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The Microwave-assisted Preparation and X-Ray Structure of 3-Bromocarbazole-N-Acetic Acid

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Abstract: The rapid synthesis of 3-bromocarbazole-N-acetic acid was performed using microwave irradiation. Under the optimal conditions the yield was 85.6 %. The crystal structure showed that the carboxylic groups form bifurcated hydrogen bonds and the hydroxyl oxygen atoms serve as proton donors and also acceptor. Each carboxylic group was involved in four hydrogen bonds. The packing of crystal was dominated by links of these hydrogen bonds.

Keywords: Microwave-assisted synthesis, 3-bromocarbazole-N-acetic acid, X-ray determination, bifurcated hydrogen bonds.

Carbazole and its derivatives have attracted the attention due to its photophysical and photochemical properties as well as biological activities[1]. So far considerable amounts of carbazole derivatives were prepared to probe the nature of electronic states. Among these carbazole derivatives, carbazole-9-carboxylic acids were important intermediates because the carboxylic group is an active function group for further transformation into other functions.

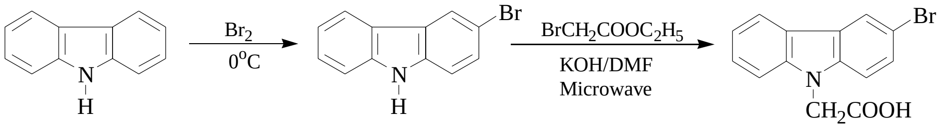
The molecular packing modes of carboxylic acids have been investigated intensively[2]. It was proved that the hydrogen bonds governed the molecular packing with several kinds of interaction modes[3]. Among these hydrogen bonds, 'three-center' hydrogen bonds were also observed. In view of our interest in photophysical property of carbazole-9-carboxylic acids, we synthesized a series of carbazole-9-carboxylic acids using microwave irradiation. Herein we report the preparation of the 3-bromocarbazole-N-acetic acid and its crystal structure.

Results and Discussions

Although the synthesis of bromocarbazoles was described before, bromination of carbazole generally yielded the mixture of polybromination products which were separated difficultly[4]. We used a simple method of bromination under the ice-bath condition to obtain 3-bromocarbazole in 52.2% yield.

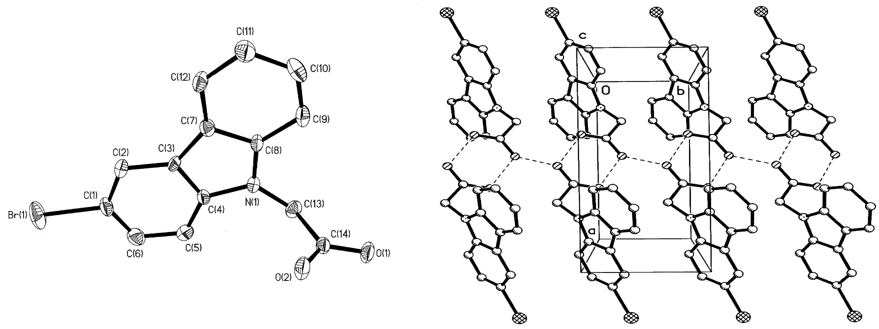
The 3-bromocarbazole-N-acetic acid was synthesized rapidly with microwave assistance. Various attempts have been carried out for this reaction under 'dry' condition using silica gel, alumina, or activated carbon as the support. But the tests were not successed. A one-pot of 'wet' reaction condition was effected using DMF as a solvent. When the microwave power was 375 W, varying the irradiation time from 2,4 to 6 minute, the yields of the 3-bromo-carbazole-N-acetic acid were 66.1, 85.6 and 52.1%, respectively. When the irradiation time kept 4 minute, changing the microwave powers with 225 W, 300 W, 375 W, 450 W and 525 W, the yields of the 3-bromocarbazole-N-acetic acid were 64.6, 73.7, 85.6, 73.5 and 53.4%, respectively. These results show that the yields are dependent upon the irradiation time and microwave power (**Scheme 1**).

Scheme 1



The crystal structure of 3-bromocarbazole-N-acetic acid was determined and the perspective view in general orientation and packing view are showed in **Figure 1**. Selected bond lengths and bond angles are listed in **Table 1**.

Figure 1 X-Ray crystal structure and packing view of 3-bromocarbazole-N-acetic acid



The Br (1) and C (13) are out slightly from the same side of the ring. The deviation of Br (1) from the mean plane through the ring defined by C (1) - C (2) - C (3) - C (4) - C (5) - C (6) is 0.0538 (0.0128) Å. The deviation of C (13) from C (3) - C (4) -C (7) - C (8) - N (1) least-squares plane is 0.0308 (0.0125) Å. The C (13), C (14), O (1) and O (2) are in one plane, which is almost perpendicular to the ring plane. The dihedral angle is 89.78° (0.21).

In the unit cell, four molecules in two orientations with two-two parallel are stacked. The Br atoms are oriented outwards from the hydrogen-bonded chains, and do not interfere sterically with the hydrogen bonds. From the topology and geometry of the packing in this neutral molecular crystal, the length of O(2)—O(1)#2 2.670 (8) Å and O(1)—O(1)#1 2.843 (12) Å and their characters are suitable to form hydrogen bonds. Furthermore, it was found that all hydrogen atoms H (1A) of hydroxyl groups were connected with three oxygen atoms simultaneously. So, it was judged that there were

Table 1 Selected bond lengths [Å] and angles [deg]

Br(1)-C(1)	1.919(8)	O(1)-C(14)	1.253(8)
O(1)-O(1)#1	2.843(12)	O(2)-C(14)	1.226(9)
O(2)-O(1)#2	2.670(8)	N(1)-C(8)	1.378(9)
N(1)-C(4)	1.405(8)	N(1)-C(13)	1.434(9)
C(1)-C(6)	1.337(13)	C(1)-C(2)	1.397(12)
C(2)-C(3)	1.425(9)	C(3)-C(4)	1.374(11)
C(11)-C(12)	1.369(10)	C(13)-C(14)	1.516(11)
C(14)-O(1)-O(1)#1	130.4(6)	C(14)-O(2)-O(1)#2	117.7(5)
C(8)-N(1)-C(4)	107.1(6)	C(8)-N(1)-C(13)	125.4(6)
C(4)-N(1)-C(13)	127.3(7)	N(1)-C(13)-C(14)	113.3(7)
O(2)-C(14)-O(1)	125.2(8)	O(2)-C(14)-C(13)	120.5(7)

Symmetry transformations used to generate equivalent atoms: #1 –x+1, -y, -z+2, #2 –x+1, -y+1, -z+2

involved in three-center hydrogen bonds, which were asymmetric as two of the hydrogen bond angles were 169.05° (O (1)—H (1A)…O (2)#2) and 151.03° (O (1)—H (1A)…O (1)#1), and dominated the packing of crystal structure[5]. This induces shorter bond length of O (1)-C (14) 1.253 (8) Å than it of acetic acid (1.43 Å) and its dimer (1.36 Å). The data of the hydrogen bond length of O (2)—O (1)#2 and O (1)—O (1)#1 illustrate that the strength of the former is at the middle range between the strong H-bonding and medium strength H-bonding, the latter is the medium strength H-bonding[6]. It is shown that each carboxylic group involves four H-bonds.

Synthesis of 3-bromocarbazole

To a solution of carbazole (20.04g , 0.12 mol) in pyridine (60 mL), in ice-bath, was added bromine (19.2 g, 0.12 mol) in pyridine (30 mL). After stirring for 2.5 hours, the reaction mixture was poured slowly in 0°C hydrochloric acid (6 mol/L, 600 mL). The crude product was collected by filtration and washed with water, dried *in vacuo.* The product was recrystallized from toluene to yield light brown crystals of 3-bromocarbazole (15.4 g, 52.2%). mp 198-199°C. Found: C 58.42, H 3.28, N 5.67 for $C_{12}H_8NBr$ calcul: C 58.54, H 3.31, N 5.69.

Synthesis of 3-bromocarbazole-N-acetic acid

A mixture of 3-bromocarbazole (4.9 g, 0.02 mol), sodium hydroxide (5.7 g, 0.1 mol), and the ethyl bromo-acetate (4.3 g, 0.026 mol) in DMF was heated in a domestic microwave oven in an open round-bottomed flask for 4 min. Then water was poured into the flask. The filtrate was acidified by adding hydrochloric acid until complete precipitation. The precipitate was filtered, washed with water, and dried *in vacuo*. The crude product was purified by recrystallization from chloroform and alcohol (90:10) to give the product (5.2 g, 85 %), mp 194-196°C. Found: C 55.24; H 3.18; N 4.63 for $C_{14}H_{10}NO_2Br$ calcul: C 55.29; H 3.31; N 4.61; ^1H NMR (CD_3COCD_3 δ ppm) 5.23 (s, CH_2), 7.20-8.18 (m, 7H, Ar-H); IR ν (KBr cm^{-1}) 3050 (m), 2931 (m), 1713 (s), 1625 (w), 1597 (m), 1491 (s), 1476 (s), 1364 (m), 1274 (m), 1247 (s), 1056 (s), 900 (m), 814 (s), 791 (s), 747 (m), 738 (m). MS (*m/z*) M^+ 303 (54).

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References and note

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