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PHOTOCHEMISTRY OF QUINONE DIAZIDES. INTRAMOLECULAR OXYGEN TRANSFER AND CARBENOID ADDITION DURING PHOTOLYSIS OF N-ALLYLSULFONAMIDO QUINONE DIAZIDES

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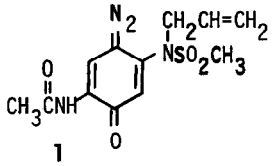
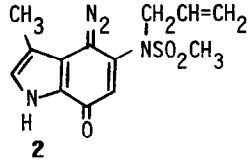
Summary: An indole quinone diazide, 5-(N-allylsulfonamido)-4-diazo-3-methyl-4,-7-dihydroindol-7-one, which is a potential precursor of a spiro-cyclopropane-indol-7-one structure has been prepared. A study of its photolysis and that of a model compound has identified oxygen transfer from the sulfonamido substituent as a process which competes with intramolecular carbenoid addition.

We have been investigating the indole quinone diazide 2 as a precursor of the spiro-cyclopropane-indol-7-one ring found in the anti-tumor antibiotic CC-1065.[1,2,3] In this letter we describe the synthesis of 2 and the model compound 1 and report on the photolysis of both compounds.



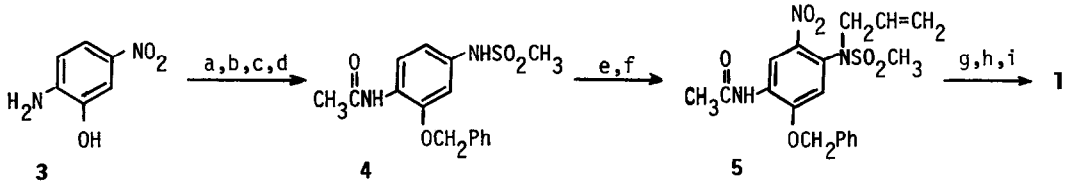
1



2

Compound 1 was prepared by the reaction sequence in Scheme I. A key step is the efficient regioselective nitration in step e. Debenzylation of 5 occurred cleanly with boron tribromide to give the expected nitrophenol which was reduced and then converted to the quinone diazide 1 using conditions described by Kraus.[4] NMR confirmed the quinone diazide structure, revealing aromatic protons at 6.47 and 8.53 ppm as singlets. The MW was 310 by mass spectrometry.

SCHEME I.

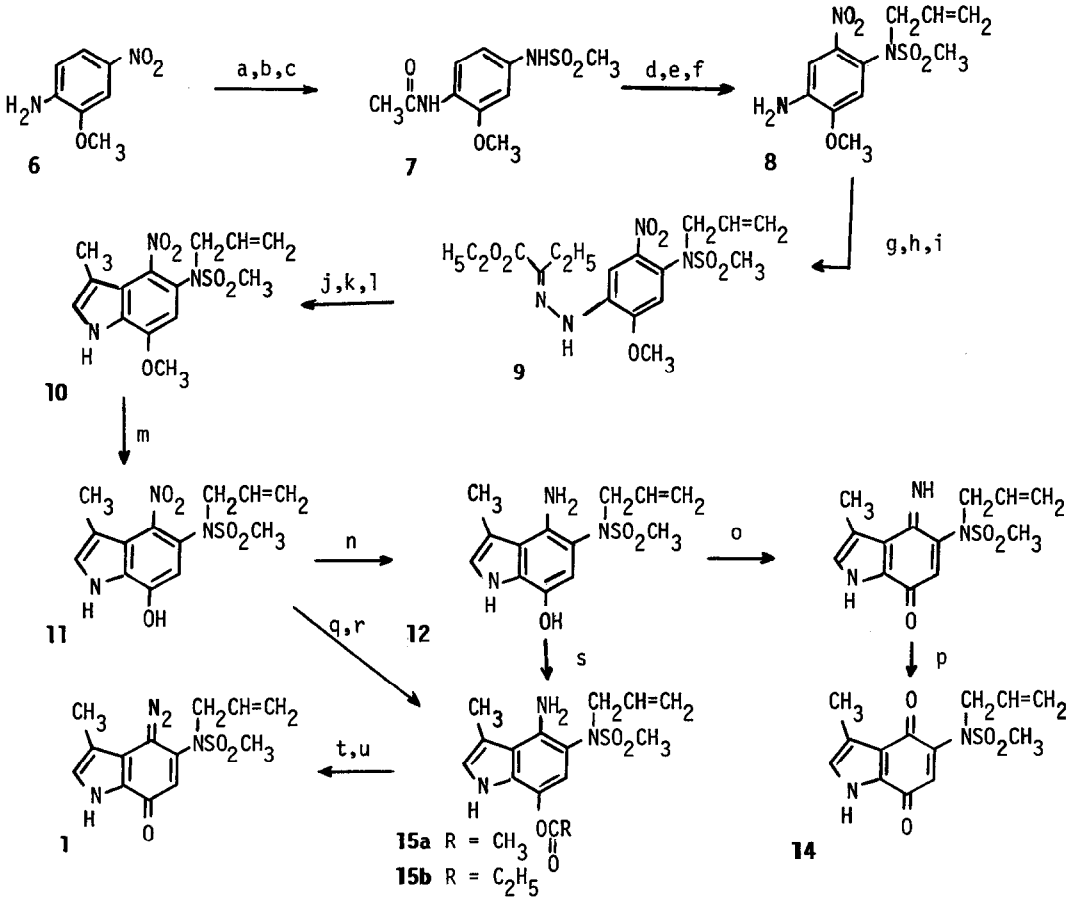


3 4 5

a: AcCl, pyridine then H_2O, K_2CO_3; b: K_2CO_3, KI, $PhCH_2Cl$; c: Zn, EtOH (Ref 5); d: CH_3SO_2Cl, pyridine; e: HNO_3, $Hg(OAc)_2$, Ac_2O (Ref 6); f: $KOC(CH_3)_3$, $BrCH_2CH{=}CH_2$, DMF; g: BBr_3; h: Zn, EtOH; i: MeOH, HCl, i-$C_5H_{11}ONO$ (Ref 4).

Compound 11, a properly functionalized indole precursor of 2 was prepared as shown in Scheme II. The early stages of the synthesis parallel those in Scheme I. After hydrolysis of the acetamide in step f, a Japp-Klingeman coupling and Fischer indole cyclization are carried out in steps g-j. The product of the Japp-Klingeman coupling is obtained as an azo compound and deacetylation must be carried out in separate step using sodium carbonate in step i.[7] Of various Fischer cyclization conditions which were tried, the best results were obtained using trifluoroacetic acid in toluene. These conditions were adapted from the report of Danishefsky and Phillips[8] in which these conditions were found advantageous in a mechanistically related aza-Claissen rearrangement. Steps k and l effect removal of the carboethoxy group by hydrolysis and decarboxylation. Demethylation was achieved by heating 10 with lithium thiophenoxide in HMPA. The overall yield of 11 from 6 is about 5%.

SCHEME II.

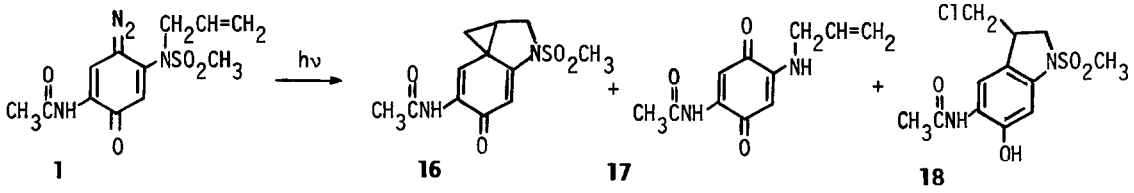


a: AcCl, pyridine; b: H_2, Pd-C; c: CH_3SO_2Cl, pyridine; d: HNO_3, $Hg(OAc)_2$, HOAc, Ac_2O (Ref 4); e: $KOC(CH_3)_3$, $CH_2{=}CHCH_2Br$, DMF; f: H_2O, NaOH, EtOH; g: $NaNO_2$, HCl; h: $CH_3COCH(C_2H_5)CO_2C_2H_5$, KOH; i: Na_2CO_3, EtOH; j: CF_3CO_2H, toluene (Ref 8); k: H_2O, NaOH; l: CuO, $AcNMe_2$; m: PhSLi, HMPA; n: Zn, EtOH; o: i-$C_5H_{11}ONO$ or $ONOSO_3H$; p: H^+, H_2O; q: EtO_2CCl; r: Zn, EtOH; s: $CF_3CO_2OCCH_3$ (Ref 9); t: i-$C_5H_{11}ONO$; u: $NaHCO_3$, H_2O.

Compound 11 was reduced to the 4-amino-7-hydroxyindole 12 using Zn. The N,O-diacetyl derivative of 12 was characterized. Diazotization of 12 with either isoamyl nitrite or nitrosylsulfuric acid under a variety of conditions led primarily to the quinone imine 13 which was identified by spectral data; NMR at 360 MHz; 2.39 (s, 3H), 3.16 (s, 3H), 4.21 (br s, 2H), 5.22 (d, J = 9, 1H), 5.23 (d, J = 18, 1H), 5.75-5.91 (m, 1H), 6.47 (br s, 1H), 6.09 (d, J = 2, 1H) and 9.63 (br s, 1H) ppm; MW 293 by mass spectrometry. It was also hydrolyzed to the quinone 14. The formation of the imine must occur either by an oxidation or by an unusual 1,6-elimination at the stage of the N-nitrosoamine intermediate.

Quinone diazide 2 was obtained from derivatives of 12 which were acylated at oxygen. The acetyl derivative 15a was obtained by reaction of the hydrochloride of 12 with acetic-trifluoroacetic mixed anhydride.[9] The carbonate 15b was obtained by conversion of 11 to the ethyl carbonate ester with ethyl chloroformate and then reducing with zinc in ethanol. Both 15a and 15b were converted to 2 by reaction with isoamyl nitrite followed by exposure to aqueous sodium carbonate. Unstable acyloxydiazonium species are presumed to be intermediates. Spectroscopic data were in accord with the assigned structure; NMR at 360 MHz: 2.27 (s, 3H), 3.05 (s, 3H), 4.25 (br s, 2H), 5.24 (d, J = 10, 1H), 5.27 (d, J = 18, 1H), 5.74-5.90 (m, 1H), 6.35 (s, 1H), 7.07 (br s, 1H); IR in KBr: 2105 cm^{-1}; UV_{max} 380 nm; MW 306 by mass spectrometry. These transformations are summarized in Scheme II.

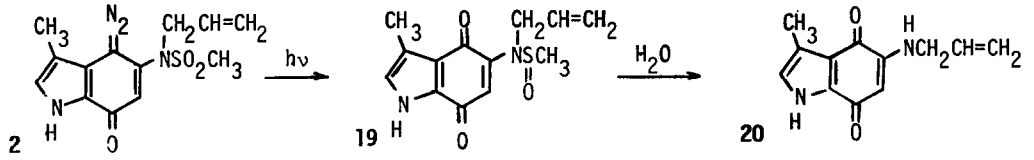
Photolysis of 1 in methylene chloride with light filtered through $CuSO_4$ and $NaNO_2$ gave two major products 16 and 17 and variable small amounts of a third product 18. The spiro-cyclopropane-cyclohexadienone 16 exhibited upfield signals charactreristic of the cyclopropane ring; NMR at 360 MHz: 1.50 (t, J = 5.4, 1H), 1.86 (d of d, J = 7.9, 5.4, 1H), 2.17 (s, 3H), 2.64-2.72 (m, 1H), 3.06 (s, 3H), 3.97 (d of d, J = 10, 5.4, 1H), 4.09 (d, J = 10, 1H), 6.42 (s, 1H), 7.48 (s, 1H), 8.35 (br s, 1H); MW 282 by mass spectrometry. This product accounted for 40-50% of the starting material. Minor product 18 was tentatively identified on the basis of spectroscopic data; NMR at 360 MHz: 2.26 (s, 3H), 2.92 (s, 3H), 3.57-3.75 (m, 3H), 3.95 (d of d, J = 11, 4, 1H), 4.03-4.13 (m, 1H), 7.08 (s, 1H), 7.43 (br s, 1H), 8.26 (br s, 1H); MW 318/320 (Cl isotope pattern) by mass spectrometry. The second major product 17 was identified on the basis of spectrtoscopic data: NMR at 360 MHz: 2.24 (s, 3H); 3.80 (t, J = 6, 2H), 5.25-5.34 (m, 2H), 5.44 (s, 1H), 5.78-5.91 (m, 1H), 6.28 (br s, 1H), 7.37 (s, 1H), 8.59 (br s, 1H); MW 220 by mass spectrometry.



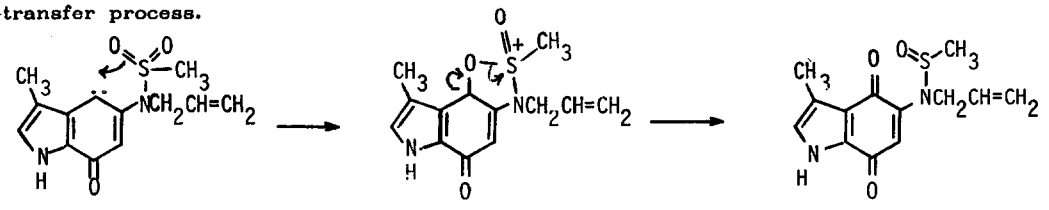
1 16 17 18

Photolysis of 2 under similar conditions gave mainly 20 after workup and no spiro-cyclopropane-indol-7-one was detected. In experiments done with rigorous exclusion of oxygen and moisture the sulfinamido quinone 19 was identified as an intermediate by NMR spectroscopy; NMR at 360 MHz: 2.23 (s, 3H), 2.93 (s, 3H), 3.78, 4.58 (AB quartet, J = 18, each doublet is further split, 3.78 d of d, J = 4, 4.58 d of m, J ~ 2, 2H), 5.21-5.30 (m, 2H), 5.73 (s, 1H), 5.69-5.88 (br m, 1H), 6.77 (br s, 1H), 9.68 (br s, 1H). Purification by chromatography

resulted in the isolation of **20**. The spectral data and transformation to **20** permit assignment structure **19** to the initial photolysis product. In particular, the nonequivalence of the two protons of the allyl methylene group, provides direct evidence for the presence of the chiral sulfinamide group. An alternative explanation of the nonequivalence based on hindered rotation of the allyl group is eliminated by the fact that the structurally similar N-allylsulfonamido quinone **14** displays a sharp doublet for the methylene protons. The facile hydrolysis to **20** is consistent with the known chemistry of sulfinamides.[10]



The formation of **17** from **1** and **20** from **2** is assumed to result from an intramolecular oxygen-transfer process.



The occurrence of the oxygen transfer reaction to the exclusion of carbenoid addition in the case of **2** is surprising in view of the observation of the desired cyclopropanation with the model compound **1**. Although models do not indicate severe steric hindrance, the 3-methyl group in **2** may bias the conformation of the N-allylsulfonamido substituent sufficiently to disfavor the addition reaction.

REFERENCES

1. Structure of CC-1065: Chidester, C. G.; Krueger, W. C.; Mizsak, S. A.; Duchamp, D. J.; Martin, D. G. J. Am. Chem. Soc. **1981**, 103, 7629.
2. Previous syntheses of Ring A: Wierenga, W. J. Am. Chem. Soc. **1981**, **103**, 5621; Magnus, P.; Gallagher, T. J. Chem. Soc. Chem. Commun. **1984**, 389; Kraus, G. A.; Yue, S.; Sy, J. J. Org. Chem. **1985**, 50, 283.
3. Sundberg, R. J.; Nishiguchi, T. Tetrahedron Lett. **1983**, 24, 4773.
4. Kraus, G. A.; Nagy, J. O.; DeLano, J. Tetrahedron, **1985**, 41, 2337.
5. Kuhn, W. E. Org. Synth., Coll. Vol. II, **1943**, 447.
6. Stock, L. M.; Wright, T. L. J. Org. Chem. **1977**, 42, 2875.
7. Parmerter, S. M., Org. Reactions, **1959**, 10, 2.
8. Danishefsky, S.; Phillilps, G. B. Tetrahedron Lett. **1984**, 25, 3159.
9. Wolfe, S.; Kazmaier, P. M. Can. J. Chem. **1979**, 57, 2388.
10. Andersen, K. K., "Sulfinic Acids and Their Derivatives," in "Comprehensive Organic Chemistry," Vol. 3, D. N. Jones, ed., Pergamon Press, Oxford, 1979, p. 326.

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