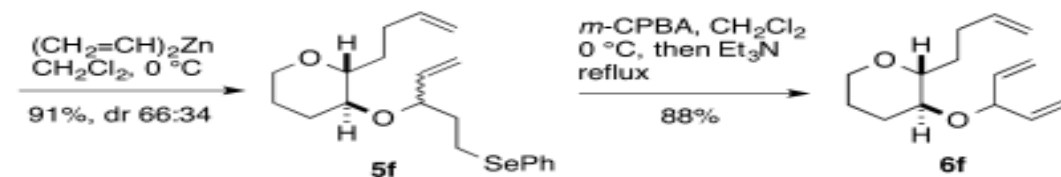
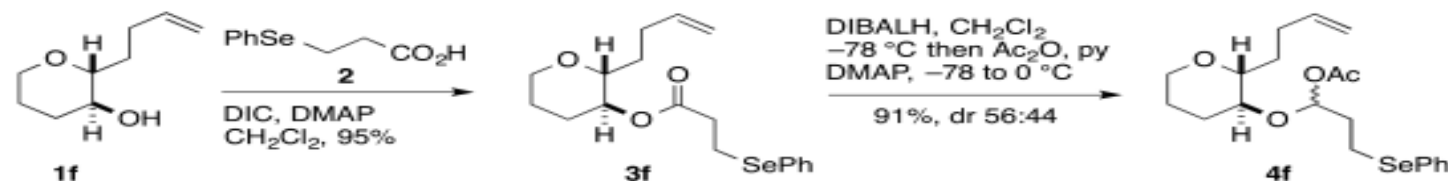
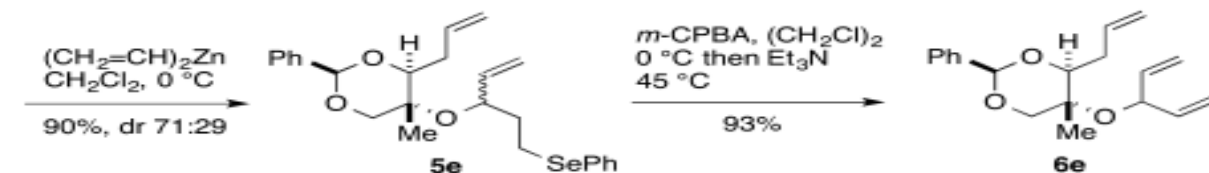
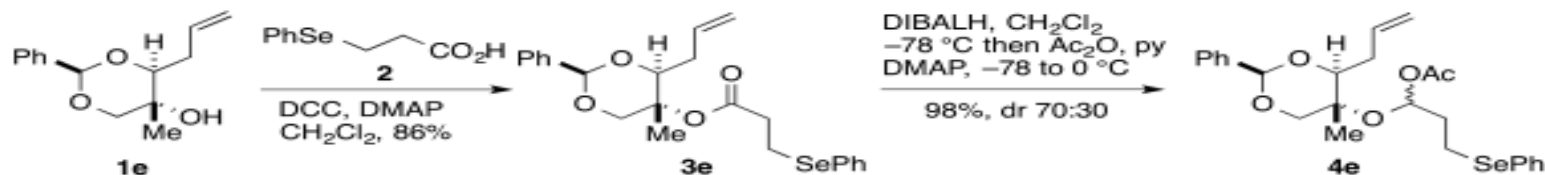
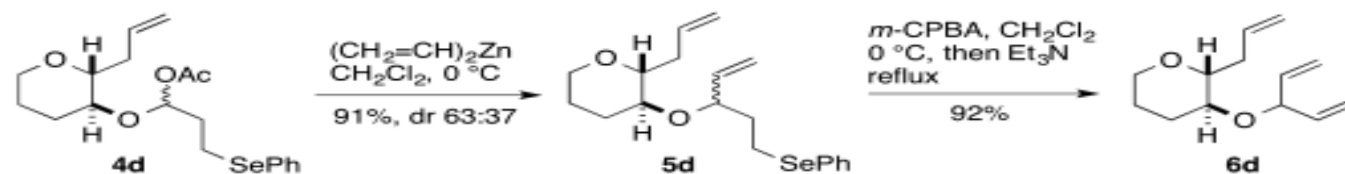
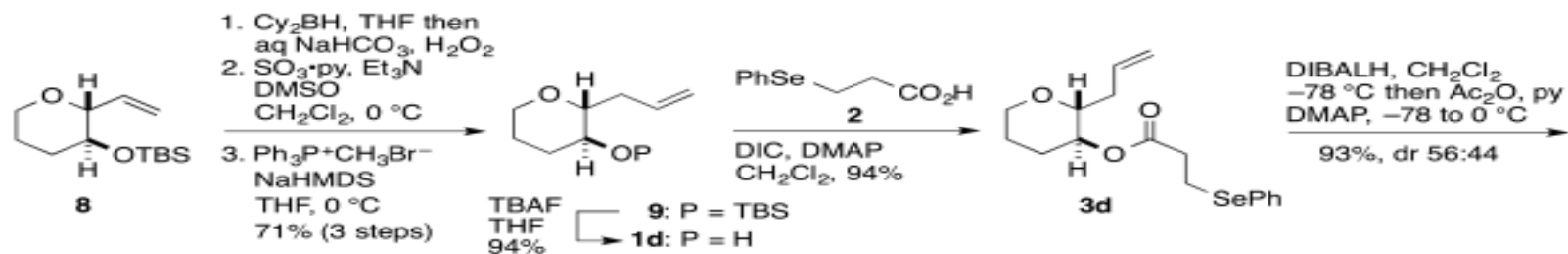


EFGH-ring domain, is responsible for potent Kv channel inhibitory activity

Synthesis of RCM Precursors 6a–c



Synthesis of RCM Precursors 6d–f



Scheme 4. Vinylation of α -Acetoxy Ether 11

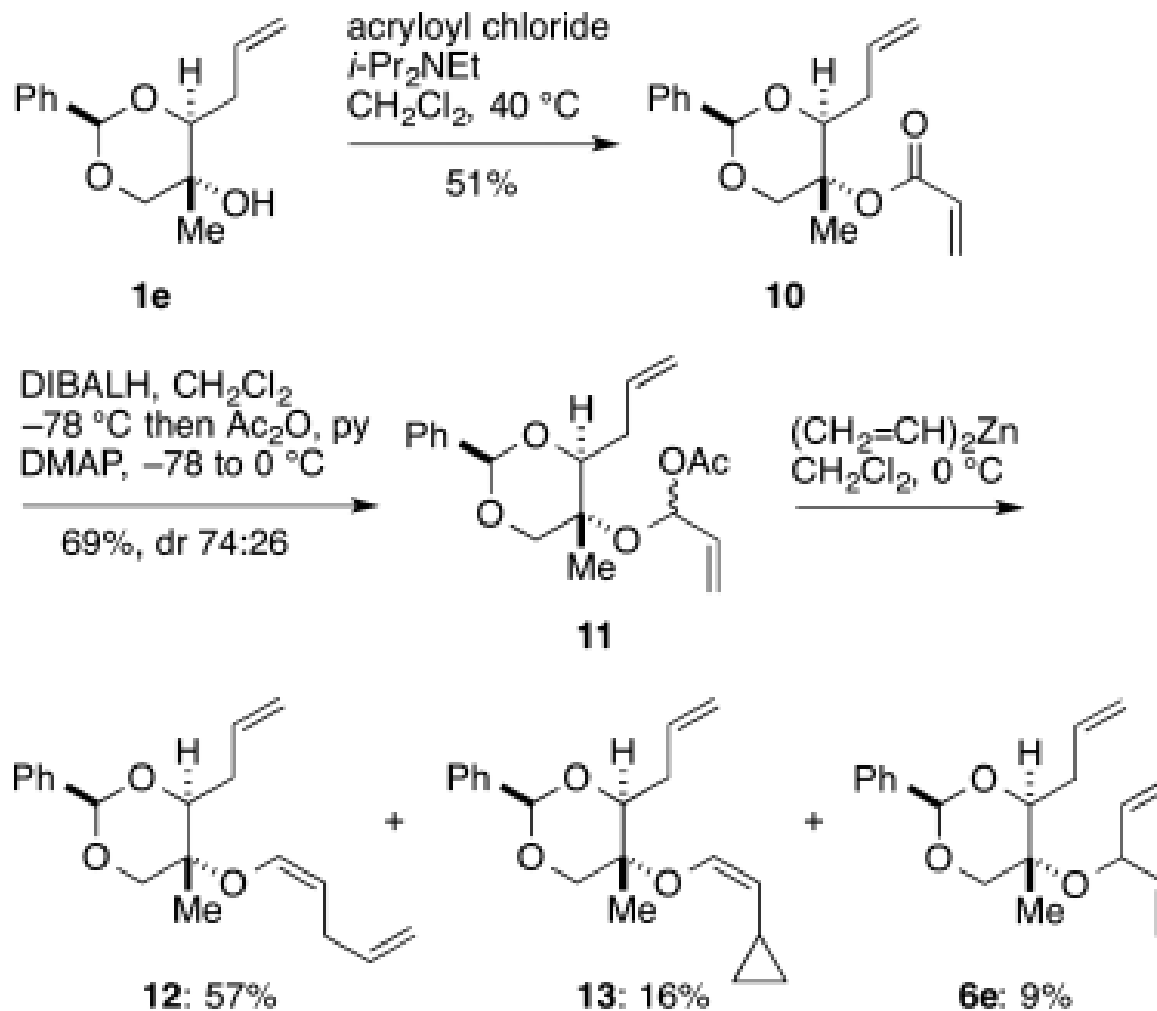
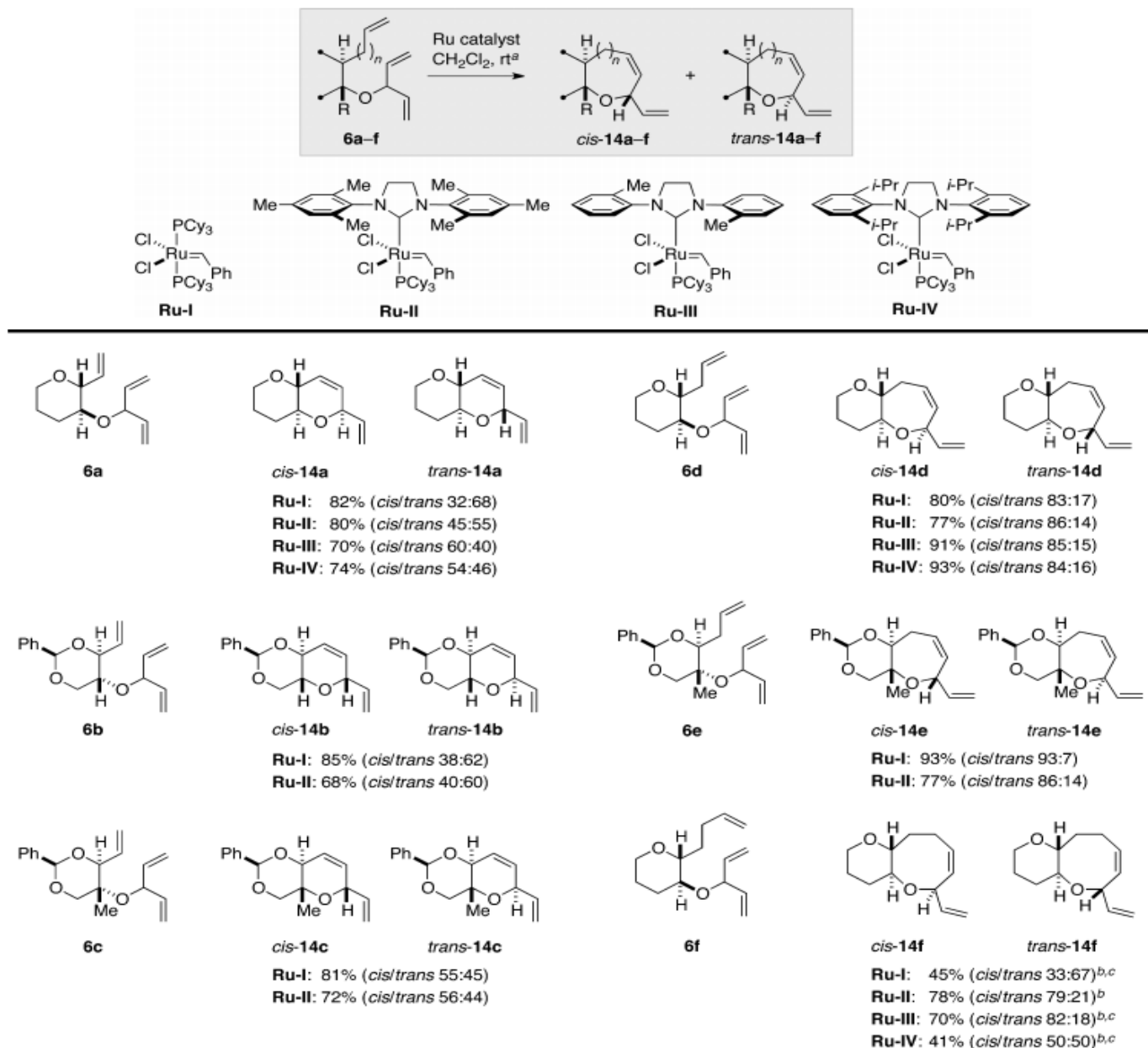
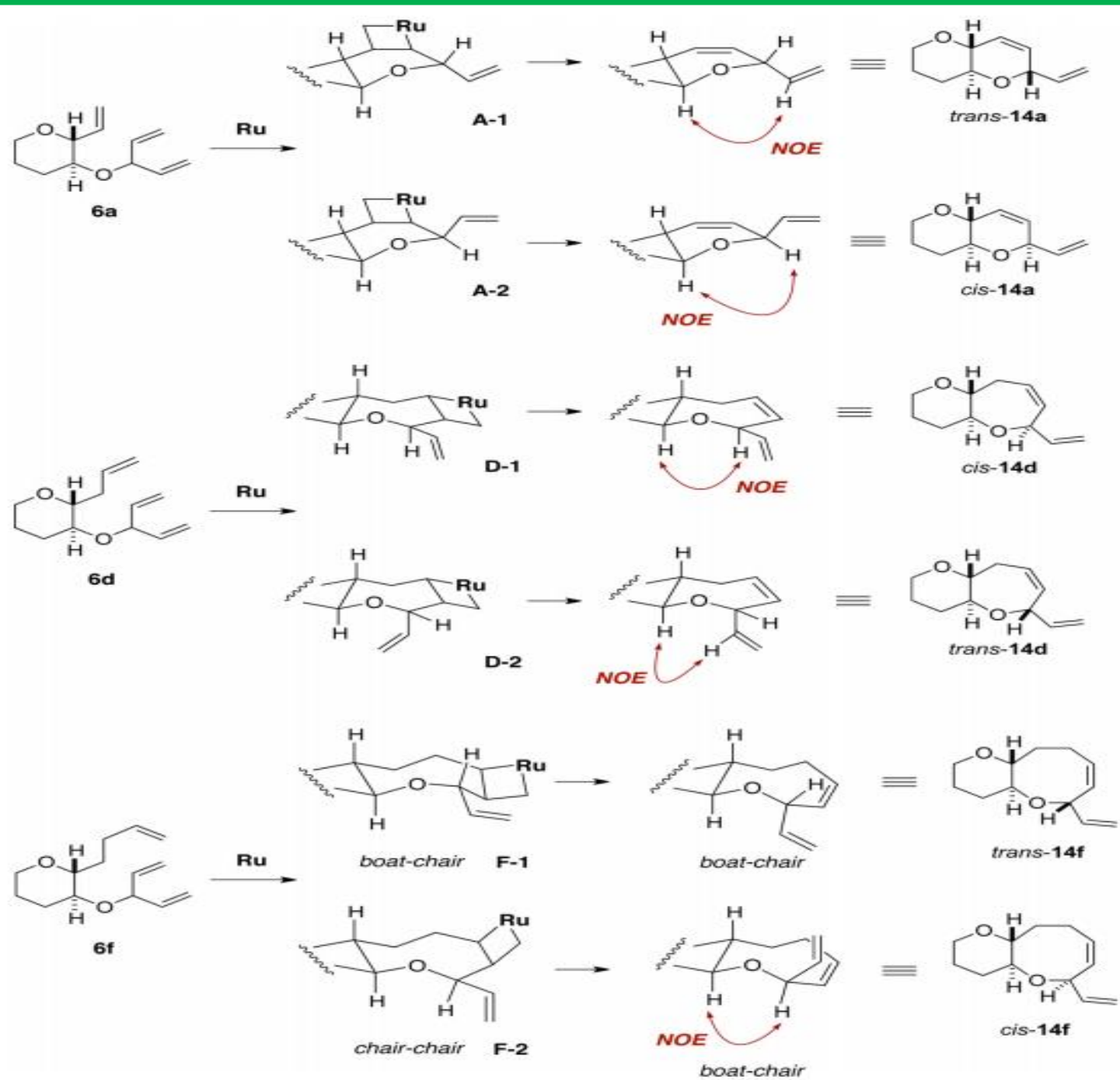


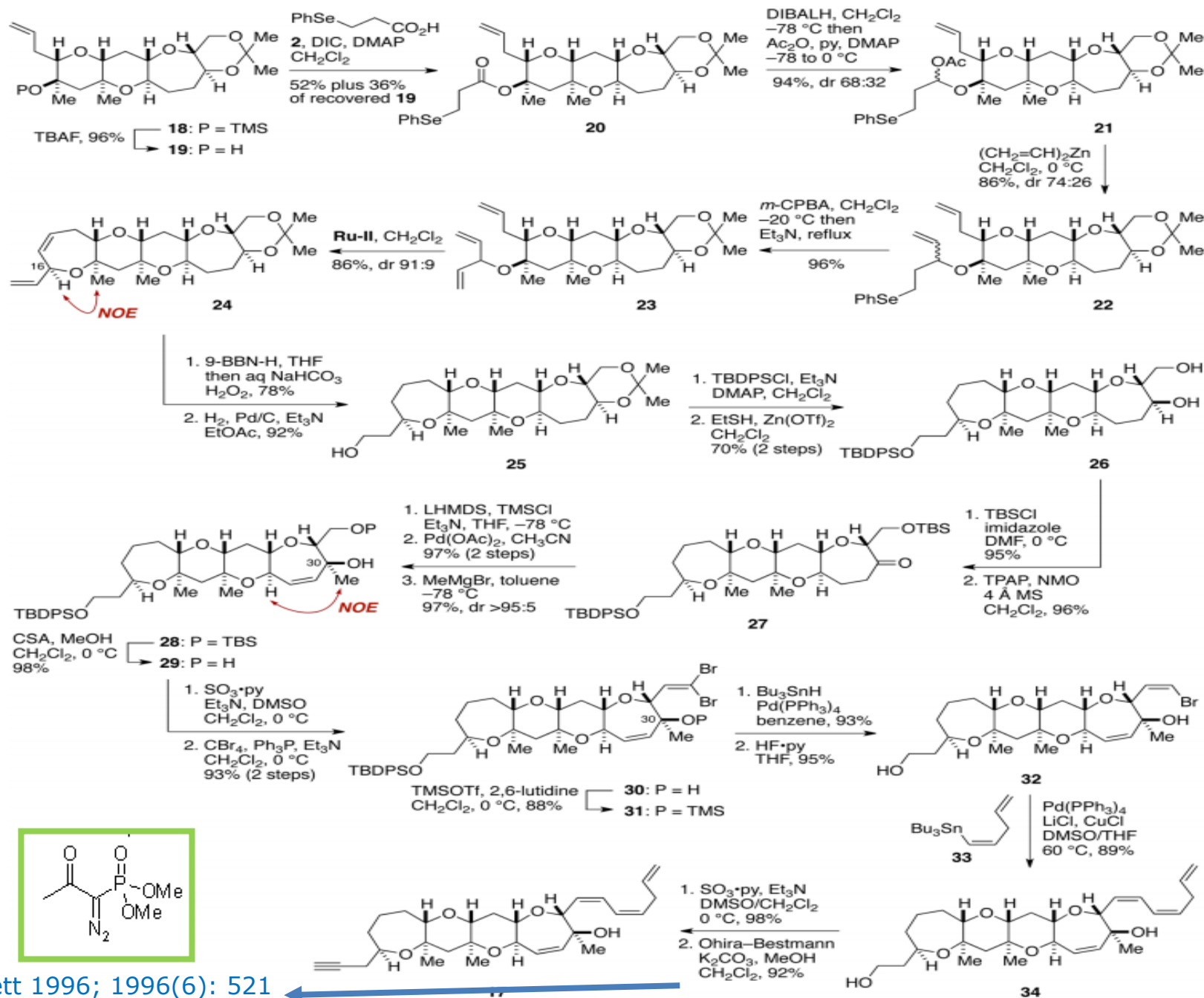
Table 1. Diastereoselective RCM of 6a–f^a



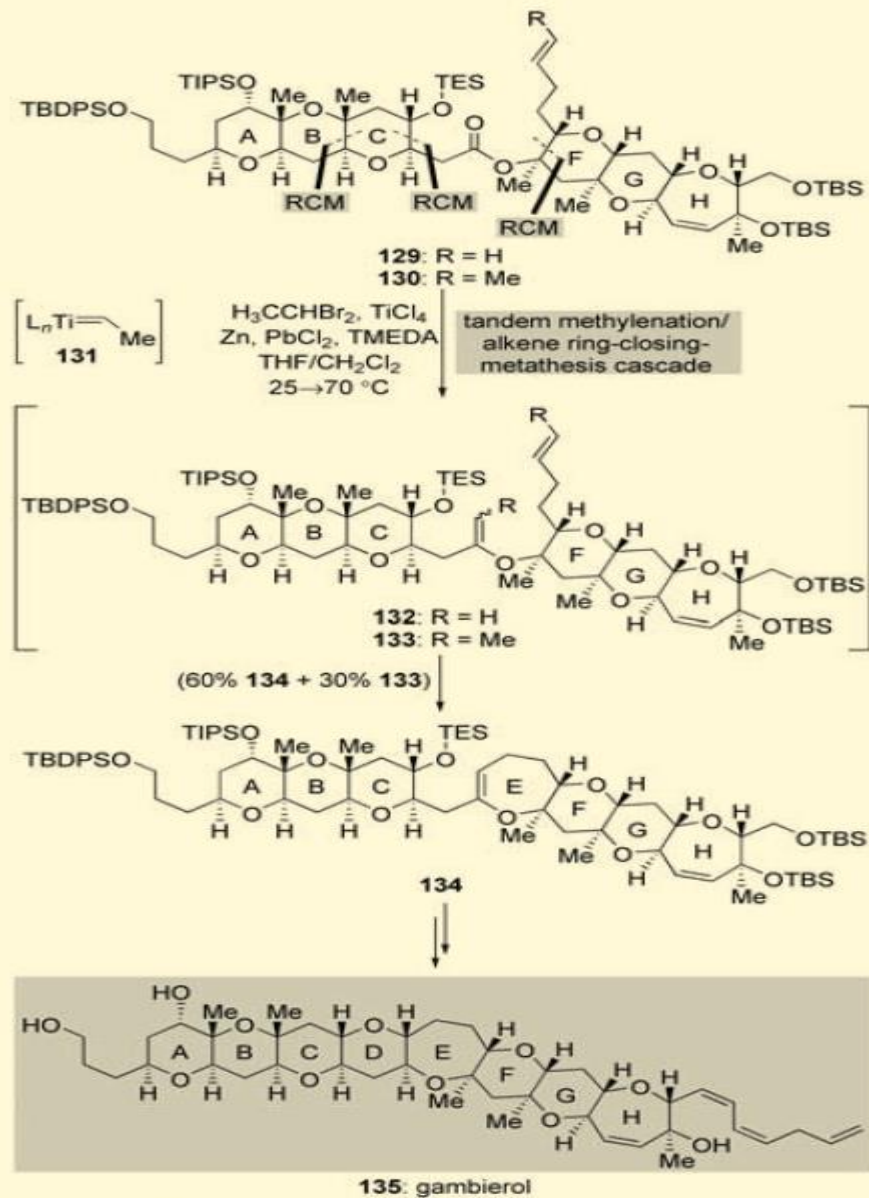
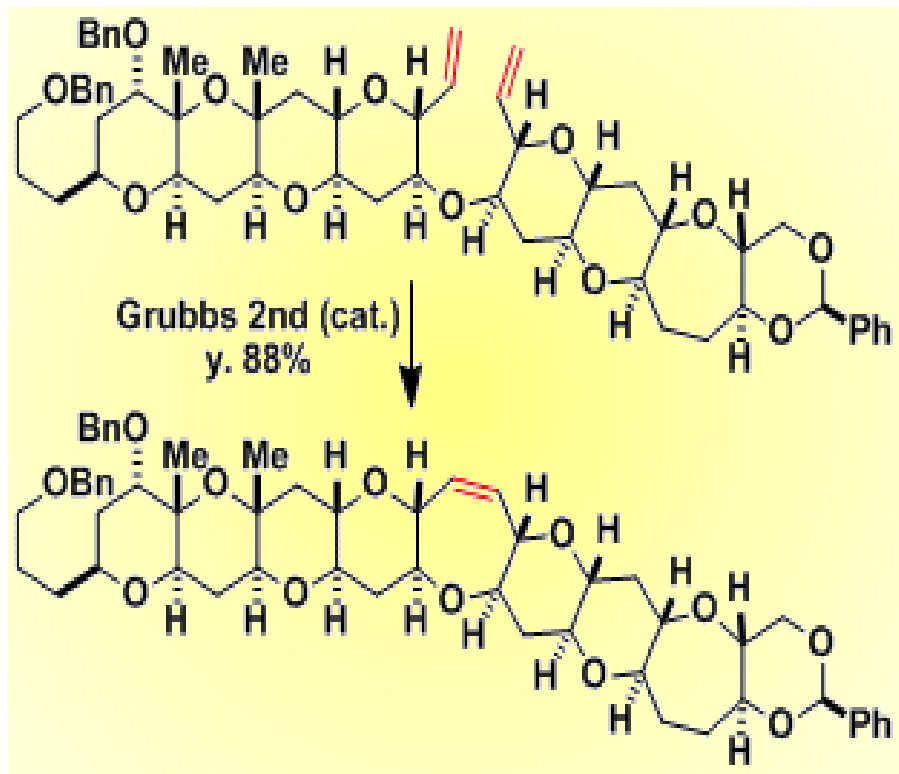
^aAll reactions were performed using 10 mol % of ruthenium catalyst in degassed CH₂Cl₂ (10 mM) at room temperature for 1–2 h, unless otherwise noted. The diastereoselectivity was estimated on the basis of ¹H NMR analysis (600 MHz). The configuration of 14a–f was assigned on the basis of NOE experiments. ^bThe reactions were performed at a concentration of 3 mM for 22 h. ^cThe reactions were performed using 30 mol % of catalyst.



Scheme 5. Synthesis of Clickable Gambierol Analogue 17

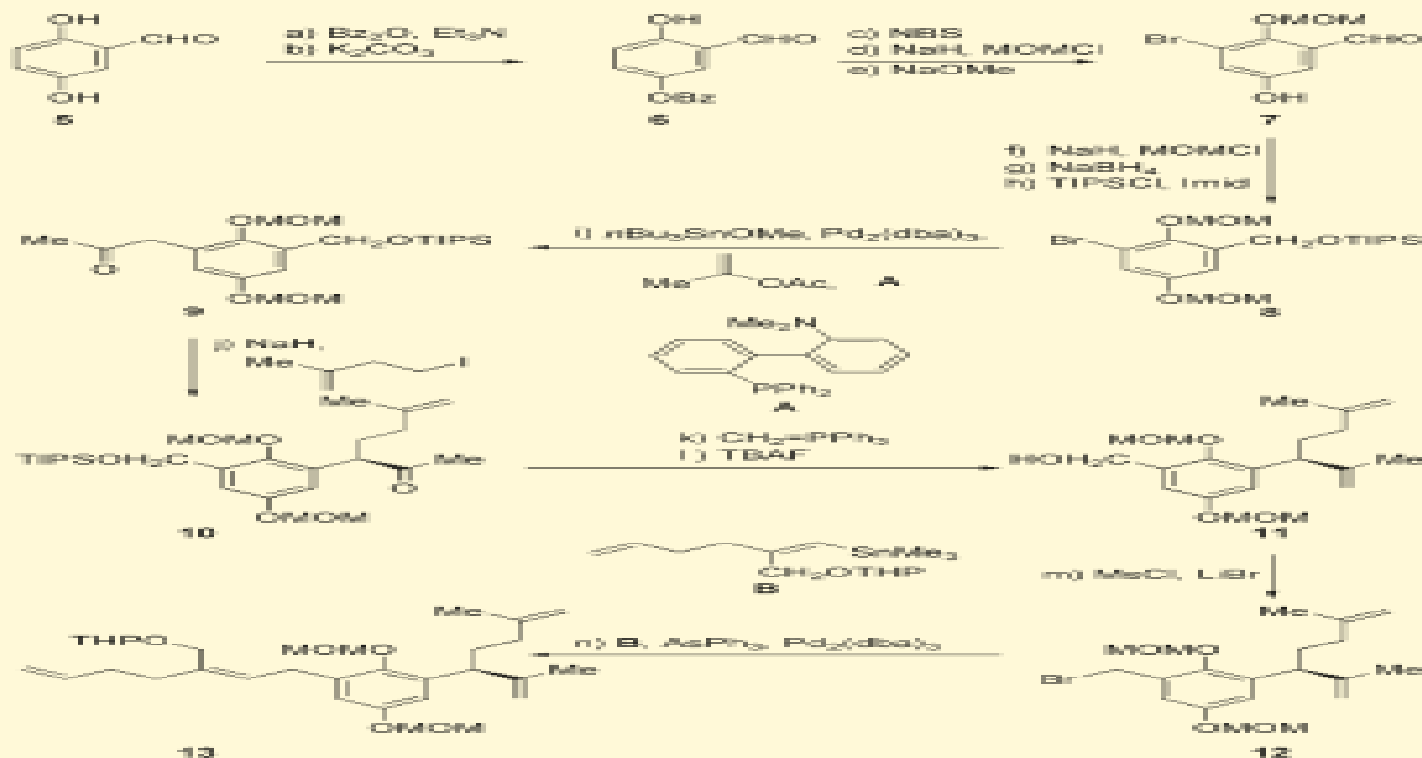


Εφαρμογή της αντίδρασης RCM στην ολική σύνθεση της γκαμπιερόλης, τοξίνης από τον θαλάσσιο οργανισμό dinoflagellate *Gambierdiscus toxicus* (Angew. Chem. Int. Ed. 2005, 44, 4490).

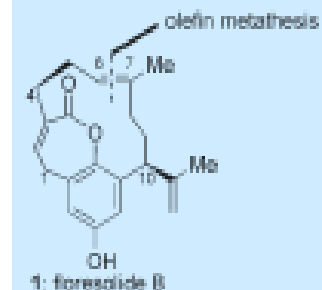


Scheme 25. The synthesis of complex polyether frameworks through tandem methylenation/ring-closing metathesis: application to the total synthesis of gambierol (135) (Rainier and co-workers, 2005).^[136]

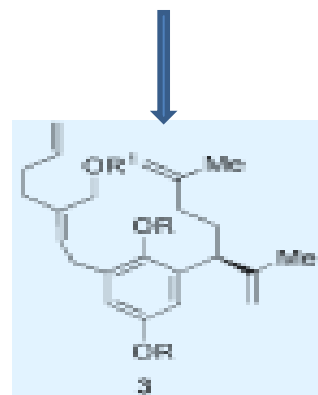
Σύνθεση Φλωρεσολιδίου B (Chem. Commun. 2006, 600).



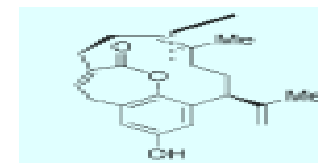
Scheme 1 Synthesis of advanced intermediate 13. *Reagents and conditions:* (a) Bz_2O (2.1 equiv), Et_3N (2.3 equiv), 4-DMAP (0.1 equiv), CH_2Cl_2 , 25 °C, 12 h, 85%; (b) K_2CO_3 (1.5 equiv), THF : MeOH (1 : 1), 0 °C, 2 h, 83%; (c) NBS (1.05 equiv), CH_2Cl_2 , 25 °C, 1 h, 95%; (d) NaH (2.0 equiv), MOMCl (1.0 equiv), DMF, 25 °C, 2 h, 90%; (e) NaOMe (1.1 equiv), THF : MeOH (1 : 1), -40 °C, 2 h, 80%; (f) NaH (2.0 equiv), MOMCl (1.0 equiv), DMF, 25 °C, 2 h, 85%; (g) $NaBH_4$ (2.5 equiv), MeOH, 0 °C, 30 min, 90%; (h) TIPSCl (1.5 equiv), imidazole (2.0 equiv), 4-DMAP (0.1 equiv), DMF, 25 °C, 12 h, 85%; (i) nBu_4SnOMe (1.4 equiv), $Pd_2(dba)_3$ (0.1 equiv), Buchwald ligand A (0.4 equiv), toluene, 90 °C, 2 h, 85%; (j) NaH (1.2 equiv), THF, 0 °C, 0.5 h; then 4-iodo-2-methylbut-1-ene (1.6 equiv), 0 °C, 4 h, 73%; (k) $CH_3PPh_3 Br^-$ (1.5 equiv), NaHMDS (1.5 equiv), THF, 0 °C, 1 h; then 10 added to the generated ylide, 0 °C, 0.5 h, 75%; (l) TBAF (1.1 equiv), THF, 0 °C, 15 min, 80%; (m) LiBr (2.0 equiv), Et_3N (2.5 equiv), MsCl (1.5 equiv), THF, -10 °C, 30 min, 82%; (n) $Pd_2(dba)_3$ (0.1 equiv), $AsPh_3$ (0.8 equiv), THF, 25 °C, 20 min; then vinyl tin compound B (1.2 equiv), 12 (1.0 equiv), 70 °C, 1 h, 85%. Bz = benzoyl, 4-DMAP = 4-dimethylaminopyridine, NBS = *N*-bromosuccinimide, MOM = methoxymethyl, DMF = *N,N*-dimethylformamide, TIPS = triisopropylsilyl, dba = dibenzylideneacetone, HMDS = hexamethyldisilazane, TBAF = tetra-*n*-butylammonium fluoride, Ms = methanesulfonyl, THP = tetrahydropyranyl.



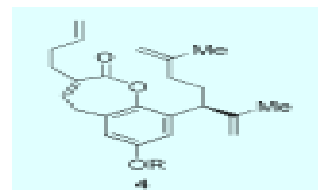
1: florescidiol B



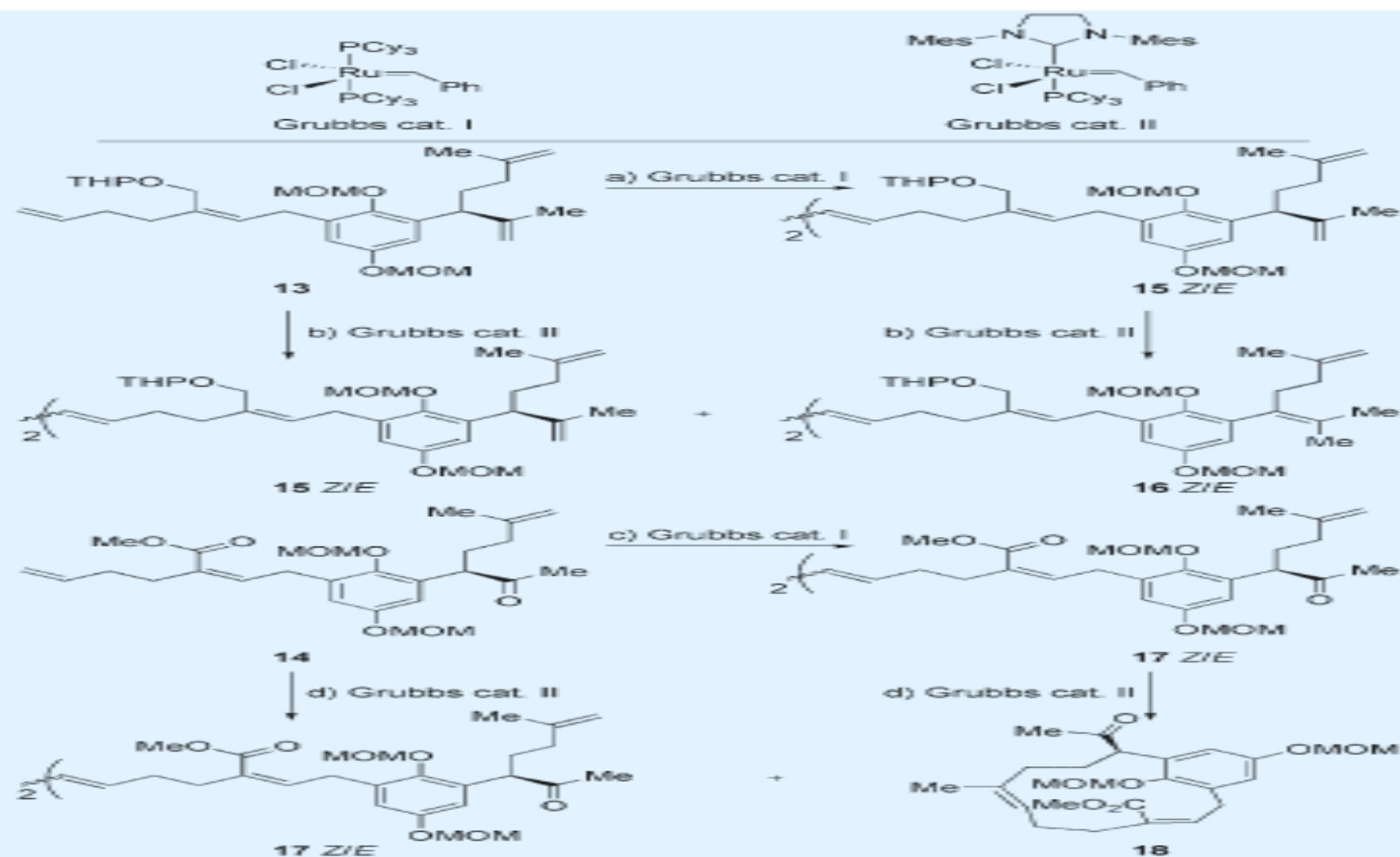
3



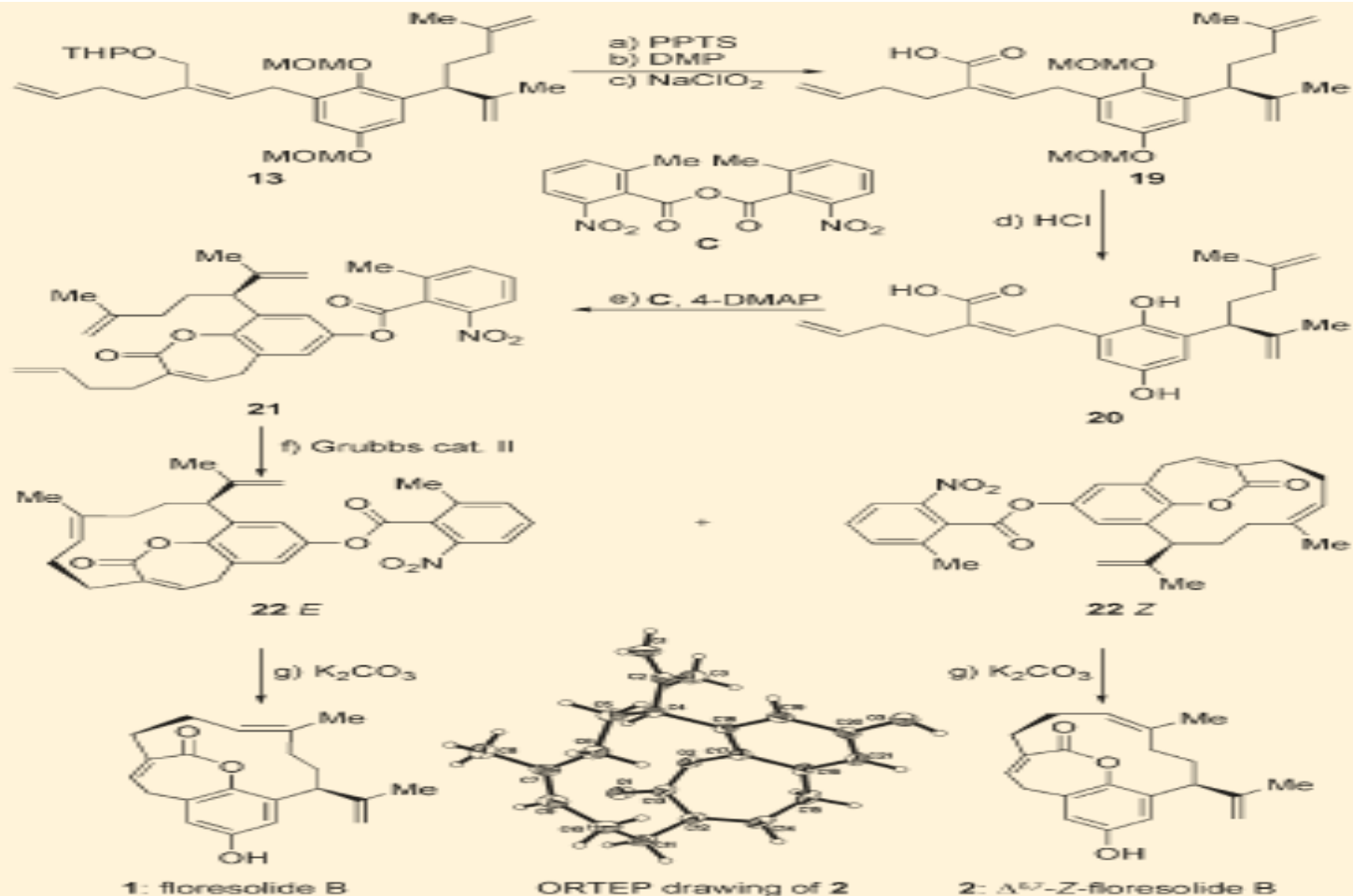
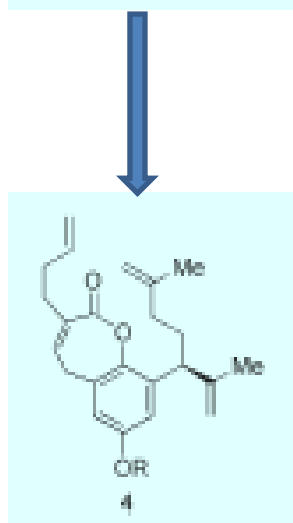
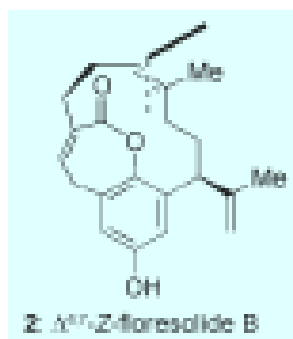
2: 2',6''-2-florescidiol B



4

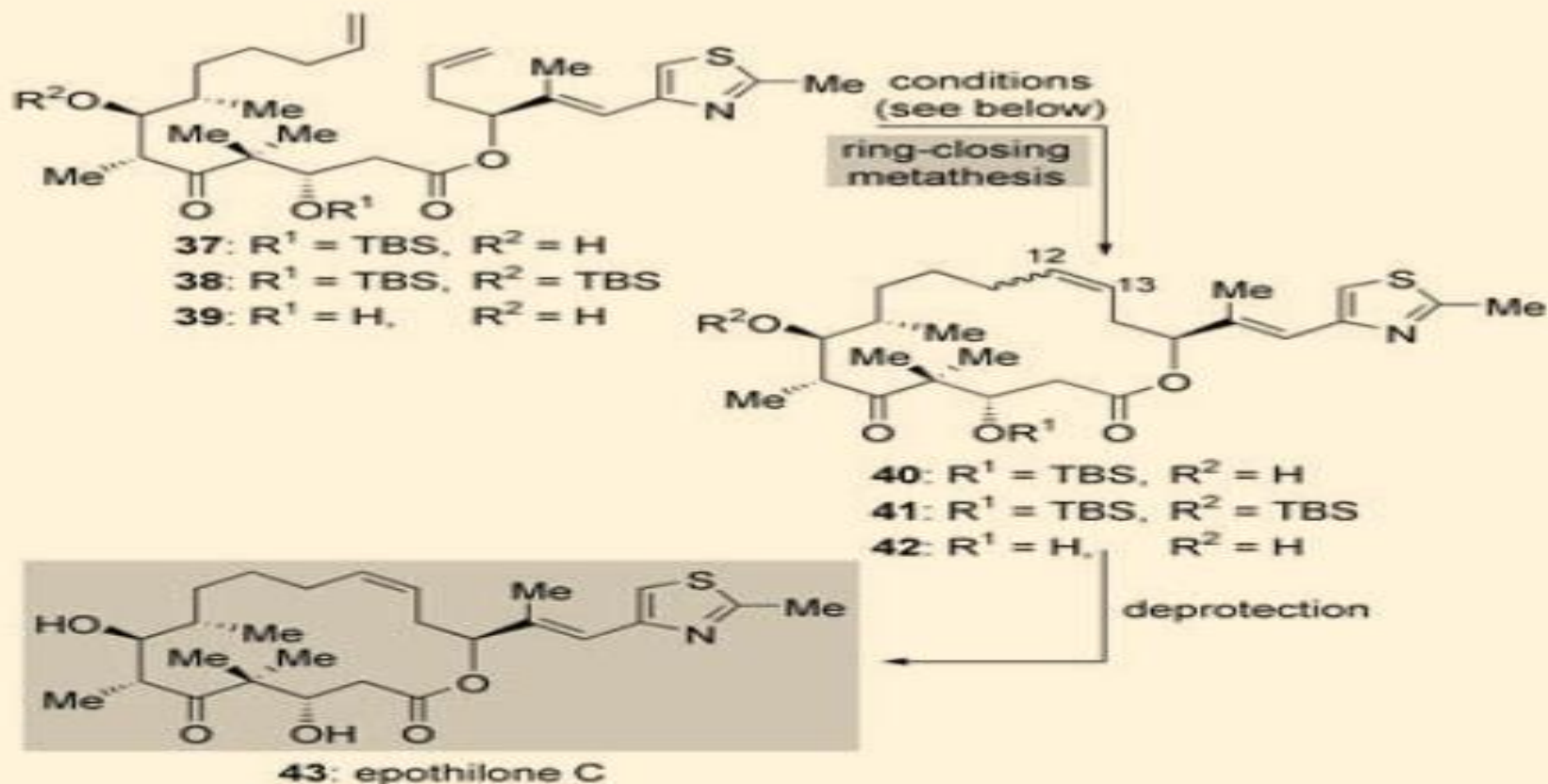


Scheme 2 Attempted ring closing metathesis of open chain substrates **13** and **14**. *Reagents and conditions:* (a) Grubbs cat. I (0.2 equiv), CH_2Cl_2 , 0.5 mM, 40 °C, 48 h, **15Z** : **15E** = 1 : 1, 75% combined yield; (b) Grubbs cat. II (0.2 equiv), CH_2Cl_2 , 0.5 mM, 40 °C, 48 h, **15Z** : **15E** = 1 : 1, 35% combined yield, **16Z** : **16E** = 1 : 1, 20% combined yield; (c) Grubbs cat. I (0.2 equiv), CH_2Cl_2 , 0.5 mM, 40 °C, 8 h, **17Z** : **17E** = 1 : 1, 90% combined yield; (d) Grubbs cat. II (0.2 equiv), CH_2Cl_2 , 0.5 mM, 40 °C, 8 h, **17Z** : **17E** = 1 : 1, 70% combined yield, **18**, 9%.



Scheme 3 Total synthesis of floresolide B (**1**) and $\Delta^{6,7}$ -Z-floresolide B (**2**) and ORTEP drawing of $\Delta^{6,7}$ -Z-floresolide B (**2**). (Only the (*S*)-enantiomer is shown from the two enantiomers present in the crystal.) *Reagents and conditions*: (a) PPTS (5.0 equiv), 0.2 M in MeOH, 25 °C, 6 h, 75%; (b) DMP (1.2 equiv), NaHCO₃ (20 equiv), CH₂Cl₂, 25 °C, 92%; (c) NaClO₂ (4.0 equiv), NaH₂PO₄ (2.0 equiv), 2-methyl-2-butene (5.0 equiv), *t*BuOH/H₂O (4 : 1), 25 °C, 4 h, 95%; (d) HCl in MeOH (0.1 M), 25 °C, 4 h, 75%; (e) 2-nitro-6-methyl-benzoic anhydride (2.0 equiv), 4-DMAP (4.0 equiv), 0.5 mM in CH₂Cl₂, then **20** was added *via* syringe pump over 12 h, 25 °C, 66%; (f) Grubbs cat. II (0.1 equiv), 0.5 mM in CH₂Cl₂, 40 °C, 15 min, 22*E* (23%), 22*Z* (66%); (g) K₂CO₃ (10.0 equiv), MeOH/H₂O (1 : 1), 25 °C, 2 h, 90%. PPTS = pyridinium *p*-toluenesulfonate, DMP = Dess–Martin periodinane.

Εφαρμογή της αντίδρασης RCM στην ολική σύνθεση της εποθιλόνης C
(*Angew. Chem. Int. Ed.* 1997, 36, 166).



Nicolaou et al.
(37→40)
2 (10 mol%)
 CH_2Cl_2 , 25 °C
(85%, *EIZ* 1:1.2)

Danishefsky et al.
(38→41)
1 (50 mol%)
benzene, 55 °C
(86%, *EIZ* 3:5)

Schinzer et al.
(38→41)
2 (6 mol%)
 CH_2Cl_2 , 25 °C
(94%, *EIZ* 3:5)

Danishefsky et al.
(39→42)
1 (50 mol%)
benzene, 55 °C
(65%, *EIZ* 2:1)

Scheme 10. Ring-closing-metathesis reactions in the total synthesis of epothilone C (43) (Nicolaou and co-workers, 1997; Danishefsky and co-workers; 1997, Schinzer and co-workers, 1999).^[68, 69, 71]

Σύνθεση 13-μελούς δακτυλίου μέσω αντίδρασης RCM σ'ένα από τα στάδια κλειδιά των 51 σταδίων στην ολική σύνθεση της (-)-σαραΐνης A (J. Am. Chem. Soc. 2007, 129, 11987).

