## Stereospecific Alkylation of Cyclopropyl Bromides by Means of Dibutylcopperlithium and Alkyl Halides

Sir:

Dehalogenative coupling reactions of organic halides have been effected by various reagents recently developed,[1] among which dialkylcopperlithium seems the most accessible one.[2] However, a side reaction sometimes encountered is the reduction of the substrates and is often ascribed to intermediary copper hydride species.[2] Notably, the newly disclosed geminal dialkylation[3] suggests an alternative reaction path proceeding through halogen–copper exchange.[4] This process involving a cyclopropylcopper intermediate is now proved to be general and synthetically useful especially for the stereocontrolled synthesis of substituted cyclopropanes by use of dibutylcopperlithium in tetrahydrofuran (THF).

When bromocyclopropanes **1** were treated with 4 molar equiv of dibutylcopperlithium[5] in THF at −48 to 0 °C and
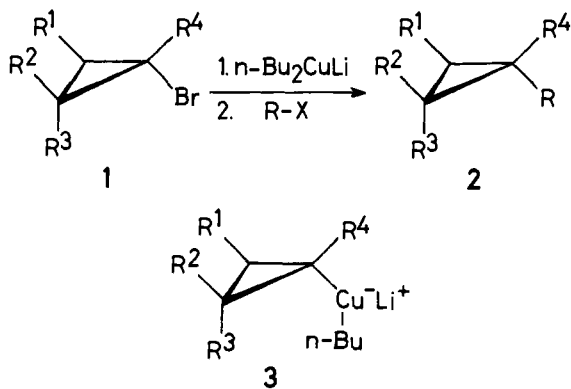
successively with excess alkyl halides at the same temperature, alkylated cyclopropanes **2** were formed. The results are collected in Table I. Noteworthy is the fact that no trace of butylated product was obtained. Besides the sequence of the reaction is found stereospecific as seen in the entries 1 and 4. The stereochemical outcome can be understood by the intermediacy of a mixed cuprate **3** whose formation and the reaction with alkyl halides proceed with retention of configuration. This scheme may be advocated by the following experiments.

Reduction of *trans*-1-bromo-2-phenylcyclopropane with dibutylcopperlithium and the reaction of the intermediary organocopper species with prenyl bromide resulted mainly in S_N2' coupling (entry 3). Decomposition of the intermediate

occurred at 60 °C to give phenylcyclopropane (56%), while oxidation with air yielded *trans*-1-butyl-2-phenylcyclopropane (60%). Treatment with benzoyl chloride afforded *trans*-1-benzoyl-2-phenylcyclopropane (95% yield) and the reaction with methyl propiolate gave methyl *trans*-β-(2-phenylcyclopropyl)acrylate (46%), whereas attempted reaction with benzaldehyde gave only a 26% yield of the adduct and the one with acetone failed to succeed.

The characteristics of the present procedure are summarized as follows.

(1) A facile approach to vicinal-disubstituted cyclopropanes is thus attained by this method coupled with stereoselective reduction of *gem*-dihalocyclopropanes[6] as exemplified in the synthesis of methyl cascarillate (entry 7).[7]

(2) Even tertiary halides are reduced by dibutylcopperlithium to give geminal-dialkylated cyclopropanes as illustrated in entries 5 and 10. The previous monoalkylation of *gem*-dihalocyclopropanes,[8] followed by the present reaction, provides us with a new, general entry to geminal-substituted cyclopropanes. It should be noted that the two different alkyl groups can be introduced as electrophiles in contrast to the previous method.[3]

(3) The present reaction is widely applicable to various bromocyclopropanes compared with the reaction via cyclopropyllithiums. Bromine–lithium exchange of *trans*-1-bromo-2-phenylcyclopropane with *tert*-butyllithium,[9] followed by treatment with excess allyl bromide, gave only a 23% yield of 1-allyl-2-phenylcyclopropane, and 7-*exo*-bromo-1-methylnorcarane failed to be transformed into the alkylated product in entry 12.

(4) The highly coordinating THF is indispensable for the present reaction, as in ether the monobromocyclopropanes are not reduced.

(5) Although a large excess of dibutylcopperlithium (4 to 5 equiv) is required for the complete reduction of bromocyclopropanes and the excess cuprate also reacts with alkyl halides, the by-products are readily removed by simple distillation or chromatography.

The following procedure for entry 1 is typical. To dibutylcopperlithium,[5] prepared from cuprous iodide (1.13 g, 6.0 mmol) and butyllithium (12 mmol) in THF (20 mL) at −48 °C, was added *trans*-1-bromo-2-phenylcyclopropane (289 mg, 1.5 mmol) at the same temperature. After 30 min allyl bromide (1.5 mL) was added and the reaction mixture was stirred for an additional 30 min. Quenching with methanol and workup followed by preparative TLC of the crude product afforded *trans*-1-allyl-2-phenylcyclopropane (224 mg, 97% yield).[10]

Table I. Alkylation of Monobromocyclopropanes

Entry	R¹	R²	R³	R⁴	R–X	Temp, °C	Yield,[a] %
1	H	Ph	H	H	$CH_2{=}CHCH_2Br$	−48	97
2	H	Ph	H	H	MeI	−48	91
3	H	Ph	H	H	$Me_2C{=}CHCH_2Br$	−48	97[b]
4	H	H	Ph	H	$CH_2{=}CHCH_2Br$	−48	91
5	H	Ph	H	Me	$CH_2{=}CHCH_2Br$	−48–0	68
6	H	$n\text{-}C_6H_{13}$	H	H	$CH_2{=}CHCH_2Br$	−48	96[c]
7	H	$n\text{-}C_6H_{13}$	H	H	$MeOCOCH_2Br$	−48–0	75
8	H	$PhCH_2OCH_2$	H	H	$CH_2{=}CHCH_2Br$	−48	65
9	−(CH₂)₄−		H	H	$CH_2{=}CHCH_2Br$	−48	57
10	−(CH₂)₄−		H	$CH_2{=}CHCH_2$	MeI	−48–0	96
11	−(CH₂)₄−		Me	H	$CH_2{=}CHCH_2Br$	−48–0	65
12	−(CH₂)₄−		Me	H	$n\text{-}C_8H_{17}Br$	−48–0	50[d,e]

[a] Isolated yield. [b] The product was a 7:3 mixture of 1-(1,1-dimethyl-2-propenyl)-2-phenylcyclopropane and 1-(3-methyl-2-butenyl)-2-phenylcyclopropane. [c] A stereoisomeric mixture (83:17) of *trans*- and *cis*-1-bromo-2-hexylcyclopropane (see ref 6i) was subjected to reaction, and the product was proved to be an 84:16 mixture of trans- and cis-allylatedcyclopropane. Oxidation of the product ($KMnO_4$–$NaIO_4$, *t*-BuOH) followed by esterification (CH_2N_2) afforded methyl *trans*- and *cis*-cascarillate (85:15, 67% yield). [d] Estimated by GLC. [e] Stereochemistry of the product was unambiguously determined by the synthesis of authentic specimen (cyclization of (E)-1-diazo-6-methyl-6-pentadecen-2-one and successive reduction).

GLC assay of the crude product revealed no contamination of the cis isomer.

Reduction of bromobenzene with dibutylcopperlithium in THF and subsequent treatment with excess allyl bromide afforded allylbenzene (64% isolated yield). This and previous findings by Whitesides et al.[4] suggest the present method is applicable not only to bromocyclopropanes but to bromoarenes. A study to find the scope and limitations of this method is now in progress.

References and Notes

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(10) The stereochemical assignment is based on the general observation that ¹H NMR absorption of the substituent cis to the phenyl group appears at higher field than that of the trans isomer. See ref 6i and 8.

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Hydrogen Transfer Photocatalyzed by Metalloporphyrins in Visible Light. Photoinduced Redox Cycling of the Catalyst

Sir:

Porphyrins have been shown to be active as chemical catalysts and electrocatalysts for hydrogen-transfer reactions.[1] Here we report the photochemical hydrogen transfer from a donor (tertiary amine) to an acceptor (nitrobenzene) at room temperature, photocatalyzed by metalloporphyrins excited with visible light. The photocatalyst cycles in these reactions between its oxidized and reduced forms, porphyrin, chlorin, and isobacteriochlorin. Similar photochemical cycles have been attempted in the past. Phlorin formed on photoreduction of water-soluble free-base porphyrins by EDTA was oxidized back to parent porphyrin in the dark by oxygen.[2] Zinc tetraphenylporphyrin (ZnTPP) was photoreduced by benzoin, using UV light absorbed by benzoin, to dihydro- and tetrahydroporphyrins which were reoxidized by oxygen in the dark.[3] Zinc tetraphenylchlorin (ZnTPC) was photooxidized to ZnTPP by quinones with visible light.[4] Pyrochlorophyll was found to sensitize the photoreduction of nitro compounds using hydrazobenzene in ethanol–pyridine solutions.[5] Tin(IV) oc-

Table I. Conversion[a] to Products as Function of Irradiation[b] Time for a Solution of 5×10^{-4} M $Sn^{IV}TPPCl_2$, 1 M NMP, and 1 M $PhNO_2$ in Benzene at Room Temperature

Irradiation time, h	Aniline	Azoxybenzene	Azobenzene	N-Methylpyrrole
10	0.20	0.28	0.10	0.60
20	0.33	0.65	0.12	1.10
30	0.46	0.77	0.14	1.56
50	0.63	1.10	0.15	2.32
80	0.96	1.60	0.19	2.80

[a] Percent of initial nitrobenzene. [b] $\lambda_{excit} > 500$ nm.
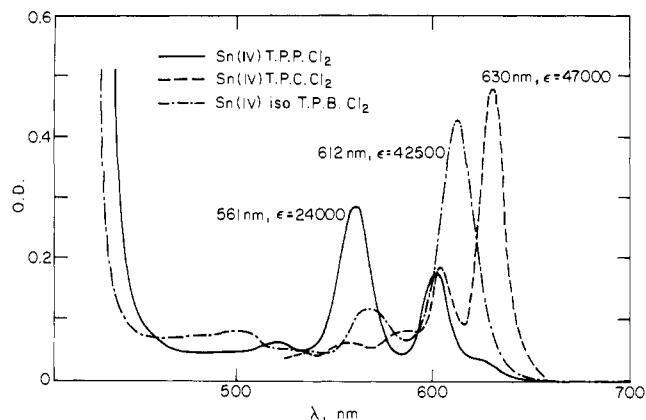
Figure 1. Absorption spectra of $Sn^{IV}TPPCl_2$, $Sn^{IV}TPCCl_2$, and $Sn^{IV}T$-$PisoBCl_2$ in benzene solution.

taethylporphyrin dihydroxide and germanium(IV) octaethylporphyrin dihydroxide were photoreduced to a mixture of the corresponding chlorins and isobacteriochlorins with EDTA in acetic acid.[6] Both octaethylporphyrin and tetraphenylporphyrin tin(IV) dichloride complexes were photoreduced to isobacteriochlorins through the chlorins by $SnCl_2 \cdot 2H_2O$ in pyridine.[7]

When degassed solutions of 10^{-4}–10^{-3} M of tin(IV) tetraphenylporphyrin dichloride ($Sn^{IV}TPPCl_2$) or germanium(IV) tetraphenylporphyrin dichloride ($Ge^{IV}TPPCl_2$) in benzene containing 1 M N-methylpyrrolidine (NMP) and 1 M nitrobenzene ($PhNO_2$) are irradiated with visible light ($\lambda > 500$ nm), aniline, azoxybenzene, and azobenzene are formed as the reduction products of $PhNO_2$, and N-methylpyrrole as the dehydrogenation product of NMP.[8] No reaction occurs in the dark or when solutions are irradiated in the absence of the porphyrin complex. Results for a typical photocatalytic run are presented in Table I.

The photoreduction and photooxidation steps can be studied separately. Irradiation of benzene solutions of $Sn^{IV}TPPCl_2$ or $Ge^{IV}TPPCl_2$ in the presence of an aliphatic tertiary amine results in the complete photoreduction of the porphyrin complexes to the corresponding metallo isobacteriochlorins via the chlorin complexes. The optical absorption spectra for $Sn^{IV}TPPCl_2$ and its reduced complexes are given in Figure 1 and are identical with those reported in the literature.[9] The rate of the photoreduction depends on the electron donor properties of the amines as was found before in the photoreduction of free base porphyrins.[10]

Irradiation of benzene solutions of tin(IV) tetraphenylisobacteriochlorin ($Sn^{IV}TPiso$-BCl_2) or $Ge^{IV}TPisoBCl_2$ in the presence of $PhNO_2$ results in their photooxidation to the corresponding porphyrins, via the chlorin complexes. The photooxidation reaction appears to be rate determining and is responsible for the low rate of the photocatalysis reaction as given in Table I. Acetic anhydride (Ac_2O) was found to accelerate the photooxidation reaction and therefore was added