

REACTION OF 1,2-DIPHENYL-1-AZASPIRO[2.2]PENTANE WITH C,N-DIPHENYLNITRONE¹

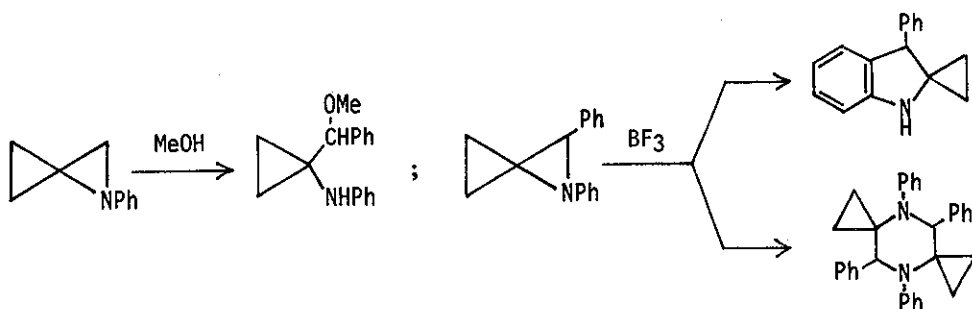
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The reaction of 1,2-diphenyl-1-azaspiro[2.2]pentane (1) with C,N-diphenylnitrone (2) has been investigated under various conditions. Azaspiropentane 1 reacts with 2 to give the 1:1 adduct 3, tetrahydro-1H-1,3-benzodiazepin-4-one compound 4, and/or its ring opening isomer 5, whose relative yields depended on the nature of solvents employed. The reaction pathways are also described.

It has been reported that the highly strained azaspiro[2.2]pentane structure is susceptible to rupture of the peripheral C-N bond as illustrated below.^{2,3}

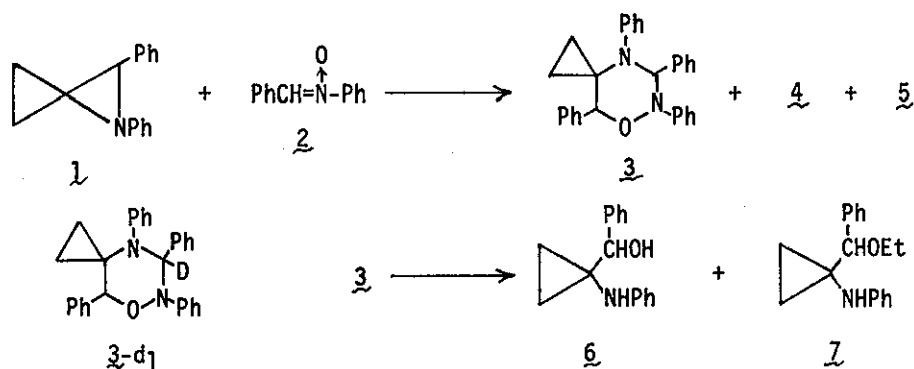


In this communication we wish to report on the capture of reactive

species generated from 1,2-diphenyl-1-azaspiro[2.2]pentane (1) by C,N-diphenylnitrone (2).

When a benzene solution of azaspiropentane 1 was refluxed with nitrone 2 under nitrogen, three crystalline products, 3, 4, and 5, were obtained together with tarry materials. On the basis of its spectral data and chemical conversion, the 1:1 adduct 3 was assigned to be 4,5,6,8-tetraphenyl-7-oxa-4,6-diaza[2.5]octane, whose structure corresponds to a [3 + 3] cycloadduct of a species generated from the peripheral C-N bond fission of 1 to 2. The reaction of 1 with C,N-diphenylnitrone- d_1 ⁴ afforded the 1:1 adduct 3- d_1 .

3: Mp 179-180°C, colorless prisms; ir (KBr) 1600, 1580, 1490 cm^{-1} ; ^1H -nmr (CDCl_3) δ 0.3-0.5 (4H, m, cyclopropyl CH_2), 5.9, 6.9 (each 1H, s, $\geq\text{CH}$), 6.7-8.0 (20H, m, ArH); MS m/e 418 (M^+), 221 ($\text{M}^+ - \underline{2}$, base peak).⁵ The singlet at δ 6.9 does not appear in the nmr spectrum of 3- d_1 .



Scheme 1

Hydrolysis of 3 with hydrochloric acid in ethanol afforded a mixture of 1-anilino-1- α -hydroxybenzylcyclopropane (6)³ and 1-anilino-1- α -ethoxybenzylcyclopropane (7).

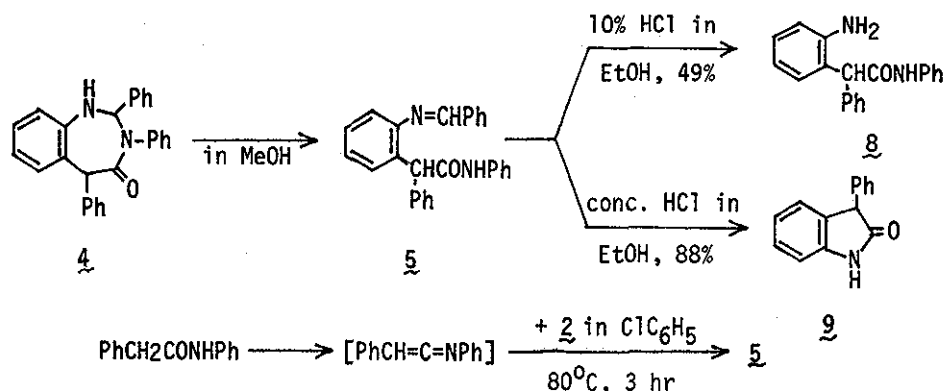
On the other hand, the molecular formulas of two isomeric products, 4 and 5, agreed with that of the compound derived from an 1:1 adduct with the elimi-

nation of ethylene. On heating in methanol 4 readily isomerized to 5.

Recently, Crandall and Conover² reported that refluxing a benzene solution of 1-phenyl-1-azaspiro[2.2]pentane for 48 hr gave 20% conversion of the azaspiropentane to a 50:50 mixture of cyclobutanone anil and N-phenylketenimine. The ketenimine corresponds to the compound derived from the azaspiropentane with the elimination of ethylene. Therefore, 4 and its isomer 5 may be considered as arising from the reaction of 2 with C,N-diphenylketenimine which would be generated from 1. In fact, C,N-diphenylketenimine, generated in situ from phenylacetanilide,⁶ reacted with 2 to give 5 in 60% yield; no 4 was isolated because of isomerization of 4 to 5 under the reaction conditions.

On the basis of their spectral data and chemical transformations, 4 and 5 were assigned to be 2,3,4,5-tetrahydro-2,3,5-triphenyl-1H-1,3-benzodiazepin-4-one and (o-benzylideneaminophenyl)phenylacetanilide, respectively.

4: Mp 156-157°C, colorless needles; ir (KBr) 3340 (NH), 1640 cm^{-1} (C=O); ¹H-nmr (pyridine-d₅) δ 5.18 (1H, s, $\geq\text{CH}$), 6.5-7.8 (21H, m, $\geq\text{CH}$, NH, and ArH); ¹³C-nmr (pyridine-d₅) δ 61.2 (C-5), 70.3 (C-2), 118.5, 119.3, 127.2, 128.1, 128.4, 128.7, 129.2, 129.5, 130.3, 136.8, 140.0, 142.5, 146.3 (aromatic C), 172.3 (C-4); MS m/e 390 (M^+), 271 ($\text{M}^+ - \text{PhNCO}$, base peak).



Scheme 2

5: Mp 165-167°C, colorless needles; ir (KBr) 3340 (NH), 1670 (C=O), 1625 cm^{-1} (C=N); ^1H -nmr (CDCl_3) δ 5.58 (1H, s, =CH), 6.9-7.6 (17H, m, ArH), 7.62-7.88 (2H, m, ArH), 8.29 (1H, s, N=CH), 8.63 (1H, br, NH); ^{13}C -nmr (CDCl_3) δ 56.3 (methine C), 118.1, 119.5, 123.8, 126.6, 126.8, 128.4, 128.7, 129.9, 131.6, 133.8, 135.7, 138.2, 138.9, 149.4 (aromatic C), 160.3 (azomethine C), 170.5 (carbonyl C); MS m/e 390 (M^+), 271 (base peak).

Hydrolysis of 5 with 10% aqueous or conc. hydrochloric acid in ethanol gave (o-aminophenyl)phenylacetanilide (8) or 3-phenyloxindole (9), mp 190-192°C (lit.⁷ mp 191°C), respectively (Scheme 2).

8: Mp 195-196°C, colorless needles; ir (KBr) 3460, 3360 (NH_2), 3300 (NH), 1650 cm^{-1} (C=O); ^1H -nmr ($\text{DMSO}-d_6$) δ 4.8 (2H, br, NH_2), 5.13 (1H, s, =CH), 6.38-7.76 (14H, m, ArH), 10.25 (1H, br, NH); MS m/e 302 (M^+), 284, 210 ($\text{M}^+ - \text{PhNH}$), 182 ($\text{M}^+ - \text{PhNHCO}$, base peak).

The results of the reaction of 1 with 2 in various solvents are summarized in Table 1.

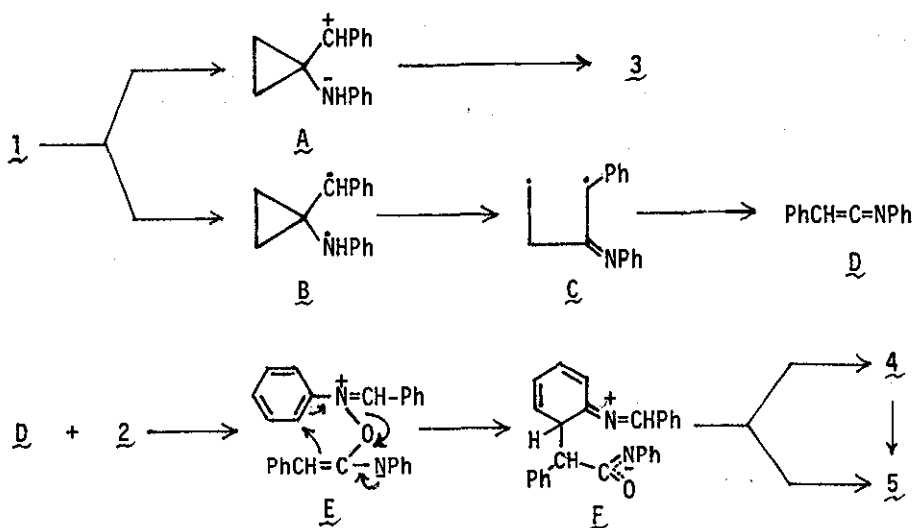
Table 1

Solvent			Products, %		
	Bp, °C	Dielectric constant	<u>3</u>	<u>4</u>	<u>5</u>
Cyclohexane	80.7	2.02	7.3	9.0	8.4
Benzene	80.1	2.28	11.4	8.7	7.2
Acetonitrile	81.6	37.5	29.4	-	7.2
Chloroform	61.7	4.81	37.2	-	-
Toluene	110.3	2.38	-	-	29.0

A solution of equimolar amounts of 1 and 2 in the solvent cited above was refluxed for 3 hr under nitrogen.

As is shown in Table 1, 3 is favorably formed in polar and lower boiling solvents, whereas the yield of 5 reverses the situation.

On the basis of the above observations and of the reported pathway for the formation of N-phenylketenimine from 1-phenyl-1-azaspiro[2.2]pentane², the pathways for the formation of products, 3-5, are outlined in Scheme 3. The heterolytic or homolytic rupture of the peripheral C-N bond of 1 yields dipolar species A or biradical B. The heterolytic rupture would be favorable in polar and lower boiling solvents, and A reacts with 2 to give 3. Ring opening of B generates new biradical C, which can lead to ketenimine D by bond fission of the 1,4-biradical moiety.



Scheme 3

Although a few reactions of N-arylketenimines with 2 have been reported in the literature,^{8,9} compounds of types 4 and 5 have not been obtained. However, it is known that the reactions of ketenes with N-arylnitrones in general give iminocarboxylic acids and oxindoles, by a reaction sequence which involves attack on the N-aryl group.¹⁰ The reaction of C,N-diphenyl-

ketenimine D with 2 proceeds in a similar manner as above. Thus, 2 reacts with D to form zwitterion E, and the subsequent attack on the N-phenyl group yields new zwitterion F. Ring closure of F with concurrent hydrogen transfer gives 4, whereas hydrogen transfer of F produces 5 directly, which is also formed via ring opening of 4 with hydrogen transfer.

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