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REACTIONS OF FLUORINATED CYCLOBUTENES WITH GRIGNARD REAGENTS*

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Summary

The reaction of an alkylmagnesium bromide with perfluorocyclobutene has been found to favor the formation of a vinylic monoalkyl product whereas an alkylmagnesium chloride favored the synthesis of a vinylic dialkyl compound. Increased branching at the α- or β-carbon of the isomeric butyl Grignard reagents caused a shift to the vinylic monoalkyl product and to reduced yields, especially with increased α-branching. Unsymmetrical vinylic dialkylperfluorocyclobutenes are reported for the first time.

Introduction

The reactions of fluorinated cyclobutenes with Grignard reagents have been under study at this laboratory for a number of years as a result of the first report of reactions in these systems by Park and Fontanelli [2]. Subsequent papers discussed the exchange reactions [3,4] and the substitution and rearrangement products [5] noted with Grignard reagents. The carbanionic nature of the carbon—magnesium bond would lead to the supposition that these reactions would follow the course of other nucleophiles with halogenated cyclobutenes, as recently summarized by Park, McMurtry and Adams [6]. This review also listed some of the factors which might be involved in directing the Grignard reaction pathway in a manner other than that predicted by the usual mechanistic interpretation of these nucleophilic substitutions. One of the possible factors considered to affect the course of reaction was steric bulk which has been cited to rationalize the results of metal hydride reductions [7] and the reaction of trialkyl phosphites [8] with halogenated cycloalkenes. The

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[*] Taken in part from ref. 1.

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present paper reports on the effect of branching at the α- or β-carbon and variation of the halogen of the alkylmagnesium halides on the reaction with perfluorocyclobutene.

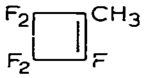
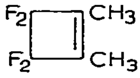
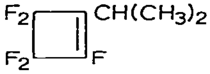
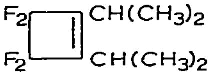
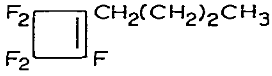
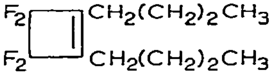
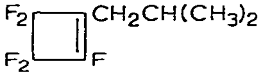
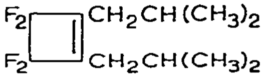
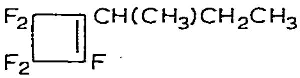
Although both the composition of Grignard reagents and the mechanism by which they react with organic functional groups remain in doubt, the question of the composition has been reviewed by Ashby [9] and the general mechanism by Salinger [10]. Any modification of either the halogen or alkyl portion of the Grignard compound would be expected to change not only the Lewis acid character of the complex itself but also to affect sterically the approach of the nucleophilic center to the fluoroalkene. The influence of solvent has remained constant since only tetrahydrofuran was utilized in this study.

Results and discussion

The results of the reaction of perfluorocyclobutene with the methyl or

TABLE 1

REACTIONS WITH PERFLUOROCYCLOBUTENE (I)[a]

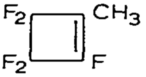
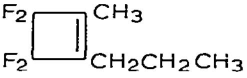
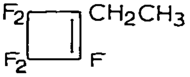
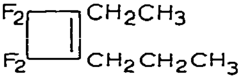
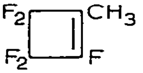
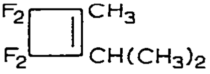
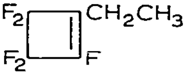
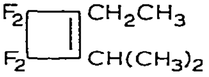
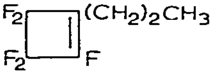
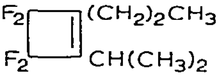
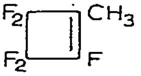
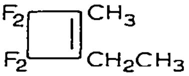
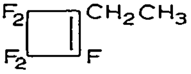
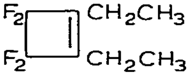
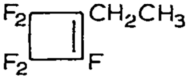
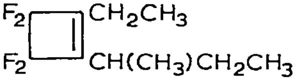
Grignard	Relative amounts of mono- and dialkyl products		Total yield (%)
CH_3MgBr	 0.7 (II)[b]	 0.3 (III)[b]	18
CH_3MgCl	0.0 (II)	1.0 (III)	21
i-PrMgBr	 1.0 (IV)	 0.0 (V)	10
i-PrMgCl	0.0 (IV)	1.0 (V)	10
n-BuMgBr	 0.4 (VI)[b]	 0.6 (VII)[b]	97
i-BuMgBr	 0.9 (VIII)	 0.1 (IX)	92
s-BuMgBr	 1.0 (X)		24

[a] Prepared by method of Henne and Ruh [11]. [b] Synthesis previously described by Dixon [12].

isopropyl Grignard reagents, summarized in Table 1, indicated that the nature of the halogen atom of the alkylmagnesium halide caused marked differences in the relative amounts of monoalkyl and dialkyl vinylic substitution produced. For example, exclusive formation of the monoalkyl product, 1-isopropyl-2,3,3,4,4-pentafluorocyclobutene, (IV), was noted with isopropylmagnesium bromide, whereas only the dialkyl compound, 1,2-diisopropyl-3,3,4,4-tetrafluorocyclobutene, (V), was found with isopropylmagnesium chloride under similar conditions. The nature of the halogen atom of the alkylmagnesium halide has been reported to affect other Grignard reactions [13] although Holm [14] indicated that the reactivity of a Grignard reagent in tetrahydrofuran did not depend greatly on the nature of the halogen, a result in marked contrast to that seen when ether was employed.

TABLE 2

REACTION OF ALKYL GRIGNARDS WITH MONOALKYL PERFLUOROCYCLOBUTENES

Cyclobutene[a]	Grignard	Product	Compd.	Yield (%)
	PrMgBr		(XI)	15
	PrMgBr		(XII)	35
	i-PrMgBr		(XIII)	4
	i-PrMgBr		(XIV)	40
	i-PrMgBr		(XV)	98
	EtMgBr		(XVI)	75
	EtMgBr		(XVII)[b]	50
	s-BuMgBr		(XVIII)	20

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[a] Prepared by the method of Park and Fontanelli [2]. [b] Synthesis previously described by Park and Fontanelli [2].

As summarized in Table 1, a distinct trend to lower total conversions and to monoalkyl products was obtained with the isomeric butyl Grignard reagents, with the sec-butylmagnesium bromide leading exclusively to the monoalkyl product, 1-sec-butyl-2,3,3,4,4-pentafluorocyclobutene, (X), in reduced yield. A similar decreased yield found with various aliphatic Grignard reagents was correlated with the increased electron releasing ability of the alkyl residue [15], which is consistent with decreasing carbanion stability [16]. However, the present study indicated that there was a large change in the relative amounts of the mono- and dialkyl products formed from the n-butyl and isobutyl Grignard compounds although both involve primary carbanionic species. A recent paper has invoked steric considerations to explain differences in reactivity of Grignard compounds as the organic ligand varied [17].

Table 2 details the results of the reactions of Grignard reagents with vinylic monoalkyl perfluorocyclobutenes. Note that the yield of 1-methyl-2-n-propyl-3,3,4,4-tetrafluorocyclobutene, (XI), increased over that found for 1-ethyl-2-n-propyl-3,3,4,4-tetrafluorocyclobutene, (XII), although the Grignard reagent was the same in both cases. An even more dramatic increase in yield occurred with the isopropyl Grignard compound in the formation of compounds (XIII), (XIV) and (XV) produced from the vinylic methyl, ethyl and n-butyl perfluorocyclobutene, respectively.

The data collected in Table 2 do reflect a decrease in the yield of the dialkyl products, compounds (XVI), (XI) and (XIII), from the vinylic methyl cyclobutene, (II), with ethyl-, n-propyl- and isopropylmagnesium bromides. Therefore, this trend is similar to the previously described reduction in yield involving the isomeric butyl Grignard reagents and perfluorocyclobutene. Generally, decreasing yields are also observed in the formation of compounds (XVII), (XII), (XIV) and (XVIII) from 1-ethyl-2,3,3,4,4-pentafluorocyclobutene as the Grignard reagent changes from ethyl-, n-propyl-, isopropyl, and sec-butylmagnesium bromide.

Experimental

The infrared spectra were taken on a Perkin—Elmer Infracord spectro-

TABLE 3

PHYSICAL PROPERTIES OF NEW FLUOROCYCLOBUTENES

Compd.	n_D^{25}	d^{25}	B.p. (°C/630 mm)	Analyses, found (calcd.) (%)		
				C	H	F
(IV)	1.3433	1.19	77—79	45.5 (45.2)	3.9 (3.7)	50.7 (50.5)
(V)	1.3892	1.05	155—156	57.1 (57.4)	6.8 (6.7)	36.0 (36.2)
(VIII)	1.3509	1.19	101—101.5	47.8 (48.0)	4.6 (4.5)	47.5 (47.5)
(IX)	1.3983	1.08	187—188	58.5 (58.1)	7.4 (7.3)	30.9 (30.7)
(X)	1.3522	1.17	98—100	48.0 (48.0)	4.7 (4.5)	47.3 (47.5)
(XI)	1.3700	1.11	138	52.7 (52.8)	5.3 (5.6)	41.6 (41.8)
(XII)	1.3845	1.09	150	54.8 (55.1)	6.4 (6.1)	38.5 (38.8)
(XIII)	1.3716	1.11	129—130	52.8 (52.8)	5.3 (5.5)	41.8 (41.7)
(XIV)	1.3831	1.08	144—145	55.0 (55.1)	6.1 (6.1)	38.5 (38.8)
(XV)	1.3894	1.06	159—161	57.0 (57.4)	6.7 (6.7)	36.3 (36.2)
(XVI)	1.3611	1.14	121	49.9 (50.0	5.0 (4.8)	45.3 (45.2)
(XVIII)	1.3898	1.04	163—164	57.1 (57.3)	6.9 (6.7)	36.4 (36.2)

photometer, and NMR spectra were obtained from a Varian Model A-60, using carbon tetrachloride as solvent and tetramethylsilane as reference [18]. Product analyses and preparative scale separations were carried out on a F and M Model 300 programmed temperature gas chromatograph, with a Texas Instruments Inc. Servariter model recorder with a disc integrator, utilizing a column with a fluorosilicon 1265 (QF-1) substrate. A Bausch and Lomb refractometer was used to measure the refractive indices. Microanalyses were performed by the Galbraith Laboratories, Knoxville, Tenn. Densities were determined by weight difference with a calibrated 10μl syringe.

Reaction of perfluorocyclobutene (I) with isobutylmagnesium bromide

A 1000 ml three-neck flask, fitted with a gas inlet tube, a mechanical stirrer, and a Dry-Ice condenser connected to a bubbler, was swept with nitrogen gas and 500 ml of 2.2 *M* isobutylmagnesium bromide in tetrahydrofuran introduced and cooled to 0°. Over a period of 1 h, 81 g of perfluorocyclobutene was bubbled into the rapidly stirred solution. The temperature was allowed to rise to room temperature, refluxed for 3 h, and finally stirred overnight at room temperature. The reaction product was worked up by destroying the excess Grignard reagent with dilute hydrochloric acid, extracting with tetrahydrofuran, and drying with anhydrous magnesium sulfate. Distillation gave 44 g (84%) of 1-isobutyl-2,3,3,4,4-pentafluorocyclobutene, (VIII), and 10 g (8%) of 1,2-diisobutyl-3,3,4,4-tetrafluorocyclobutene, (IX).

The preparations of the other derivatives in general followed along similar lines. For those reactions carried out with perfluorocyclobutene, the molar ratio of Grignard reagent to the fluoroalkene was normally 2.1 to 2.2. In those

TABLE 4

SPECTRAL PROPERTIES OF FLUOROCYCLOBUTENES

Compd.	IR, C=C	NMR	
	(cm^{-1})	τ (ppm)[a]	Coupling (Hz)
(IV)	1720	8.77 d	7.0
		7.38 m	
(V)		8.79 d	6.9
		7.23 septet	
(VIII)	1730	9.00 d	6.5
		7.89, 8.0 broad, m	
(IX)		9.03 d	6.4
		7.90, 8.03 broad, m	
(X)	1720	9.03 t	6.6
		8.78 d	7.0
		7.58, 8.44 m	
(XIV)		8.83 d	7.0
		8.88 t	7.0
		7.4, 7.79 m	
(XV)		9.03 t	7.0
		8.80 d	7.0
		8.40 m	
		7.79, 7.35 m	
(XVIII)		8.84 t	7.6
		9.08 t	6.6
		8.82 d	6.6
		8.49, 7.69 m	

[a] TMS = 10.0.

cases where the monoalkyl-substituted perfluorocyclobutene was added to the tetrahydrofuran Grignard solution, a water condenser could be substituted for the Dry-Ice condenser and a dropping funnel for the gas inlet tube. Here, a two-fold molar ratio of Grignard reagent to monoalkyl cyclobutene was used. The physical properties of the new vinylic alkyl perfluorocyclobutenes are tabulated in Table 3, along with spectral properties in Table 4.

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