The most widespread use of the Birch reaction (or the modification proposed by Nelson and Wilds) in syntheses of steroid compounds is the reduction of an aromatic ring. Thanks to this reaction, various 19-norsteroids distinguished by high physiological activity have become available [1].

The Birch reduction of steroids of type (I) containing a styrene grouping is not often useful, although in some investigations on the complete synthesis of steroids it has given good results [2, 3]:

So far as concerns the reduction of phenylbutadiene steroid systems of type (II), it has scarcely been studied, although it is of interest since it would lead, in the final analysis, to compounds possessing anabolic activity. The experiments carried out previously in our laboratory on the reduction of the ethylene ketal of 3-methoxy-Δ^{1,9,13,14}-D-homoestratriaconta-17-α-one (III) were of an exploratory nature [4]: the reaction product (after hydrolysis) was provisionally assigned the structure of Δ^{4,8}-19-nor-D-homoandrostadienedione which, as it will be seen below, has proved to be incorrect.

It might be assumed that the action of lithium under Birch's conditions (i.e., in liquid ammonia in the presence of alcohol) would first lead to the reduction of the butadiene system and then that of the aromatic nucleus. This would give (after hydrolysis) Δ^{4}-19-nor-D-homoandrostanedione (IV). If, in the first stage, the reduction takes place partially, the final reaction product should be the dienedione (V). Under these conditions, the dione (IV) can be formed only if the unreduced double bond migrates to a position conjugated with the aromatic ring during the reaction:

We have investigated the Birch reduction of the ketal (III), the corresponding ketone (IIIa), and 3-methoxy-Δ^{1,9,13,14}-D-homoestratriaconta-17α-ol (VI). When the ketal (III) was reduced with a 15 to 20-fold excess of lithium (calculated at the rate of two atoms of lithium per double bond), it was impossible to isolate the intermediate ether of the enol (VII) and the reaction product was subjected to hydrolysis by means of hydrochloric acid in chloroform. As a result, the dienedione (VIII) was obtained as the main reaction product. The structure of the dienedione (VIII) as Δ^{4,9(14)}-19-nor-D-homoandrostadiene-3,17α-dione was shown by its IR and NMR spectra and by the following reactions:
Reduction of the carbinol (VI) under the same conditions followed by hydrolysis gave the ketol (IX), differing from 19-nor-D-homotestosterone and its two isomers previously obtained by the same route from 3-methoxy-Δ^{1,3,5(10)}-8,14-D-homoestratriaen-17αβ-ol. The oxidation of the ketol (IX) with chromic anhydride in pyridine led to the dienedione (VIII), which shows that the course of the reduction is similar for the ketal (III) and the carbinol (VI). In the analogous reaction with the ketone (IIIa), no crystalline products could be isolated; the ketol (IX) was detected chromatographically. In addition, the reaction mixture contained compounds of a phenolic character.

The IR spectrum of the dienedione (VIII) exhibits frequencies at 1688 and 1695 cm⁻¹ corresponding to a Δ⁴,8-keto grouping and a 17α-keto group. It is interesting to note that the frequency of the 17α-keto group in the dienedione (VIII) is 10 cm⁻¹ lower than the same frequency in the dione (IV) (1695 as compared with 1705 cm⁻¹). This can be ascribed to the influence by the 8,14 double bond. A similar influence was noted in the NMR spectrum of the dione (VIII), where the chemical shift of the 18-CH₃- group is characterized by a signal with a δ of 1.25 ppm while the corresponding signal for the dione (IV) is at 1.15 ppm. This difference can be caused only by a closely adjacent double bond (Δ⁴(14) or Δ⁸(14)); the Δ⁸(9) bond, being more remote, cannot exert such a strong influence and is therefore excluded. Examples of a similar influence of a double bond and its position on the chemical shift of angular methyl groups have been reported previously [5].

The choice between Δ⁴(14) and Δ⁸(14) double bonds was determined by the behavior of the dienedione (VII) on hydrogenation, when only one molecule of hydrogen was absorbed (with the formation of the diketone (X)). Consequently, the second double bond must be located in the 8-14 position, since, as is well known, hydrogenation in the 14-15 position takes place readily.

According to published data, the rate of reduction in the Birch reaction is considerably higher for a double bond than for a benzene ring conjugated with this bond [6]. This made it possible to assume that the action of lithium on the ketal (III) first led to 1,4-addition to the butadiene system and then to the reduction of the aromatic nucleus. To confirm this assumption, we carried out the reduction of the ketal (III) by potassium in liquid ammonia with the addition of a mixture of alcohol and ammonium chloride, i.e., under milder conditions than described above. This gave the ketal of 3-methoxy-Δ⁸(9)-14(14)-D-homoestratriaen-17α-one (XI), the UV spectrum of which exhibited a maximum at 277 μm (log ε 3.27) which signified that the presence of a double bond in the 8-9 position could be excluded, since if it were present the extinction would be considerably higher (log ε 4.1-4.3). The position of the double bond in ring D is also excluded, since the ketal (XI) did not hydrogenate with a palladium catalyst under the usual conditions. Thus, the structure given above remained to be adopted:

Further reduction of the ketal (XI) with lithium and alcohol in liquid ammonia led to the ketal (VII), the aromatization of which by means of chromic anhydride in pyridine gave the initial ketal (XI). Hydrolysis of the ketal (VII) with hydrochloric acid gave the above-described dienedione (VIII).