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THE DIRECT ALKYLATION OF PYRROLE WITH ALLYL BROMIDE

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Abstract -- In the presence of silver carbonate, potassium carbonate, or sodium bicarbonate, pyrrole reacts with allyl bromide to form 2-allylpyrrole together with smaller amounts of 3-allylpyrrole and di(poly)allylpyrroles.

Although the alkylation of metal derivatives of pyrrole has been investigated extensively, very little work has been done on reactions of pyrrole with alkyl halides in the absence of a Friedel-Crafts catalyst.[1-5] Pyrrole has been reported to yield polymethylpyrroles upon treatment with methyl iodide,[6] and the reaction of 1-methylpyrrole with methyl iodide and potassium carbonate in methanol at 140° has been found to lead to N,C,C-trimethylpyrroles as well as 1,3,4,5,5-pentamethyl-2-methylene-Δ^3-pyrroline and 1,2,2,4,5-pentamethyl-3-methylene-Δ^2-pyrroline.[7,8] Treatment of pyrrole with trianisylmethyl chloride in benzene has been shown to yield 2-trianisylmethylpyrrole.[9]

In the course of a study of the reactions of metal salts of pyrrole with allyl bromide,[5] it was observed that pyrrole reacts violently with allyl bromide at room temperature to form a partially charred polymeric material. Polymerization however is prevented and the reaction is controlled when it is run in the presence of sufficient base to neutralize the hydrogen bromide formed by the alkylation reaction. Thus the reaction of pyrrole with allyl bromide in toluene or tetrahydrofuran, in the presence of potassium carbonate or sodium bicarbonate and water, with or without addition of a silver salt, yields 2-allylpyrrole as the principal product together with smaller amounts of 3-allylpyrrole and di(poly)allylpyrroles (Table I). In general, the composition of the product is analogous to that of the reaction of pyrrolylmagnesium bromide with allyl chloride,[10] except that in the present case the relative percentage of 3-allylpyrrole is significantly lower and that of di(poly)allylpyrroles somewhat higher. The best overall yields were obtained when the reaction was run in toluene, in the presence of silver carbonate (58%), and in toluene/water, in the presence of potassium carbonate (51%).

TABLE I

REACTION OF PYRROLE WITH ALLYL BROMIDE

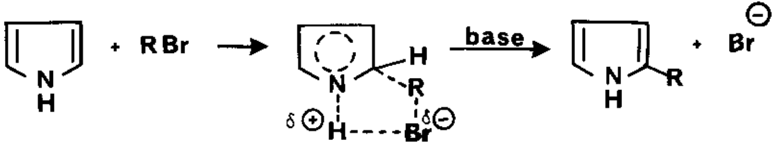
Medium	Added Reagents	% Yield Monoallylpyrroles	% Yield Di(poly)allylpyrroles	Relative Percent		
				2-Allylpyrrole	3-Allylpyrrole	Di(poly)allylpyrroles[a]
Toluene	Silver carbonate	40	18	57	5	38
Toluene-water	Sodium bicarbonate, silver nitrate	31	12	57	8	35
Tetrahydrofuran-water	Sodium bicarbonate, silver nitrate	29	13	54	9	37
Toluene	Sodium bicarbonate	20	9	59	4	37
Tetrahydrofuran	Sodium bicarbonate	21	9	58	6	36
Toluene-water	Potassium carbonate, silver nitrate	30	14	53	8	39
Tetrahydrofuran-water	Potassium carbonate, silver nitrate	28	13	51	9	40
Toluene-water	Potassium carbonate	42	9	67	10	23
Tetrahydrofuran-water	Potassium carbonate	30	10	60	9	31
Tetrahydrofuran	Sodium carbonate	10	2	72	9	19
Toluene	Dimethylamine	4	1	61	9	30
Toluene	Pyridine	9	0.5	86	8	6

[a] Calculated as diallylpyrroles.

Because of the simplicity of the experimental procedure and the fact that 2-allylpyrrole may be more easily separated from di(poly)allylpyrroles than from its 3-isomer, the reaction described in this report may be considered a more convenient approach to 2-allylpyrrole than the route involving a Grignard reaction.[10]

No clear pattern has been observed correlating the composition of the product with the reaction conditions. The presence of water increases somewhat the overall yield, whereas addition of a silver salt seems to favor polyalkylation.[11] Reactions in tetrahydrofuran afford consistently lower yields than reactions in toluene and the use of an amine as base gives poor results presumably because of considerable side reaction between the amine and allyl bromide.

With regard to a probable reaction pathway, the fact that in no case has any 1-allylpyrrole been detected in the product indicates that pyrrole itself, and not its anion, is the species undergoing substitution.[5] It is interesting to note that no reaction takes place when 1-allylpyrrole is treated with allyl bromide and sodium bicarbonate in toluene, at 65°, for 24 hours. Under the same conditions, however, the use of silver carbonate, instead of sodium bicarbonate, causes a reaction to occur. Gas-liquid chromatography of the product shows the presence in it of 58% of unreacted 1-allylpyrrole, 24% of two compounds with retention times corresponding to 1,2- and 1,3-diallylpyrroles, and 18% of two compounds with longer retention times, presumably more highly substituted pyrroles. These results indicate that the presence of hydrogen on the nitrogen atom of the pyrrole ring is essential for the reaction to occur in the absence of silver ions. This requirement is consistent with the expected stabilization of the transition state of the substitution reaction by the simultaneous formation of a proton and a bromide ion in close proximity.[5] When an alkyl group is attached to the pyrrole nitrogen atom, such a relatively low-energy transition state is not possible and the reaction takes place only when the C-Br bond of the alkyl halide is polarized enough by a silver ion to allow an S_N1-type pathway.



Experimental[12]

With minor modifications, the reactions were run as described in the following representative cases. The reaction products were analyzed by gas-liquid chromatography as described in reference 5.

Reactions in the Presence of Silver Carbonate. The dropwise addition over 0.5 h of 60.5 g (0.50 mole) of allyl bromide to a stirred mixture of 33.5 g (0.50 mole) of pyrrole, 69.0 g (0.25 mole) of silver carbonate and 100 ml of toluene caused a vigorous, exothermic reaction accompanied by evolution of carbon dioxide. After an additional stirring period of 6 h, the reaction mixture was filtered and the solid material was washed with ethyl ether. Removal of the solvents from the combined organic solutions by distillation under reduced pressure yielded a liquid residue which was analyzed by gas-liquid chromatography.

Reactions in the Presence of Sodium Bicarbonate. A mixture of 33.5 g (0.50 mole) of pyrrole, 42.0 g (0.50 mole) of sodium bicarbonate, 60.5 g (0.50 mole) of allyl bromide, and 100 ml of toluene or tetrahydrofuran was stirred at 65° for 24 h. The resulting mixture was treated as described above.

Reactions in the Presence of Potassium Carbonate and Water. A mixture of 33.5 g (0.50 mole) of pyrrole, 35.0 g (0.25 mole) of potassium carbonate dissolved in 100 ml of water, 60.5 g (0.50 mole) of allyl bromide, and 100 ml of toluene or tetrahydrofuran was stirred at 65° for

24 h. The product was cooled, the layers were separated, and the aqueous layer was extracted with ethyl ether. The combined organic solutions were dried ($MgSO_4$) and further treated as described earlier.

Reactions in the Presence of Potassium Carbonate, Silver Nitrate, and Water. A solution of 85.0 g (0.50 mole) of silver nitrate in 100 ml of water was added dropwise, over a period of 1 h, to a stirred mixture of 33.5 g (0.50 mole) of pyrrole, 35.0 g (0.25 mole) of potassium carbonate, 60.5 g (0.50 mole) of allyl bromide, and 100 ml of toluene or tetrahydrofuran. After an additional stirring period of 24 hours, the reaction mixture was filtered, the solid material was washed with ethyl ether, and the combined organic solutions were treated as described previously.

References and Notes

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