

Synthesis and Process of Bisamides Compounds Derived From Benzoyl Hydrazine

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Five bisamides compounds were synthesized from benzoyl hydrazine and alkyl diacyl dichloride which was deprived from alkyl diacid *via* acylation and the structures of these synthesized compounds had been characterized by Fourier transform infrared spectroscopy, ¹H nuclear magnetic resonance techniques and mass spectrometry. The reactive process also was investigated by orthogonal experiment. At the same time, theoretical calculations using the semiempirical method PM3 showed the consistency between theoretical and practical reaction.

Key Words: Benzoyl hydrazine, Bisamides, Alkyl diacyl dichloride, Theoretical calculations.

INTRODUCTION

Amides are very important organic compounds. Owing to their antitumour¹, antibacterial² and nucleating properties³, *etc.*, Amides and its derivatives have a wide range of applications in synthetic intermediates⁴⁻⁷, material chemistry⁸⁻¹¹, drug discovery¹², polymer^{13,14} and so on. For example, the importance of the amides in polymer has been recently highlighted by Angela and co-workers¹³. In that article, it is reported that ethylene *bis*-stearamide can serve as a nucleating agent for dramatic increasing in crystallization rate and final crystalline content as indicated by isothermal and nonisothermal crystallization measurements.

Usually, amides are synthesized by the typical reaction of carboxylic acids with amines at high temperature. Due to the long time of reaction, various methods for their activation have been reported in the literature¹⁵, the most common being conversion of a carboxylic acid to an acyl chloride. According to the development of new routes to the synthesis of amides, five bisamides compounds were synthesized from benzoyl hydrazine and alkyl diacyl dichloride which was deprived from alkyl diacid *via* acylation and optimum conditions of these reaction was investigated. The consistency between theoretical and practical reaction was discussed by theoretical calculations using the semiempirical method PM3.

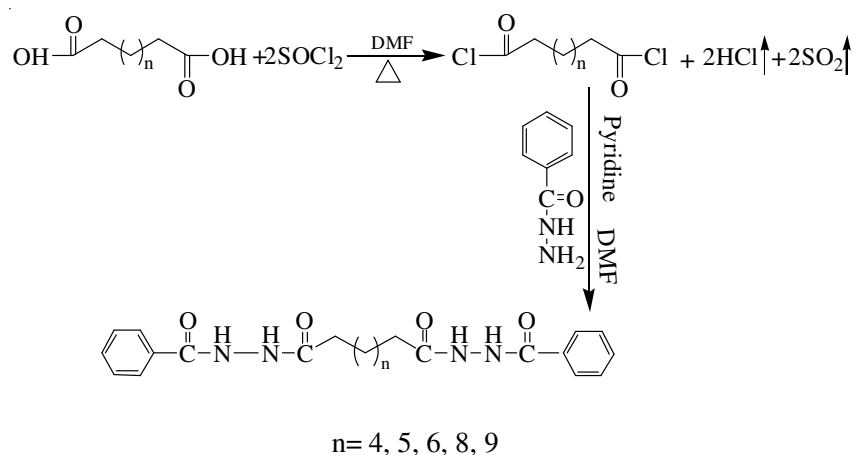
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EXPERIMENTAL

The materials used in this study were of analytical grade (AR) grade. Benzoyl hydrazine and suberic acid were procured from Beijing Chemical Reagents Company (Beijing, China) and Chengdu Kelong Chemical Reagents Company, respectively (Sichuan Province, China), azelaic acid, sebacic acid, dodecanedioic acid, brassylic acid, thionyl dichloride, pyridine and N,N-dimethylacetamide were procured from Mianyang Rongshen Chemical Reagents Company (Sichuan Province, China).

Typical synthesis procedure of preparation of bisamides compound: Five bisamides compounds were prepared as shown in **Scheme-I**: alkyl diacid, thionyl dichloride of 50 mL in the presence of N,N-dimethylacetamide as catalyst was mixed and the mixture was heated up to 80 °C and held at same temperature for 12 h with stirring. After cooling to room temperature and evaporation of thionyl dichloride in vacuum, the residue was alkyl diacyl dichloride.

Benzoyl hydrazide and N,N-dimethylacetamide (each 50 mL) was mixed and the mixture was purged under nitrogen atmosphere. Alkyl diacyl dichloride was added slowly onto the mixture, followed by adding pyridine of 0.057 mol and the mixture was heated up to certain temperature and kept for some time with constant stirring. Reaction mixture was poured onto water of 300 mL and stirred, followed by filtrating. Obtained crude product was washed four times by water of each 300 mL at room temperature and finally washed by 300 mL methanol at 55 °C to eliminate raw materials and by-products, the resulting product was dried in a vacuum at 65 °C.



Scheme-I: Preparation of five bisamides compounds

RESULTS AND DISCUSSION

Structures of compounds

N, N'-Bis(benzoyl) suberic acid dihydrazide (compound 1): IR (KBr, ν_{\max} , cm^{-1}): 3390, 3215, 2930, 2854, 1691, 1647, 1604, 1574, 1498, 1468, 1415, 1321,

1245, 1150, 794, 692, 640. ^1H NMR (DMSO, 500 MHz) δ : ppm; 10.29 (s, 1H, NH), 9.85 (s, 1H, NH), 7.48-7.88 (m, 5H, Ar), 2.18-2.21 (t, 2H, CH₂), 1.56-1.59 (t, 2H, CH₂), 1.35-1.36 (d, 2H, CH₂); MS (MAIDI-TOF) m/z: 410 ([M]⁺), 257 ([M-2Ar]⁺).

N,N'-Bis(benzoyl)azelaic acid dihydrazide (compound 2): IR (KBr, ν_{max} , cm⁻¹): 3219.1, 2927.1, 2854, 1689, 1647.7, 1605.6, 1574, 1507, 1468.5, 1312.6, 900.1, 794, 693. ^1H NMR (DMSO, 500 MHz) δ : ppm; 10.29 (s, 1H, NH), 9.84 (s, 1H, NH), 7.47-7.88 (m, 5H, Ar), 2.17-2.20 (t, 2H, CH₂), 1.32-1.58 (t, 2H, CH₂), 1.32 (s, 2H, CH₂); MS (MAIDI-TOF) m/z: 424 ([M]⁺), 229 ([C₁₀N₃H₁₇O₃ + 2H]⁺).

N,N'-Bis(benzoyl)sebacic acid dihydrazide (compound 3): IR (KBr, ν_{max} , cm⁻¹): 3215.4, 3028.9, 2927.6, 2852.7, 1689, 1648.6, 1606.9, 1575, 1499.9, 1468.9, 1415.2, 1312.4, 1270.9, 1229.5, 1152.3, 1067.7, 1027.9, 897.7, 869.1, 794, 711, 691.9, 632. ^1H NMR (DMSO, 500 MHz) δ : ppm; 10.28 (s, 1H, NH), 9.83 (s, 1H, NH), 7.47-7.87 (m, 5H, Ar), 2.17-2.19 (t, 2H, CH₂), 1.55-1.58 (t, 2H, CH₂), 1.3 (s, 2H, CH₂); MS (MAIDI-TOF) m/z: 438 ([M]⁺), 285 ([M-2Ar + H]⁺), 229 ([M-2(Ar-CO) + H]⁺).

N,N'-Bis(benzoyl) dodecanedioic acid dihydrazide (compound 4): IR (KBr, ν_{max} , cm⁻¹): 3215, 2924.3, 2847, 1644.2, 1603.7, 1573.9, 1535.9, 1461.8, 1416.9, 1159.7, 1075, 996.4, 949.7, 860.2, 781.6, 683.6, 619.8, 547.7, 520.3, 474.7. ^1H NMR (DMSO, 500 MHz) δ : ppm; 10.29 (s, 1H, NH), 9.84 (s, 1H, NH), 7.47-7.88 (m, 5H, Ar), 2.16-2.19 (t, 2H, CH₂), 1.54-1.57 (t, 2H, CH₂), 1.21-1.28 (d, 2H, CH₂); MS (MAIDI-TOF) m/z: 466 ([M]⁺), 256 ([M - 2(Ar-CO)]⁺).

N,N'-Bis(benzoyl) brassylic acid dihydrazide (compound 5): IR (KBr, ν_{max} , cm⁻¹): 3439, 3221.3, 2920.9, 2850, 1642.9, 1604.8, 1574.3, 1503.2, 1468.4, 1407.8, 1382.9, 1358.1, 1266.9, 1158.7, 1072.5, 997, 951.2, 861.4, 711.1, 691.6, 636.4, 548.3, 522.9, 449.8. ^1H NMR (DMSO, 500 MHz) δ : ppm; 10.28 (s, 1H, NH), 9.83 (s, 1H, NH), 7.48-7.88 (m, 5H, Ar), 2.16-2.19 (t, 2H, CH₂), 1.54-1.55 (d, 2H, CH₂), 1.21-1.27 (d, 2H, CH₂); MS (MAIDI-TOF) m/z: 480 ([M]⁺).

Theoretical analysis of reactive process: The influence of the molar ratio, reaction temperature and reaction time to the yields of product were investigated by orthogonal experiment. The relevant reaction conditions and yield of final products were indicated in Table-1.

TABLE-1
RELEVANT REACTION CONDITIONS AND YIELD OF FINAL PRODUCTS

Compound	Molar ratio*	Reaction temperature (°C)	Reaction time (h)	Yield (%)
1	3:1	60	2	91.4
2	3:1	70	4	89.7
3	2:1	70	4	92.5
4	3:1	70	6	87.3
5	2:1	80	6	90.1

*Benzoic hydrazide: alkyl diacyl dichloride.

In order to discuss the consistency between theoretical and practical reaction, we calculated the HOMO and LUMO energy levels for the reactants employed. Calculations were performed with the program VAMP using the semiempirical quantum chemical method PM3. Frontier molecular orbital theory indicated that the reaction model was based upon the interaction between the HOMO of benzoic hydrazide and the LUMO of alkyl diacyl dichloride. The possibility of the reaction was related to the LUMO (alkyl diacyl dichloride)-HOMO (benzoic hydrazide) energy gap ΔE (Fig. 1). The calculation results are summarized in Table-2. Usually, the smaller the value of the LUMO-HOMO gap is, the easier the reaction condition is. The energy gap ΔE between benzoic hydrazide and suberoyl chloride was the smallest, consequently, the reaction condition was easiest as shown in Table-1. The energy gap ΔE between benzoic hydrazide and undecyl diacyl dichloride was 9.967 eV,

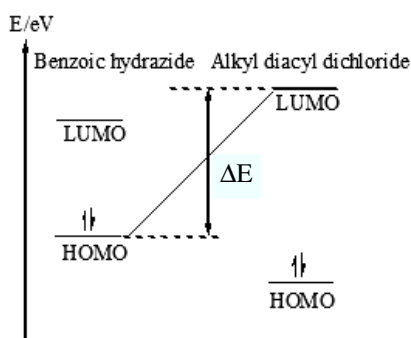


Fig. 1. Energy gap ΔE between LUMO of alkyl diacyl dichloride and HOMO of benzoic hydrazide

TABLE-2
HOMO AND LUMO LEVELS OF RAW MATERIALS CALCULATED WITH PM3

Compound	E (eV)	ΔE (eV)
	LUMO: -0.534 HOMO: -9.802	-
	LUMO: 0.059 HOMO: -11.074	9.861
	LUMO: 0.101 HOMO: -11.06	9.903
	LUMO: 0.09 HOMO: -11.047	9.892
	LUMO: 0.124 HOMO: -11.038	9.926
	LUMO: 0.165 HOMO: -11.041	9.967

which was biggest, so the highest reaction condition was required. The calculation results explained practical reaction conditions. Beside from the reaction of sebacoyl chloride with benzoic hydrazide, the remaining reaction of alkyl diacyl dichloride with benzoic hydrazide occur more difficulty with the increase of methylene number, which result from conjugated effect strengthened with the increase of methylene number. The distribution of electronic density of the entire system was averaged, which resulted in weakening of positively charged of carbonyl and nucleophiles attack the carbonyl more difficulty. Thus, the reaction get more difficult.

Conclusion

In this paper, five bisamides compounds were synthesized from benzoyl hydrazine and alkyl diacyl dichloride which was deprived from alkyl diacid *via* acylation and the structures of these synthesized compounds had been characterized. We investigated influence of the molar ratio, reaction temperature and reaction time to the yields of product and theoretical calculations explained the consistency between theoretical and practical reaction.

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