The Reaction of 1,1-Diethylaminoprop-1-yne with Benzylidene Ketones

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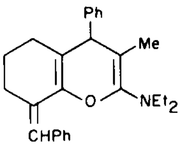
In previous communications (1) the formation of dihydropyran adducts from enamines and benzylidene ketones has been described. This reaction has now been extended to give substituted 4*H*-pyrans by reaction of the ynamine, 1,1-diethylaminoprop-1-yne with benzylidene ketones. Similar 4*H*-pyran products from ynamines and methyl vinyl ketone have recently been reported (2) by Ficini *et al.*

Reaction of 2,6-dibenzylidenecyclohexanone with 1,1-diethylaminoprop-1-yne in boiling ethanol gave a 32% yield of the crystalline pyran (1). In accord with its structure, **1** showed ir absorption at 1648 and 1700 cm^{-1} (3) and in the nmr spectrum the benzylic proton at C-8 appeared as a singlet at τ 6.35. Benzylidenedeoxybenzoin reacted in a similar manner to give the crystalline pyran (**2**; R_1 = R_2 = Ph). Mild hydrolysis of **1** yielded the corresponding γ,δ-unsaturated lactone (**3**).



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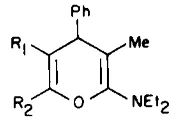

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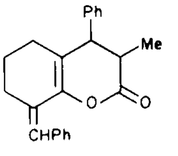

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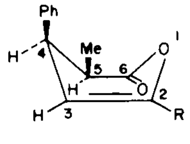

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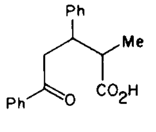

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Reaction of dibenzylidene acetone with the same ynamine at ambient temperature failed to give the crystalline adduct (**2**; R_1 = H, R_2 = Ph-CH=CH-) but direct hydrolysis of the oily product furnished the lactone (**4**; R = Ph-CH=CH-). The nmr spectrum of (**4**; R = Ph-CH=CH-) contains a triplet at τ 6.39 and a quintet at τ 6.98 which were assigned to the protons at C-4 and C-5 respectively. Double irradiation experiments revealed that the coupling between these two protons was 7 Hz and this suggests that the stereochemistry is as depicted in (**4**; R = Ph-CH=CH-) where the angles between the proton at C-4 and the adjacent C-3 and C-5 protons are both 20°. Similar hydrolysis of the non-crystalline pyran (**2**; R_1 = H, R_2 = Ph) from chalcone and the ynamine gave the lactone (**4**; R = Ph) with identical stereochemistry to (**4**; R = Ph-CH=CH-). A small amount of the keto-acid (**5**) resulting from further hydrolysis of (**4**; R = Ph) was also obtained.

EXPERIMENTAL

Materials and methods have previously been described (1).

5,6,7,8-Tetrahydro-8-benzylidene-2-diethylamino-3-methyl-4-phenyl-4*H*-1-benzopyran (**1**).

To a stirred suspension of 2,6-dibenzylidenecyclohexanone (5 g., 0.018 mole) in 50 ml. of ethanol at 0°, was added 5 g. (0.045 mole) of 1,1-diethylaminoprop-1-yne. The mixture was allowed to warm up to room temperature and then heated under reflux for 2.5 hours. Removal of ethanol gave a non-crystalline residue which was chromatographed on alumina (Grade I). Elution with light petroleum, b.p. 40-60°, gave 2.2 g. (32%) of product which solidified on trituration with ethanol-light petroleum. Recrystallisation from light petroleum gave white needles, m.p. 80-82°; ir ν max (potassium bromide) 1709, 1648 (enol ether C=C), 1597 (Ar C=C) cm^{-1}; uv λ max (ethanol) 276 (ϵ, 21,100) nm; nmr τ (deuteriochloroform) 8.93 (t, 6H, J 7.5 Hz, 2 x CH_2CH_3), 8.47 (s, 3H, CH_3), 7.08 (q, 4H, J 7.5 Hz, 2 x CH_2CH_3), 6.35 (s, 1H, Ph C-H), 3.07 (s, 1H, Ph CH=), 2.5-2.9 (m, 10H, 2 x Ph).

Anal. Calcd. for $C_{27}H_{31}NO$: C, 84.1; H, 8.1; N, 3.6. Found: C, 83.9; H, 8.0; N, 3.7.

6-Diethylamino-5-methyl-2,3,4-triphenyl-4*H*-pyran (**2**; R_1 = R_2 = Ph).

To a stirred suspension of benzylidenedeoxybenzoin (5 g., 0.0175 mole) in 20 ml. of ethanol at 0°, was added 8 g. (0.027 mole) of the ynamine. The mixture was stirred at 0° for 1 hour and then heated under reflux for 8 hours. Removal of the solvent gave 2.23 g. (32%) of a solid product which was recrystallised from ether-light petroleum, m.p. 111.5-112°; ir ν max 1712, 1647 (enol ether C=C), 1597 (Ar C=C) cm^{-1}; nmr τ (deuteriochloroform) τ 8.94 (t, 6H, J 7Hz, 2 x CH_2CH_3), 8.35 (s, 3H, CH_3), 7.06 (q, 4H, J 7 Hz, 2 x $C\mathit{H}_2CH_3$), 6.18 (s, 1H, PhC-H), 2.5-3.3 (m, 15 H, 3 x Ph).

Anal. Calcd. for $C_{28}H_{29}NO$: C, 85.1; H, 7.4; N, 3.55. Found: C, 85.0; H, 7.2; N, 3.2.

Hydrolysis of **1**.

The benzopyran (**1**) (4 g., 0.0104 mole) in 100 ml. of benzene was stirred with a buffer solution of sodium acetate (6 g.) and acetic acid (12 ml.) in 40 ml. of water for 1 hour. Dilute hydrochloric acid was then added (*p*H 2) and the benzene layer separated. The aqueous layer was extracted once more with ether and the combined organic layers were washed with water and dried. Removal of solvent gave 2.72 g. (79%) of product which was recrystallised from ethyl acetate-light petroleum, m.p. 149-151°; ir ν max 1750 (C=O), 1594 (ArC=C) cm^{-1}; nmr τ (deuteriochloroform) 8.98 (d, 3H, J 6 Hz, CH_3), 6.53-7.10 (m, 2H, Ph C-H and Me C-H), 2.33-3.07 (m, 1H, 2 x Ph and PhCH=).

Anal. Calcd. for $C_{23}H_{22}O_2$: C, 83.55; H, 6.7. Found: C, 83.8; H, 6.8.

Reaction of Dibenzylideneacetone and 1,1-Diethylaminoprop-1-yne.

To a stirred suspension of dibenzylideneacetone (5 g., 0.021 mole) in 10 ml. of ethanol at 0°, was added 5 g. (0.045 mole) of the ynamine. The solution was allowed to warm up to room temperature and when reaction was judged to be complete (tlc), the solvent was removed and the residue, in 40 ml. of benzene, was hydrolysed as above. Recovery gave 1.12 g. (18%) of a white solid which was crystallised from ethanol, m.p. 128-130°; ir ν max 1763 (C=O), 1650, 1618, 1600 (C=C) cm^{-1}; nmr (deuteriochloroform) τ 9.03 (d, 3H, J 6 Hz, CH_3), 6.98 (quintet, 1H, J 7 Hz 5-H), 6.39 (t, 1H, J 7 Hz, 4 - H), 4.47 (d, 1H, J Hz, 3-H), 3.50 (d, 1H, J 15 Hz, -C*H*=CH-), 2.4-3.1 (m, 1H, 2 x Ph and -CH=CH-). Double irradiation at both τ 9.03 and τ 4.47 revealed an AB quartet (J 7 Hz) due to the interaction between the adjacent protons at C-4 and C-5.

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 82.7; H, 6.2. Found: C, 82.5; H, 6.1.

Reaction of Chalcone and 1,1-Diethyl-aminoprop-1-yne.

To a stirred suspension of chalcone (7.5 g., 0.036 mole) in 20 ml. ethanol at 0°, was added 8 g. (0.072 mole) of the ynamine and the solution was maintained at 0-5° for 15 hours. Removal of solvent gave an oily residue which hydrolysed as before. Recovery gave a gum which partly solidified on standing*. The keto acid (**5**) (0.91 g., 9%) was collected and crystallised from ether-light petroleum in fine needles, m.p. 150-151°; ir ν max 1693, 1681 (Ph-C=O and CO_2H) cm^{-1}.

Anal. Calcd. for $C_{18}H_{18}O_3$: C, 76.6; H, 6.4. Found: C, 71.1; H, 6.3.

The residue from above (*) was allowed to stand overnight and was then triturated with ether to give 2.32 g. (24%) of lactone which was crystallised from ether-light petroleum in needles, m.p. 99.5-100°; ir ν max 1767 (C=O), 1660 (C=C), 1600 (Ar C=C) cm^{-1}; nmr (deuteriochloroform) τ 8.97 (d, 3H, J 7 Hz, CH_3) 6.91 (quintet, 1H, J 7 Hz, 5-H) 6.30 (t, 1H, J 6.5 Hz, 4-H), 3.99 (d, 1H, J 6.5 Hz, 3-H), 2.2-3.1 (m, 10H, 2 x Ph).

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 81.7; H, 6.1. Found: C, 81.8; H, 6.1.

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REFERENCES

(1) J. W. Lewis, P. L. Myers and M. J. Readhead, *J. Chem. Soc. (C)*, 771 (1970); J. W. Lewis and P. L. Myers, *Chem. Ind.* (London), 1625, (1970).

(2) J. Ficini, J. Besseyre, J. D'Angelo and C. Barbara, *C. R. Acad. Sc. Ser. C.*, 271, 468 (1970).

(3) Y. L. Chow and H. H. Quon, *J. Org. Chem.*, 34, 1469 (1969) and refs. *loc. cit;* J. Wolinsky and H. S. Hauer, *ibid.*, 34, 3169 (1969).