Journal of Labelled Compounds and Radiopharmaceuticals—Vol. XXVIII, No. 11

PREPARATION OF CARBAZOLE-3,6-d_2 and CARBAZOLE-1,3,6,8-d_4

Arthur Chestand, Ling Yang, and Robert I. Walter*
Chemistry Department
University of Illinois at Chicago
P.O. Box 4348, Chicago, Illinois 60680

SUMMARY

Carbazole-3,6-d_2 and carbazole-1,3,6,8-d_4 were prepared by reduction of the corresponding di- and tetrabromocarbazoles in alkaline ethanol with deuterium gas and Pd/C catalyst.

Key words: Carbazole-3,6-d_2, carbazole-1,3,6,8-d_4, 3,6-dibromocarbazole, and 1,3,6,8-tetrabromocarbazole.

INTRODUCTION

A number of specifically deuterated carbazoles have been prepared: 1,2,3,4,5,6,7,8-d_8 by ring closure of 2-nitroperdeuterobiphenyl heated with triethylphosphite (1a); 2,4,5,7-d_4 by back exchange of the d_8 compound with HCl in ethanol (1b); and the 1,8-d_2 isotopomer by successive metallations and deuterations of carbazole (1c). We report here the preparation of the 3,6-d_2 and 1,3,6,8-d_4 isotopomers. Both compounds were made by catalytic reduction of the corresponding dibromo and tetrabromocarbazoles with deuterium gas in alkaline ethanol solution, over Pd/C catalyst (2).

The reliability of this synthesis depends upon the structures of the bromo compounds, which we have prepared by controlled direct bromination of carbazole. Mazzara and Leonardi (3) first prepared a dibromocarbazole by bromination of N-benzoyl carbazole, followed by saponification of the benzoyl group. They gave a rather convoluted argument that their product is the 3,6-isomer; among other steps, it requires acceptance of the structures of the products from various hot tube reactions which convert 2,n-aminobiphenyls to n-aminocarbazoles. The direct

0362–4803/90/111239–04$05.00

Received January 22, 1990
Revised June 26, 1990

evidence for the structure of tetrabromocarbazole is equally tenuous. For both compounds, the strongest support for the proposed (and accepted) structures lies in their general consistency with the pattern of electrophilic substitution reactions of carbazole: 3,6-disubstitution occurs most readily, followed by 1,8-disubstitution. These observations are also consistent with the calculated partial rate factors for substitution in carbazole (4).

In view of the lack of direct evidence for the structures of these two bromination products, we have submitted samples for crystallographic study (5). The data show that the dibromo compound is certainly 3,6-disubstituted. Unfortunately, we have not yet been able to grow a crystal of the tetrabromo compound which is suitable for x-ray study.

EXPERIMENTAL SECTION

Commercial carbazole contains 1% or more of an impurity which is claimed (6) to be anthracene and/or phenanthrene. We have not been able to confirm this identification by the positions of impurity lines in the ^{13}C NMR spectrum, although both of these compounds have the R_f value 0.83, or the same as the impurity in commercial carbazole. Futhermore, a considerable range of melting points has been reported over the years for carbazole and its bromination products. Consequently, we have given greatest weight to purity demostrated by a single spot on a TLC plate. All TLC's were carried out on silica plates developed with CH_2Cl_2 and imaged under UV light. The R_f value for carbazole is 0.73 with a violet fluorescence, while that for the impurity commonly present is 0.83, with orange-brown fluorescence. All of the reaction products described below give a single TLC spot under these conditions, so the impurity in carbazole is removed at some stage in the preparation or purification of these compounds.

3,6-Dibromocarbazole: This compound was prepared by bromination in CS_2 solution at room temperature, a procedure originally reported by Lindemann and Muhlhaus (7). Commercial carbazole (20.9 g or 0.125 mol) in 210 ml CS_2 was stirred in a one liter flask equipped with a condenser with its outlet connected to a trap filled with H_2O to absorb the HBr formed. Bromine (12.8 ml or 0.25 mol) in 150 ml CS_2 was dropped into the stirred solution over 1.8 h, and stirring then continued for another 0.5 h. The crude product precipitates out; it was removed and then crystallized by Soxhlet extraction into 350 ml ethanol. The product obtained by cooling this extract

was dried and then sublimed at 190° to give 20.3 g or 50% colorless crystals with mp 210-211°. TLC: R_f = 0.76. MS: m/e 323(M, 47%), 325(M+2, 100%), 327(M+4, 40%). ^{13}C NMR in DMSO-d_6: δ = 137.9, 127.7, 122.4, 122.3, 112.2, and 110.0.

1,3,6,8-Tetrabromocarbazole (8): Carbazole (41.8 g, or 0.25 mol) was stirred into 500 ml acetic acid and warmed to 30° with a water bath. A solution of 25.6 ml (0.50 mole) bromine in 75 ml acetic acid was dropped in over 0.8 h. The temperature was then raised to 60°, another portion of 25.6 ml bromine in 75 ml acetic acid dropped in, and the mixture stirred over night at 60°. Cooling gave 85 g yellow crystals which were purified by Soxhlet extraction into chlorobenzene, followed by sublimation at 220°. The yield was 80 g, or 66%, and the mp 225-226°. TLC: R_f = 0.83, with orange-brown flourescence. MS: m/e 479(M, 10%), 481(M+2, 35%), 483(M+4, 50%), 485(M+6, 31%), 487(M+8, 7%). ^{13}C NMR in DMSO-d_6: δ = 137.0, 130.6, 124.2, 122.2, 111.0, 104.2.

Catalytic deuteriodebromination procedure: Pd/C catalyst (10%), 300 ml ethanol, 17 g KOH (0.3 moles) and the bromocarbazole were placed in the 500 ml pressure bottle for the Parr hydrogenation shaker and shaken under deuterium gas until the pressure drop indicated complete reduction. The ethanol solution was filtered hot to remove catalyst, cooled, and the deuteriocarbazole filtered off. The product was purified by sublimation at 170°.

3,6-Dideuteriocarbazole: Dibromocarbazole (32.5 g or 0.1 mole) was reduced in the presence of 0.5 g catalyst; the pressure drop indicated reaction of 0.204 moles of bromine. The colorless product weighed 12.2 g, or 73% yield. TLC: R_f = 0.73. MS: m/e 168(M-1, 16%), 169(M, 100%), 170(M+1, 16%). ^{13}C NMR in DMSO-d_6: 138.8, 124.5, 121.5, 119.1, 117.5 (C-H), 117.3 (C-D triplet), 110.0.

1,3,6,8-Tetradeuteriocarbazole: Tetrabromocabazole (24.2 g, or 0.05 mole) was reduced with 1.0 g of catalyst under the conditions given above. The yield was 80%, and the mp 219-220°. TLC: R_f = 0.73. MS: m/e 169(M-2, 5%), 170(M-1, 29%), 171(M, 100%), 172(M+1, 35%), 173(M+2, 13%). ^{13}C NMR in DMSO-d_6: 138.9, 124.6, 121.6, 119.3, 117.6 (C-H), 117.4 (C-D triplet), 110.1 (C-H), 109.9 (C-D triplet).

It is possible to exchange carbazole slowly in refluxing ethanol-O-d with D_2SO_4 catalyst (1b). The product is again 1,3,6,8-tetradeuteriocarbazole. The ^{13}C NMR shows three to five impurity lines which do not serve to identify the impurity. TLC: product has R_f = 0.73, together with the usual impurity with R_f = 0.82, and

two additional impurities with R_f = 0.64 and 0.56. This method was not used for the synthesis because of the impurities present.

Acknowledgment: Most of this research was supported by U.S. Department of Energy contract number 81er10910.

REFERENCES

1. a. F. A. Neugebauer, H. Fischer, S. Bamberger, and H. O. Smith, Chem. Ber., **105**, 2694-2713 (1972).

   b. F. A. Neugebauer, Chem. Ber., **106**, 1716-1723 (1973).

   c. A. Hallberg and A. R. Martin , J. Heterocycl. Chem. **21**, 837-840 (1984).

2. W. A. Doak, C. Knessl, H. Labaziewicz, S. E. O'Connor, L. Pup, G. Putz, M. Schranz, R. I. Walter, L. Yang, and N. H. Werstiuk, Can. J. Chem., **63**, 3371-3373 (1985).

3. G. Mazzara and A. Leonardi, Gazz. Chim. Ital., **22**, 569-582 (1892).

4. a. P. B. D. de la Mare, O. M. H. el Dusouqui, and E. A. Johnson, J. Chem. Soc., 521 (1966).

   b. M. J. S. Dewar and D. S. Urch, J. Chem. Soc., 345 (1957) and 1079 (1958).

5. We are indebted to Professor Boon Teo and his coworkers for carrying out the crystallographic study.

6. J. M. Clark, Ind. Eng. Chem. **11**, 208 (1919).

7. H. Lindemann and F. Muhlhaus, Ber., **58**, 2371-2377 (1925).

8. J. Pielichowski and J. Kyziol, Monatsh. Chem., **105**, 1306-1312 (1974).