

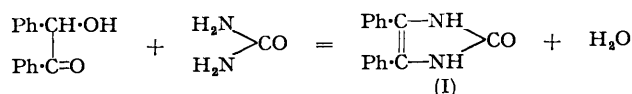
*Studies in Stereochemical Structure. Part XI.\* Heterocyclic  
Compounds from Benzoin.*

By ROBERT ROGER, KENNETH C. REID, and ROBERT WOOD.

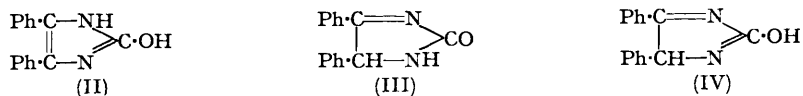
[Reprint Order No. 4303.]

(-)-Benzoin and urea in boiling glacial acetic acid yield optically inactive 2 : 3-dihydro-2-oxo-4 : 5-diphenylglyoxaline. We have found, however, that (-)-benzoin is racemised in glacial acetic acid. The dienolic formula for benzoin explains the accepted structure for the glyoxaline and its racemisation. Most important is the fact that substituted benzoin, *e.g.*, ethylbenzoin, do not condense with urea, probably because they cannot react in an enolic form.

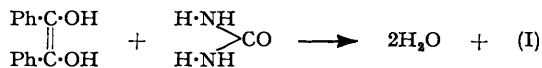
THE formation of 2 : 3-dihydro-2-oxo-4 : 5-diphenylglyoxaline from *rac.*-benzoin and urea is usually depicted as :



(Biltz, *Annalen*, 1909, **368**, 173; Chattaway and Coulson, *J.*, 1929, 1363). Three other formulations for the glyoxaline (II—IV), however, are possible, (III) and (IV) possessing centres of asymmetry and (II) and (IV) conjugated double-bond systems.



The condensation of (-)-benzoin with urea was carried out just as with *rac.*-benzoin *viz.*, by boiling in glacial acetic acid for some hours, the glyoxaline isolated then being optically inactive. This does not necessarily support formula (I) for the structure of the glyoxaline since experiment showed that optically active benzoin is slowly racemised at room temperature and more quickly at the boiling point in glacial acetic acid solution. The mechanism of formation of the glyoxaline is depicted conveniently by utilising the stilbenediol form of benzoin.



and this form has also been used extensively to explain the catalytic racemisation of optically active benzoin and related compounds (see Roger and McGregor, *J.*, 1934, 1545). More

\* Part X, *J.*, 1954, 811.

important and convincing experimental evidence in favour of this mechanism is now adduced in the following facts. We had hoped to realise the synthesis of optically active glyoxalines [*e.g.* (III) and (IV)] thus :



and, moreover, optically active ethylbenzoin had already been prepared in these laboratories (McKenzie and Ritchie, *Ber.*, 1937, **70**, 23; Roger, *J.*, 1937, 1048; 1939, 108). However, the condensation of *rac.*-ethylbenzoin and urea under even more drastic conditions than those recorded for benzoin and urea failed completely, most of the ketol being recovered unchanged. Similar lack of success attended the use of phenylbenzoin. Ketols such as ethylbenzoin offer no possibility of change into isomeric dienolic forms such as are possible with benzoin and, furthermore, the optically active forms are not susceptible to catalytic racemisation with alkali. These results support the foregoing mechanism for the formation of dihydro-oxodiphenylglyoxaline and formula (I) as its probable structure.

Stilbenediol diacetate (Barnes and Tulane, *J. Amer. Chem. Soc.*, 1940, **62**, 896) and urea in boiling glacial acetic acid yielded no dihydro-oxo-4 : 5-diphenylglyoxaline but only unidentified products. Perchance, glacial acetic acid may not be the proper condensing agent in this case. We found that desyl chloride and urea in boiling acetic acid did yield small amounts of the glyoxaline, but once again the main products were unidentified solids.

#### EXPERIMENTAL

2 : 3-Dihydro-2-oxo-4 : 5-diphenylglyoxaline (cf. Biltz, *Annalen*, 1905, **339**, 265; *Org. Synth.*, 1932, **12**, 34). *rac.*-Benzoin (32 g.) and urea (11 g., 1.85 mols.) were refluxed in glacial acetic acid (80 c.c.) for 7 hr. The crystals which separated on cooling were filtered off, washed with ether, and crystallised from glacial acetic acid; the product (22.1 g.) had m. p. 325—328°.

*Attempted Preparation of Optically Active 2 : 3-Dihydro-2-oxo-4 : 5-diphenylglyoxaline.*—(+)-Benzoin (3.6 g.;  $[\alpha]_{5461}^{20} + 144.0^\circ$  in acetone) and urea (1.75 g., 1.85 mols.) yielded a product (3.25 g.), m. p. 324—326°, identical with the compound obtained above.

*Condensation of Stilbenediol Diacetate and Urea.*—The diacetate (0.65 g.) (Barnes and Tulane, *loc. cit.*) and urea (0.25 g., 1.8 mols.) were refluxed for 6½ hr. in glacial acetic acid (2.5 c.c.). A white unidentified solid (0.4 g.), m. p. 200—203°, separated on cooling. No other product was isolated.

*Condensation of rac.-Desyl Chloride and Urea.*—*rac.*-Desyl chloride (5.5 g.) and urea (2.6 g., 1.8 mols.) were refluxed in glacial acetic acid (20 c.c.) for 6 hr. Ammonium chloride (0.5 g.) separated on cooling, and on dilution of the liquors with water 2 : 3-dihydro-2-oxo-4 : 5-diphenylglyoxaline (0.4 g.), m. p. 330—333°, was precipitated. An ether extract of the dilute acid liquors yielded a small amount of unidentified yellow crystals, m. p. 213—214°. On neutralisation of the acid liquors with sodium hydrogen carbonate an unidentified solid, m. p. 243—245°, separated.

*Attempted Condensation of rac.-Ethylbenzoin and Urea.*—*rac.*-Ethylbenzoin (4.8 g.) and urea (2.2 g., 1.8 mols.) were refluxed for 30 hr. in glacial acetic acid (16 c.c.). Unchanged *rac.*-ethylbenzoin (4.5 g.), m. p. 65—70°, slowly separated from the liquors on cooling.

*Attempted Condensation of Phenylbenzoin and Urea.*—Phenylbenzoin (0.4 g.), m. p. 80—82°, was recovered unchanged after glacial acetic acid (2 c.c.), urea (0.21 g., 1.8 mols), and *rac.*-phenylbenzoin (0.55 g., 1 mol.), m. p. 83—84°, had been refluxed for 16 hr.

*Racemisation of (+)-Benzoin in Glacial Acetic Acid.*—(+)-Benzoin (1 g.;  $[\alpha]_{5461}^{20} + 144.6^\circ$  in acetone) was dissolved in glacial acetic acid (30 c.c.), and the solution halved ( $l = 0.5$ ,  $c = 3.3$  for all readings). (i) One half was kept at room temperature, and rotations (all positive) were read every few days :

Time, days ...	0	1	2	5	12	21	30	40	55	70	500
$\alpha_{5461}^{20}$ .....	4.52°	4.48°	4.45°	4.33°	4.14°	3.99°	3.68°	2.88°	2.01°	1.27°	1.12°
$[\alpha]_{5461}^{20}$ .....	273.9°	271.5°	269.8°	262.4°	250.9°	241.8°	223.0°	174.6°	121.8°	96.8°	67.9°

The (+)-benzoin recovered from the liquors had m. p. 127—128°,  $[\alpha]_{5461}^{20} + 93.58^\circ$  in acetone, after one crystallisation from ethyl alcohol.

(ii) The other half was boiled for several hours, the optical rotation (positive) being read every hour :

Time of boiling, hr. ....	*	1	2	3	4	5	6
$\alpha_{5461}^{20}$ .....	4.3°	2.38°	0.58°	0.26°	0.17°	0.17°	0.17°
$[\alpha]_{5461}^{20}$ .....	260.6°	144.2°	35.15°	15.76°	10.3°	10.3°	10.3°

\* Time required for solution to be heated to the b. p.

The partially racemised (+)-benzoin recovered from the liquors had m. p. 129—130°,  $[\alpha]_{5461}^{20}$  +10.1° (in acetone), after one crystallisation from ethyl alcohol. A small amount of benzil, m. p. 94—95°, was also recovered.

We thank the Carnegie Trust for the Universities of Scotland and the Department of Scientific and Industrial Research for the support which made this work possible.

UNIVERSITY COLLEGE, DUNDEE, UNIVERSITY OF ST. ANDREWS. [Received, May 11th, 1953.]