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FREE RADICAL PHENYLATION OF ISOTHIAZOLE AND METHYL-ISOTHIAZOLES

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In some recent papers we exposed our work concerning the free radical arylation of thiazoles and pyridines. We wish to report now, some preliminary results dealing with the free radical phénylation of isothiazole and methyl-isothiazoles.

I - ISOMER RATIOS AND REACTIVITY -

The phenylation method has been described in previous papers (I, 2, 3, 4). The reactivity is given towards benzene, equimolecular amount of benzene or nitrobenzene being used in the experimental process of competitive reactions. In the benzene experiments, some oxidising agent is added to the reaction mixture to prevent excessive dimerization or disproportionation of the intermediate complexes (5, 6).

We obtained:

substrates	medium	isomer ratios 3	4	5	reactivity towards benzene
isothiazole	neutral	47	9	44	0,95
3-methyl isothiazole	neutral		38,5	6I,5	0,65
4-methyl isothiazole	neutral	40		60	I,85
5-méthyl isethiazole	neutral	69	3I		

All the results are given with + or - 2%.

In acidic medium (e.g. acetic acid, acetic anhydride, hydrochloric acid) we found an increase of substitution of about 15 to 20% for the 3 position.

II - REACTIVITY TOWARDS ONE POSITION OF BENZENE AND DISCUSSION -

a) Reactivity towards one position of benzene in neutral medium:

substrates	positions	partial rate factors
isothiazole	3	2,68
	5	2,5I
	4	0,5I

substrates	positions	partial rate factors
3-methyl isothiazole	4	I,5
	5	2,4
4-methyl isothiazole	3	4,43
	5	6,65
5-methyl isothiazole	3	I,25
	4	0,56

b) Discussion:

The partial rate factors show that the reactivity of isothiazole is almost the same for the 3 or 5 positions, adjacent to nitrogen or sulfur. This fact, emphasize the results already obtained for the thiazole (4). In the same way, substitution of the isothiazole ring by a methyl group , give the greatest increase of reactivity when the methyl group substitutes a weakly reactive position, as in the case of pyridine and thiazole (7, 8, 9).

I - H.JM.DOU and B.M.LYNCH Tetrahedron Letters I965, p.897

2 - G;VERNIN, H.JM.DOU et J.METZGER Bull.Soc.Chim.France I967, p.45I4

3 - G.VERNIN, H.JM.DOU, L.BOUSCASSE et J.METZGER Bull.Soc.Chim.France I967, p.3387

4 - H.JM.DOU, G.VERNIN et J.METZGER Tetrahedron Letters I967, p.2223

5 - H.JM.DOU, G.VERNIN et J.METZGER Tetrahedron Letters I968, p.953

6 - G.VERNIN, H.JM.DOU et J.METZGER Bull.Soc.Chim.France I968, p.3280

7 - R.A.ABRAMOVITCH et J.G.SAHA J.Chem.Soc. I964, p.2175
and, M.SAHA Ph.D. Thesis SASKATCHEWAN Canada I966

8 - JM.BONNIER, J.COURT et M.GELUS C.R.Acad.Sci. 1966, p.262

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