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Studies on the action of sodium-ethylenediamine on α-diketo compounds

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ABSTRACT

*Reactions of sodium / ethylenediamine (Na / EDA) have been carried out on α-diketones e.g. benzil (**1**), 4, 4′-dibromo benzil (**2**) and on diketo triterpenoids e.g. 2, 3 diketo lupene (**3**) and 2, 3 diketo methyl dihydro betulonate (**4**). The resulting 1, 4 pyrazine derivatives have been characterized by UV, IR, NMR (^{1}H and ^{13}C), optical rotation, mass spectra and by comparison with authentic samples.*

Key words: Benzil, diketo triterpenoids, sodium / ethylenediamine.

INTRODUCTION

Alkali metals in presence of bases are known to act as a reducing agent for the reduction of organic compounds since early years. The well known Birch reduction is the first example where these types of reagents are used. In Birch reduction, a number of experimental variants have been proposed from one another by the ratio and the order of addition of the reagents - the alkali metals, liq. ammonia and the alcohol and also presence or absence of supplementary solvents. According to Birch's method [1], the alkali metal (sodium or potassium) was added to a well stirred mixture of an alcohol, liq. ammonia and the substance to be reduced. This method of reduction was highly effective for the reduction of simple aromatic compounds; but for more complex compounds, the amount of reduction fall sharply [2] because of the low solubility of the compounds.

Regel and co-workers [3] reported first time a new metal-amine reducing system, lithium in ethylenediamine for reduction of organic compounds. Although Kraus [4] predicted that methyl-

amine, ethylamine and ethylenediamine would be valuable solvents for studying the physio-chemical properties of solutions of metals in amines at high temperatures; ethylenediamine had not hitherto been used in a metal-amine reducing system. The first use of the lower aliphatic amines for metal-amine reduction was reported by Benkeser et al [5] who showed that aromatic rings were reduced to mono olefins by lithium-ethylenediamine. However, their attempt to replace ethylamine by higher primary amines gave poor yields [6] perhaps because lithium becomes progressively less soluble in these monofunctional amines as the ratio of nitrogen to carbon decreases. Since ethylenediamine contains one amine group per carbon atom, and possess a relatively high boiling point (117^0 C), people got encouraged to investigate its use in a metal-amine system.

In continuation of our studies towards the introduction of greener approaches in organic transformations [7-9], we have attempted sodium-ethylenediamine instead of lithium-ethylenediamine for the transformative reaction of α-diketo compounds. As was expected [10] the combination yielded a condensed product which got aromatized simultaneously rather than producing a reduced system. More interestingly the investigation indicated that the more eco-friend sodium in ethylenediamine could be a very good replacement of more toxic lithium [11-14] in forming the pyrazine derivative from α-dicarbonyl compounds, as was reported earlier [15-17]. Considering the less toxicity, easy availability and the cost of sodium metal [18-20] in comparison to lithium, the combination of sodium and ethylenediamine would be an excellent protocol for preparation of 1, 4-pyrazine derivatives from α-diketones. Less reactivity of sodium would be an added advantage to get a high yield of product out of this reaction [21]. This is probably the first report of the above combination for a single step pyrazine ring formation.

EXPERIMENTAL SECTION

Melting points are uncorrected. Petroleum ether (bp 60-80 ^oC) was used during the investigations. IR spectra were recorded in nujol on Beckmann IR–20 spectrophotometer. UV spectra were recorded in methanol on Shimadzu– UV 240 spectrophotometer. Mass spectra were recorded on Varian Mat 711(70 eV) and JMS-D 300(70 eV) by EI/CI method. All the rotations were taken in $CHCl_3$ solution. Column chromatography was performed over silica gel (60 – 120 mesh, BDH). TLC was performed on chromatoplate of silica gel G (Glaxo and BDH) and the spots were located by exposing to iodine chamber.

General Procedure for Reduction

Small pieces of sodium metal (0. 5 gm) were added at intervals to a solution of compound (0.5 gm) in dry ethylenediamine (150 ml) and refluxed for two hours under nitrogen blanket. The reaction mixture was cooled and treated with solid NH_4Cl to destroy excess of sodium. It was acidified with dilute hydrochloric acid and extracted with ether. The ether solution was washed with water till neutral and dried over anhydrous Na_2SO_4. Evaporation of solvent (ether) furnished a gummy residue (0.4 gm). The residue was dissolved in minimum volume of toluene and chromatographed over silica gel (15 gm); a solid compound obtained which after crystallization from chloroform-methanol mixture afforded pale yellow crystals.

Spectroscopic and Analytical Data:

Compound 5:

Yield 84%; mp 119-20 ^oC (lit.[23] mp 118-19 ^oC); IR (Nujol): 1600, 1110 cm^{-1} (pyrazine ring) [22]; UV: 263 nm (€=5711) and 385 nm (€=1009) [15], [16]; ^1H NMR ($CDCl_3$): δ 7.23-7.28 (m, 6H, Ar-H), 7.40-7.46 (m, 4H, Ar-H), 8.55 (s, 2H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 128.21, 128.44, 128.61, 129.29, 129.59, 138.52, 142.02, 152.69; Mass: m/z 232, other peaks of prominence

appeared at 231 (base peak), 205, 204, 176, 103, 76; Anal. Calcd for $C_{16}H_{12}N_2$ (232): C, 82.76; H, 05.17; N, 12.10; Found: C, 82.71; H, 05.11; N, 12.06%. Thus from spectrum analysis the structure for the compound-5 has been assigned as 2, 3-diphenyl pyrazine (**5**) [23].

Compound 6:

Yield 82%; mp 122-25 ^oC; IR (Nujol): 1600, 1110 cm^{-1} (pyrazine ring) [22]; UV: 263 nm (€=5711) and 385 nm (€=1009) [15], [16]; ^1H NMR ($CDCl_3$): δ 7.23-7.50 (m, 8H, Ar-H), 8.51 (s, 2H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 128.31, 128.75, 129.67, 138.46, 142.07, 152.85; Anal. Calcd for $C_{16}H_{10}N_2Br_2$ (492): C, 39.06; H, 02.07; N, 05.53, Br, 32.87; Found: C, 39.10; H, 02.21; N, 05.67, Br, 32.92%. Thus from spectrum analysis the structure for the compound-6 has been assigned as 2, 3 diphenyl pyrazine derivative of dibromobenzil (**6**).

Compound 7:

Yield 85%; mp 213-14^o C; $[\alpha]_D$+24^o; IR (Nujol): 1650, 1430, 1120 cm^{-1} (Heterocyclic ring) [22] and 1630, 990, 825 cm^{-1} (for vinyl ethylene); UV: 272 nm (€=5700) and 278 nm (€=5600). ^1H NMR ($CDCl_3$): δ 0.81 (s, 6H, 2t-CH_3), 1.00, 1.11, 1.28, 1.30 (4s, 16H, 4t-CH_3), 1.27 (CH-CH_3), 2.45 and 3.04 (2d, 2H, -CH_2, J=16 Hz), 4.6 (m, 2H, =CH_2), 4.71 (d, 2H, 29-CH_2, J= 3 Hz), 8.27 and 8.405 (2d, 2H, J= 3 Hz 2 pyrazine ring protons); Mass: m/z 460, other peaks of prominence appeared at 445 (base peak), 438, 377, 350, 257, 256, 241, 229, 191, 189, 175, 149, 121, 109, 55; Anal. Calcd for $C_{32}H_{48}N_2$ (460): C, 83.48; H, 10.43; N, 06.10; Found: C, 83.40; H, 10.31; N, 06.86%. Thus from spectrum analysis the structure for the compound-7 has been assigned as pyrazine derivative of lupene (**7**) [10], [24-25].

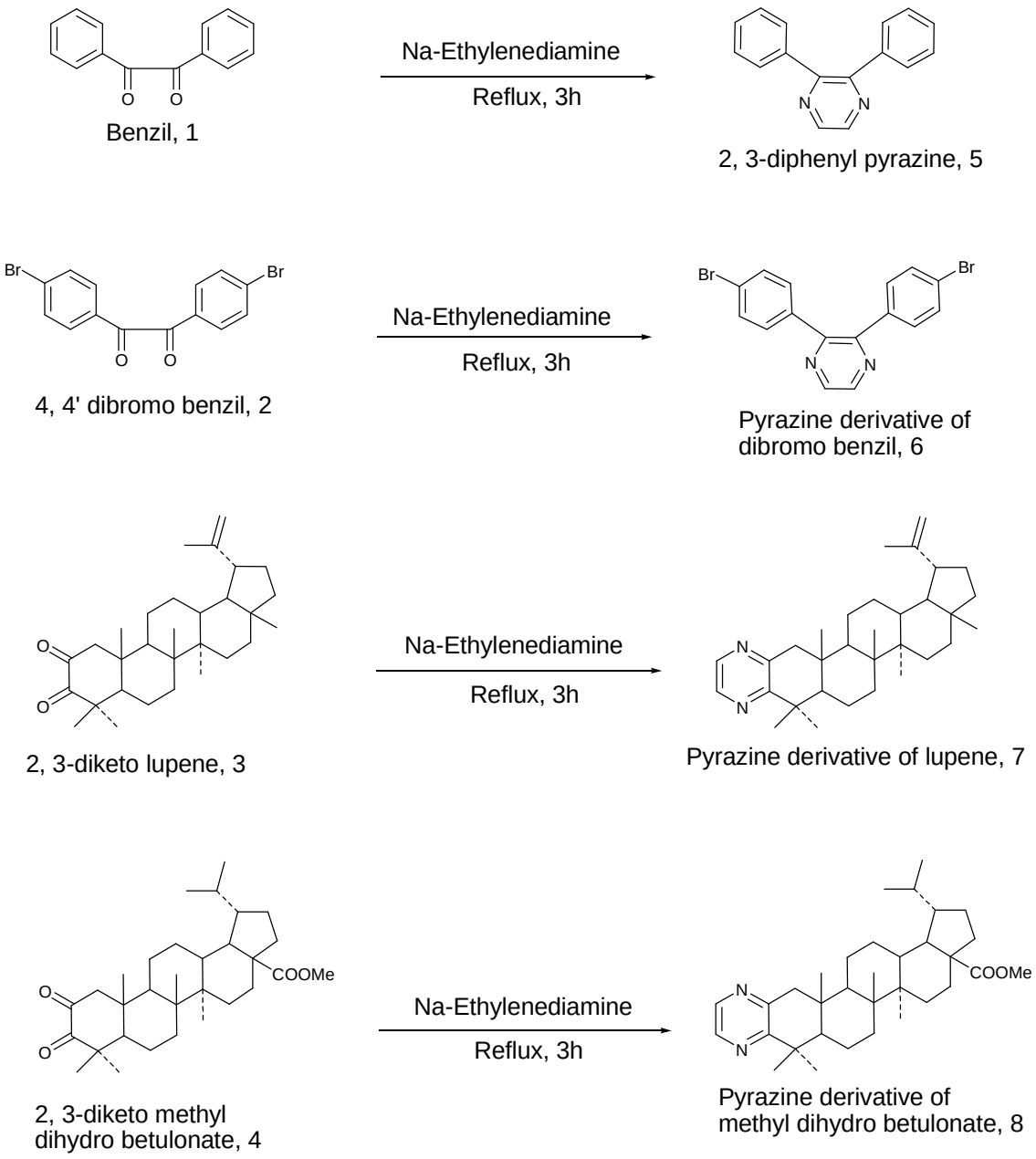
Compound 8:

Yield 82%; mp 220^o C; IR (Nujol): 1710-20 (COOMe), 1650-70, 1430, and 1120 cm^{-1}(pyrazine ring) [22]; UV: 272 nm (€=5712) and 278 nm (€=5603). ^1H NMR ($CDCl_3$): δ 0.82-1.305 (5s, 15H, 5t-CH_3), 0.76 and 0.88 (2d, 6H, $CH(CH_3)_2$, J= 7 Hz), 2.48 and 3.04 (2d, 2H, 1-CH_2, J= 16 Hz), 8.27 and 8.41 (2d, 2H, pyrazine ring proton, J= 3 Hz), 3.66 (s, 3H, -$COOCH_3$); Mass: m/z 506, other peaks of prominence appeared at 491 (base peak), 463, 447, 432, 431, 258, 256, 241, 191, 187, 175, 159, 147, 133, 95, 55; Anal. Calcd for $C_{33}H_{50}O_2N_2$ (506): C, 78.26; H, 09.88; N, 05.40; Found: C, 78.25; H, 09.73; N, 05.33%. Thus from spectrum analysis the structure for the compound-8 has been assigned as pyrazine derivative of methyl dihydro betulonate (**8**) [10, 22].

RESULT AND DISSCUSSION

Each of Benzil (**1**), 4, 4′-dibromobenzil (**2**), 2, 3-diketo lupene (**3**) and 2, 3-diketo methyl dihydro betulonate **(4)** was refluxed with sodium-ethylenediamine for two hours under nitrogen atmosphere. After usual work-ups [2], the residue in each case was chromatographed over a column of silica gel and eluted with petroleum ether-toluene (4:1) to furnish pure 2, 3-diphenyl pyrazine (**5**) [22], [23], pyrazine derivative of dibromobenzil (**6**), pyrazine derivative of lupene (**7**) [10], [24] and pyrazine derivative of methyl dihydrobetulonate (**8**) [10] (**Scheme 1**). These were identified by spectral data (IR, NMR and Mass) and by comparison with the data reported in the literature (except compound 6, which is being reported for the first time).

Scheme 1



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