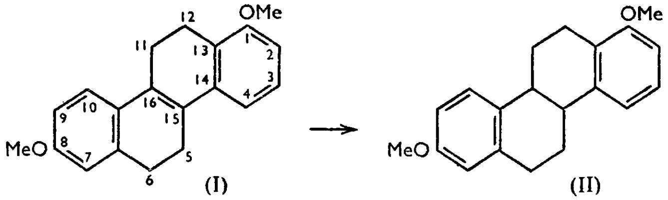
996. *Absence of Stereochemical Selectivity in the Reduction of* 5 : 6 : 11 : 12-*Tetrahydro- to* 5 : 6 : 11 : 12 : 15 : 16-*Hexahydro*-1 : 8-*dimethoxychrysene by Dissolving Metals.*

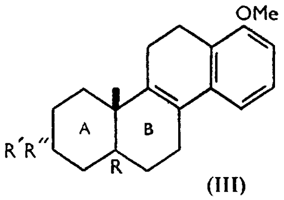
By P. A. Robins and James Walker.

Reduction of the 15 : 16-double bond in 5 : 6 : 11 : 12-tetrahydro-1 : 8-dimethoxychrysene (I) with (*a*) sodium and butan-1-ol, or (*b*) sodium, lithium, or potassium and an alcohol in liquid ammonia, gave mixtures containing approximately equal proportions of *cis*- and *trans*-5 : 6 : 11 : 12 : 15 : 16-hexahydro-1 : 8-dimethoxychrysene (II).

Birch and Smith [1] have recently described the reduction of 5 : 6 : 11 : 12-tetrahydro-1 : 8-dimethoxychrysene (I) by sodium in boiling butan-1-ol to 5 : 6 : 11 : 12 : 15 : 16-hexahydro-1 : 8-dimethoxychrysene (II), an intermediate in the preparation of some D-homo-18 : 19-bisnor-steroids, and claimed that the *trans*-form of (II) is the major constituent of the mixture of *cis*- and *trans*-isomers formed. At the time of their communication we had almost completed an extensive investigation * of this reduction, our starting material being obtained by an alternative route.[2] We now report our results, which indicate that this reduction appears to be non-stereoselective, although appropriate experimental conditions [1] may permit the isolation of more of the *trans*-form of (II) than of the *cis*-stereoisomer. There is also no evidence to show that the similar reduction of the 2 : 8-dimethoxy-isomer of (I) takes place stereoselectively.[3] In contrast to these observations, Johnson and his collaborators [4, 5] have reported that reduction with lithium and alcohol in liquid ammonia of a series of substances (III) takes place with varying degrees of stereoselectivity, depending upon the nature of the substituents (R, R′, R″) and the *trans*- or *cis*-arrangement of rings A and B, to give the products of *trans*- [4] or *cis*-reduction [5] of the styrene double bond.



(I) (II)



(III)

We have already described [2] the catalytic reduction of the compound (I) to give the *cis*-stereoisomer (II). Reduction of the substance (I) with sodium in boiling butan-1-ol gave a mixture, from which the *trans*-stereoisomer of (II) was isolated in relatively poor yield by repeated crystallisation, whereas Birch and Smith,[1] more fortunate than ourselves in finding satisfactory conditions for crystallisation, obtained a fraction rich in *trans*-isomer directly from the reaction mixture in 40% yield, but further crystallisation, or chromatography, was necessary to obtain a completely pure product. The infrared absorption spectra of the two pure stereoisomers of (II) were recorded (Figure; *a*, *b*), and

---

* The essence of the present paper was communicated, and the figure was shown as a slide, at a meeting of the Society on October 18th, 1956, during the discussion of the paper by Professor Birch and Dr. Smith.

[1] Birch and Smith, *J.*, 1956, 4909.

[2] Robins and Walker, *J.*, 1956, 3249, 3260.

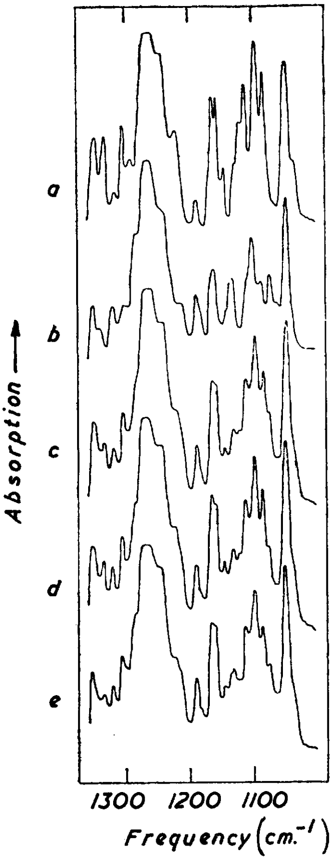
[3] Birch and Smith, *J.*, 1951, 1882.

[4] Johnson, *J. Amer. Chem. Soc.*, 1956, **78**, 6278; Johnson, Rogier, Szmuszkovicz, Hadler, Ackerman, Bhattacharyya, Bloom, Stalman, Clement, Bannister, and Wynberg, *ibid.*, p. 6289.

[5] Johnson, Ackerman, Eastham, and DeWalt, *ibid.*, p. 6302.

the spectrum of a 1 : 1 mixture of the two (Figure; *c*) was compared with that of the crude product from another reduction of (I) with sodium and butan-1-ol; the last pair of spectra were indistinguishable (Figure; *c, e*) over the region in which substantial differences were discernible in the spectra of the pure *cis*- and *trans*-stereoisomers of (II).

In view of the apparent absence of stereoselectivity in the above reduction a series of experiments employing alkali-metal–alcohol–liquid ammonia systems was carried out. In these cases also the reduction of the tetrahydro- (I) to the hexahydro-compound (II) was non-stereoselective (cf. Figure; *d*). Although with a large excess of sodium and propan-2-ol in liquid ammonia reduction did not proceed beyond the introduction of two hydrogen atoms to give compound (II), reduction readily proceeded further with lithium or potassium and ethanol in liquid ammonia, even when low temperatures and small excesses of metal were employed, to give crude products giving some ketonic material on acid hydrolysis (cf. Birch and Smith[1]). The hexahydro-compound (II) in every case appeared to be a 1 : 1 mixture of *cis*- and *trans*-stereoisomers. The tetrahydro-compound (I) was not reduced by lithium aluminium hydride in boiling tetrahydrofuran or by Goodman's lithium aluminium hydride–Carbitol reagent,[6] the starting material being recovered in each case.



Infrared spectrum of: (*a*) cis-5 : 6 : 11 : 12 : 15 : 16-*hexahydro*-1 : 8-*dimethoxychrysene*; (*b*) trans-5 : 6 : 11 : 12 : 15 : 16-*hexahydro*-1 : 8-*dimethoxychrysene*; (*c*) *a* 1 : 1 *mixture of* cis- *and* trans-5 : 6 : 11 : 12 : 15 : 16-*hexahydro*-1 : 8-*dimethoxychrysene*; (*d*) 5 : 6 : 11 : 12 : 15 : 16-*hexahydro*-1 : 8-*dimethoxychrysene from the reduction of* 5 : 6 : 11 : 12-*tetrahydro*-1 : 8-*dimethoxychrysene with sodium and propan*-2-*ol in liquid ammonia*; *and* (*e*) 5 : 6 : 11 : 12 : 15 : 16-*hexahydro*-1 : 8-*dimethoxychrysene from the reduction of* 5 : 6 : 11 : 12-*tetrahydro*-1 : 8-*dimethoxychrysene with sodium and butan*-1-*ol.*

It thus appears from our results that reduction by dissolving metals of the 15 : 16-double bond in the almost planar molecule (I) is non-stereoselective, and that the stereoselective reductions observed by Johnson and his collaborators[4,5] are controlled to a considerable extent by steric and polar[5] factors.

---

[6] Goodman, *J.*, 1951, 2209.

EXPERIMENTAL

Reduction of 5 : 6 : 11 : 12-*Tetrahydro*-1 : 8-*dimethoxychrysene* (I) *with Sodium and Butan-1-ol.*—Sodium (0·24 g., 30 atom-equiv.) was added to a solution of the tetrahydrodimethoxychrysene (I) (0·1 g.) in boiling butan-1-ol. When all the sodium had dissolved the butanol was removed by steam-distillation, and the product was recovered by extraction with ether. The solid residue obtained on evaporation of the dried ethereal solution showed strong ultraviolet absorption of the anisole type at 279 mμ (log ε 3·66), while absorption at 330 mμ indicated that less than 2% of the starting material remained unchanged. The infrared absorption spectrum (Figure; *e*) (carbon tetrachloride solution) was indistinguishable from that of a 1 : 1 mixture of the pure *cis*- and *trans*-stereoisomers of 5 : 6 : 11 : 12 : 15 : 16-hexahydro-1 : 8-dimethoxychrysene (II).

Repetition on a larger scale, followed by repeated recrystallisation of the crude product from methanol–chloroform, gave, with poor recovery, *trans*-5 : 6 : 11 : 12 : 15 : 16-hexahydro-1 : 8-dimethoxychrysene (II) as needles, micro-m. p. 130·5—131·5° (Found: C, 81·2; H, 7·5; MeO, 20·6. Calc. for $C_{20}H_{22}O_2$: C, 81·6; H, 7·5; 2MeO, 20·7%), $\lambda_{max.}$ (in hexane) 274 (infl.), 279, 286 (infl.) mμ (log ε 3·50, 3·55, and 3·31 respectively). On another occasion the *trans*-compound (II) was obtained as leaflets, micro-m. p. 133—137°, which on recrystallisation and seeding with the needle form gave the latter. The leaflets on melting and cooling then remelted at 129—130° repeatedly. The infrared spectra in carbon tetrachloride solution of the two crystalline forms were indistinguishable. Birch and Smith[1] record needles, m. p. 133·5—134·5°.

In another experiment chromatography on alumina was employed in an attempt to separate the mixture of stereoisomers obtained in the reduction. Some concentration of the *cis*-stereoisomer was obtained in the earlier fractions, but the m. p. fell on recrystallisation until the 1 : 1 mixture of stereoisomers resulted. Later fractions contained a concentration of the *trans*-isomer, which could be obtained in poor yield only after several crystallisations.

Reduction of 5 : 6 : 11 : 12-*Tetrahydro*-1 : 8-*dimethoxychrysene* (I) *by Alkali-metal–Alcohol–Liquid Ammonia.*—Experiments were carried out using 4, 10, and 12·5 atomic proportions of sodium, 3, 4, 5, and 10 of lithium, and 10 of potassium, and the following experiment is typical. Potassium (0·14 g., 10 atom-equiv.) was added in several pieces with stirring to a solution of the tetrahydrodimethoxychrysene (I) (0·1 g.) in dry tetrahydrofuran (20 c.c.) and liquid ammonia (100 c.c.). After 10 min. ethanol (5 c.c.) was added to discharge the blue colour and the ammonia was allowed to evaporate. Water was then added and the product was recovered, washed, and dried in ether. The crude sticky product showed 89% of the expected absorption at 279 mμ for the hexahydro-compound (II), and gave with acid alcoholic 2 : 4-dinitrophenylhydrazine a copious precipitate of an orange derivative. Hydrolysis in ethanol (25 c.c.) with concentrated hydrochloric acid (3 c.c.) under reflux for ½ hr., followed by dilution with water and extraction with ether, gave an oil. This was dissolved in benzene–light petroleum (b. p. 40—60°) (1 : 4) and allowed to percolate down a column of activated alumina (10 g.).

Elution with the same solvent mixture left the ketonic material adsorbed on the column. The total eluate was taken to dryness, and the infrared absorption spectrum of the residue was indistinguishable from that of the 1 : 1 mixture of *cis*- and *trans*-5 : 6 : 11 : 12 : 15 : 16-hexahydro-1 : 8-dimethoxychrysene (II).

NATIONAL INSTITUTE FOR MEDICAL RESEARCH,
THE RIDGEWAY, MILL HILL, LONDON, N.W.7.

[*Received, July 5th,* 1957.]