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Metalation of 2-Methyl-*N*-phenylbenzamide with *n*-Butyllithium. Formation of *N*,3-Diphenyl-1-isoquinolinamine by Subsequent Reaction with Benzonitrile

Short Communication

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2-Methyl-*N*-phenylbenzamide was metalated with two equivalents of *n*-butyllithium. Benzonitrile was allowed to react with the organometalic intermediate thus formed to yield *N*,3-diphenyl-1-isoquinolinamine.

(Keywords: Benzamide, iminophenylethyl-phenyl; Cyclodehydration; Isoquinolinamine, diphenyl; Lithiation)

Metallierung von 2-Methyl-N-Phenyl-benzamid mit n-Butyllithium und Bildung von N,3-Diphenyl-1-isochinolinamin durch anschließende Reaktion mit Benzonitril

Reaktion von Benzonitril mit der Di-Lithiumverbindung aus 2-Methyl-*N*-phenylbenzamid und 2 mol *n*-Butyllithium liefert *N*,3-Diphenyl-1-isochinolinamin.

In order to determine if 1,2-dihydro-2,3-diphenyl-1-isoquinolinone (**1**) was among the products resulting from the thermally induced intramolecular cycloaddition reaction of *N*-phenyl-2-phenylethylbenzamide (**2**)[1], synthetic routes to **1** were investigated. In this connection, synthesis via directed metalation of benzamides appeared to be applicable[2,3].

Metalation of 2-methyl-*N*-phenylbenzamide (**3**) in anhydrous tetrahydrofuran (*THF*) with two equivalents of *n*-butyllithium gave *N*-lithio-2-lithiomethyl-*N*-phenylbenzamide (**4**). The dimetalated species

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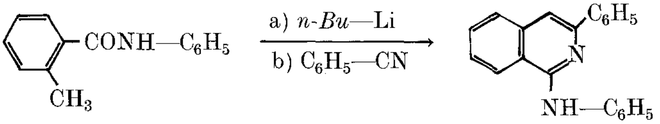
4 was expected to react with benzonitrile to give 2-(2-oxo-2-phenylethyl)-*N*-phenylbenzamide (**5**) after hydrolysis with aqueous acid. Compound **5** was then expected to undergo an acid catalyzed cyclodehydration reaction to yield **1**.

Indeed, metalation of 2-methyl-*N*-phenylbenzenesulfonamide (**6**) in anhydrous *THF* with two equivalents of *n*-butyllithium and subsequent reaction of the dilithio intermediate with benzonitrile gives 2,3-diphenyl-2*H*-1,2-benzothiazin-1,1-dioxide (**7**) after hydrolysis followed by cyclodehydration[2].

However, the product of the reaction of **4** with benzonitrile was shown to be *N*-3-diphenyl-1-isoquinolinamine (**8**). Apparently, instead of undergoing hydrolysis, the expected imino compound which resulted from the addition of **4** to benzonitrile, enaminized efficiently, and cyclodehydration occurred by addition of the enamine nitrogen to the carbon atom of the amide carbonyl function. No other reaction product was present.



3 **8**

The nitrogen atom of benzanilide has been shown to be an efficient nucleophile for intramolecular addition to imine functions. For example, *ortho*metalated benzanilide condensed with benzonitrile to form the imine carboxamide which equilibriated in favour of the corresponding cyclic amine carboxamide[2]. In this case, however, enaminization of the imino group cannot take place. In the case of the addition product of dimetalated **6** and benzonitrile, the imino compound formed could enaminize. The sulfonamide moiety, however, contained no good leaving group, and therefore the imino group was hydrolyzed.

The desired compound **1** was obtained by the reaction of *N*-phenylbenzimidoyl chloride and 3,4-dihydro-1*H*-2-benzopyran-1,3-dione (homophthalic anhydride) in refluxing chlorobenzene[1].

Experimental

Spectrometers Used: Varian EM360A 60 MHz ^1H NMR spectrometer (chemical shifts are given in ppm from internal *TMS*); Beckman 1R 33 spectrophotometer; Du Pont 21-490 chemical ionization mass spectrometer (ionizing voltage 70 eV, source temperature 200°, sample temperature given, methane as ionizing gas).

2-Methyl-N-phenylbenzamide (**3**) was made by the reaction of two equivalents of aniline with one equivalent of *o*-toluoyl chloride in anhydrous ether, at room temperature, under nitrogen in 100% yield; mp. 126–126.5° (from CH_2Cl_2-petrol ether); Lit.[4] 125–126°.

^1H NMR ($CDCl_3$): 2.5 (s, 3), 6.6–8.3 (m, 10).

N,3-Diphenyl-1-isoquinolinamine (**8**)

Under nitrogen, *n*-butyllithium (31.2 mmol, 18.5 ml of a 1.69 *M* solution in hexane) was added dropwise to a cold (ice bath), stirred solution of 2-methyl-*N*-phenylbenzamide (3.0 g, 14.2 mmol) in 40 ml of anhydrous *THF*. Addition of *n*-butyllithium beyond the first equivalent caused the solution to turn deep red (dianion formation). After the completion of the addition of butyllithium, stirring was continued for 0.5 h (ice bath). The red color of the dianion was then discharged by the dropwise addition of benzonitrile (1.6 ml, 15.7 mmol) in 10 ml of anhydrous *THF*. The cooling bath was then removed and the contents of the reaction vessel was stirred overnight under nitrogen at room temperature.

Water (100 ml) was added to the reaction flask and the water layer was neutralized by the dropwise addition of conc. HCl. The reaction mixture was extracted with methylene chloride (2 × 100 ml), and the combined organic phase was washed with water and dried ($MgSO_4$). The crude solid obtained on evaporation of the organic layer was taken up in methanol (100 ml). Concentrated HCl (20 ml) was then added and the solution was refluxed for 2 h. Work up as before by extraction with methylene chloride yielded 3.38 g of an off-white solid which was adsorbed on to 30 g of silica gel and then chromatographed on 270 g of the adsorbent. Elution with 20% methylene chloride in petroleum ether (bp. 38.4–55.2°) yielded a white solid (0.25 g, mp. 232.5–233.5°) from the initial fractions which was identified as 2,4,6-triphenyl-1,3,5-triazine, resulting from the trimerization of unreacted benzonitrile. The identification was based on comparison of the infrared spectrum of this substance with that of a published spectrum[5], and on mass spectral data:

MS (180°): 339 (4), 338 (24.5, *M* + 29), 324 (4, *M* + 15), 312 (2), 311 (24.5), 310 (100, *M*), 309 (22.4), 221 (2), 194 (6.1), 193 (67.3), 192 (8.2), 103 (12.2), 104 (2), 108 (2).

8 was then eluted as a white solid. The initial fraction (0.1 g, softened at 97°, mp. 117.5–118.5°) was discolored yellow due to trace impurities [undetectable by thin layer chromatography (TLC)]. The later fractions gave 1.4 g of white crystals (mp. 118.5–119.5°), the melting point of which did not change on recrystallization from methylene chloride-petroleum ether. The total yield was 50% based on 2-methyl-*N*-phenylbenzamide consumed. Calc. for $C_{21}H_{16}N_2$: C 85.10; H 5.44; N 9.45. Found: C 84.81; H 5.20; N 9.98.

^1H NMR ($CDCl_3$): 7–8.9 (m).

MS (200°): 326 (trace); 325 (20, *M* + 29), 298 (28), 297 (100, *M* + 1), 296 (52, *M*), 295 (12).

After most of the product had been eluted, elution with methylene chloride gave unreacted 2-methyl-*N*-phenylbenzamide (**3**), contaminated with **8** (TLC).

TLC of the crude product on silica gel (50% methylene chloride in petroleum ether) indicated the presence of only three components, 2,4,6-triphenyl-1,3,5-triazine (*Rf* = 0.8), **8** (*Rf* = 0.3), and **3** (*Rf* = 0.1).

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References

[1] *Abraham T.*, J. Polym. Sci., Polym. Chem. Ed., to be published.

[2] *Watanabe H.*, *Mao C.-L.*, *Barnish I. T.*, *Hauser C. R.*, J. Org. Chem. **34**, 919 (1969).

[3] *Iwao M.*, *Watanabe M.*, *de Silva S. O.*, *Snieckus V.*, Tetrahedron Lett. **22**, 2349 (1981).

[4] *Smith P. A. S.*, *Antoniades E. P.*, Tetrahedron **9**, 210 (1960).

[5] Sadtler Research Laboratories, Inc., grating infrared spectrum 31570 K (1974).