TRANSITION METAL CATALYZED REACTIONS OF DIAZOESTERS

CYCLOPROPANATION OF DIENES AND TRIENES

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Abstract—The regioselectivity of the cyclopropanation of polyenes by cycloaddition of carbenes generated by catalyzed decomposition of diazoesters in the presence of Rh, Pd and Cu catalysts can be controlled to some extent by selecting proper reaction parameters. For a particular diene, the regioselectivity depends both on the catalyst and on the nature of the double-bond (conjugation, substitution).

The cyclopropanation of trienes containing both a conjugated diene system and an isolated double bond is reported as an application of these reactions. The practical interest of the present study is further demonstrated by the synthesis of a pyrethroid precursor by the rhodium(II) carboxylates catalyzed-cyclopropanations of 1,1-dichloro-4-methyl-1,3-pentadiene.

Our previous studies on the control of carbene reactivity by Transition metal complexes revealed some unusual efficiencies and selectivities when applied to cyclopropanation,[1] cyclopropenation,[2] insertion reactions[3] and ring enlargement of aromates.[4]

The influence of the catalyst on the *regioselectivity* of attack of polyfunctionnal substrates has also been investigated in the case of unsaturated alcohols[5] and nitriles.[6] We now stress the role of the catalyst on the regioselectivity of the cycloaddition of carbalkoxycarbenes (carbenoids) to polyenes, a problem already approached by different authors.[7,8]

RESULTS AND DISCUSSION

Dienes. As already observed in the case of monoolefins,[1] the room temperature decomposition of diazoesters by rhodium(II) acetate (RhOAc) promotes the formation of electrophilic species that are very efficient for the cyclopropanation of unsaturated bonds. Indeed, quite generally, rhodium(II) carboxylates are more efficient cyclopropanation catalysts than Pd(II) acetate and than Cu(II) triflate (Cu(Tf)$_2$) (Table 1 and Ref. 1 for monoolefins). The distribution of the positional isomers formed with some typical substances is summarized in Table 2. It is apparent that the regioselectivity of the addition depends much on the nature of the catalyst and of the double bonds. Pd(OAc)$_2$ shows a marked preference for terminal, little hindered double bonds (Table 2: 1, 2, 3) when present. The case of 2,4-hexadiene (Table 2: 4), where the two olefinic centers are cyclopropanated to about the same extent seems exceptional and is to be related to the selective cyclopropanation of the *E*-bond of *E,Z*-1,5-cyclodecadiene with Pd(OAc)$_2$ as catalyst,[9] whereas Rh and Cu display no selectivity in that particular case. Rh(II) acetate works especially well with electron-rich olefins, such as alkyl disubstituted·*Z*-olefins. Moreover, it is an especially smooth catalyst which permits the cyclopropanation of sensitive substrates (Table 2: 5, see also Ref. 2).

A comparison between the regioselectivities of cyclopropanation of 1,3-pentadiene and of isoprene is worthy of comment (Table 2: 1,2). While RhOAc cyclopropanates both substrates at the electron-rich double-bond, the less hindered one (the best coordinating one) is prefered with Pd acetate as catalyst.

The results of the present study are additional examples of the two fundamental mechanisms we have previously proposed for explaining the results of competitive cyclopropanations of mono olefins with transition metal complexes as catalysts:

(i) A "carbenoid" mechanism is exclusively involved in Rh(II) carboxylates catalyzed decomposition of diazoesters, where an electrophilic carbenoid (or "complexed carbene") cyclopropanates a non coordinated olefin.

(ii) a "coordination" type of mechanism which is operative with Pd(OAc)$_2$ and to some extent with Cu(Tf)2, and where coordination of the olefin dictates the selectivities.

As a consequence, the relative selectivities observed with the various catalytic systems described in this study eventually result from a delicate balance between steric, electronic and coordination factors.

Similarly, the stereoselectivity of the reaction which leads to the preferential formation of the *E*-isomer (although with a *E/Z* ratio close to 1 in Rh catalysis) is relevant to specific steric interactions within the coordination sphere of the metal in the transition state and has been adequately discussed in the chemistry of carbenes.[7]

The Rh(II) carboxylate catalyzed regioselective cyclopropanation of halogenated dienes has been successfully applied to the preparation of permethric acid derivatives (**B**) (Table 3), via the cyclopropanation of
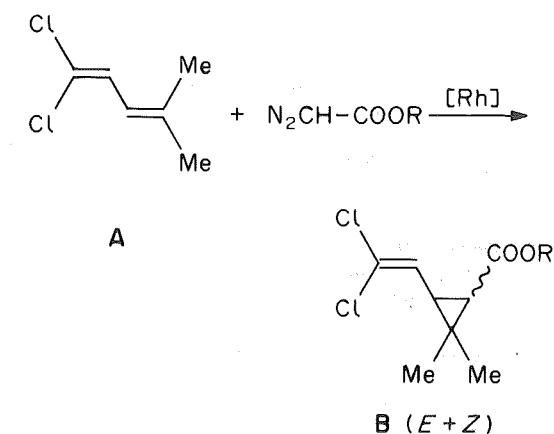
A

B (*E* + *Z*)

Table 1. Yields of the catalyzed cyclopropanation of dienes with ethyldiazoacetate (EtDA)

Olefin	Yiels(%) of Cyclopropanes		
	$Rh_2(O_2C-CH_3)_4$	$Cu(Tf)_2^a$	$Pd(O_2C-CH_3)_2$
1,5-hexadiene	80	60	37
1,4-hexadiene (E+Z)	87	56	53
1,3-pentadiene (E+Z)	96	82	48
Isoprene	93	74	48
E,E-2,4-hexadiene	76	85	30
Z,E-2,4-hexadiene	87	81	60
2,5-diMe-2,4-hexadiene	83	77	35
2,3-diMe-1,3-butadiene	85	76	35
1-chloro-1,3-butadiene	$55(80)^d$	$0^{b,c}$	0^b
1,1-dichloro-4-Me-1,3-pentadiene	54	42	12
hexachlorobutadiene	0	0	0
1,3-cyclohexadiene	90	70	20
Z,Z-1,5-cyclooctadiene	64	25	10
Z,E-1,5-cyclodecadiene	50	23	41

Reaction conditions : 22°C, 20mmoles of olefin, 5mmoles of EtDA,

0,025mmoles of catalyst. Perfusion time 4h.

a : $Cu(Tf)_2$ = Cu(II) trifluoromethanesulfonate = Cu(II) triflate,

b : the substrate polymerized in the presence of the catalyst,

c : 55% yield using Cu (pyridine)$_2$Tf$_2$ as catalyst,

d : 80% yield using n-butyldiazoacetate (BuDA) in place of EtDA

Table 2. Stereo- and regioselectivities of the cyclopropanation of polyenes

Substrate	Catalyst	Δx^a,yield%	Δy^a,yield%	$\Delta x/\Delta y$
1. Isoprene[b]	$Rh_2(OAc)_4$	1(29:28)	3(12:24)	1.6
	$Cu(Tf)_2$	(25:24)	(8:17)	2
	$Pd(OAc)_2$	(6:5)	(15:22)	0.3
2. 1,3-pentadiene (E+Z)	$Rh_2(OAc)_4$	1(E:75)^c	3(-)	> 4
	$Cu(Tf)_2$	(E:65)	(-)	> 4
	$Pd(OAc)_2$	(E:35)	(-)	> 3
3. 1,4-hexadiene (E+Z)	$Rh_2(OAc)_4$	1(25:40)	4(11:11)	2.9
	$Cu(Tf)_2$	(11:26)	(12:7)	1.7
	$Pd(OAc)_2$	(17:28)	(5:3)	5.6
4. Z,E-2,4-hexadiene	$Rh_2(OAc)_4$	2(E≈66)^d	4(E≈21)	3.1
	$Cu(Tf)_2$	idem		
	$Pd(OAc)_2$	(E≈30)	(E≈30)	1
5. Z-1-chloro-1,3-butadiene	$Rh_2(OAc)_4$	1(∿0)	3(18:36)	0.02
	$Cu(Tf)_2^e$	-	-	
	$Pd(OAc)_2^e$	-	-	

Reaction conditions : same as in Table I (see Table I for overall yields).

a : Δx,cyclopropanation of the double bond x (x given), Δy idem for double

bond y (y given). Values in brackets represent the yields of the Z and E

isomers, respectively as determined by ^{1}H NMR and VPC. b : small amounts of

dicyclopropanation were identified in this case (yield ≈5%).c : % of 1-(E)

isomer calculated in the total amounts of cyclopropanes : Rh 78%,Cu 80%,

Pd 73%. d : other isomers also present as minor components. e : see note b

in Table I.

1,1-dichloro-4-methyl-1,3-pentadiene (A). The low reactivity of the halogenated double bond is probably the result of a deactivating effect of the Cl atoms (Table 2:5). For this reaction, the triflate is clearly less efficient than Rh(II) derivatives, whereas Pd acetate and Ru acetate are practically inactive as catalysts. Moreover, the efficiency of the Rh(II) carboxylates strongly depends on the nature of the catalyst counter-ions and on the diazoacetate alkoxy group (Table 3 for some examples).

Trienes: The cyclopropanation of trienes containing a conjugated diene unit and an isolated double bond are applications of an intramolecular competition between both types of unsaturation (Table 4).

In general, the conjugated system is selectively cyclopropanated with the three catalysts, as expected by comparison with an intermolecular competition between 1,3-pentadiene and 1-dodecene (Table 4B). The overall selectivity is actually higher with myrcene and 1,3,7-octatriene than with 2,7-dimethyl-E-1,3,7,-octatriene, the three catalysts (and particularly PdOAc) showing a reduced efficiency with the latter substrate. Moreover, the especially poor reactivity of E-disubstituted or of the triply substituted double bonds is a further indication that steric factors take over electronic effects in such intramolecular competitions. The cyclopropanation of myrcene has been extensively studied by Anteunis *et al.*:[8] the carbenes (carbenoids) were then generated either by thermolysis or by CuSO$_4$ decomposition of the diazoester.

The CuSO$_4$ catalyzed reaction, although considered to be of a purely carbenoid type, displayed a regioselectivity closer to that of Pd acetate than of Rh acetate, an observation that again points out the importance of structural features for imposing the regioselectivity of the reaction.

When the three double bonds are conjugated as in the case of 1,3,5-cycloheptatriene, the regioselectivity of the cycloaddition also shows a marked preference for the 1-double bond with all three catalysts (overall yield 90% with Rh, a few percentage of the 3-cycloaddition product being however formed, Table 5).

Generally, *monocyclopropanation* products are obtained under our conditions but *di-* and *tri-cyclopropanated* compounds are progressively formed by increasing the diazoester to olefin ratio (e.g.: 1,3,5-cycloheptatriene, Table 5).

CONCLUSION

The present work further illustrates the interest of applying transition metal catalysis for controlling carbene reactions. Rh(II) carboxylates, which are air-stable and easily accessible compounds, proved to be exceptionaly efficient catalysts for promoting the cyclopropanation of mono- and polyolefins. Moreover, unusual selectivities may be achieved by a proper tailoring of the catalyst.

Table 3. Rhodium(II) carboxylate catalyzed cyclopropanation of 1,1-dichloro-4-methyl-1,3-pentadiene (A)

Rh(II) Carboxylate	Ethyl diazoacetate Yield(%) in cyclopropane B (Z/E ratio)	t-Bu diazoacetate Yield(%) in cyclopropane B (Z/E ratio)
Acetate	54 (1)	56 (1.29)
trifluoroacetate	29 (0.93)	45 (0.8)
pentafluorobenzoate	64 (0.94)	56 (0.87)
pivalate	56 (1.15)	32 (1.29)

Reaction conditions : same as in Table I.

Table 4. Intramolecular competitions between conjugated and non conjugated double bonds

A. Myrcene (7-methyl-3-methylene-1,6-octadiene)

double bond cyclopropanated	Yields,% with catalysts		
	$Rh_2(OAc)_4$	$Cu(Tf)_2$	$Pd(OAc)_2$
	87[a]	72	33
1-	39(16:23)[b]	31(13:18)	25(11:14)
3-	48(23:25)	41(18:23)	8 (3:5)
6-	0	0	0

B. 1,3,7-octatriene[c]

	97[a]	64	27
1-	87	56	20
3-	10	8	7
7-	traces	traces	traces

C. 2,7-dimethyl-E-1,3,7-octatriene

	72[a]	38	17
1-	38(18:20)	20(10:10)	8(4:4)
3-	0	0	0
7-	28(14:14)	13(5:8)	5(2:3)

D. 1,3-pentadiene + 1-dodecene (intermolecular competition)[d]

	75	74	28
	25	13	17

Reaction conditions : Same as in Table I, a : overall yield, b : respective yields of (Z and E) isomers, total yields reported when identification of isomers was not possible, c : mixture of 55% E and 45% Z, d : 20 mmoles of each olefin.

Table 5. Cyclopropanation of 1,3,5-cycloheptatriene (CHT)

Catalyst	Cyclopropanated double bond, yield %		
	monoaddition	diaddition	triaddition
	1-	1,3-	1,3,5-
$Rh_2(OAc)_4$	90[a](41)[b]	8(20)	0 (5)
$Cu(Tf)_2$	78 (40)	5(20)	0 (2)
$Pd(OAc)_2$	22	0	0

Reaction conditions : same as in Table I. a : mixture of endo+exo isomers, b : values in brackets refer to the yields obtained when using equimolecular amounts of CHT and EtDA .

EXPERIMENTAL

Analytical techniques. Analysis of the cyclopropane carboxylates were run on Varian 1700 and 2800 gas liquid chromatographs (Catharometers-W filaments) using analytical (4 ft, 1/4 in.) or preparative (10 ft, 3/8 in.) columns (Se30 or FFAP, 15% on chromosorb W, acid washed)Carrier gas: He, 40 ml/min. Temp programme from 70 to 230° (15°/min).

The results of GLC were also checked by HPLC in some cases on Waters PREP LC system 500 and Tracor 995 chromatographs using silicagel columns (respectively equiped with a PREPAK-500 silica and a 250 × 4.6 mm silicagel 10 μ columns). The NMR spectra were recorded on a Varian HA 100 spectrograph.

The olefins were carefully distilled under N_2. The reactions were carried out under N_2 at room temp. Most olefins are commercial products (Aldrich). 1,3,7-octatriene was kindly supplied by Professor Keim (RWTH, Aachen) as a mixture of cis (45%) and trans (55%) isomers. 1,1-dichloro-4-methyl-1,3-pentadiene was kindly supplied by ICI (Mond Division). 2,7-dimethyl-E-1,3,7-octatriene was prepared from isoprene according to Anteunis' procedure.[16]

Ethyl diazoacetate is a Fluka product whereas t-butyl diazoacetate was prepared according to the reported procedure.[10]

Cyclopropanation of olefins (standard procedure). The diazoester (5 mM) was added continuously with an automatic syringe

(SAGE, model 352) to the olefin (20 mM) containing the catalyst (0.025 mM) within 4 hr while stirring magnetically. After having checked the absence of any absorption at $2175 cm^{-1}$ (diazogroup), the product was distilled and analysed by GLC and NMR. Cyclopropanes were identified with authentic samples when previously described. Otherwise, the LIS technique was used for identifying the various isomers, when possible. The paramagnetic complex used was Eu (DPM)₃. The results of the analysis are summarized hereafter for some samples.

Cyclopropanation of 1,4-hexadiene (E + Z). The cyclopropanation products (prepared from ethyl diazoacetate) were isolated by distillation −BP 82°/15 torr. Found: C, 71.6, H, 9.4. Calc for $C_{10}H_{16}O_2$: C, 71.4, H, 9.5%· mass spectrum: M/e = 168, Calc. 168. The major isomer was purified by preparative GLC IR (neat, cm^{-1}): 1725 (ester), 1640(C=C), 967 and 730 (trans and cis sp^2CH). No absorption was detected at $990–910 cm^{-1}$, no monosubstituted olefinic group is therefore present. ¹H NMR ($CDCl_3$, TMS), δ (ppm): 5.43 (m, 1H, −CH=CH−), 4.78 (m, 1 H, −CH=CH), 4.12 (q, 2H, −O-CH₂-CH₃), 2.59−1 (broad m, 12H, remaining H). The minor isomers showed the typical IR absorption of the vinyl group at $990–910 cm^{-1}$.

Cyclopropanation of 1,3-pentadiene (E + Z).[1,11]
Cyclopropanation of isoprene.[1,12]
Cyclopropanation of Z-1-chloro-1,3-butadiene.[12]
Cyclopropanation of 1,3,7-cycloheptatriene.[8,13]
Cyclopropanation of 1,1-dichloro-4-methyl-1,3-pentadiene.[14]
Cyclopropanation of E,Z-2,4-hexadiene.[15]

In the Rh acetate catalyzed reaction, the mixture of isomers from methyl diazoacetate shows a strong IR absorption (neat) at $965 cm^{-1}$ (trans olefin), a very weak at $710 cm^{-1}$ (cis olefin). This latter absorption is much stronger in the Pd acetate catalyzed reaction.

Cyclopropanation of E,Z-1,5-cyclodecadiene. Mixture of isomers, BP 90–95°/0.01 mm. Found; C, 74.5, H, 9.7%. Calc. for $C_{13}H_{20}O_2$: C 75.0, H 9.7% M/e = 208, Calc. 208. IR (neat, cm^{-1}): 1730 and 1180 (ester), 980 (trans olefin), 705 (cis olefin). The relative ratio of the 2 latter absorptions depends much on the catalyst, with Rh acetate and Cu triflate, the cis to trans relative intensity is slightly lower than in the starting material, whereas the trans absorption is very weak relatively to the cis one in the Pd catalyzed reaction. ¹H NMR (CCl_4, TMS); δ (ppm): 5.2 (m, 2H, CH=CH), 3.35 (S, 3H, −OCH₃), 2.3−1.0 (m, 15H, remaining H).

Cyclopropanation of myrcene. The analysis of the cyclopropanes was performed by comparison with authentic sample provided by Professor M. Anteunis.[8]

Cyclopropanation of 1,3,7-octatriene (E + Z). Isomeric mixture of cyclopropanes (from ethyldiazoacetate, Rh acetate): b.p. 78°/1 mm. Found: C, 74.7, H, 9.0. Calc. for $C_{12}H_{18}O_2$: C, 74.2, H, 9.3%. M/e = 194. The separation of the mixture of isomers could not be completely realized by GLC or HPLC, the analysis were consequently performed on enriched fractions. Main fraction: UV and IR show the lack of conjugated double bond. ¹H NMR ($CDCl_3$, TMS) δ (ppm): 6.10−5.20 (m, 3H, −CH=CH₂), 5.10−4.68 (m, 2H, −CH=CH−), 4.13 (q, 2H, O-CH₂-CH₃), 1.23 (t, 3H, −O-CH₂-CH₃) 2.4−0.8 (m, 4H, cyclopropane). The fraction presenting the above spectroscopic features contains 4 geometric isomers and the results fit well with an attack of the conjugated double bond. Another isomer, resulting from the cyclopropanation of the 3-double bond displayed the following ¹H NMR: δ(ppm): 6.35−5.32(m, 2H, two CH=CH₂), 5.30–4.70 (m, 4H, two−CH=CH₂), 4.11 (q, 2H, O-CH₂-CH₃), 2.06 (d, of t, 2H, allylic H), 1.84 (d of t, 2H, 5-CH₂), 1.25 (t, 3H, −O-CH₂-CH₃), 2.10−0.8 (m, 3H, cyclopropane).

Cyclopropanation of 2,7-dimethyl-E-1,3,7-octatriene, mixture of isomers from methyl diazoacetate (Rh acetate) b.p. 104°/1 mm. Found C, 75.4, H, 9.8, Calc. C, 75.7, H, 9.9%. The four main isomers C,D,E,F were isolated by preparative GLC. IR (neat) C and D: 1735 (ester), 1648 and $885 cm^{-1}$ (−CH=CH₂) no conjugated double bond. E and F: 1735 and $1610 cm^{-1}$. C and D, E and F, respectively show very similar ¹H NMR spectra (CDCl₃ and C₆D₆, TMS), δ (ppm) for C: 5.54 (broad S, 2H, −CH=CH−), 4.66 (S, 2H, =CH₂), 3.64 (S, 3H, O-CH₃), 2.08 (m, 4H, allylic CH₂), 1.68 (broad S, 3H, C-CH₃), 1.24 (S, 3H, 2-CH₃), 2.4–0.8 (m, 3H,

cyclopropane). The NMR of D is very similar to that of C, the Me group on the cyclopropyl ring is 0.04 ppm downfield and the ester Me appears at 3.65 ppm.

For E: δ (ppm): 6.3−5 (m, 2H, −CH=CH−), 4.82 (broad S, 2H, −C=CH₂), 3.62 (S, 3H, −OCH₃), 1.80 (s, 3H, 2-CH₃), 1.14, 1.14 (S, 3H, 7-CH₃), 2.4–0.8 (m, 5H, three cyclopropyl H + 2C=C-CH₂-CH₂); 2.08 (m, 2H, allylic CH₂). The spectrum of F is very similar but the Me on the cyclopropyl ring absorbs 0.04 ppm downfield (1.18 ppm) and the Me group of the ester is at 3.63 ppm.

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[9] It is noteworthy that E,Z-1,5-cyclodecadiene is selectively cyclopropanated on the E-double bond with Pd acetate whereas Rh acetate and Cu triflate display no selectivity: total yield of cyclopropanes, in brackets, yields of cyclopropanation of the Z-and E-double bonds, respectively: Rh: 50(25 + 25); Cu: 22(11 + 11), Pd: 41(1 + 40). The selectivity displayed in the Pd catalyzed reaction is similar to that of vinyl carbene with the same substrate.
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