

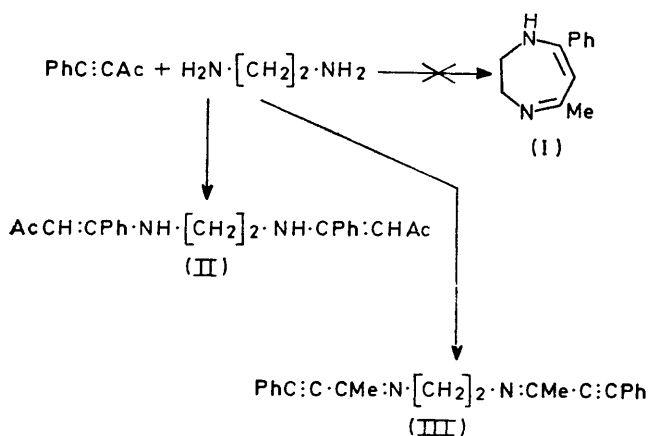
Reaction Products from 4-Phenylbut-3-yn-2-one and Aliphatic Diamines or 2-Aminoethanethiol, and from 2-Aminoethanethiol and some $\alpha\beta$ -Enones

By Olga H. Hankovszky and Kálmán Hideg,* Central Laboratory, Chemistry, University of Pécs, Pécs, Hungary
Douglas Lloyd,* Department of Chemistry, Purdie Building, University of St. Andrews, St. Andrews, Fife

4-Phenylbut-3-yn-2-one reacts with α,ω -diamino-ethane and -propane either by conjugate addition or by conjugate addition, dependant on the reaction conditions, but cyclisation products were not obtained. 2-Aminoethanethiol reacts with this ynone by conjugate addition of the amino-group, with benzylideneacetone to give a tetrahydrothiazepine, and with chalcone to give mono- or bis-conjugate addition products.

ETHYLENEDIAMINE reacts with $\alpha\beta$ -unsaturated ketones either by conjugate addition to two molecules of ketone to give an uncyclised adduct, or by conjugate addition plus condensation at the carbonyl group to give either tetrahydrodiazepines or tetra-azacyclotetradecadienes; the nature of the principal product depends on the structure of the enone.^{1,2}

It was hoped that reaction of ethylenediamine with an $\alpha\beta$ -acetylenic ketone might provide an alternative mode for the preparation of 2,3-dihydro-1*H*-1,4-diazepines (I) or alternatively provide tetra-azacyclotetradecatrienes, but when it reacted with 4-phenylbut-3-yn-2-one it gave only uncyclised products (II) or (III).



When the reactants were heated in refluxing benzene-ether in the presence of anhydrous potassium carbonate, conjugate addition of the diamine to two molecules of the ynone took place to give product (II). Since amines normally add readily to $\alpha\beta$ -ynones in the absence of a catalyst,³ it is surprising that when the reactants were heated without a catalyst, condensation to give product (III) rather than conjugate addition took place. The presence of an acid catalyst, either toluene-*p*-sulphonic

¹ K. Hideg and D. Lloyd, *Chem. Comm.*, 1970, 929.

² K. Hideg and D. Lloyd, *J. Chem. Soc. (C)*, 1971, 3441.

acid or zinc chloride, also led to formation of the condensation product (III). Possibly (II) arises by thermodynamic and (III) by kinetic control, but no rationale for these different reaction paths is presently obvious. The structures of these products are clearly shown by their n.m.r. spectra.

The failure of adduct (II) to react with a further equivalent of ethylenediamine to give a 14-membered ring, as happens when benzylideneacetone reacts with this diamine, must be due to the deactivation of the carbonyl groups in (II) owing to their being parts of extended amide systems. A similar effect would explain why the bis-adduct (II) is formed from the presumed mono-adduct intermediate rather than cyclisation of this mono-adduct ensuing to form the dihydrodiazepine (I), but the preferential formation of the bis-condensation product (III) from an intermediate mono-condensation product is more surprising since the intermediate possesses a conjugated ynimine structure which might well undergo an intramolecular Michael-type reaction.

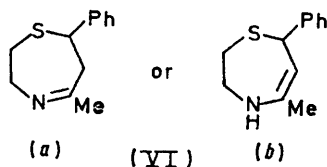
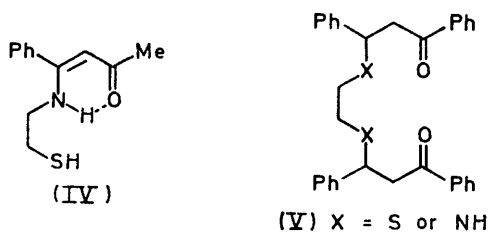
When product (III) was heated with more ethylenediamine in the presence of potassium carbonate, *i.e.* the conditions which led to conjugate addition to the original ynone, no addition to the triple bonds occurred, although they are conjugated with electron-withdrawing imino-groups, and (III) was recovered unchanged after 6 h.

In contrast 2-aminoethanethiol reacted with the ynone in the absence of catalyst to give the conjugate adduct (IV). That the amino-group rather than the thiol group has added to the acetylene bond is evident from the n.m.r. spectrum of (IV). Two multiplets represent the two methylene groups, that centred at τ ca. 7.4 appearing at the same field as in related compounds with an S-CH₂ group, and that centred at ca. 6.7 appearing at the same field as methylene groups in systems ·CH₂·CH₂·NH·CH:CH·C(R)=X but at lower field than is normal for CH₂NH₂.

Preferential addition by the amino-group contrasts with the behaviour shown by the adducts (V) formed

³ R. A. Raphael, 'Acetylenic Compounds in Organic Synthesis,' Butterworths, London, 1955, p. 39.

from chalcone and ethylenediamine or ethane-1,2-dithiol, for, when the adduct (V; X = NH) is heated with ethanedithiol the diamine portion is displaced by the dithiol to give (V; X = S).² In the case of (IV) this

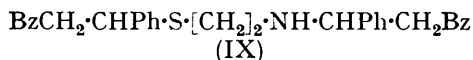
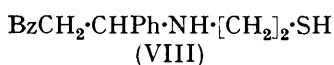
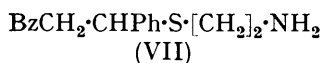


adduct is stabilised with respect to the alternative sulphur adduct by the conjugated chelate system, which is absent in (V; X = NH).

When 2-aminoethanethiol reacted with benzylideneacetone under the same conditions the product was the tetrahydrothiazepine (VI). It seems that both forms (a) and (b) are present for the n.m.r. spectrum is complex. A singlet (τ 3.05) equivalent to less than one proton [relative to Ph, τ 2.23 (5H)] disappears when the solution in deuteriochloroform is shaken with deuterium oxide, and is attributed to the NH of form (VIb). There are two methyl signals at τ 8.0 and 8.45, equivalent together to 3H. The remaining protons appear as a complex pattern at τ 5.5–7.9, equivalent to 6–7H [(VIa) and (VIb) require 7H and 6H respectively]. The molecular weight (mass spectrum) of (VI) is 205 as required. The reaction of 2-aminothiols with aliphatic $\alpha\beta$ -enones to give tetrahydrothiazepines has been reported previously.⁴

The formation of (VIa and b) involves a different mode of reaction of the aminothiols with the enone system from that with the ynone, with the thiol group undergoing conjugate addition while the amine condenses with the carbonyl group. This may again be attributed to the lack of special stabilisation of the possible amine adduct by conjugate chelation.

Whereas benzylideneacetone forms a tetrahydrothiazepine on reaction with 2-aminoethanethiol, chalcone forms mono-adducts [(VII), (VIII)] or a bis-adduct (IX), depending on the molar ratios used. Formation of such adducts rather than cyclised products is in



accord with previous work on the reaction between

chalcone and diamines.^{1,2} The n.m.r. spectrum of the mono-addition product is complex and indicates that addition of either the thiol or the amine groups to the enone takes place to give a mixture of adducts (VII) and (VIII). In particular, two well-defined doublets at τ 6.5 and 6.7 appear to be associated with COCH₂ groups in (VII) and (VIII) respectively [cf. corresponding signals from (V; X = S)² at τ 6.55 and from (V; X = NH)² at 6.7]. A similar pair of doublets is given by the bis-adduct (IX). Also in both the mono- and bis-adducts, the CH₂·CHPh proton, which in compounds (V; X = S or NH) appears as a sharp triplet, gives a multiplet, the result of two superimposed triplets, due in each case to two methine protons in different environments. In view of the normal preferred addition to enones of thiol groups rather than amines (cf. ref. 2) the presence of both mono-adducts had not been expected.

1,3-Diaminopropane reacted with benzylideneacetone in the presence of potassium carbonate to form a hexahydrodiazocine,^{2,5} but with 4-phenylbut-3-yn-2-one conjugate addition to give the trimethylene analogue of (II) again ensued; in the absence of carbonate a condensation reaction gave the trimethylene analogue of (III).

EXPERIMENTAL

N.m.r. spectra were recorded for solutions in deuteriochloroform unless otherwise indicated. I.r. spectra were recorded from KBr discs.

4,9-Diphenyl-5,8-diazadodeca-3,9-diene-2,11-dione (II).—A solution of ethylenediamine (0.60 g) and 4-phenylbut-3-yn-2-one (1.44 g) in benzene-ether (1:2; 25 ml) was stirred and heated under reflux, with anhydrous potassium carbonate (1.0 g) present, for 3 h. The mixture was cooled, filtered, and kept overnight in a refrigerator. Crystals separated and were filtered off. This *diazadienedione* (2.5 g, 72%) had m.p. 123–124° (from ether), ν_{max} . 3200m (NH) and 1610s (CO) cm⁻¹, τ -0.64br (2H), 2.4–2.9 (10H, complex), 4.95 (2H, s), 6.75–6.90 (4H, m), and 7.93 (6H, s); on addition of D₂O signal at -0.64 disappears and that at 6.75–6.90 becomes 6.83 (s) (Found: C, 76.0; H, 6.8; N, 8.3. C₂₂H₂₄N₂O₂ requires C, 75.85; H, 6.95, N, 8.05%).

3,8-Dimethyl-1,10-diphenyl-4,7-diazadeca-3,7-diene-1,9-diyne (III).—A solution of ethylenediamine (0.60 g) and 4-phenylbut-3-yn-2-one (1.44 g) in benzene (65 ml) was heated under reflux for 2 h. Solvent was evaporated off *in vacuo*, leaving the *diazadienediyne* as yellow crystals (2.65 g, 85%), m.p. 132–134° (from ether), ν_{max} . 2210s (C:C) and 1610s (N:C) cm⁻¹, τ (CCl₄) 2.4–2.8 (10H, complex), 6.15 (4H, s), and 7.75 (6H, s) (Found: C, 84.4; H, 6.9; N, 8.8. C₂₂H₂₀N₂ requires C, 84.6; H, 6.45; N, 8.95%). The same product was obtained if the reactants were heated in benzene in the presence of toluene-*p*-sulphonic acid or anhydrous zinc chloride.

Attempted Reaction of Diyne (III) with Ethylenediamine.—Molar equivalents of the diyne (III) and ethylenediamine were heated under reflux in benzene or ether-benzene in the presence of anhydrous potassium carbonate for 6 h. When the solution was cooled, filtered, and evaporated *in vacuo*, unchanged diyne was recovered quantitatively.

⁴ L. K. Mushkolo and Z. I. Shokol, *Zhur. obshchei Khim.*, 1960, **30**, 1023.

⁵ K. Hideg and D. Lloyd, *Chem. Comm.*, 1971, 372.

4-Phenyl-7-mercapto-5-azahept-3-en-2-one (IV).—A solution of 4-phenylbut-3-yn-2-one (1.44 g) and 2-aminoethanethiol (0.77 g) in benzene (65 ml) was heated under reflux for 2 h. The solution was evaporated *in vacuo* and the residue was dissolved in ether (30 ml) and kept in a refrigerator. Yellow crystals separated and were filtered off and washed with ether. The mercaptoazaheptenone (1.1 g, 50%) had m.p. 114–115° (from ether), ν_{\max} 3200s (NH) and 1610s (CO) cm^{-1} , τ (CCl_4) 0.77 (flattened), 2.63 (5H, s), 5.0 (1H, s), 6.46–6.82 (2H, m), 7.25–7.55 (2H, m), and 8.0 (3H, s) (Found: C, 65.1; H, 6.45; N, 6.5; S, 14.5. $\text{C}_{12}\text{H}_{15}\text{NOS}$ requires C, 65.15; H, 6.85; N, 6.35; S, 14.5%).

Reaction of 2-Aminoethanethiol with Benzylideneacetone.—A solution of benzylideneacetone (1.46 g) and 2-aminoethanethiol (0.77 g) in benzene (65 ml) was heated under reflux for 2 h. The dark solution was evaporated *in vacuo*. The residue, which slowly solidified, was suspended in ether (10 ml) and filtered. The brown 2,3,6,7- and/or 2,3,4,7-tetrahydro-5-methyl-7-phenyl-1,4-thiazepine (VIa, b) (1.64 g, 80%) had m.p. 112–114° (Found: C, 70.35; H, 6.75; N, 6.5; S, 15.0%; M^+ , 205. Calc. for $\text{C}_{12}\text{H}_{15}\text{NS}$: C, 70.2; H, 7.35; N, 6.8; S, 15.6%; M , 205).

6-Amino-1,3-diphenyl-4-thiahexan-1-one (VII) and 6-Mercapto-1,3-diphenyl-4-azahexan-1-one (VIII).—A solution of chalcone (2.08 g, 0.01 mol) and 2-aminoethanethiol (0.74 g, 0.01 mol) in benzene (30 ml) was heated under reflux for 3 h. Benzene was distilled off and the residual yellow oil slowly solidified to give a mixture (2.4 g, 85%) of the thiahexanone and the azaheptanone, m.p. 38–39° (from ether), ν_{\max} 3300m (NH_2) and 1656s (CO) cm^{-1} , τ 1.8–3.0 (10H, m), 5.3–6.0 (1H, m), 6.5 (1H, d), 6.7 (1H, d), 7.0–7.8

(~4.5H, m), and 8.25 (~1.5H, s) (Found: C, 71.7; H, 6.75; N, 5.15; S, 11.35. Calc. for $\text{C}_{17}\text{H}_{19}\text{NOS}$: C, 71.55; H, 6.7; N, 4.9; S, 11.25%).

1,3,8,10-Tetraphenyl-4-thia-7-azadecane-1,10-dione (IX).—Chalcone (4.16 g, 0.02 mol) and 2-aminoethanol (0.74 g, 0.01 mol) in benzene (30 ml) were heated under reflux for 3 h. When the solution was cooled the thia-azadecanedione precipitated as an almost colourless solid (4.0 g, 81%), m.p. 101–102° (from benzene), ν_{\max} 3300m (NH) and 1654s (CO) cm^{-1} , τ 1.8–3.0 (20H, m), 5.3–6.0 (2H, m), 6.5 (2H, d), 6.75 (2H, d), 7.5br (4H, s), and 8.25br (1H, s) (Found: C, 77.65; H, 6.55; N, 3.05; S, 6.55. $\text{C}_{32}\text{H}_{31}\text{NO}_2\text{S}$ requires C, 77.85; H, 6.35; N, 2.85; S, 6.5%).

4,10-Diphenyl-5,9-diazatrideca-3,10-diene-2,12-dione.—Prepared in the same way as the diazadecadienedione homologue (II) this diazadienedione (69%) had m.p. 67–69° (from ether), ν_{\max} 3620m (NH) and 1610s (CO) cm^{-1} , τ 2.45–2.75 (10H, complex), 5.05 (2H, s), 6.8–7.1 (4H, m), 7.8–7.9 (2H, m), and 8.05 (6H, s) (Found: C, 76.35; H, 7.6; N, 8.0. $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_2$ requires C, 76.2; H, 7.25; N, 7.75%).

3,9-Dimethyl-1,11-diphenyl-4,8-diazaundeca-3,8-diene-1,10-diyne.—Prepared in the same way as the diazadecadienedione homologue (III) this diazadienediyne (87%) had m.p. 75–76° (from ether), ν_{\max} 2210s (C:C) and 1610s (N:C) cm^{-1} , τ (CCl_4) 2.40–2.90 (10H, complex), 6.15–6.50 (4H, t), 7.65–8.15 (2H, m), and 7.83 (6H, s) (Found: C, 84.85; H, 6.4; N, 8.5. $\text{C}_{23}\text{H}_{22}\text{N}_2$ requires C, 84.65; H, 6.8; N, 8.6%).

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