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CATALYTIC SYNTHESIS OF FLUORO-DERIVATIVES OF 2,4-DIPHENYL-5, 6-BENZOQUINOLINE

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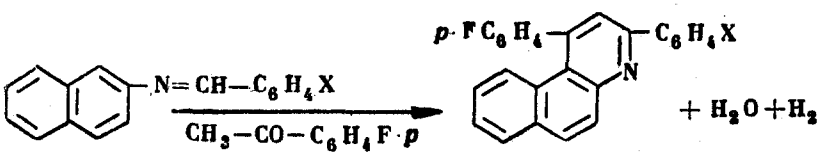
A study is made of the condensation of fluorine-containing azomethines with mixed aliphatic aromatic ketones containing fluorine as a substituent, and it is used as a basis for synthesizing 10 new fluoro-derivatives of 2,4-diphenyl-5,6-benzoquinolines.

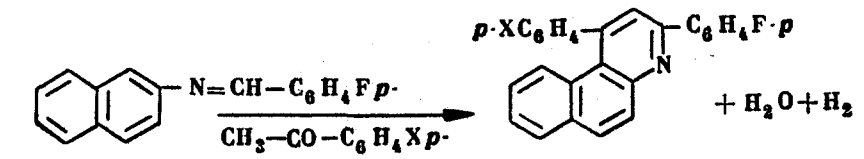
A new method of synthesizing 2,4-diphenyl-5,6-benzoquinoline and its derivatives was previously described, [1,2] it being based on condensation of ketones with Schiff's bases, prepared from 2-naphthylamine and aromatic aldehydes. It is known from the literature [3-6] that quinoline derivatives have a varied physiological action. At the same time there are numerous indications [7-9] that introduction of a fluorine atom into an organic molecule can sharply alter its physicochemical properties, and in particular, its physiological activity.

Hitherto fluoro-derivatives of 2,4-diphenyl-5,6-benzoquinoline have not been described in the literature. The present paper investigates two variants of a method of synthesizing them. According to the first variant the azomethine, prepared from 2-naphthylamine and an aromatic aldehyde, is caused to react with p-fluoroacetophenone. It was used to synthesize 2,4-diphenyl derivatives of 5,6-benzoquinoline, where the fluorine atom was para- in the benzene ring at position 4:



X=H, *m*- и *p*-NO_2, *p*-F, *p*-Cl, *p*-Br, *p*-CH_3, *p*-$N(CH_3)_2$, *p*-OCH_3.

In the second variant, the azomethine, prepared by condensing 2-naphthylamine with p-fluorobenzaldehyde, was reacted with a mixed aliphatic aromatic amine. It was used to synthesize 2,4, -diphenyl-5,6-benzoquinolines where the fluorine was para- in the benzene ring at position 2 or at both position 2 and 4:



H, F.

The catalyst used for these reactions was concentrated hydrochloric acid. Actually, formation of the benzoquinoline is preceded by formation of the corresponding β-naphthylaminoketone which is cyclized by the action of a proton to the corresponding benzoquinoline base [10]. In the present work no attempt was made to isolate the intermediates, and reaction was effected under more vigorous conditions, in sealed tubes.

Experimental

A mixture of 0.01 mole azomethine, 10 ml alcohol, 0.01 mole ketone, and 5 drops of conc. HCl, was heated in a sealed tube on a steam bath for 30 min. After cooling the crystals were separated, treated with aqueous ammonia, and crystallized from alcohol-toluene (1:1). The table gives name, yield, mp and elementary analytical data for the compounds.

Compound	Mp °C	Formula	N, %		% Yield
			Found	Calculated	
2-phenyl-4-p-fluorophenyl-5, 6-benzoquinoline	165—167	$C_{25}H_{16}FN$	3.88 4.09	4.01	30.2
2-p-tolyl-4-p-fluorophenyl-5, 6-benzoquinoline	155—156	$C_{26}H_{18}FN$	3.89 3.82	3.85	29
2-p-methoxyphenyl-4-p-fluorophenyl-5, 6-benzoquinoline	169—171	$C_{26}H_{18}FNO$	3.74 3.57	3.69	32
2-p-chlorophenyl-4-p-fluorophenyl-5, 6-benzoquinoline	189—190	$C_{25}H_{15}ClFN$	3.61 3.59	3.65	40
2-p-bromophenyl-4-p-fluorophenyl-5, 6-benzoquinoline	195—196	$C_{25}H_{15}BrFN$	3.07 3.09	3.27	52
2-m-nitrophenyl-4-p-fluorophenyl-5, 6-benzoquinoline	244—246	$C_{25}H_{15}FN_2O_2$	6.97 6.82	7.10	46
2-p-nitrophenyl-4-p-fluorophenyl-5, 6-benzoquinoline	249	$C_{25}H_{15}FN_2O_2$	6.82 6.87	7.10	35
2-p-dimethylaminophenyl-4-p-fluorophenyl-5, 6-benzoquinoline	204—206	$C_{27}H_{21}FN_2$	6.90 7.01	7.14	25
2-p-fluorophenyl-4-phenyl-5, 6-benzoquinoline	171—172	$C_{25}H_{16}FN$	4.03 4.18	4.01	42
2,4-bis (p-fluorophenyl)-5, 6-benzoquinoline	177—179	$C_{25}H_{15}F_2N$	3.76 3.87	3.81	28

The compounds synthesized formed hydrochlorides, picrates, and platinates, which decomposed on heating.

The IR spectra of the compounds synthesized did not exhibit an absorption band characteristic of the carbonyl group (1690 cm^{-1}).

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