Condensed 1,2,4-Triazines, II
Synthesis and Structure of Some Phenanthro[9,10-e]-1,2,4-triazolo[4,5-b]-as-triazine Derivatives

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(Z. Naturforsch. 32b, 569-572 [1977]; received October 29, 1976)

Triazines, Phenanthro-triazolo Derivatives

3-Hydrazinophenanthro[9,10-e]-1,2,4-triazine (2) was prepared and condensed with aromatic aldehydes to give the corresponding arylidene derivatives (3a-f). Phenanthro[9,10-e]-1,2,4-triazolo[4,5-b]-as-triazine (11), its 3-mercapto-(4a), 3-alkylmercapto-(9a-d) and 3-hydroxy- (4b) derivatives were prepared and their structures have been established.

Condensed derivatives of 1,2,4-triazine have recently become the subject of several patents due to their pronounced biological activity. In continuation of the work, that has been started in this laboratory on condensed 1,2,4-triazines1. We are describing the synthesis and structure of some new products of this system. Thus 3-hydrazinophenanthro[9,10-e]-1,2,4-triazine (2) has now, been prepared by the action of hydrazine hydrate on either 3-mercapto-, 3-methylmercapto- or 3-chlorophenanthro[9,10-e]-1,2,4-triazines (la-c). Compound 2 condenses readily with aromatic aldehydes, namely; benzaldehyde, anisaldehyde, 3,4-dimethoxybenzaldehyde, 3,4-diethoxybenzaldehyde, and piperonal to give the corresponding arylidene derivatives (3a-f) (Table I).

Table I. Arylidene derivatives of 3-hydrazinophenanthro[9,10-e]-1,2,4-triazine (3a-f).

<table>
<thead>
<tr>
<th>Products</th>
<th>m.p. [°C]</th>
<th>Formula (mol. wt.)</th>
<th>Analysis Found/Calcd</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>320°*</td>
<td>C22H22N5 (349.4)</td>
<td>C 75.52  H 4.30  N 19.84</td>
</tr>
<tr>
<td>b</td>
<td>300°*</td>
<td>C23H24N6O2 (394.39)</td>
<td>C 66.74  H 3.57  O 21.31</td>
</tr>
<tr>
<td>c</td>
<td>303</td>
<td>C22H22N2O (379.42)</td>
<td>C 72.80  H 4.52  O 18.46</td>
</tr>
<tr>
<td>d</td>
<td>296</td>
<td>C23H22N3O2 (409.44)</td>
<td>C 69.99  H 4.67  O 18.89</td>
</tr>
<tr>
<td>e</td>
<td>295</td>
<td>C23H22N3O2 (437.49)</td>
<td>C 71.37  H 5.29  O 16.01</td>
</tr>
<tr>
<td>f</td>
<td>305</td>
<td>C23H22N3O2 (401.46)</td>
<td>C 68.81  H 5.77  O 17.45</td>
</tr>
</tbody>
</table>

* Decomposition.

The reaction of compound 2 with carbon disulfide in pyridine led to the formation of a red compound. On the basis of the elemental analysis and its ready solubility in aqueous sodium carbonate solution, this product can be assigned either structure 4a or 5a.

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The structure of the product was proved to be phenanthro[9,10-e]-3-mercaptotriazolo[4,5-b]-as-triazine (4a) by independent synthesis via the condensation of phenanthraquinone with 3,4-diamino-5-mercapto-1,2,4-triazole (7a). This completely rules out the other isomer; viz, phenanthro[9,10-e]-3-mercaptotriazolo[5,4-c]-as-triazine (5a).

The reaction of 2 with carbon disulfide in pyridine presumably involves the formation of the pyridinium salt (6) which cyclizes preferentially at N2 rather than N4 leading to the formation of 4a. This preferential cyclization may be attributed to: (a) the hydrogen atom, at position 1 in the phenanthrene moiety, sterically inhibits cyclization at N4, (b) of the two possible cyclization products (i.e. 4 and 5), compound 5a is expected to be less sterically stable (similar steric instability was reviewed). The synthesis of compound 4a has, also, been achieved by fusion of an intimate mixture of 2 and thiourea. Similarly fusion of 2 with urea led to the formation of phenanthro[9,10-e]-3-hydroxy-1,2,4-triazolo[4,5-b]-as-triazine (4b).

The reaction of 2 with thiourea and urea probably proceeds via the intermediate formation of the thiosemicarbazido (8a) and semicarbazido (8b) derivatives respectively. This is followed, again, by the preferential cyclization at N2 via the loss of a molecule of ammonia. In favour of this presumption is the ready formation of compounds 4a, b by fusion of 2 with phenylisothiocyanate and phenylisocyanate, respectively. In this later case the intermediates phenylthiosemicarbazido (8c) and phenylsemicarbazido (8d) are doubtless the first reaction products which lose a molecule of aniline to yield compounds 4a, b, respectively.

The action of alkylating agents, namely; methyl iodide, ethyl iodide, benzyl chloride and ethylmonobromacetate, on 4a in an aqueous alkaline solution led to the formation of the S-alkyl derivatives (9a-d), respectively (Table II). That the products are S-alkyl (9) and not N-alkyl (10) derivatives was established by the ready formation of the methyl derivative (9a) by the condensation of phenanthraquinone with 3,4-diamino-5-methylmercapto-1,2,4-triazole (7b).

The trials to obtain 4b by the hydrolysis of the corresponding S-alkyl derivatives (9) according to the previously reported methods were unsuccessful. Instead, we have obtained products which still contain sulfur, the structure of which are under further investigation.

Finally the behaviour of compound 2 towards formic acid has, also, been undertaken. Thus when 2 was refluxed with formic acid cyclization was effected and phenanthro[9,10-e]-1,2,4-triazolo[4,5-b]-as-triazine (11) was obtained. Again in favour of the linear structure 11 is the independent formation of the same compound from phenanthraquinone and 3,4-diamino-1,2,4-triazole (7) when refluxed in alcoholic potassium hydroxide solution.
From what has been said, we come to the conclusion that, steric factor presumably plays an important part in preventing cyclisation at N4 of the triazine ring to give the angular structures 5 as it is observed in benzo-1,2,4-triazine derivatives.

**Experimental**

All melting points are uncorrected.

**3-Hydrazinophenanthro[9,10-e]-1,2,4-triazine (2)**

a) From 1a: Compound 1a (1 g) was refluxed with hydrazine hydrate (5 ml, 90%) for 1/2 h, left to cool, filtered, washed with water. The solid obtained was crystallised from pyridine as yellowish-brown crystals, m.p. 233 °C, yield ca. 98%.

Analysis for C_{15}H_{11}N_{5}

Caled C 68.95  H 4.24  N 26.80,
Found C 69.00  H 4.30  N 27.10.

b) From 1b: Compound 1b (1 g) was refluxed in alcohol (10 ml) with hydrazine hydrate (3 ml, 90%). The reaction mixture was refluxed for 6 h, during which methylmercaptan was noticeably evolved. After cooling, the solid was collected, and crystallised from pyridine. This was proved to be 2 (mixed m.p.), yield was almost quantitative.

c) From 1c: Compound 1c (1 g) was refluxed with hydrazine hydrate (5 ml, 90%) for 6 h. The solid obtained was collected, washed with water, crystallised from pyridine and proved to be 2 (mixed m.p.), yield ca. 95%.

**Action of aromatic aldehyde on 2**

General procedure: The following exemplifies the procedure. Compound 2 (0.002 mole) was refluxed with the appropriate aldehyde (0.002 mole) and alcohol (5 ml) on a water bath for 1/2 h. The solid obtained was crystallised from dimethylformamide as orange or yellow fibers of 3a–f in an almost quantitative yield (Table I).

**Phenanthro[9,10-e]-3-mercapto-1,2,4-triazolo-[4,5-b]-as-triazine (4a)**

a) Compound 2 was refluxed in pyridine (10 ml) with carbon disulfide (1 ml) for 1 h, during which hydrogen sulfide was evolved and a reddish-brown precipitate began to separate. The solid was collected and crystallised from DMF as reddish-brown crystals, m.p. 340 °C, yield ca. 84%.

The product can also be purified by dissolution in aqueous 5% sodium or potassium carbonate solution, filtered, and reprecipitated with concentrated hydrochloric acid.

Analysis for C_{14}H_{10}N_{8}S

Caled C 61.31  H 6.11  N 22.35  S 10.23,
Found C 61.50  H 6.30  N 22.1  S 10.40.

b) Phenanthraquinone (2.0 g) was dissolved in acetic acid (30 ml), then 3.4-diamino-5-mercaptop-1,2,4-triazolo-8 (7a) (1.3 g) in 5 ml water was added. The reaction mixture was refluxed for 3 h, during which a reddish-brown precipitate separated. This was filtered, washed, crystallised from DMF and proved to be 4a (mixed m.p.), yield 80%.

c) An intimate mixture of 2 (1 g) and thiourea (2 g) was heated at 220 °C (oil bath) till no ammonia evolves (30 minutes). The obtained product was cooled, dissolved in 5% potassium carbonate solution, filtered, cooled and finally acidified with conc. hydrochloric acid. The solid was filtered, washed with water, crystallised from DMF and proved to be 4a (mixed m.p.), yield ca. 50%.

d) Compound 2 (0.4 g) and phenylisothiocyanate (1 ml) were heated at 220 °C (oil bath) for 10 minutes. The reddish product was worked up as in experiment (c) to give compound 4a, yield ca. 70%.

**Action of methyl iodide, ethyl iodide and benzyl chloride on 4a**

General procedure: The following exemplifies the procedure. 4a (1 g) was dissolved in 5% aqueous potassium carbonate solution (50 ml), then the alkylating agent (0.035 mole) was added. The reaction mixture was shaken for 1/2 h and left overnight at room temperature. The precipitate was collected and crystallised from pyridine into orange needles of 9a–e (Table II).

**Action of ethylmonobromoacetate on 4a**

4a (0.5 g) was boiled in pyridine (5 ml), then ethylmonobromoacetate (0.2 ml) was added. The reaction mixture was boiled for few minutes, left overnight at room temperature then poured over iced-cooled water. The solid formed was collected washed with alcohol and crystallised from dilute acetic acid as orange crystals of 9d (Table II).

**Condensation of phenanthraquinone and 3,4-diamino-5-methylmercapto-1,2,4-triazole (7b)**

Phenanthraquinone (0.2 g) was dissolved in alcohol (10 ml) then compound 7b (0.15 g) was added. The reaction mixture was refluxed for 1/2 h, then potassium hydroxide (0.01 g) was added whereupon immediately the solution become deeply colored and orange crystals began to separate. After further 1/2 h of reflux the crystals were collected, and crystallised from pyridine. This was found identical with the product 9a obtained from the previous reaction (mixed m.p.).

**Phenanthro[9,10-e]-3-hydroxy-1,2,4-triazolo-[4,5-b]-as-triazine (4b)**

a) From 2 and urea: An intimate mixture of 2 (1 g) and urea (2 g) was heated at 220 °C (oil bath) for 1/2 h. The product was cooled and dissolved in hot 5% potassium carbonate solution filtered and then acidified with conc. hydrochloric acid. The precipitate was collected and crystallised from DMF as red crystals of 4b, m.p. 336 °C, yield 40%.
Analysis for C_{16}H_9N_5O  
Caled C 66.88 H 3.15 N 24.38,  
Found C 70.20 H 2.90 N 23.80.

b) From 2 and phenylisocyanate: 2 (0.5 g) heated at 220 °C (oil bath) for 11/2 h. The reaction mixture was triturated with alcohol and the solid precipitate was collected and purified as in (a). The product was found identical with compound 4b obtained in the previous reaction (mixed m.p.), yield ca. 45%.

Phenanthro[9,10-c]-1,2,4-triazolo[4,5-b]-astriazine (11)  
a) To compound 2 (0.2 g) was added formic acid (1.5 ml, 85%), the reaction mixture was refluxed for 5 h, cooled and poured over crushed ice. The residue was collected and crystallised from DMF into yellow needles of 11, m.p. 293 °C, yield ca. 98%.

Analysis for C_{18}H_9N_5  
Caled C 70.83 H 3.34 N 25.82,  
Found C 70.50 H 3.50 N 26.20.

b) Phenanthraquinone and 3,4-diamino-1,2,4-triazole (7c) was condensed together following the same procedure described before for the synthesis of 9a from 7b. Compound 11 obtained in this case is identical with that prepared in the previous reaction (mixed m.p.) from 2 and formic acid.

The authors wish to thank Prof. Dr. A. K. Mansour, Chem. Dept., Faculty of Science, Cairo University, A. R. Egypt for his help and encouragement during the work.

5 S. Tadashi and M. Masayoshi, Chem. Ber. 102(11), 3818 [1969]; C. A. 72, 12692b [1970].