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Dialkylation of *gem*-Dibromocyclopropanes with Trialkylmanganate and Manganese(II) Chloride-Catalyzed Reaction with Alkylmagnesium Bromide

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Abstract: Treatment of gem-dibromocyclopropanes with trialkylmanganate, derived from manganese(II) chloride and three equivalents of Grignard reagent or alkyllithium, followed by an addition of electrophiles provided dialkylated cyclopropanes in good yields. It was found the reaction with alkylmagnesium halide proceeded in the presence of a catalytic amount of manganese(II) chloride. Copyright © 1996 Elsevier Science Ltd

Cyclopropane derivatives are versatile synthetic intermediates. Double alkylation of gemdihalocyclopropanes, which can be easily prepared by the addition of dihalocarbene to olefins, provides us with an effective route to a variety of functionalized cyclopropane derivatives. The transformation of gemdihalocyclopropanes into 1-alkyl-1-butylcyclopropanes has been reported to proceed by successive treatment with dibutylcuprate¹ or tributylzincate^{2,3} and several electrophiles. In this paper we describe that the reaction of gem-dibromocyclopropanes with trialkylmanganate⁴ followed by treatment with electrophiles provides dialkylated cyclopropanes as in the case of the reaction with cuprates or zincates and also that the reaction of gem-dibromocyclopropanes with alkylmagnesium halides takes place in the presence of a catalytic amount of manganese(II) chloride.

Manganese(II) chloride (151 mg, 1,2 mmol) was sonicated in tetrahydrofuran (THF, 10 ml) under argon atmosphere for 15 min. Butylmagnesium bromide (1.0 *M* ether solution, 3.6 ml, 3.6 mmol) was added to the suspension of MnCl₂ in THF at 0 °C. The mixture turned into a clear brown solution and then, after being stirred for 20 min at 0 °C, a part of the manganese(II) chloride precipitated as a white solid. A solution of dibromocyclopropane **1a** (0.28 g, 1.0 mmol) in THF (2 ml) was added at 0 °C and the whole was stirred at 0 °C for 1 h and then at 25 °C for 20 min. The mixture was poured into 1*M* HCl and extracted with hexane (3 x 20 ml). Purification of the products by silica-gel column chromatography gave a mixture of **2a** and **3a** (162 mg) in 89% combined yield (**2a/3a** = 71/29).



Various *gem*-dibromocyclopropanes were allowed to react first with trialkylmanganate, triallylmanganate or tris(phenyldimethylsilyl)manganate⁵ and then with a variety of electrophiles. The results are summarized in Table 1. Among the solvent systems examined (THF, ether, DME), THF gave the best results. Several

	R Br	1) R ¹ ₃ MnMtl	E'	R	R ¹
	Br -	2) Electrophile	R^1 +	∇	Έ'
Entry	Substrate 1	R ¹ 3MnMtl	Electrophile	Yield	Isomeric Ratio
				(%)	of 2/3
1		Me3MnLi	H ₂ O	65	82/18
2		n-Bu3MnLi	EtOHb	53	68/32
3		n-Bu3MnMgBr	H ₂ O	89	71/29
4		n-Bu3MnMgBr	CH ₂ =CHCH ₂ Br	77	89/11
5	<i>n</i> -C ₆ H ₁₃ Br	n-Bu3MnMgBr	Mel	65	94/6
6	\succ	n-Bu3MnMgBr	PhCOCI	72	83/17
7	Br	n-Bu3MnMgBr	I2	54 ^c	72/28
8	1a	n-Bu3MnMgBr	CH ₂ =CHBr ^d	58	99/1
9		n-Hex3MnMgBr	H ₂ O	61	86/14
10		n-Hex3MnMgBr	CH ₂ =CHCH ₂ Br	69	88/12
11		(PhMe2Si)3MnLi	H ₂ O	84	58/42
	Br				
12	~ 1	n-Bu3MnLi	H_2O	56	87/13
13	Br	n-Bu3MnMgBr	H ₂ O	82	97/3
14		n-Bu3MnMgBr	CH ₂ =CHCH ₂ Br	88	97/3
	1b				
15	Br	n-Bu3MnMgBr	H ₂ O	64	87/13
16		n-Bu3MnMgBr	PhCOCI	75	84/16
17	1c Br	(CH ₂ =CHCH ₂) ₃ MnMgBr	H ₂ O	64	83/17
18	Ph Br	n-BuoMnMaBr ^e	HaO	78	87/13
10		n DuaMnMaDre		70 50	07/8
19	1d	n-bu3ivilivigbi-	сп2=спсп2ы	30	9210
20	PhCH ₂ OCH ₂ B	r n-BuaMnMøBr	HaQ	75	88/12
20	\succ	n-BuoMnMgBr	CHa-CHCHaBr	66	88/12
<i>1 -</i> 2	le b		enz-enenzbi	w.	00/12
	Me Br				
22	Me	(PhMe ₂ Si) ₃ MnLi	H ₂ O	62	
	Me 1f				

Table 1. Stereoselective Dialkylation of gem-Dibromocyclopropanes^a

a) The reactions were performed at 0 °C unless otherwise stated. b) Quenching the reaction with EtOH or H_2O gave the same results (yield and isomeric ratio of 2/3). c) See Ref 6. d) Pd(PPh₃)₄ (10 mol%) was added. e) The reaction was performed at -48 °C.

comments are worth noting. (1) In contrast to the reaction with cuprate or zincate which has been performed at -48 °C or -85 °C, the reaction with manganate could be performed conveniently at 0 °C. The reaction of 1a with n-Bu₂MnLi at -78° C for 30 min provided 1-bromo-2-hexylcyclopropane⁷ (cis/trans = 1/2) in 65% yield in addition to an isomeric mixture of 1-butyl-2-hexylcvclopropane (2a/3a = 76/24, 30% vield). Moreover, treatment of 1a with *n*-Bu₃MnMgBr at -78 °C for 30 min resulted in almost complete recovery of 1a. (2) Tributylmanganesemagnesium bromide, derived from MnCl₂ and three equivalents of butylmagnesium bromide, afforded better vields of butylated cyclopropanes 2 and 3 than tributylmanganeselithium generated from butvllithium (Entry 2 vs 3, 12 vs 13). (3) Triphenylmanganate Ph3MnMgBr or Ph3MnLi gave phenylated cyclopropane in 34% or 30% yield, respectively, upon treatment of 1a. (4) (CH₂=CH)₃MnMgBr and (Me3Si-C≡C)3MnMgBr gave a minimal amount of the corresponding alkenvl- or alkynylcyclopropanes (<5%). Manganates having secondary and tertiary alkyl ligands such as i-Pr3MnMgBr and t-Bu3MnMgCl gave 1-bromo-2-hexylcyclopropane in 50-55% yield along with an unidentified complex mixture which did not contain the desired isopropylevelopropane or *tert*-butylevelopropane. (5) The intermediary cyclopropylmanganese reagents 5 could be trapped by acid chloride,⁸ iodine, and vinvl bromide (in the presence of Pd(PPh₃)_{Δ} (10mol%))⁹ as well as methyl iodide and allyl bromide. (6) 1,1-Dichlorocyclopropane such as 9.9-dibromobicvclo[6,1,0]nonane was found to be unreactive.

We are tempted to assume a similar reaction mechanism to the reaction with cuprate and zincates: (1) the initial halogen-manganese exchange at the less hindered bromine to afford 4, (2) alkyl migration under Br^- elimination producing 5 (inversion on the cyclopropane carbon), (3) the second alkylation by R^2X with retention of the configuration. The stereoselective formation of 2 might be attributed to the bulkiness of the manganese reagents which attack the less hindered halogen selectively.



Moreover, the reaction proceeded in the presence of a catalytic amount of manganese(II) chloride. For instance, an addition of a solution of dibromocyclopropane **1a** (1.0 mmol) to a THF solution of butylmagnesium bromide (3.0 mmol) and manganese(II) chloride (12 mg, 10 mol%) at 0 °C gave 1-butyl-2-hexylcyclopropane **2a** and **3a** in 75% combined yield after aqueous workup. In contrast, the reaction of **1a** with butylmagnesium bromide without manganese provided 1,2-nonadiene in 95% yield. The representative results of the catalytic reactions are shown in Table 2.

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Entry	Substrate 1	RMtl (3.0 mmol)	Electrophile	Yield (%)	Isomeric Ratio
	(1.0 mmor)				66/24
1		n-Duli	H ₂ O	00	00/34
2	n-CoHao Br	n-BuMgBr	H ₂ O	15	79/21
3		<i>n</i> -BuMgBr	CH ₂ =CHCH ₂ Br	57	81/19
4	<pre>✓ Br</pre>	CH ₂ =CHCH ₂ MgBr	H ₂ O	79	58/42
5	1a	CH ₂ =CHCH ₂ MgBr	CH ₂ =CHCH ₂ Br	47	
6		PhMe ₂ SiLi	EtOH	43	79/21
	Br				
7	$\wedge \downarrow_{a}$	<i>n</i> -BuLi	H ₂ O	62	85/15
8		<i>n</i> -BuMgBr	EtOH	51	93/7
9	Ph Br Br 1d	n-BuMgBr	H ₂ O	51	77/23

Table 2. Manganese(II) Chloride-Catalyzed Reaction of gem-Dibromocyclopropanes^a

a) The reactions were performed in the presence of 0.1 mmol of MnCl₂.

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- 6. 1-Butyl-2-hexyl-1-iodocyclopropane (*cis/trans* = 72/28): Bp 130–140°C (bath temp, 0.5 Torr); IR (neat) 3058, 2954, 2924, 2852, 1466, 1379, 1294, 1261, 1211, 1164, 1116, 1031, 942, 914, 800, 724 cm⁻¹; ¹H NMR (CDCl₃) δ –0.05–0.10 (m, 0.72H), 0.32 (t, J = 6.3Hz, 0.28H), 0.68 (t, J = 6.0 Hz, 0.72H), 0.80–0.98 (m, 6H), 1.02–1.75 (m, 17.28H); ¹³C NMR (CDCl₃) δ 13.98, 14.01, 21.81, 22.00, 22.51, 22.56, 22.80, 23.67, 24.02, 24.67, 28.63, 28.70, 29.01, 29.17, 30.17, 31.68, 31.77, 32.50, 36.95, 39.15, 46.00. Found: C, 50.79; H, 8.40%. Calcd for C₁₃H₂₅I: C, 50.66; H, 8.17%.
- 7. Monobromide could be obtained by quenching an intermediary manganate 4 with H_2O before being converted to 5.
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- 9. 1-Alkylcyclopropylzincates have been reported to react with alkenyl halide in the presence of a Pd catalyst. See ref 2.

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