Triphosgene in Heterocyclic Chemistry, Novel Synthesis of Pyrazolo (2, 3-c) Quinazoline from 2-Acetamido Acetophenone Hydrazone

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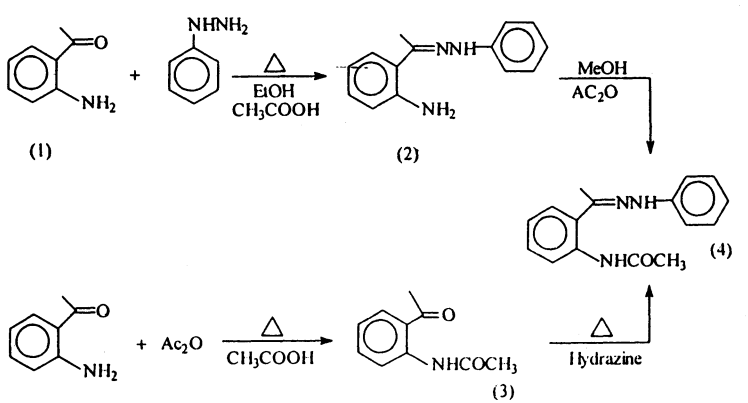
5-Methyl-3-phenyl pyrazolo-[2,3-c]-quinazoline-2-one was prepared from the reaction of triphosgene (BTC) with 2-acetamido acetophenone hydrazone.

INTRODUCTION

Hydrazones have previously been used for the synthesis of heterocyclic compounds in a variety of methods[1]. In this study we planned to obtain benzodiaziepine from the reaction of 2-acetamido acetophenone hydrazone with triphosgene (BTC), in a method used previously with 2-phenyl acetophenone derivatives[2], but instead we obtained a fused heterocyclic system which was identified as 5-methyl-3-phenyl pyrazolo-[2,3-c]-quinzoline-2-one.

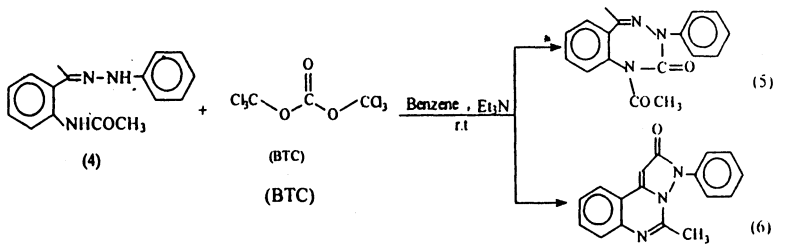
RESULTS AND DISCUSSION

In the first part of this paper, the preparation of the hydrazone acetamide was investigated. There were two methods for preparing the last compound as shown in Scheme-I. Both have given the same compound. In the first method, we started the reaction by refluxing 2-aminoacetophenone with phenyl hydrazine; therefore we got 2-aminoacetophenone phenyl hydrazone. Then, we added acetic anhydride



Scheme (I)

to the hydrazone[3] with methanol as a medium at room temperature with stirring in second step, and we got hydrazone acetamide.

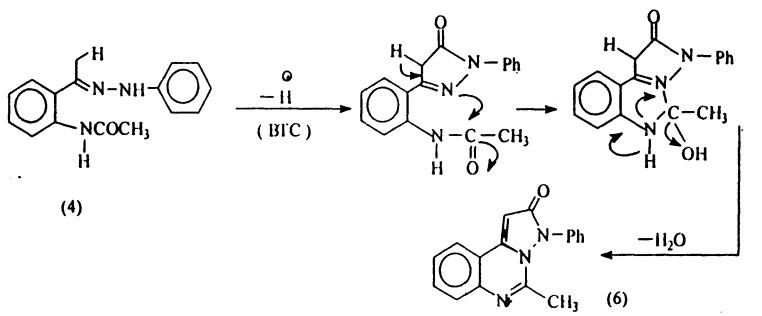


Scheme (II).

In the second method, we mixed 2-aminoactophenone with acetic anhydride[4] in a medium of acetic acid and refluxed for 2 h until we got N-(2-acetylphenyl) acetamide; then we added phenyl hydrazone to get the same compound as in the first method.

In the second part of this paper we used triphosgene instead of phosgene to react with our last compound[5] due to safety[6] of handing. We were expecting to get benzotriazepine[7], but instead of that we got fused pyrazole-quinazoline as shown in Scheme-II.

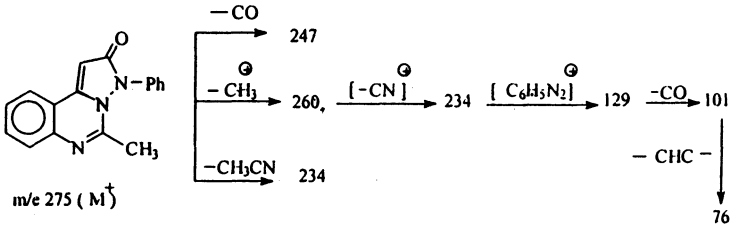
The structure of **(6)** was determined based up on the following observations. First there is only one carbonyl group absorbance at 1685 ν (cm^{-1}) in the IR spectrum. Second, the ^{13}C-NMR spectrum shows one-carbonyl absorbance at



Scheme (III)

δ 169.39. Lastly, the MS spectrum of this compound shows molecular ion at m/z 275 (100%).

Thus, accordingly the reaction may follow the routes shown in scheme (III).



EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 883 spectrophotometer as KBr pellets. NMR spectra were recorded on a Jeol FX-100 (100 MHz) using TMS as an internal standard in the indicated solvents and reported in the δ (ppm) values. The MS spectra were recorded on GC ms-QP5050A Shimadzu GC-17A at the College of Science, Central Research Laboratory, King Saud University.

2-Aminoacetophenone-phenyl hydrazone (2)

To a solution of 2-aminoacetophenone (4.19 g, 0.03 mole) in 50 mL of absolute ethanol was added phenyl hydrazine (3.3 g, 0.03 mole) with 1.5 mL of AcOH. The mixture was refluxed for 3 h in a water bath. The solvent was evaporated under vacuum and the resulting solid was recrystallized from ethanol to give **2** in 85% yield; m.p. 105°C.

IR (cm^{-1}): 3399, 3288 ν(NH_2, NH), 1601 ν(C=N).

^{1}H-NMR ($CDCl_3$): δ 2.28 (s, 3H), 5.43 (s, 2H), 6.75–7.29 (Ar, 9H)

^{13}C-NMR ($CDCl_3$): 13.39, 112.94, 116.70, 116.88, 120.23, 128.21, 128.63, 129.39, 145.13, 145.31, 145.66.

MS (m/e): 225 (M^+).

N-[2-Acetylphenyl] acetamide (3): To 2-aminoacetophenone (22.5 mL, 0.18 mole) in 120 mL of AcOH, 30 mL of Ac_2O was added and the reaction mixture was then refluxed for 2 h. The mixture was poured in a little crushed ice with water. A white solid powder was precipitated. Recrystallization from warm water with a little ethanol gave **3** in 80% yield; m.p. 55°C.

IR (cm^{-1}): 3238 ν(NH), 1690, 1655 ν(CO).

^{1}H-NMR ($CDCl_3$): 2.23 (S, 3H), 2.67 (S, 3H), 7.04–7.93 (Ar, 4H) 8.69 (S, 1H).

MS (m/e): 177 (M^+).

N-(2-Acetophenone-phenyl hydrazone) acetamide (4):

First method: To a solution of 1.0 g, 0.004 mole of **(2)** in 30 mL of MeOH, 1 mL of Ac_2O was added and the mixture was under stirring for a few minutes; white solid crystals of compound **(4)** were precipitated. The yield was around 75%; m.p. 173°C.

IR (cm^{-1}): 3238 ν(NH), 1707, 1690 ν(CO), 1602 ν(C=N).

^{1}H-NMR ($CDCl_3$): δ 2.16 (S, 3H), 2.35 (S, 3H), 7.16–7.40 (Ar, 9H) 8.52 (S, 1H), 8.60 (S, 1H).

^{13}C-NMR ($CDCl_3$): 14.39, 113.12, 121.05, 121.23, 122.99, 125.34, 127.81, 128.80, 129.52, 136.04, 144.31, 144.54, 168.74.

MS: m/e 276 (M^+).

Second Method: To a solution of (1.0 g, 0.006 mole) **(3)** in 30 mL of methanol, 1.2 eq of phenyl hydrazine was added. The solution was refluxed for 4 h. The resulting solid was collected and recrystallized from ethanol. Yield 93%; m.p. 173°C.

IR, ^{1}H-NMR, ^{13}C-NMR: all same as above.

2-Methyl-4-(N-phenyl) pyrazolo-[2,3-C]-quinazoline-5-one (6)

To a solution of (0.5 g, 0.0019 mol) **(4)** in 40 mL of henzene with 1 mL of Et_3N, 1.1 eq of triphosgene (BTC) was added dropwise. The solution was kept stirring at room temperature for 3 h. The mixture was extracted with water. The solvent was evaporated and the product was precipitated by the addition of ether. m.p. 195°C.

IR (cm^{-1}): 1685, 1624, 1555, 1482, 1389 and 1352.

^{1}H-NMR ($CDCl_3$): 2.19 (S, 3H), 5.89 (S, 1H), 7.32–7.89 (Ar, 9H) ppm.

^{13}C-NMR ($CDCl_3$): 22.55 85.52, 116.94, 124.81, 125.10, 127.39, 128.39, 129.57, 132.91, 138.61, 141.25, 147.42, 150.24, 169.39.

MS m/e 275 (M^+).

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