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THE REACTION OF 3-(1-IMIDAZOLYL)-2-ALKEN-1-ONES WITH ORGANOMETALLIC COMPOUNDS

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Abstract ——In the reaction with organometallic compounds, 3-(1-imidazolyl)-2-alken-1-ones (1) gave both 1,2- and 1,4-addition products in a comparable ratio. This fact showed that the chemical properties of 1 were analogous to those of 3-phenyl-2-alken-1-ones (2) and 3-amino-2-alken-1-ones (3).

Since Staab reported the general preparation of N-acylimidazoles,[1)] the reaction of N-acylimidazoles with nucleophiles such as alcohols, amines, thiols, organometallic compounds and metal hydride complexes has been extensively investigated and these compounds have been found to behave as the convenient acylating reagent.[2)] Although 3-(1-imidazolyl)-2-alken-1-ones (1) are the vinylogues of N-acylimidazoles, the paper concerning the compound 1 has scarcely been reported in the literature. Recently we succeeded in the preparation of 1 from 2-alkyn-1-ones, 3-chloro-2-alken-1-ones[3)] or 2,3-dibromoalkan-1-ones[4)] by the treatment with imidazole.

Since imidazole is a heteroaromatic compound, 1 could be regarded as an analogue of 3-phenyl-2-alken-1-ones (2) such as benzalacetone and chalcones. Also 1 could be an analogue of 3-amino-2-alken-1-ones (3), because imidazole could be considered as an amine. From these considerations, 1 was expected to have the character of both 2 and 3.

It is well-known that the reactions of 2-alken-1-ones with organometallic compounds afford 1,2- and 1,4-addition products, whose ratios depend on the kind of metal. For example, in the reaction of 3-phenyl-2-alken-1-ones (2) with alkyllithium, the main products were found to be 3-phenyl-2-alken-1-ols (7) by the 1,2-addition reaction, while the reaction products with alkyl Grignard reagent were mainly 3-phenyl-alkan-1-ones (8) by the 1,4-addition (conjugated addition).[5)] On the contrary, 3-amino-2-alken-1-ones (3) gave the

1,4-addition products (5) in the reaction with either an alkyllithium or an alkyl Grignard reagnt without any metal effect.[6] Further, the reactions of 2-alken-1-ones with organocuprate reagents afford predominantly 1,4-addition products.[7] From these facts, the reactions of 1 with alkyllithium, alkyl Grignard and dialkylcuprate reagents were of interest in the clarification of the behaviours of 1.

When 1-(4-methyl)phenyl-3-(1-imidazolyl)-2-propen-1-one (1) was treated with methylmagnesium iodide at room temperature, two products (4a and 5a) were obtained. One, 5a, was identical with the 1-(4-methyl)phenyl-2-buten-1-one by the comparison of spectral data, which seemed to be formed by the 1,4-addition reaction accompanied with the removal of imidazoles. On the other, carbonyl absorption band disappeared and new band due to the hydroxyl group appeared at 3400 cm^{-1} in the IR spectrum. The NMR spectrum showed the olefinic protons at δ 6.13 and 6.98 ppm with J=14 Hz and two methyl singlet signals at δ 1.74 and 2.35 ppm. From these spectral data and elemental analysis, the product (4a) was found to be 3-(4-methyl)phenyl-1-(1-imidazolyl)-1-buten-3-ol, which was an allyl alcohol derivative owing to 1,2-addition reaction. In the case of methyllithium and sodium borohydride, 1 afforded the corresponding 4 and 5. The product ratios of 4 : 5 in these reactions were determined by means of HPLC, and were summarized in Table. Further, by the treatment with lithium dimethylcuprate, 1 afforded predominantly 1-(4-methyl)phenyl-3-methyl-1-butanone (6a), which was identified by the comparison of the spectral data with those of authentic sample. In this cuprate reaction, the compound 6a was formed by the reactions of 1,4-addition, removal of imidazole and again 1,4-addition, and any trace of 1,2-addition was not observed. The ratio of the products in the reactions of 1-(4-methyl)phenyl-3-phenyl-2-propen-1-one (2) and 1-(4-methyl)phenyl-3-pyrrolidinyl-2-propen-1-one (3) with nucleophiles was also shown for comparison.

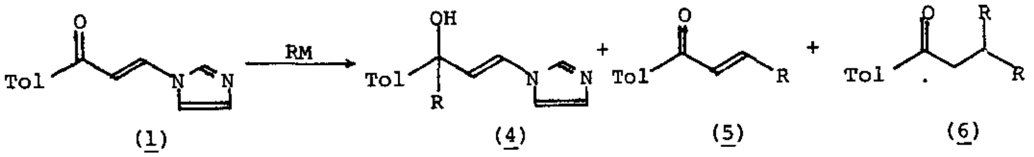
As the result, 1,2- and 1,4-addition products were formed almost in the same ratios as in the reaction of 1, and the metal effect of the organometallic compound was rather small. Also, in the case of alkyllithium and sodium borohydride, the product ratio from 1 was intermediate between those from 2 and 3. These tendencies coincide with the expectation based on the fact that 1 is regarded as the analogues of both 2 and 3.

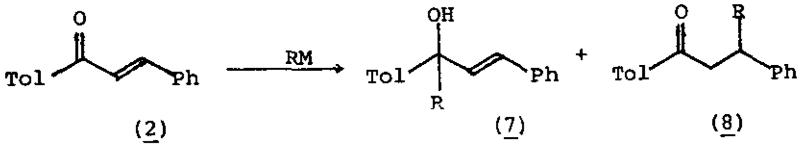
Table

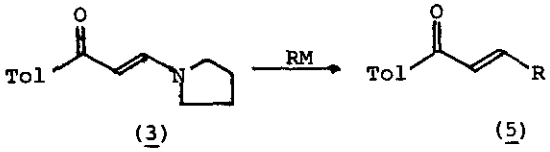
Product Ratios in the Reaction of

3-Substituted 1-(4-Methyl)phenyl-2-propen-1-ones with Organometallic Compounds

Substrate	3-Substituent	RM	Total Yield (%)	1,2-Adduct % (Product)	1,4-Adduct % (Product)
1	Imidazolyl	MeMgI	60	50 (4a)	50 (5a)
1	Imidazolyl	BuMgBr	47	30 (4b)	70 (5b)
1	Imidazolyl	MeLi	44	70 (4a)	30 (5a)
1	Imidazolyl	BuLi	50	35 (4b)	65 (5b)
1	Imidazolyl	$NaBH_4$	60	65 (4c)	35 (5c)
1	Imidazolyl	Me_2CuLi	55	0	100 (6a)
2	Phenyl	MeMgI	97	10 (7a)	90 (8a)
2	Phenyl	BuMgBr	39	5 (7b)	95 (8b)
2	Phenyl	MeLi	94	90 (7a)	10 (8a)
2	Phenyl	BuLi	65	65 (7b)	35 (8b)
2	Phenyl	$NaBH_4$	98	100 (7c)	0
3	Pyrrolidinyl	MeMgI	44	0	100 (5a)
3	Pyrrolidinyl	BuMgBr	75	0	100 (5b)
3	Pyrrolidinyl	MeLi	80	0	100 (5a)
3	Pyrrolidinyl	BuLi	70	0	100 (5b)
3	Pyrrolidinyl	$NaBH_4$	40	0	100 (5c)







a: R=Me
b: R=Bu
c: R=H

Similarly, the reactions of 1-phenyl-3-(1-imidazolyl)-2-buten-1-one, 4-methyl-1-(1-imidazolyl)-1-penten-3-one and 1-(1-imidazolyl)-2-buten-3-one with organometallic compounds gave the mixture of 1,2- and 1,4-addition products.

EXPERIMENTAL

Reaction with Organometallic Compound

The 3-(1-imidazolyl)-2-alkene-1-one (1) (1 mmol) in tetrahydrofuran (10 ml) was added to an ethereal solution of organometallic compound. After the mixture was stirred for 3 h, water was added to the reaction mixture and the product was extracted with dichloromethane three times. The organic layer was washed with water three times and then dried over anhydrous magnesium sulfate. After removal of the solvent, the ratio of the products was measured by HPLC, and the crude products were chromatographed on a silica gel column with chloroform-acetone-ethanol (100:20:4) mixture.

Reaction with Sodium Borohydride

To a solution of 1 (1 mmol) in ethanol (10 ml), sodium borohydride was added. After stirring for 3 h, the reaction mixture was diluted with water, and the product was extracted with dichloromethane three times.

The organic layer was washed with water three times and then dried over anhydrous magnesium sulfate. After removal of the solvent, the ratio of the products was determined by HPLC, and the crude products were chromatographed on a silica gel column with chloroform-acetone-ethanol (100:20:4) mixture.

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