A new Tröger's Base Content Dicarboxyl Groups

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Abstract
Four Tröger's base (TB) molecules were synthesized by reaction of derivative of aminobenzoic acid with a methylene suppler of methylal (dimethoxymethane) (DMM)) with a strong acid from trifluoroacetic acid (TFA) which used a solvent and catalyst. This method were afforded a ratio of products between 34-66%, all products were conforming by FTIR, XRD, HRMs, 1HNMR, and 13CNMR.
Keywords: Tröger base, heterocyclic compounds, new carbocyclic acids.

1. Introduction

Julius Tröger was synthesized and isolated the first Tröger base 1 (TB1) from condensation of 4-aminotoluene with formalin in catalyst present. [1, 2]. Many substrates do not work well with this approach, likely due to solubility issues. [3] Later, many different of reagents of methylene donors, such as dimethoxymethane, paraformaldehyde, hexamethylenetetramine or dimethylsulfoxide; in an acidic media, such as hydrochloric acid, acetic acid, or trifluoroacetic acid [4], were used to synthesize a variety of aromatic and heterocyclic Tröger's bases with various functional groups. [5] M. A. Spielman used acylation, nitrosation, and reduction to prove the structure of Tröger base (TB1) in 1935, concluding that it was (TB) [6], Larson and Wilcox used single crystal X-ray diffraction to validate this structure in 1986 [7]. The Tröger base has rigid twisted of V-shaped structure which contains two stereogenic nitrogen atoms [7, 8], because of quick inversion of the bridgehead N atoms at room temperature, enantiomers of chiral amines (N-centered) are frequently impossible to distinguish. However, because the stiff bicyclic unit inhibits inversion of the bridgehead N atoms, TB exists as two enantiomers [9]. Tröger's base analogues are used to build chelating and biomimetic systems because they are reasonably rigid chiral armatures [8]. Tröger's base contains variations of synthesis using the Brnsted acid catalyzed condensation of formaldehyde with aniline's derivatives. Formaldehyde, paraformaldehyde, hexamethylenediamine or methylal is suitable to form Troger bases. The ratio of product were varying degrees of success depend on various reagents and media of reaction such as acetic acid, aqueous of hydrochloric acid solutions, methanesulfonic acids, or TFA [9]. Troger bases (TBs) are chiral heterocyclic with a saturated bicyclic core that are naturally chiral [10]. In 2014 Peng-Fei Li et al. were reported synthesized a series of Tröger's bases based on triptycene-derived by one-pot condensation with PFA (paraformaldehyde) in the presence of TFA [11].

2. Experimental

2-1- Chemicals and instruments

Chemicals, One of the most important chemicals that were used in the research and its manufacturer's m-amino benzoic acid & p - amino benzoic acid and o – amino benzoic acid were supplied from CHD.4-amino-2-nitrobenzoic acid. The trifluoro acetic acid was supplied from fluorochem, dimethoxymethane (DMM) was supplied from fisher chemical , ethanol was supplied from Ecochem and diethyl ether was supplied from Riedel-denHaën.

Instrumental

Melting point smp 30 Stuart [UK] at Chemistry department – College of science for woman –University Babylon. FTIR Spectrophotometer 8400s Shimadzu "Japan" at Chemistry department /College of science for woman / University Babylon. NMR bruker 400 MHz SWITZERLAND
XRD xpert paanaltycal Philips Holland, MASS Instrument Specifications: Manufacturer Company: Agilent Technology (HP), MS Model: 5973 Network Mass Selective Detector.

General Procedure

A Dimethoxymethane (DMM) was added to an amino benzoic acid, then the mixture was cooled to zero centigrade. TFA was added drop by drop to the mixture, then allow the mixture to be stirred at room temperature for 72 h, then, washed with water, and collected by filter paper. The resulting materials were dried by an electric drying oven.

2-2- Synthesis of 6, 12-dihydro-5,11-methanodibenzo[b,f][1,5]diazocine-3,9-dicarboxylic acid (TBCOOH-1)

Broadly was a method the following is mixing the o-Aminobenzoic acid (8.00 g , 58.33 mmol), DMM (12 ml, 10.30 g, 135.462 mmol) and trifluoroacetic acid (35 ml) to give (12.00 g , 66.29 %) as a red powder. MP = 186 - 189 °C,FTIR (KBr disk , cm-1) υ= [3030 cm-1 C-H stretch Aromatic] , [3377- 2767 cm-1 for O-H of carboxyl group] , [1716 cm-1 C=O for carboxyl group] , [1670, 1575 and 1458 cm-1 (C=C of Aromatic)] , [1373 cm-1 (Caromatic -N)] , [1190 cm-1 (Caliph-N)] 1H NMR (499 MHz, (DMSO) δ 12.21 (s, 2H, COOH), 8.22 (d, J = 105.9 Hz, 2H, Ar), 7.71 (d, J = 69.5 Hz, 2H , Ar), 6.91 (t, 2H , Ar), 5.16 (s, 2H, aliphatic), 4.60 (s, 4H , aliphatic). 13C NMR (126 MHz, DMSO) δ 169.14(COOH) , 145.71(Ar –N) , 131.91(Ar) , 129.94(Ar) , 121.82(Ar) , 117.40(Ar) , 108.45(Ar-COOH) , 71.74(N-C aliphatic -N) , 60.39(N –C aliphatic -Ar).

2- Synthesis of 6,12-dihydro-5,11-methanodibenzo[b,f][1,5]diazocine-2,8-dicarboxylic acid (TBCOOH -2)

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Broadly was a method the following is mixing the p-Aminobenzoic acid (8.00 g , 58.33 mmol), DMM (12 ml, 10.30 g, 135.462 mmol) and triflouroacetic acid (35 ml) to give (11.00 g, 60.76 %) as a red powder. MP = 230 - 233 °C , FTIR (KBr disk , cm-1)υ = [3030 cm-1 C-H stretch Aromatic] , [3300 & 2515 cm-1 O-H for carboxyl group] , [1714 cm-1 C=O for carboxyl group] , [1668, 1595 and 1450 cm-1 (C=C of Aromatic)] , [1398 cm-1 (CAr- N)] ,[1197 cm-1 (Caliph – N)] 1H NMR (499 MHz, DMSO) δ 12.00 (s, 2H, COOH), 7.79 (s, 2H,Ar), 7.75 (d, J = 7.4 Hz, 2H, Ar), 7.14 (d, J = 9.2 Hz, 2H, Ar), 5.49 (s, 2H, aliphatic), 4.69 (s, 4H,aliphatic). 13C NMR (126 MHz, DMSO) δ 166.80(COOH), 153.91(Ar), 131.20 (Ar), 130.22 (Ar) , 121.92(Ar), 119.28(Ar) , 111.20(Ar-COOH), 71.95(N-C aliphatic -N) , 60.89(N-C aliphatic -Ar).

Synthesis of 6,12-dihydro-5,11-methanodibenzo[b,f][1,5]diazocine-4,10-dicarboxylic acid (TBCOOH -3)

Broadly was a method the following is mixing the m-aminobenzoic acid (8.00 g, 58.33 mmol), DMM (12 ml, 10.30 g, 135.462 mmol) and trifluoro acetic acid (35 ml) to give (10.6 g , 58.56 %) as a red powder. M.P. = 91 -94o C; FTIR (KBr disk, cm-1) υ = [3034 cm-1 C-H stretch Aromatic] , [3377 - 2623 cm-1 for O-H of carboxyl group] , [1707 cm-1 for C=O of carboxyl group] , [1670, 1587 and 1491 cm-1 (C=C of Ar)] , [1325 cm-1 (Ar-N)] , [1195 cm-1 (Caliph-N)] , 1H NMR (499 MHz, DMSO) δ 11.31 (s, 2H, COOH), 7.46 (d, J = 8.0 Hz, 2H, Ar), 7.33 (s, 2H, Ar), 7.26 (d, J = 8.2 Hz, 2H, Ar), 5.43 (s, 2H, aliphatic), 4.57 (s, 4H,aliphatic). 13C NMR (126 MHz, DMSO) δ 166.75(COOH), 147.03(Ar-N) , 133.04(Ar), 129.86 (Ar), 127.56 (Ar), 120.61(Ar) , 115.64 (Ar) , 70.46 (N- Caliphatic -N) , 60.75(Ar-C aliphatic –N).

4- Synthesis of 4,10-dinitro-6,12-dihydro-5,11 methanodibenzo[b,f][1,5]diazocine-2,8-dicarboxylic acid (TBCOOH -4)

Broadly was method the following is mixing the 4-Amino -2-Nitro benzoic acid (2.00 g, 10.98 mmol), DMM (4 ml, 3.43 g, 45.172 mmol) and TFA (40 ml) to afforded (1.5g, 34.15 %) as a yellow powder. MP = 159-161° C; FTIR (KBr disk , cm-1) υ = [3096, 2978, 2943, 1660, 1620, 1577, 1510 (asy. NO2, 1334 sy. NO2, 1264) 1H NMR (499 MHz, DMSO) δ 13.58 (s, 2H,COOH), 8.74 (s, 2H, Ar), 8.21 (s, 2H, Ar), 5.60 (s, 2H, aliphatic), 5.29 (s, 4H, aliphatic) 65.88. 13C NMR (126 MHz, DMSO) δ 162.50(COOH), 147.79(Ar), 139.65(Ar), 136.20(Ar-NO2), 132.52(Ar), 121.86(Ar-Caliphatic –N), 116.40(Ar-COOH), 79.90(N-Caliphatic –N) , 65.88(Ar-Caliphatic –N).

No. of compounds	R1	R2	R3	R4	Yield	Code
1	**COOH**	**H**	**H**	**H**	**66.29 %**	**TBCOOH-1**
2	H	H	COOH	H	60.76 %	TBCOOH-2
3	H	COOH	H	H	58.56 %	TBCOOH-3
4	NO2	H	COOH	H	34.15 %	TBCOOH-4

3. Results and Discussion

Tröger base was synthesized as described in the patent, with the addition of amino benzoic acid dimethoxymethane (DMM which is a source of methyl, in a super acid (catalyst and solvent) like trifluoro acetic acid (TFA). One equivalent of pure amino benzoic acid is combined with 2.5 equivalent of (DMM) and chilled to cold temperature in this synthesis. The trifluoroacetic acid (4-5 ml per gram of amino benzoic acid) is then gradually added slowly, drop by drop. For 72 hours, Can mix the reaction with a magnetic stirrer at 25 °C temperature in an inert environment. The color of the solution will change from pink to red. Water was used to quench the mixture, then was wished by hot ethanol and recrystallized by diethyl ether.

We can prove the compounds by FTIR, NMR, and XRD. FTIR :It can show the disappearance of the sharp weak peaks of the amine, and shows the Caliph –N peak at 1190 cm-1, showing a carboxyl group between 3300 -2500. 1HNMR which showing disappearance of the peak amine[N-H] and showing Tröger bases are cyclic from through values peaks for Ar-N-CH2 between 4.57 - 5.29 ppm and [N-CH2-N] between 5.16- 5.60 ppm.13CNMR of Tröger base showed to COOH 162 -169 ppm, [C Aromatic –N] 145.7 - 153.3 ppm, , [N- Caliph –N] 70.8 – 79.9 ppm , [Ar-CH2 –N] 61.39 – 66.88 ppm (Figure 1 - 4) ,but in the chart of amino benzoic acid not found this a peaks. We can check the molecular structure of Tröger's bases by X-ray diffraction. The[Figure 5] shows this. The X-ray diffraction patterns show that all synthesized molecules possess a crystalline structure. In the two compound , the highest intensity of the peaks is at the angles 18.27°, 26.32°and 27.17° where was the highest intensity at 18.27 can be measured the crystallite size of all compound by law Sherrer

$$D = \frac{0.9\,\lambda}{\beta cos\theta}$$

β *is a full width at half maximum* $(FWHM)$, *and* θ *is the diffraction angl*

Where (λ =1.5406 A°), The crystalline size value of the highest intensity is found to be equal to (6.262 nm), when adding a group NO2 to the compound, the orientation will change at (15.52° , 23.92° and 27.92°)

at the neighboring system, but when converting the system to the opposite system, the intensity decreases to become the highest peaks at the angles. In the fourth compound, that is, in the mutual system, the peaks return to increase in intensity at the angles 27.92°, 15.52°and 23.29°. As for the fourth system, the intensity of the peaks of the previous systems decreases, so that other peaks appear with a higher intensity at the angles 194.1° , 165.1° , 150.1°. That is , the best structure will be at the angles mentioned in the fourth system

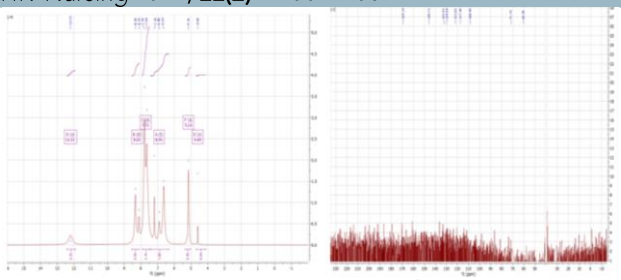

Figure 1 : 1HNMR and 13CNMR for TBCOOH-1

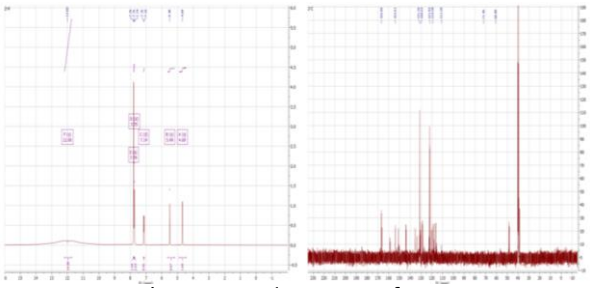

Figure 2 : ^{1}HNMR and 13CNMR for TBCOOH-2

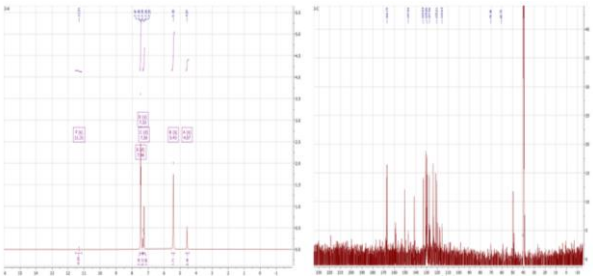

Figure 3 : 1HNMR and 13CNMR for TBCOOH-3

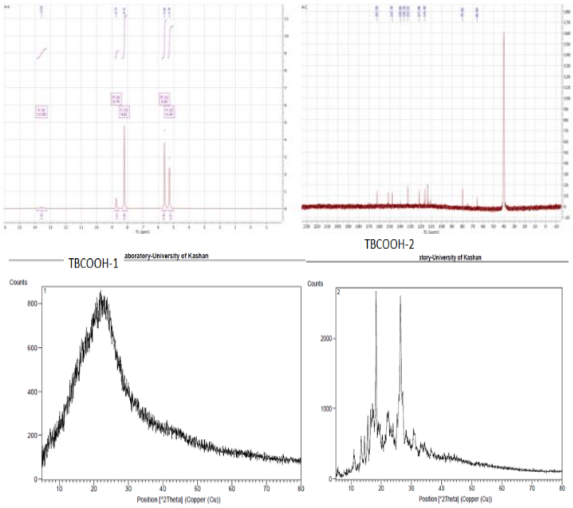

Figure 4 : 1HNMR and 13CNMR for TBCOOH-4

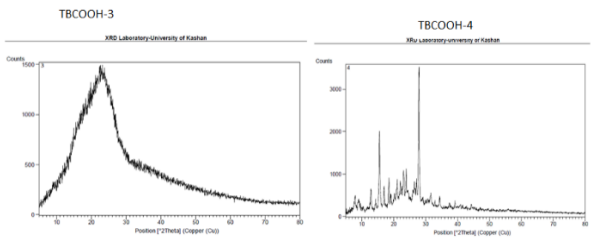

Figure 5 : XRD of Tröger's base

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