Brief Communications

New catalytic system $Cu(OAc)_2$—2,4-lutidine—$ZnCl_2$ for olefin cyclopropanation with methyl diazoacetate

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A new efficient catalytic system consisting of $Cu(OAc)_2$, 2,4-lutidine, and $ZnCl_2$ was found for the cyclopropanation of unsaturated compounds with methyl diazoacetate. In the case of conjugated dienes, the process occurs regioselectively at the most alkylated C=C bond.

Key words: olefins, diazo esters, dienes, cyclopropane carboxylates, catalytic systems, cyclopropanation.

Olefin cyclopropanation with alkyl diazoacetates is widely used in organic synthesis as a convenient method for the preparation of cyclopropanecarboxylic acid derivatives,[1—6] many of which are practically important compounds (cilastatin, pyrethroids, dictyopterenes, *etc.*). It is noteworthy that the majority of the known catalysts for cyclopropanation[3—8] based on Cu, Co, Ru, Pd, and Rh provide no high regioselectivity in the case of dienes and, as a rule, require the application of a 5—10-fold excess of an unsaturated compound for the suppression of alkoxycarbonylcarbene dimerization. The repeated use of these catalysts is usually impossible and, hence, search for new highly efficient catalysts for the cyclopropanation of unsaturated compounds remains to be an urgent problem.

In the present work, we showed for the first time that the $Cu(OAc)_2$—2,4-lutidine—$ZnCl_2$ three-component system with a molar ratio of 6 : 5 : 1 is an efficient catalyst for the cyclopropanation of olefins and conjugated dienes (**1a—h**, Scheme 1, Table 1) with methyl diazoacetate (MDA). The reaction is carried out at 40 °C by the addition of a solution of MDA in CH_2Cl_2 to the unsaturated compound and the catalyst, with the molar ratio MDA : olefin : catalyst (based on $Cu(OAc)_2$) being 1 : 1 : 0.06. The study of the effect of the nature of pyridinium compounds (Py, 2,4-lutidine, 2,6-lutidine, 2-picoline, 2-cyanopyridine, 2,6-diaminopyridine, 3- and 4-aminopyri-dines, 3,5-dibromo-2-aminopyridine), Lewis acids ($AlCl_3$, KBF_4, $ZnCl_2$), and various copper, palladium,

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Scheme 1

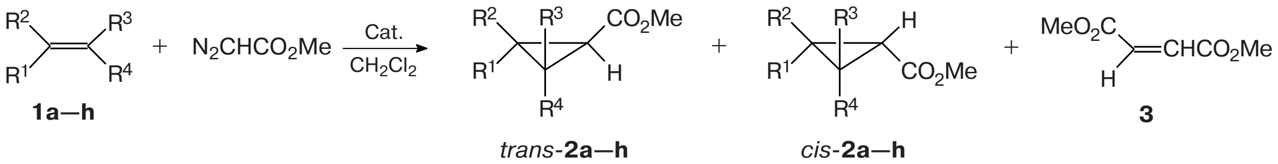

Table 1. Yields of the products and the ratio of the *trans-* and *cis-*isomers of compound **2**

Compounds **2a—h**	R^1	R^2	R^3	R^4	Yield (%)		Ratio of isomers *trans/cis*
					2	**3**	
a	H	H	H	Bu	28	25	1.9
b	H	H	H	Ph	72	26	2.0
c	H	H	H	$CH=CH_2$	49	9	1.3
d	H	H	Me	$CH=CH_2$	52	9	1.3
e	H	Me	H	$CH=CH_2$	50	8	1.3
f	Me	H	H	$CH=CH_2$	50	—	1.3
g	Me	Me	H	$CH=CMe_2$	65	20	1.9
g*	Me	Me	H	$CH=CMe_2$	81	9	1.9
g**	Me	Me	H	$CH=CMe_2$	72	11	2.0
h	Me	Me	H	$CH=CCl_2$	48	—	1.5

*Sixth cycle of the catalyst use.
**Seventh cycle.

and rhodium compounds ($Cu(OAc)_2$, $[CuOTf] \cdot C_6H_6$, $Cu(OTf)_2$, $Pd(OAc)_2$, $Rh_2(CF_3CO_2)_4$, $Rh_2(OAc)_4$) on the reaction products showed that a combination of the components $Cu(OAc)_2$—2,4-lutidine—$ZnCl_2$ provided the best results. In the absence of at least one of the components of this system, MDA does not interact with unsaturated compounds **1a—h**. When this system is used, the cyclopropanation of 1,3-dienes **1c—h** with MDA occurs regioselectively at the most alkylated C=C bond to form mixtures of diastereomeric methyl vinylcyclopropanecarboxylates **2c—h** with prevailing of *trans*-isomers in 49—81% yields (see Scheme 1). It should be mentioned that for diene **1g** no double cyclopropanation products were observed even when using a twofold molar excess of MDA. The double bond of chrysanthemate **2g** is not subjected to cyclopropanation under these conditions.

It was found for the cyclopropanation of 2,5-dimethylhexa-2,4-diene (**1g**) as an example that the $Cu(OAc)_2$—2,4-lutidine—$ZnCl_2$ catalytic system did not lose its activity even being used eight times. Moreover, it turned out that recycling of the catalyst increased the yield of methyl chrysanthemate (**2g**) up to 81%. The obtained catalytic system is an oily dark brown substance soluble in methylene chloride and insoluble in petroleum ether, which allows easy isolation of the catalyst from the reaction mixture for repeated use.

Thus, we proposed a new rather simple and efficient catalyst for the synthesis of cyclopropanecarboxylates from methyl diazoacetate and unsaturated compounds.

Experimental

The structures of compounds **2a—h** were confirmed by the ^1H and ^{13}C NMR spectral data. ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer (300.13 and 75.47 mHz, respectively) in $CDCl_3$ using Me_4Si as an internal standard. GLC analysis was carried out on a Chrom-5 chromatograph with a flame-ionization detector (column 1200×3 mm with 5% SE-30 on Chromatone N-AW-HMDS) using helium as a carrier gas. 2,5-Dimethylhexa-2,4-diene (**1g**), 2,4-lutidine, $[CuOTf]_2 \cdot C_6H_6$, and $Cu(OTf)_2$ (Aldrich) and $Cu(OAc)_2$ (ZAO Vekton, Russia) were used. Unsaturated compounds **1a—h** were distilled under an argon flow and stored over hydroquinone. The solvents used (CH_2Cl_2 and petroleum ether) were purified using standard procedures.[9]

Catalytic cyclopropanation of olefins 1a—h with methyl diazoacetate (general procedure). Unsaturated compound **1a—h** (18 mmol) was added to a stirred solution containing anhydrous $ZnCl_2$ (4.1 mg, 0.03 mmol), 2,4-lutidine (16.0 mg, 0.15 mmol), and $Cu(OAc)_2$ (32.7 mg, 0.18 mmol) in CH_2Cl_2 (5 mL). Then at 40 °C (in the case of diene **1c**, the reaction was carried out at room temperature) methyl diazoacetate (1.80 g, 18 mmol) in CH_2Cl_2 (7 mL) was slowly added until gas evolution has ceased. The solvent was removed *in vacuo*, petroleum ether (b.p. 40—70 °C) was added to the residue, and the catalytic system was separated as a dark brown oil (the catalytic system obtained for the cyclopropanation of diene **1g** was used seven times more in experiments on cyclopropanation). The petroleum ether solution was concentrated *in vacuo*, and the residue was analyzed by GLC and ^1H NMR spectroscopy. The yields of compounds **2a—h** were determined by GLC using tetradecane as an internal standard calibrated by an authentic sample of methyl chrysanthemate **2g**. The isomers were characterized in a mixture by NMR spectroscopy, and their ratio was determined on the basis of the integral intensity of signals of the methinic protons at the C(1) atom for compounds **2a—c,g,h** and the vinylic protons for compounds **2d—f** in the ^1H NMR spectra. The physicochemical and spectral characteristics of compounds **2a—h** corresponded to the published data.[4,10,11]

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