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# Metal-Assisted Oxidative Cyclization of Arylamidrazones I. Synthesis of 3-Acetyl-1,4-dihydro-1-phenyl-1,2,4-benzotriazine

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**Summary.** In the presence of $RuCl_3$, *N*-phenylamidrazone underwent oxidative cyclization into 1,4-dihydro-1-phenyl-1,2,4-benzotriazine, the structure of which is established by spectral and X-ray diffraction data.

**Keywords.** Arylamidrazones; Ruthenium(III) chloride; Dihydro-1,2,4-benzotriazines.

## Introduction

Functionally-substituted arylamidrazones are utilized for the construction of various condensed aza-heterocycles [1, 2]. Surprisingly, the reaction of 1-(phenylamino)-1-(phenylhydrazono)-2-propanone (**2**) with ruthenium(III) chloride led to the formation of 3-acetyl-1,4-dihydro-1-phenyl-1,2,4-benzotriazine (**3**, Scheme 1), as evidenced from NMR and X-ray data (*vide infra*). This class of heterocyclic compounds is of interest generating stable dihydro-1,2,4-benzotriazinyl free radicals (**4**, Fig. 1) [3] and as non-steroidal anti-inflammatory drugs (*e.g.* azapropazone (**5**) [4], Fig. 1) used to treat various forms of arthritis.

## Results and Discussion

Addition reactions of a variety of nucleophilic species onto nitrile imines (generated *in situ* by the action of triethylamine on hydrazonyl chorides) provide direct

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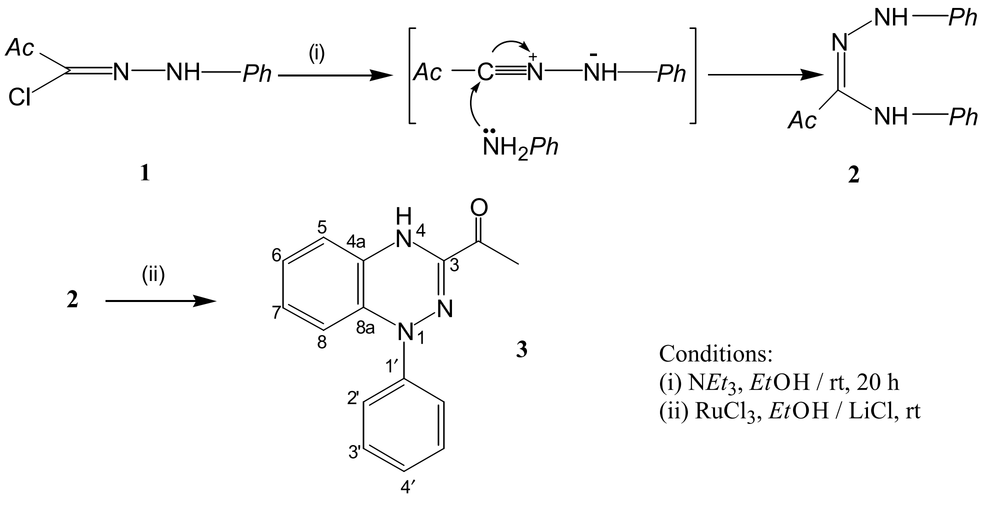

Conditions:
(i) $NEt_3$, $EtOH$ / rt, 20 h
(ii) $RuCl_3$, $EtOH$ / LiCl, rt

**Scheme 1**

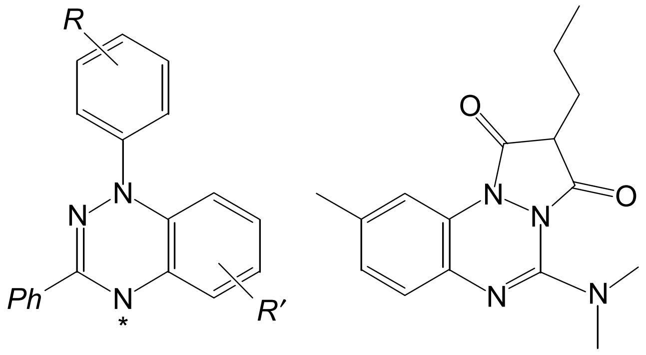

**Fig. 1.** Structures of dihydro-1,2,4-benzotriazinyl free radicals (**4**) and azapropazone (**5**)

access to diverse acyclic systems [5–7]. In this way, **2** was prepared *via* interaction of 1-phenylhydrazono-1-chloropropanone (**1**) with aniline (Scheme 1) following Ref. [8]. Direct interaction of **2** with $RuCl_3$ in ethanol gave 3-acetyl-1,4-dihydro-1-phenyl-1,2,4-benzotriazine (**3**) in 52% yield. $^1H$ and $^{13}C$ NMR spectral data and X-ray diffraction measurements confirm the assigned structure of **3** and are given in the experimental section.

In the present study, single crystal X-ray diffraction measurements for **3** were performed, and the results are listed in Tables 1 and 2 and shown in Fig. 2. The dihydrotriazine moiety comprising N1, C13, N3, N2, C6, and C1 exhibits a significant ring-puckering with a root mean square deviation of these six fitted atoms of 0.1381; the hydrogen atom positioned at N1 is 0.4957 Å out of the plane of the dihydrotriazine moiety. The half heteroring encampassing N1, C1, C6, and N2 is nearly planar to the benzo-fused ring (C1–C6) with a dihedral angle of 1.2° (0.2), while the second half heteroring (comprising N1, C13, N3, N2) shows a dihedral

**Table 1.** Summary of the crystal data and structure refinement parameters for **3**

| | |
|---|---|
| Empirical formula | $C_{15}H_{13}N_3O$ |
| Formula weight | 251.28 Da |
| Temperature/K | 293(2) |
| Wavelength/Å | 0.71073 |
| Crystal system | Monoclinic |
| Space group | $C2/c$ |
| Unit cell dimensions | |
| $a$/Å | 20.367(4) |
| $b$/Å | 17.319(4) |
| c/Å | 7.4310(15) |
| $\beta$/° | 101.37(3) |
| Volume/$Å^3$ | 2569.7(9) |
| $Z$ | 8 |
| Calculated density/g $cm^{-3}$ | 1.299 |
| Absorption coefficient/$mm^{-1}$ | 0.085 |
| $F$ (000) | 1056 |
| Theta range for data collection/° | 2.04–25.03 |
| Completeness to $\theta = 25.03°$ | 90.8% |
| Index range | $-24 \leq h \leq 24$; $-20 \leq k \leq 20$; $-8 \leq l \leq 7$ |
| Reflections collected | 8480 |
| Independent reflections | 2062 [$R_{\text{int}} = 0.0740$] |
| Weight scheme | Calcd $w = 1/[\sigma^2 (F_O)^2 + (0.0701P)^2 + 0.0000P]$ where $P = [(F_0)^2 + 2(F_c)^2]/3$ |
| Data/restraints/parameters | 2062/0/172 |
| Goodness-of-fit on $F^2$ | 0.914 |
| Final $R$ indices [$I > 2\sigma$ ($I$)] | $R_1 = 0.0734$, $wR_2 = 0.1649$ |
| $R$ Indices (all data) | $R_1 = 0.1872$, $wR_2 = 0.1991$ |
| Largest difference peak/e · $Å^{-3}$ | 0.280 |
| Largest difference hole/e · $Å^{-3}$ | −0.177 |

angle of 27.4° (0.2) with respect to the first half. In other words, there is a folding of 27.4° along the N1⋯N2 axis bisecting the dihydrotriazine ring (Fig. 1). Moreover, the dihedral angle between the two benzenoid (phenylene and phenyl) rings is 59.7° (0.1), while the dihedral angle between the plane containing the acyl carbonyl group, namely C13, C14, C15, and O1, and that of the dihydrotriazine ring is 9.9° (0.2). Currently, we are exploring the scope and generality of this one-pot metal-assisted reaction as well as the consequent mechanistic aspects, and the results will be reported in due course.

## Experimental

Rhuthenium(III) chloride and 3-chloro-2,4-pentanedione were purchased from Acros. Melting points were determined on a Gallenkamp electrothermal melting temperature apparatus. $^1H$ and $^{13}C$ NMR spectra were measured on a Bruker DPX-300 instrument with *TMS* as internal reference. EIMS spectra were obtained using a Finnigan MAT TSQ-70 spectrometer at 70 eV and an ion source temperature of 200°C. IR spectra were recorded as KBr discs on a Nicolet Impact-400 FT-IR spectrophotometer.

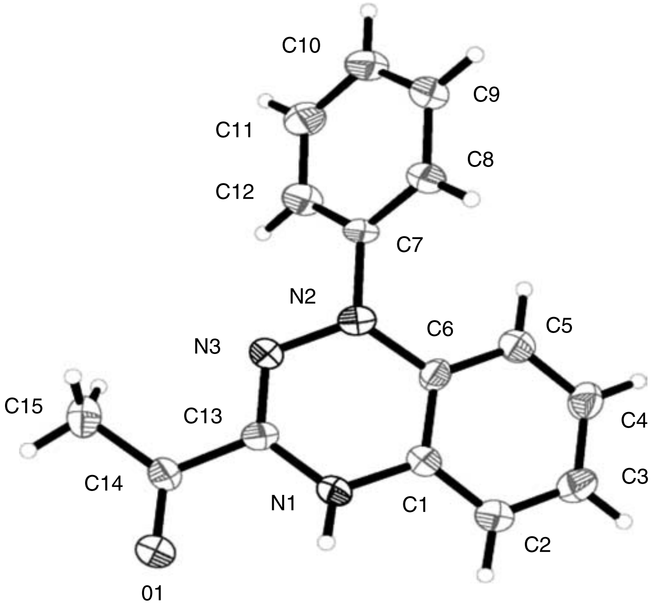

**Fig. 2.** Molecular stucture of *3-acetyl-1,4-dihydro-1-phenyl-1,2,4-benzotriazine* (**3**); thermal ellipsoids are drawn at the 50% probability level; numbering of the atoms in this ORTEP plot (and in Table 1) is arbitrary, being different from the IUPAC numbering adopted in Scheme 1

Microanalyses were performed at the Microanalytical Laboratory of the Chemistry Department of Hashemite University, Zarka-Jordan, and the results agreed with the calculated values within experimental error (±0.4%).

*1-Phenylhydrazono-1-chloropropanone* (**1**)

The hydrazonoyl chloride **1** was previously characterized and is prepared in this study *via* the *Japp–Klingemann* reaction [9] that involves direct coupling of benzenediazonium chloride with 3-chloro-2,4-pentanedione following the standard procedure [10].

*1-(Phenylamino)-1-(phenylhydrazono)-2-propanone* (**2**)

This compound is prepared *via* direct interaction of **1** with aniline in methanol in the presence of triethylamine following the procedure of Ref. [8]. Yield 94%; mp 95°C (Ref. [8] yield 96%, mp 94°C).

*3-Acetyl-1,4-dihydro-1-phenyl-1,2,4-benzotriazine* (**3**, $C_{15}H_{13}N_3O$)

A mixture of 266 mg $RuCl_3$ (1.0 mmol) and 253 mg **2** (1.0 mmol) in 200 $cm^3$ absolute ethanol was refluxed for 4 h. Then, additional 1.0 mmol **2** was added to the reaction mixture, which was further heated for 1 h. Excess LiCl (500 mg, 12 mmol) was then introduced and the reaction mixture was refluxed for l h. The solvent was evaporated *in vacuo* and the residue taken up in $CH_2Cl_2$. The resulting solution was washed with water ($3\times30\,cm^3$) to remove unreacted $RuCl_3$, dried ($MgSO_4$), and the solvent removed under reduced pressure. The residual brown solid was purified by column chromatography over alumina using $CH_2Cl_2$/acetonitrile (3/1, *v*/*v*) as eluent. Yield 52%; mp 173–174°C; $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 2.39$ (s, $CH_3$), 6.34 (m, H-5 + H-8 + NH), 6.61 (dd, $J = 7.3$, 7.4 Hz, H-7), 6.71 (dd, $J = 7.3$, 7.4 Hz, H-6), 7.19 (tt, $J = 2.0$, 6.7 Hz, H-4′), 7.41 (m, H-2′, H-6′, H-3′, H-5′); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta = 23.6$ ($CH_3$), 112.6 (C-8), 113.7 (C-5), 122.9 (C-2′ + C-6′), 123.8 (C-7), 124.6 (C-6), 125.3 (C-4′), 129.2 (C-3′ + C-5′), 132.8 (C-1′), 142.9 (C-8a), 143.5 (C-4a), 149.6 (C-3), 191.3 (C=O); MS (EI, 70 eV): $m/z$ (%) = 250 (100) [$M^+$-1], 208 (65) [$M^+$-O=$CCH_3$], 181 (18) [$M^+$-1-N=C–C(O)$CH_3$].

*Crystal Structure Determination of* ***3***

Crystals (brown, parallelpiped) were obtained by allowing a hot solution of **3** in ethanol/$H_2O$ (5/1, *v*/*v*) to stand at rt for 4–5 d (crystal dimensions: $0.30 \times 0.20 \times 0.05\,mm^3$). Crystal data collection was made on a Rigaku MSC Mercury CCD diffractometer using graphite-monochromated Mo–K$\alpha$ radiation. Data collection and reduction were performed using Crystal Clear 1.3.5 [11] and Crystal Structure 2.00 [12]. The data were then transferred *via* interface command to SHELXTL [13] and solved by direct phasing using SHELXS [14] and refined using SHELXL [15]. Graphics and calculations were performed by SHELXP, and Table 1 was generated using SHELXCIF. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares procedure based on $F^2$ using all unique data. The hydrogen atoms were placed geometrically and then refined isotropically using a 'riding model' with $U_{iso}$ constrained to be 1.2 $U_{eq}$ of the carrier atom. Crystallographic data for the structural analysis of **3** have been deposited with the Cambridge Crystallographic Data Center under the depository no. CCDC – 275956. Copies of further information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk, or http://www.ccdc.cam.ac.uk).

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