Phosphoramides; III[1]. Phenyl *N,N'*-Dimethylphosphorodiamidate as a New Reagent for the Synthesis of 3-Methyl-4-oxo-3,4-dihydroquinazolines

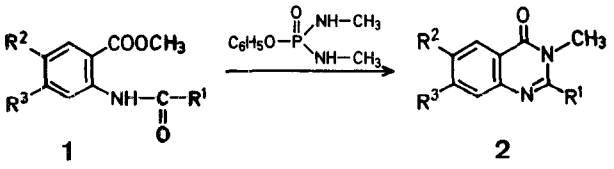
E. B. PEDERSEN

Department of Chemistry, Odense University, DK-5000 Odense, Denmark

3-Methyl-4-oxo-3,4-dihydroquinazolines [**2**, 3-Methyl-4(3*H*)-quinazolinones) have been prepared by heating the corresponding quinazolinones with methyl iodide in alcoholic potassium hydroxide[2] or by heating an appropriate *N*-methyl-2-acylaminobenzamide[3]; other methods have also been employed[4,5]. Compounds **2** are of general interest in terms of their biological and pharmacological activities such as lowering of blood pressure[6], inhibition of plant-cell mitosis[7,8], muscle-relaxing effects[9], and antispasmodic activity[10].

Phosphoramides have in recent years frequently been used in organic synthesis[11]. In particular, hexamethylphosphoric triamide (HMPT) has been shown to be an interesting solvent and reagent. Thus for example, 2,4-bis[dimethylamino]-quinoline could be obtained by heating ethyl 2-acetylaminobenzoate in HMPT at reflux temperature[1]. This simple quinoline synthesis made it attractive to investigate the reaction of anthranilic acid derivatives of the above-mentioned type with other phosphoramides.

It was found that heating of methyl 2-acylaminobenzoates (**1**) with equimolar amounts of phenyl *N,N'*-dimethylphosphorodiamidate at 250° leads to the formation of 3-methyl-4-oxo-3,4-dihydroquinazolines (**2**) in an exothermic reaction.



1 2

Table. 3-Methyl-4-oxo-3,4-dihydroquinazolines (**2**) prepared

R^1	R^2	R^3	Yield [%]	m.p. (from solvent)	Lit. m.p.
H	H	H	32	104–106° (toluene/petroleum ether 80–100°)	105°[2]
CH_3	H	H	74	70–72°[c] (diisopropyl ether)	70°[2]
CH_3	CH_3	H	40[a]	109–112° (petroleum ether 80–100°)	—
CH_3	OCH_3	OCH_3	54[b]	218–220° (xylene/petroleum ether 100–140°)	—
C_2H_5	H	H	72	119–121° (petroleum ether 80–100°)	121°[12]
C_6H_5	H	H	67	134–135° (xylene/petroleum ether 80–100°)	131–132°[13]

[a] $C_{11}H_{12}N_2O$ (188.2) calc. C 70.18 H 6.43 N 14.88; found 70.85 6.87 14.64

^{1}H-N.M.R. ($CDCl_3$): $\delta = 2.47$ (s, 3H); 2.58 (s, 3H); 3.60 (s, 3H); 7.48 (m, 2H); 8.00 ppm (m, 1H).

[b] $C_{12}H_{14}N_2O_3$ (234.2) calc. C 61.52 H 6.02 N 11.96; found 61.35 6.13 11.78

^{1}H-N.M.R. ($CDCl_3$): $\delta = 2.55$ (s, 3H); 3.58 (s, 3H); 3.97 (s, 6H); 6.90 (s, 1H); 7.45 ppm (s, 1H).

[c] As hydrate.

It should be noted that the reaction gives also good results when two methoxy groups are on the aromatic ring in **1**. The yields are around 70% for the *N*-acetyl ($R^1 = CH_3$), *N*-propanoyl ($R^1 = C_2H_5$), and *N*-benzoyl ($R^1 = C_6H_5$) compounds **1**, whereas with the *N*-formyl compound (**1**, $R^1 = H$) only a 32% yield of the corresponding **2** is obtained.

Preparation of 3-Methyl-4-oxo-3,4-dihydroquinazolines (2); General Procedure:

A mixture of the methyl 2-acylaminobenzoate **1** (0.05 mol) and phenyl *N*,*N'*-dimethylphosphorodiamidate (12 g, 0.66 mol) is heated on a silicone-oil bath at 250°. The temperature of the reaction mixture increases to 275–290° within 4–6 min. Heating is then continued for 5 min. The hot reaction mixture is poured directly into ice (~200 g) in a separating funnel, and 2 normal aqueous sodium hydroxide (100 ml) is added. The mixture is extracted with dichloromethane (50 ml portions) until all solid material has dissolved. The organic extract is dried and evaporated and the residue is recrystallized from the solvent given in the Table with the addition of decolorizing carbon (2 g).

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