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Ring Opening of Methylenecycloalkenes via the C−C Bond Cleavage

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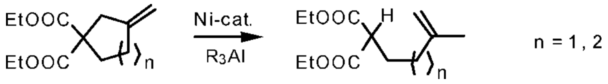
ABSTRACT



3-Methylenecycloalkene-1,1-dicarboxylates underwent facile ring opening via the cleavage of the unactivated C−C bond to yield aliphatic alkenes. The reaction (intramolecular deallylation) was catalyzed by “Ni−H” species generated in situ from a $NiX_2(phosphine)_n/R_3Al$ mixture and proceeded under ambient conditions. In addition, the skeletal rearrangement of a diene could be carried out by a one-pot cycloisomerization/deallylation sequence.

A transition metal complex catalyzed carbon−carbon bond cleavage under mild reaction conditions has been a long pursued process of considerable theoretical and practical interest. Generally, it can be facilitated by the presence of an activating group and driven by a decrease of steric strain.[1] Nevertheless, the ultimate goal in this area is to achieve the cleavage of unstrained and unactivated carbon−carbon bonds under mild reaction conditions.[2] We have recently reported the C−C bond cleavage in allylmalonates and related compounds under a transition metal complex catalysis in the presence of alkylaluminums. It resulted in the clean and selective removal of the allyl moiety (deallylation).[3,4] Although this process was catalyzed by a number of transition-metal complexes (Fe, Ru, Co, Rh, Ni, and Pd), the highest catalytic activity and generality with respect to the substitution pattern of the allylic moiety was achieved with simple $NiX_2(PPh_3)_2$ complexes.[3b,c] Since it was shown that the prenyl group (sterically hindered double bond) could also be cleaved,[3b] we wanted to explore a possibility of the cleavage of an unstrained ring system possessing a R(C=O)−C−C−C=C moiety, e.g., methylenecycloalkanes (Scheme 1). If the reaction could proceed, then the net result would be a skeletal rearrangement accompanied by the double-bond shift.[5]

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(1) (a) Bishop, K. C., III. *Chem. Rev.* **1976**, *76*, 461–486. (b) Crabtree, R. H. *Chem. Rev.* **1985**, *85*, 245–269. (c) Jennings, P. W.; Johnson, L. L. *Chem. Rev.* **1994**, *94*, 2241–2290. (d) Murakami, M.; Ito, Y. *Top. Organomet. Chem.* **1999**, *3*, 97–129.

(2) For leading references, see: (a) Watson, P. L.; Roe, D. C. *J. Am. Chem. Soc.* **1982**, *104*, 6471–6473. (b) Bunel, E.; Burger, B. J.; Bercaw, J. E. *J. Am. Chem. Soc.* **1988**, *110*, 976–978. (c) Kesti, M. R.; Waymouth, R. M. *J. Am. Chem. Soc.* **1992**, *114*, 3565–3567. (d) Yang, X.; Li, J.; Marks, T. J. *J. Am. Chem. Soc.* **1993**, *115*, 3392–3393. (e) Hajela, S.; Bercaw, J. E. *Organometallics* **1994**, *13*, 1147–1154. (f) Rossier, C.; Niccolai, G. P.; Basset, J.-M. *J. Am. Chem. Soc.* **1997**, *119*, 12408–12409.

(3) (a) Nečas, D.; Kotora, M.; Císařová, I. *Eur. J. Org. Chem.* **2004**, 1280–1285. (b) Nečas, D.; Turský, M.; Kotora, M. *J. Am. Chem. Soc.* **2004**, *126*, 10222–10223. (c) Nečas, D.; Turský, M.; Tišlerová, I.; Kotora, M. *New J. Chem.* **2006**, *30*, 671–674. (d) Turský, M.; Nečas, D.; Drabina, P.; Sedlák, M.; Kotora, M. *Organometallics* **2006**, *25*, 901–907. (e) Nečas, D.; D.; Drabina, P.; Sedlák, M.; Kotora, M. *Tetrahedron Lett.* **2007**, *48*, 4539–4541.

(4) For Ti-mediated deallylation, see: Yamazaki, T.; Kasatkin, A.; Kawanaka, Y.; Sato, F. *J. Org. Chem.* **1996**, *61*, 2266–2267.

(5) For pioneering work on the nickel/organoaluminum-promoted skeletal rearrangement, see: (a) Miller, R. G. *J. Am. Chem. Soc.* **1967**, *89*, 2785–2787. (b) Miller, R. G.; Pinke, P. A.; Baker, D. J. *J. Am. Chem. Soc.* **1970**, *92*, 4490–4492. (c) Gosser, L. W.; Parshall, G. W. *Tetrahedron Lett.* **1971**, 2555–2558. (d) Miller, R. G.; Golden, H. J.; Baker, D. J.; Stauffer, R. D. *J. Am. Chem. Soc.* **1971**, *93*, 6308–6304. (e) Miller, R. G.; Pinke, P. A.; Stauffer, R. D.; Golden, H. J.; Baker, D. J. *J. Am. Chem. Soc.* **1974**, *96*, 4211–4220.

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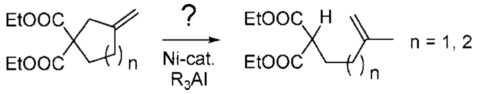
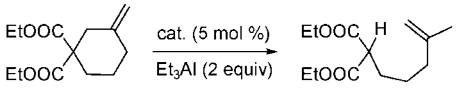
Scheme 1. Cleavage of Methylenecycloalkanes



As a model substrate **1a** was chosen for the above-mentioned study (it was prepared within five steps according to the previously published procedure[6]). Initially, **1a** was subjected to action of the previously used complexes[3] and Et_3Al (Table 1). Rh and Co complexes showed a low catalytic activity, and the ring-opened product **2a** was obtained in 52 and 26% yields, respectively (entries 1 and 2). Ru, Pd, and Pt complexes did not react at all (entries 3−5). Also, previously catalytically active Rh and Fe complexes failed to meet expectations: the use of the former afforded **2a** in just 20% yield, whereas the latter could cleave the ring only in 1% (entries 6 and 7). On the other hand, nickel chloride and bromide PPh_3 complexes catalyzed deallylation cleanly in an almost quantitative manner affording **2a** in 99 and 98% yields, respectively (entries 8 and 9). Good catalytic activity was also achieved with the PBu_3 complex (entry 10). As for bidentate phosphine complexes, only the dppm complex promoted deallylation to **2a** in 69% yield (entry 11). Other complexes such as dppe, dppp, and dppb were negligibly active if at all (entries 12−14). The Ni−BIAP complex (BIAP = bis(imidazolonyl)pyridine) and a combination of nickel hexanoate and tris(*o*-tolyl)phosphine[7] gave **2a** in good 85 and 88% yields, respectively (entries 15 and 16).

Table 1. Transition Metal Complex Catalyzed Ring Opening of **1a**



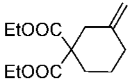
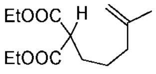
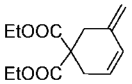
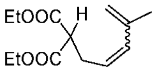
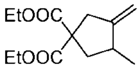
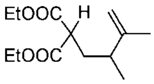
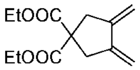
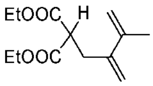
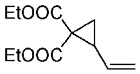
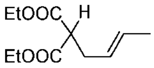
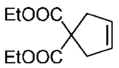
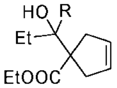
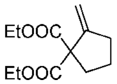
1a **2a**

entry	catalyst	yield[a] (%)	entry	catalyst	yield[a] (%)
1	$CoCl_2(PPh_3)_2$	52	9	$NiBr_2(PPh_3)_2$	98
2	$RhCl(PPh_3)_3$	26	10	$NiBr_2(PBu_3)_2$	91
3	$RuCl_2(PPh_3)_3$	nr[b]	11	$NiBr_2$(dppm)	69
4	$PdCl_2(PPh_3)_2$	nr	12	$NiBr_2$(dppe)	2
5	*cis*-$PtCl_2(PPh_3)_2$	nr	13	$NiBr_2$(dppp)	nr
6	$RhCl_3$−BIAP	20	14	$NiBr_2$(dppb)	nr
7	$FeCl_3$−BIAP	1	15	$NiBr_2$−BIAP	85
8	$NiCl_2(PPh_3)_2$	99	16	$Ni(OEtHex)_2$/ 2(*o*-tol)$_3$P	88

[a] ^1H NMR or GC yields. [b] nr = no reaction.

Since the best results were obtained with a combination of Et_3Al and $NiX_2(PPh_3)_2$, we decided to use it in further studies. In the next stage, the C−C bond cleavage of various cyclic compounds with the double bond was tested. The results are presented in Table 2 (in entry 1 is presented the reaction of **1a** for comparison). The C−C bond cleavage of **1b** possessing the diene moiety proceeded cleanly giving diene **2b** as 9/8 mixture of trans/cis isomers in a nice yield of 95% (entry 2). The reaction with **1c** proceeded almost quantitatively (98%) to afford butenyl derivative **2c** (entry 3). Analogous reaction of **1d** yielded diene **2d** in good 90% yield (entry 4). The reaction of vinylcyclopropane **1e** gave a mixture of products, the distribution of which was not very different from the uncatalyzed reaction with Et_3Al.[8] The expected intramolecularly deallylated product **2e** was obtained only in ~5% yield (entry 5). Evidently, the rate of the catalytic deallylation reaction could not override the rate of the uncatalyzed process. Surprisingly, the C−C bond cleavage did not take place with **1f**; instead, nucleophilic addition to one ester moiety gave rise to a mixture of **2f** and **2f′** (entry 6). Finally, deallylation of **1g** did not proceed (entry 7).

Table 2. Intramolecular Deallylation of **1**

entry	1		2		yield (%)[a]
1		**1a**		**2a**	99
2		**1b**		**2b**	95
3		**1c**		**2c**	98
4		**1d**		**2d**	90
5		**1e**		**2e**	5
6		**1f**		**2f**, R = H **2f′**, R = Et	45 5
7		**1g**			nr[b]

[a] ^1H NMR or GC yields. [b] nr = no reaction.

As for the reaction mechanism, we assume that it proceeds analogously to the one proposed earlier by us (Scheme 2).[3b,c] At the outset, Et_3Al generates a cationic nickel hydride **3** that hydronickelates the double bond giving a tertiary alkyl nickel species **4**. The favorable spatial arrangement of the nickel atom and the carbonyl group (1-nickela-6-oxo species) enable a lone electron pair of the carbonyl oxygen to coordinate into the empty coordination place on the nickel

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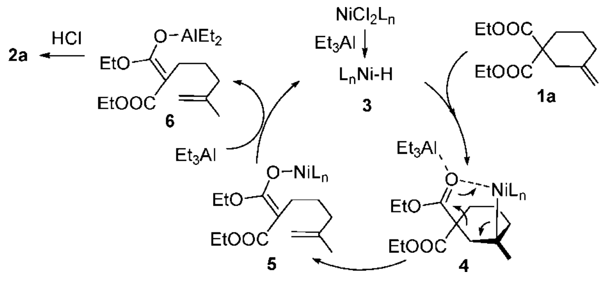
[6] Pérez-Hernández, N.; Febles, M.; Pérez, C.; Pérez, R.; Rodríguez, M. L.; Foces-Foces, C.; Martín, J. D. *J. Org. Chem.* **2006**, *71*, 1139–1151.

[7] Nečas, D.; Ramella, D.; Rudovská, I.; Kotora, M. *J. Mol. Catal. A: Chem.*, **2007**, *274*, 78–82.

[8] Hiyama, T.; Morizawa, Y.; Yamamoto, H.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2151–2160.

Scheme 2. Reaction Mechanism of the C—C Bond Cleavage

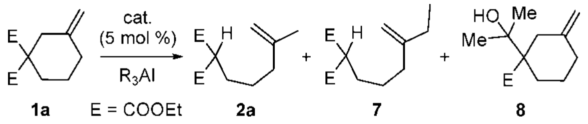


atom allowing electron pairs to migrate via a six-membered cyclic transition state. The electron-pair migration accompanied by the cleavage and formation of the C—C bonds yields a nickel enolate **5**. The formation of **5** with the strong Ni—O bond is probably the driving force of the whole process. Additional activation of the carbonyl group by Et_3Al through Lewis acid and base pairing is probably also involved.[3d] Subsequent transmetalation of **5** by Et_3Al forms the aluminum enolate **6** and releases the nickel species back into the catalytic cycle.

In this regard, it is rather surprising that the hydronickelation of **1f** did not proceed to give a secondary alkylnickel intermediate. From a steric point of view, it should be easier than in the case of methylidenecycloalkanes **1a**−**d**. Perhaps other so far unknown factors disfavor the addition of the Ni—H species to the double bond. As for the reaction with **1g**, the condition of the favorable spatial arrangement enabling a six-membered cyclic transition state was not fulfilled.

As for other organoaluminums, the C—C bond cleavage proceeded also in the presence of $(i\text{-Bu})_3Al$, albeit in average yield of 50% (Table 3, entry 1). Of a special interest was the reaction in the presence of Me_3Al. The intermediate methylnickel species could not undergo β-hydrogen elimination, and thus, the transfer of methyl group onto the double bond followed by the C—C bond cleavage was expected. Although a small amount of the expected product **7** was formed when Me_3Al (25%, entry 2) or MAO (8%, entry 3) were used, the major product was a compound with alkylated ester group **8** (ca. 50%). An increase of the amount of MAO (Entry 4) or the use of its combination with Me_3Al did not have a positive effect on the formation of **7** (entries 4 and 5). An attempt to generate nickel species with noncoordinating tetraphenyl borate also failed (entry 6). Evidently, nucleophilic addition to the carbonyl group was the prevailing process.

Table 3. Reaction of **1a** with Various Organoaluminums

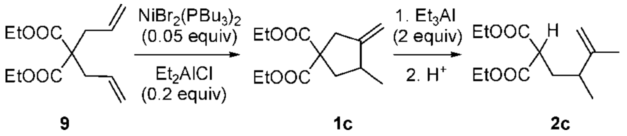


entry	organoaluminum	equiv	product	yield[a] (%)
1	$(i\text{-Bu})_3Al$	2	**2a**	50
2	Me_3Al	2	**7** + **8**	25 + 50
3	MAO	2	**7** + **8**	8 + 50
4	MAO	5	**8**	99
5	MAO + Me_3Al	2 + 2	**8**	99
6	Me_3Al + $NaBPh_4$	2	**7** + **8**	10 + 50

[a] ^1H NMR or GC yields.

Finally, we realized one-pot cycloisomerization[3c,7,9] followed by skeletal rearrangement of diallylmalonate **9** (Scheme 3).

Scheme 3. One-Pot Cyclization−Rearrangement Sequence of **9**



Initial treatment of diallylmalonate **9** with $NiBr_2(PBu_3)_2$/Et_2AlCl (0.05/0.2 equiv) resulted in smooth cycloisomerization to methylenemethylcyclopentane **1c**, which after addition of Et_3Al (2 equiv) underwent the C—C bond cleavage to give butenylmalonate **2c** in 75% isolated yield. The neat result of this two-step reaction is molecular rearrangement with transfer of an alkyl moiety.

In conclusion, we have shown that the C—C bond cleavage of unactivated methylenecycloalkenes with 5- and 6-membered rings is feasible with high selectivity. The reaction seems to be general with respect to nickel based catalytic systems. The reaction could also proceed via methylnickelation of the double bond combining methyl group transfer with the C—C bond cleavage in one step, albeit in low yields. Last but not least, a combination of cycloisomerization/skeletal rearrangement (migration of alkyl moiety) could be carried out in a one-pot reaction resulting in a skeletal rearrangement.

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Supporting Information Available: Experimental procedures and spectral data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) For other Ni-catalyzed cycloisomerizations, see: (a) Bogdanović, B. *Adv. Organomet. Chem.* **1979**, *17*, 105–140. (b) Radetich, B.; RajanBabu, T. V. *J. Am. Chem. Soc.* **1998**, *120*, 8007–8008. (c) Böing, C.; Franciò, G.; Leitner, W. *Chem. Commun.* **2005**, 1456–1458. (d) Böing, C.; Franciò, G.; Leitner, W. *Adv. Synth. Catal.* **2005**, *347*, 1537–1541. (e) Diez-Holz, C. J.; Böing, C.; Franciò, G.; Hölscher, M.; Leitner, W *Eur. J. Org. Chem.* **2007**, 2995–3002. (f) Böing, C.; hahne, J.; Franciò, G.; Leitner, W. *Adv. Synth. Catal.* **2008**, *350*, 1073–1080.