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

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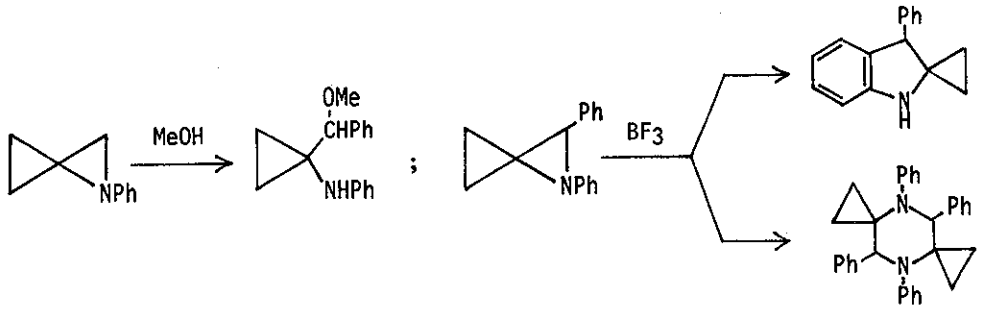
The reaction of 1,2-diphenyl-1-azaspiro[2.2]pentane (1) with C,N-diphenylnitrone (2) has been investigated under various conditions. Azaspiropentane 1 reacts with 2 to give the 1:1 adduct 3, tetrahydro-1H-1,3-benzodiazepin-4-one compound 4, and/or its ring opening isomer 5, whose relative yields depended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

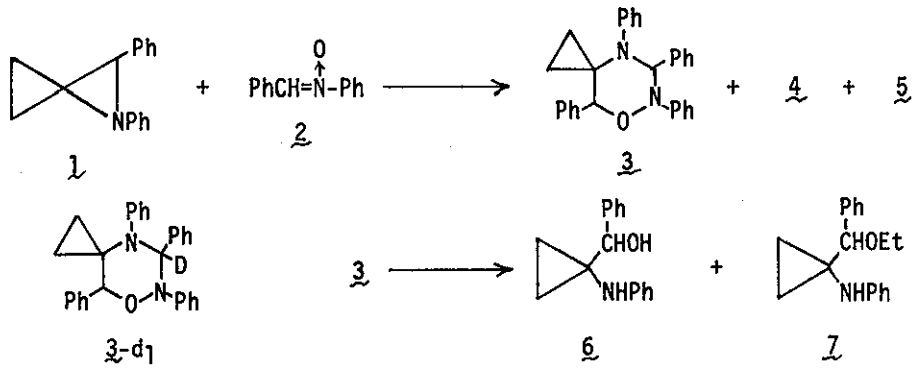


In this communication we wish to report on the capture of reactive

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}; ^{1}H-nmr ($CDCl_3$) δ 0.3-0.5 (4H, m, cyclopropyl CH_2), 5.9, 6.9 (each 1H, s, >CH), 6.7-8.0 (20H, m, ArH); MS m/e 418 (M^+), 221 (M^+ - 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).

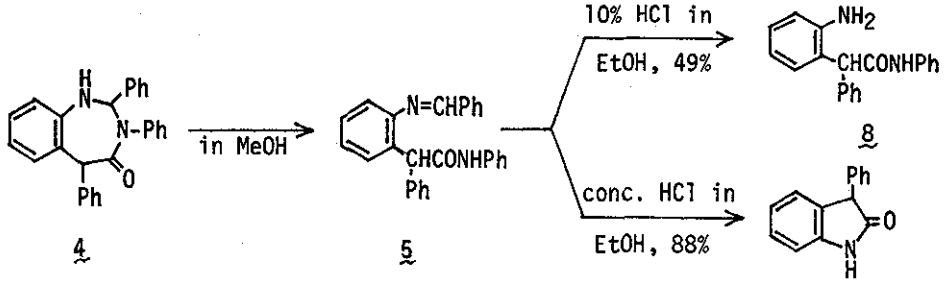
On the other hand, the molecular formulas of two isomeric products, 4 and 5, agreed with that of the compound derived from an 1:1 adduct with the elimi-

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

Recently, Crandall and Conover[2] 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); ^{1}H-nmr (pyridine-d_5) δ 5.18 (1H, s, ≥CH), 6.5-7.8 (21H, m, ≥CH, NH, and ArH); ^{13}C-nmr (pyridine-d_5) 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 (M^+ - PhNCO, base peak).



Scheme 2

5: Mp 165-167°C, colorless needles; ir (KBr) 3340 (NH), 1670 (C=O), 1625 cm^{-1} (C=N); ^{1}H-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); ^{1}H-nmr (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 (M^+ - PhNH), 182 (M^+ - PhNHCO, base peak).

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

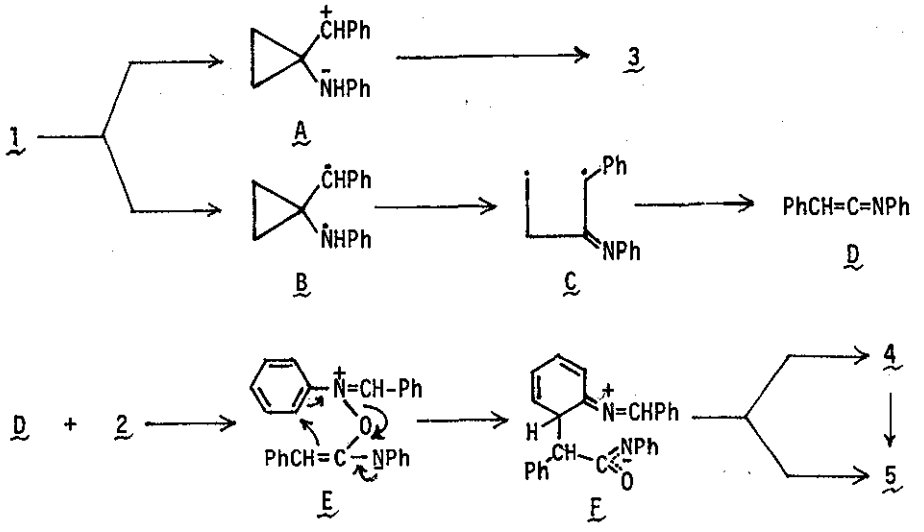
Table 1

Solvent			Products, %		
	Bp, °C	Dielectric constant	3	4	5
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]pentane[2], 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 trnasfer gives 4, whereas hydrogen transfer of F produces 5 directly, which is also formed via ring opening of 4 with hydrogen transfer.

REFERENCES

1. Studies of Highly Strained Heterocycles. Part II. Part I of this series: O. Tsuge and H. Watanabe, Heterocycles, 1976, 4, 1905.
2. J. Crandall and W. W. Conover, J. Org. Chem., 1974, 39, 63.
3. O. Tsuge and H. Watanabe, Heterocycles, 1976, 4, 1905.
4. C,N-Diphenylnitrone-d1 was prepared from phenylhydroxylamine and benzaldehyde-d1 which was prepared from phenylglyoxylic acid azine with D_2O.
5. All compounds gave satisfactory analytical values.
6. H. J. Bestmann, J. Lienert, and L. Mott, Liebigs Ann. Chem., 1968, 718, 24.
7. J. M. Bruce and F. K. Sutcliffe, J. Chem. Soc., 1957, 4789.
8. N. Murai, M. Komatsu, Y. Ohshiro, and T. Agawa, J. Org. Chem., 1977, 42, 448.
9. D. P. Del'tsova, N. P. Gambaryan, and I. L. Knunyants, Dokl. Akad. Nauk SSSR, 1972, 206, 620. Chem. Abstr., 1973, 78, 15959.
10. R. N. Pratt, D. P. Stokes, G. A. Taylor, and P. C. Brookes, J. Chem. Soc. (C), 1968, 2086.

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