Attempts to hydrolyze the pentaacetate of m.p. 153° to the corresponding free bromoquercitol, by means of aqueous ethanolic hydrogen chloride or bromide, and by other methods, failed to yield any pure product.

DL-(1)R-5-Cyclohexene-1,2,3,4-tetrol Tetraacetate ("Conduritol-*C*" Tetraacetate, M.p. 92°).—The above bromoquercitol pentaacetate (0.55 g.) was treated by the procedure[1c] previously described for making conduritol-*B* tetraacetate from bromo*vibo*quercitol-*A* pentaacetate. The crude product melted at 85–91° and weighed 0.37 g. It was recrystallized from methanol–water (1:2), giving 0.20 g. (58%) of pure conduritol-*C* tetraacetate, m.p. 90–92°.

A mixed m.p. with conduritol-*B* tetraacetate,[1c] which has almost the same m.p. was depressed.

A sample recrystallized twice more for analysis melted at 90.5–92°.

Anal. Calcd. for $C_{14}H_{18}O_8$: C, 53.50; H, 5.77. Found: C, 53.61; H, 5.90.

The compound gives a sluggish reaction with bromine in either carbon tetrachloride or water, but gives a definite positive test for unsaturation with potassium permanganate–acetone. The presence of a double bond was confirmed by hydrogenation (see below).

On ammonolysis, the tetraacetate gave conduritol-*C* (see below).

DL(1)R-5-Cyclohexene-1,2,3,4-tetrol ("Conduritol-*C*," M.p. 152°).—The above tetraacetate of m.p. 92° (0.31 g.) was dissolved in 22 ml. of saturated anhydrous methanolic ammonia. After 24 hours at 25° the solution was filtered. Methanol, ammonia and most of the acetamide were removed by vacuum distillation. The oily residue was taken up in 3 ml. of hot absolute ethanol. The crystals which separated on cooling were collected, giving 0.10 g. of product melting at 151.5–152.2°. A second crop of 0.012 g. with the same m.p. was obtained: total yield 83%. A sample recrystallized once more for analysis showed no change in m.p.

Anal. Calcd. for $C_6H_{10}O_4$: C, 49.31; H, 6.90. Found: C, 49.29; H, 6.97.

Conduritol-*C*, unlike its tetraacetate, reacts rapidly with bromine in water. The reaction with bromine in carbon tetrachloride is sluggish. The potassium permanganate test for unsaturation was positive. A negative test with dinitrophenylhydrazine showed that no rearrangement to a carbonyl compound had occurred.

On hydrogenation conduritol-*C* gave a saturated cyclohexanetetrol (see below).

Hydrogenation of Conduritol-*C* to DL(1)R-Cyclohexane-1,2,3,4-tetrol, M.p. 157°.—Conduritol-*C* (0.150 g.) in 5 ml. of water was hydrogenated with Raney nickel catalyst at 3 atm. at 28° for about two hours. After hydrogenation, the filtered mixture was vacuum distilled, giving a colorless crystalline residue of m.p. 110–154°. This was recrystallized from absolute ethanol, giving 0.057 g. (39%) of colorless crystals, m.p. 150–156°. A sample was recrystallized again, raising the m.p. to 155–157°.

The product was shown by mixed m.p. and fusion analysis[8] to be identical with the cyclohexane-1,2,3,4-tetrol (formula XI) of m.p. 157° prepared by Posternak and Friedli in 1953.[9a]

Hydrogenation of Conduritol-*C* Tetraacetate to DL(1)R-Cyclohexane-1,2,3,4-tetrol Tetraacetate, M.p. 112°.—Conduritol-*C* tetraacetate (0.12 g.) in 5 ml. of absolute ethanol was hydrogenated at 1 atm. at 26° for about two hours with Raney nickel catalyst. After hydrogenation the filtered mixture was vacuum distilled, giving 0.06 g. (50%) of a colorless crystalline residue of m.p. 108–115°. A sample of this residue was recrystallized from aqueous methanol, giving crystals of m.p. 110.5–111°. A sample recrystallized again for analysis melted at 111.0–111.5°.

Anal. Calcd. for $C_{14}H_{20}O_8$: C, 53.16; H, 6.37. Found: C, 53.37; H, 5.98.

We also attempted to prepare the tetrabenzoate of reported[9a] m.p. 154° by benzoylation of the tetrol XI, but have not yet succeeded in purifying the product obtained.

Acknowledgment.—We are indebted to Dr. Théodor Posternak of the Université de Genève, Switzerland, for providing a sample of his cyclohexanetetrol of m.p. 157°; to Mr. Kenneth Irvine for assistance in the preparation of *epi*-inositol; and to the Research Council of Ontario and the Advisory Committee on Scientific Research for generous financial support.

TORONTO 5, CANADA

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY OF THE UNIVERSITY OF VIRGINIA]

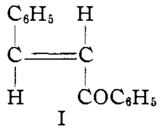
The Effect of Configuration on the Reactivity of the Chalcone System[1]

BY ROBERT E. LUTZ AND JAMES O. WEISS

RECEIVED NOVEMBER 1, 1954

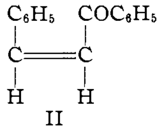
Phenylmagnesium bromide adds largely 1,4 to both *cis*- and *trans*-chalcones. Phenyllithium, which adds largely 1,2 to the *trans* isomer, adds chiefly 1,4 to the *cis*. Both isomers are reduced exclusively 1,2 at the carbonyl groups by aluminum isopropoxide and sodium borohydride, the *trans* isomer more easily than the *cis*; and both isomers are reduced 1,2 by lithium aluminum hydride. *trans*-Benzalacetomesitylene is not reduced by aluminum isopropoxide or sodium borohydride but is reduced 1,4 by lithium aluminum hydride. These results have been interpreted in terms of greater steric interferences in *cis*-chalcone, especially at the carbonyl carbon.

In the light of *cis–trans* differences in ultraviolet absorptivities and chemical reactivities of the α-phenylchalcones,[2] it was important to extend the study of such differences to the parent chalcones themselves (I, II) utilizing the now available *cis* isomer.[3]



$$\begin{array}{ccc} C_6H_5 & & H \\ | & & | \\ C & = & C \\ | & & | \\ H & & COC_6H_5 \end{array}$$

I



$$\begin{array}{ccc} C_6H_5 & & COC_6H_5 \\ | & & | \\ C & = & C \\ | & & | \\ H & & H \end{array}$$

II

Reaction with Alkaline Hydrogen Peroxide.—It has been pointed out[2a] that *trans*-chalcone (I), which has the more effectively conjugated system, reacts several times more rapidly with this reagent than does the *cis* isomer to give the same epoxide (the possible stereoisomeric epoxide is known[4b]). That this difference in rate of reaction is a true measure of the relative rates of peroxide attack and not of isomerization of the *cis* isomer first to the more reactive *trans* isomer, is now shown by the fact

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(1) This investigation (a) was supported by a grant from the National Science Foundation, and (b) is described in a Master's thesis (J.O.W.), University of Virginia, August, 1954. (c) The work on the α-phenylchalcones by Lutz and Rinker (ref. 2c) also was supported by the grant from the National Science Foundation but was erroneously credited only to a grant from the Office of Ordnance Research under which the investigation was initiated.

(2) W. B. Black and R. E. Lutz, THIS JOURNAL, (a) **75**, 5990 (1953); (b) **77**, in press (1955); (c) R. E. Lutz and E. H. Rinker, **77**, 366 (1955).

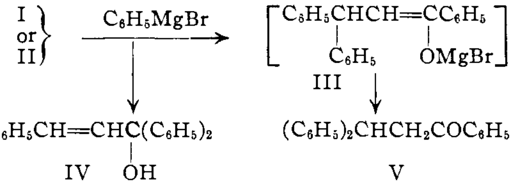
(3) (a) R. E. Lutz and R. H. Jordan, *ibid.*, **72**, 4090 (1950); (b) L. P. Kuhn, R. E. Lutz and C. R. Bauer, *ibid.*, **72**, 5058 (1950).

that *cis*-chalcone, although it is the labile isomer, is stable in the absence of hydrogen peroxide under the alkaline reaction conditions involved. The recently proposed mechanism of this peroxide reaction[4a] includes an initial 1,4-reaction step; and the reaction is limited to attack at the β-carbon and does not involve a competing reaction at the carbonyl carbon such as occurs in the addition of the Grignard reagent. The empirically greater nucleophilic reactivity of the *trans* system as compared with the *cis* is thus demonstrated.

Addition of phenylmagnesium bromide to *trans*-chalcone according to Kohler[5] gives 85% of 1,4-addition compound (III → V) and 4% of 1,2-addition (the latter was estimated by oxidation of the product IV to benzoic acid). We have confirmed these findings and obtained 89% of 1,4-addition product and accounted for the remainder of the reaction as 1,2-addition.

cis-Chalcone under comparable conditions also gave 89% of 1,4-addition, but in this case no 1,2-addition was demonstrated although it may have occurred to a small extent. It seems unlikely that *cis*-to-*trans* rearrangement occurs first during the reaction in view of retention of configuration, during the 1,2-reductions, and up to the point of reaction with phenyllithium (see below).

Information as to the relative rates of the 1,4-additions to the *cis*- and *trans*-chalcones is not available and will be hard to get because of the high speed of the reactions and because of the necessity of a large excess of reagent at all times to minimize secondary reactions.



$$\left.\begin{matrix}\text{I}\\\text{or}\\\text{II}\end{matrix}\right\}\xrightarrow{C_6H_5MgBr}\left[\begin{matrix}C_6H_5CHCH{=}CC_6H_5\\ \quad |\qquad\qquad |\\ \quad C_6H_5\qquad OMgBr\end{matrix}\right]_{\text{III}}\longrightarrow \underset{\text{V}}{(C_6H_5)_2CHCH_2COC_6H_5}$$

$$\text{I or II}\longrightarrow \underset{\text{IV}}{C_6H_5CH{=}CHC(C_6H_5)_2OH}$$

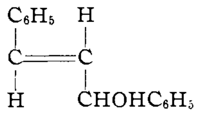
Thus it is clear that both *cis*- and *trans*-chalcones add the Grignard reagent chiefly 1,4 and that 1,2-addition occurs only to a relatively minor extent (possibly not at all in the case of *cis*-chalcone). The results parallel those in the α-phenylchalcone series.[2c]

Addition of phenyllithium to *trans*-chalcone, in repetition of the work of Michael and Saffer,[6] gave 79% of 1,2-addition (ref. 6a, 80%) and 14% of 1,4-addition, a result diametrically opposite to that of the addition of the Grignard reagent. This result seems to show a predilection of phenyllithium toward 1,2- rather than 1,4-addition when steric hindrance is at a minimum as is the case in the fully-planar *trans*-chalcone.

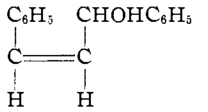
cis-Chalcone, on the other hand, is found to add phenyllithium 87% 1,4 and only 7% 1,2. This is a quite different mode of addition than in the case of the *trans* isomer and it is one which is comparable with the mode of addition of phenylmagnesium bromide to both isomers. The results parallel those found in the addition of phenyllithium to *cis*- and *trans*-α-phenylchalcones.[2c]

Additional evidence concerning the steric effects at the chalcone carbonyl is provided by the behavior of *trans*-benzalacetomesitylene (VIII) which undergoes entirely 1,4-addition of both phenylmagnesium bromide[5a] and phenyllithium.[7] Here the carbonyl carbon is effectively and prohibitively shielded by the *ortho* methyls and 1,2-addition by either reagent is thereby prevented (and presumably this would also be true of the unknown *cis* isomer).

Aluminum isopropoxide reduction of *trans*-chalcone gave 94% yield of the *trans* unsaturated carbinol VI (ref. 8, 76%). *cis*-Chalcone under identical conditions reacted definitely slower and gave 92.5% yield of the corresponding *cis* unsaturated carbinol VII, an oil which corresponds in properties to the product of partial catalytic hydrogenation of 1,3-diphenylpropiolyl alcohol.[9] Both isomers VI and VII showed infrared hydroxyl bands at *ca.* 2.8 μ and no significant carbonyl absorption in the 6 μ region (however, a very small absorption peak in the 6 μ region by the non-crystalline *cis* isomer VII indicated the presence of a carbonylic impurity, possibly unreacted *cis*-chalcone). The two isomers showed ultraviolet absorption bands at 253 and 247 mμ, respectively; the *trans* isomer VI had the higher molar absorptivity (ϵ 21,000) and the *cis* isomer VII the lower (ϵ 12,900) as would be expected in view of steric interference with planarity in the latter; the *trans* isomer did not absorb in the 300 mμ chalcone region, whereas the sample of the *cis* isomer showed very slight absorption at this point (which is another indication of the presence of a small amount of a chalcone-like impurity).



VI, m.p. 56°



VII, oil

It is significant that aluminum isopropoxide reductions of both isomers have taken place specifically 1,2 at the carbonyl groups and that the labile configuration has withstood the conditions necessary to give the corresponding *cis* product.

trans-Benzalacetomesitylene (VIII) was recovered unchanged after five times the length of treatment with aluminum isopropoxide employed above, a fact which shows the very great steric hindrance toward 1,2-reduction here, yet resistance of the fully effective conjugated cinnamoyl system toward reaction with this carbonyl-specific reagent.

Sodium borohydride reduction of *trans*-chalcone proceeded 78% to the carbinol VI, but the reaction required five hours in refluxing ethanol. *cis*-Chalcone was reduced similarly but considerably slower.

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[4] (a) C. A. Bunton and G. J. Mincoff, *J. Chem. Soc.*, 665 (1949); (b) H. H. Wasserman and H. E. Aubrey, THIS JOURNAL, **77**, 590 (1955).

[5] (a) E. P. Kohler, *Am. Chem. J.*, **38**, 511 (1907); (b) Kohler reported 94% of 1,4-addition but this is at variance with the value 85% which we calculated from his reported weight of crude product.

[6] (a) A. Michael and C. M. Saffer, *J. Org. Chem.*, **8**, 60 (1943); (b) H. Gilman and R. H. Kirby, THIS JOURNAL, **63**, 2046 (1941).

[7] (a) *C. A.*, **44**, 1402 (1950) (A. H. Nesmeyanov and V. A. Sazonova, *Izvest. Akad. Nauk S.S.S.R., Otdel Chim. Nauk*, 422 (1949); (b) the assumption of the *trans* configuration of benzalacetomesitylene is based on ref. 2b.

[8] W. L. Truett and W. N. Moulton, THIS JOURNAL, **73**, 5913 (1951).

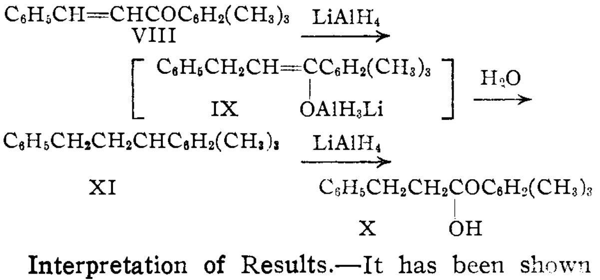
[9] K. N. Campbell, B. K. Campbell and M. J. McGuire, *Proc. Indiana Acad. Sci.*, **50**, 87 (1940).

Under these same conditions benzalacetomesitylene (VIII) was recovered unchanged.

The greater facility of 1,2-reduction of *trans*-chalcone as compared with the speed of reduction of the *cis* isomer by the above reagents seems best explained empirically in terms of the greater steric shielding of the carbonyl carbon which is inherent in the *cis* configuration as will be seen upon inspection of scalar molecular models.

Lithium aluminum hydride reduction of *trans*-chalcone receives mention in the literature but without experimental details,[10] and it is claimed that this reduction takes place 1,2 followed, depending on conditions, by reduction of the ethylene double bond.• In our hands *trans*-chalcone was reduced easily by an excess of reagent under mild conditions to the *trans*-carbinol VI in 88% yield. *cis*-Chalcone gave 95% yield of an oil which was shown to be the *cis*-carbinol VII by the near-identity of its ultraviolet and infrared absorption spectra with those of the oil obtained in the aluminum isopropoxide reduction. The reductions were rapid and no attempt was made to determine relative rates.

Reduction of *trans*-benzalacetomesitylene VIII under the same conditions gave an oil in 97% yield which was shown to be the 1,4-addition product, benzylacetomesitylene(XI), by analysis, by ultraviolet absorption spectra which showed the absence of a strongly conjugated ethylene double bond, and by infrared absorption which showed a strong carbonyl band at 5.97 μ and no hydroxyl band in the 2.8 μ region. Had reduction (of VIII) proceeded other than 1,4, by 1,2-reduction of the keto group or reduction first of the ethylene double bond, a different product would have been expected. The saturated ketone actually isolated (XI) is itself reduced to the saturated carbinol X (rather than enolized) under these conditions and could not have been formed first or present as such in the reduction mixture; and this proves that the reduction must have been 1,4 directly to the enolate IX which would be immune to further reduction by the reagent until after hydrolysis of the reduction mixture and consequent destruction first of the excess reagent.[11]



$$\underset{\text{VIII}}{C_6H_5CH{=}CHCOC_6H_2(CH_3)_3} \xrightarrow{\text{LiAlH}_4} \left[\underset{\text{IX}}{C_6H_5CH_2CH{=}\underset{\text{OAlH}_3\text{Li}}{\underset{|}{C}}C_6H_2(CH_3)_3}\right] \xrightarrow{H_2O}$$

$$\underset{\text{XI}}{C_6H_5CH_2CH_2CHC_6H_2(CH_3)_3} \xrightarrow{\text{LiAlH}_4} \underset{\text{X}}{C_6H_5CH_2CH_2\underset{\text{OH}}{\underset{|}{C}}OC_6H_2(CH_3)_3}$$

Interpretation of Results.—It has been shown that the planar *trans*-chalcone system as a whole accounts best for the ultraviolet absorption characteristics of this isomer,[2a] whereas in the *cis* isomer the existence of a "partial chromophore" is evident from the strong middle wave length absorption which is attributed to the acrylophenone or/and benzoyl group. The preference of the *cis* isomer for 1,4-addition of phenyllithium is in a sense consistent with the absorption characteristics of this isomer and possibly might have been predicted from them. However, such an interpretation involves questionable assumptions, and it does not explain the hydroperoxide reaction where it is *trans*-chalcone which reacts the more rapidly.

In a more empirical approach it may be assumed, with support from inspection of scalar molecular models, that over-all steric interferences are much greater in the *cis* configuration than in the *trans*, and are primarily responsible for the deviations from planarity and alteration of the effectiveness of the principal conjugated systems. The ultraviolet spectrum in some degree mirrors these effects but does not show the classical type steric "hindrance" and its damping effect on reaction speeds. The "hindrance" effect directly at the β-carbon is small, and the greater difficulty of the hydroperoxide reaction of the *cis* isomer may be interpreted in terms of this effect coupled possibly with appreciable diminution in the effectiveness of the vinyl ketone conjugation. On the other hand, the retardation of the carbonyl-specific 1,2-reductions is doubtless due primarily to the considerable direct steric "hindrance" at the carbonyl-carbon which accounts adequately for the preference of the *cis* isomer for 1,4-addition of phenyllithium.

Further experiments on *cis–trans* differences are in progress, and note is made of preliminary results on the addition of diazomethane; *trans*-chalcone (in our hands) gives directly the pyrazoline of m.p. 129–133°,[12] but the *cis* isomer gives a different product which has not yet been obtained in crystalline form. On the other hand, no significant difference was found in the facility of addition of sodium bisulfite to the two isomers.[13]

Experimental[14]

The ultraviolet absorption spectra were determined in isoöctane at 0.00005 *M* concentrations using a Beckman DU quartz spectrophotometer. **The infrared absorptions** were run in solutions of 50 mg. per ml. of chloroform using a Baird direct recording double-beam spectrophotometer.

The preparation of *cis*-chalcone[3a] was not carried out successfully on a large scale because of excessive polymerization that occurred under the necessarily prolonged irradiation by sunlight or "sunlamp." Experiments in an attempt to diminish this polymerization by the use of antioxidants did not appear to be helpful. The optimal procedure thus far used is as follows.

A solution of 100 g. of *trans*-chalcone in 4 l. of isoöctane was irradiated for 5 days by direct sunlight (a "sunlamp" gave poorer results). After standing about 4–6 hours at −20° until a few characteristic deep-yellow rosettes of the *cis* isomer had appeared in the mass of pale yellow crystals of the *trans* compound, the solution was quickly decanted, seeded with *cis* isomer, and again allowed to stand at −20° (2–3 days). The solution was decanted from the crystallized *cis* isomer back into the original flask containing the bulk of the *trans* isomer (for re-irradiation after addition of more *trans*-chalcone, and reprocessing, a procedure which was repeated three or four times until the accumulation of polymers became excessive). The yield of *cis* isomer of m.p. 45–46° from each irradiation was 3–5 g.

The *meta*-stability of *cis*-chalcone under the alkaline conditions used in earlier comparative peroxide reactions[2a] with

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[10] W. G. Brown, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 482.

[11] *Cf.* R. E. Lutz and D. F. Hinkley, This Journal, **72**, 4091 (1950).

[12] *Cf.* L. I. Smith and W. B. Pings, *J. Org. Chem.*, **2**, 23 (1937), who reported the m.p. 127–129°.

[13] R. Morise, *Ber.*, **37**, 4049 (1904).

[14] Microanalyses were by Miss Mai Lai.

the *cis* and *trans* isomers, was shown by recovery of material of m.p. 39–43° (80%, identified) after treatment of 0.5 g. with 0.6 ml. of 2 *N* sodium hydroxide and 6 ml. of methanol at room temperature for 15 min.

The addition of phenylmagnesium bromide to *trans*-chalcone was carried out approximately according to Kohler's procedure[5] as follows: To a solution of phenylmagnesium bromide[15] was added at −10° under stirring a solution of *trans*-chalcone in 200 ml. of dry ether, slowly enough so that the resulting yellow precipitate dissolved completely (the order of addition and large excess of reagent is necessary to minimize secondary reactions). The mixture was allowed to come to room temperature and to stand for 3 hr., and was hydrolyzed with ice and dilute hydrochloric acid. The ether layer (and ether extract) was evaporated under reduced pressure and the residue dissolved in acetone; this solution at 15° was treated with 2 g. of potassium permanganate (shaken for 1 hr.) and then with sulfur dioxide to destroy excess reagent, and was filtered from manganese dioxide. Upon basification and steam distillation, acidification and again steam distilling, 0.8 g. (13.5%) of crude benzoic acid was obtained (ref. 5, 4%), and this was presumed to be directly proportional to the carbinol IV. The residue V from the steam distillations was recovered by extraction with ether and was crystallized from an ethanol–water mixture; 12.3 g. (89%), m.p. 88–92° (ref. 5, 85%, m.p. 92°).

Addition of phenylmagnesium bromide to *cis*-chalcone (5 g.) under comparable conditions gave 6.1 g. (88.7%) of V of m.p. 87–90°; recrystallized, m.p. 90.5–91.5°; identified as V by mixture m.p. No benzoic acid was actually isolated, but a small amount could easily have escaped detection.

In parallel experiments solutions of *cis*- and *trans*-chalcones at −60° were added suddenly under vigorous stirring to twenty times the usual amounts of phenylmagnesium bromide solution also at −60°. After ten seconds the temperature had risen to −40° and the reactions were quenched by addition of carbon dioxide snow. Ultraviolet absorption analysis of the products showed absence of unreacted chalcone.

Addition of phenyllithium[16] to *trans*-chalcone according to Michael and Saffer[6] but using a fourfold excess of reagent, starting from 10 g. of I and 5.3 g. of lithium, gave 9.8 g. (71%) of m.p. 111° and 0.8 g. (8%) of m.p. 100–106°, a total of 79% of IV (ref. 6, 110–111°). The third fraction, 1.8 g. (14%) of m.p. 86–91° was identified by mixture m.p. as V. None of the compound of m.p. 160.5–161° mentioned by Michael and Saffer[6] was isolated.

Similar addition to *cis*-chalcone (4 g.) gave 4.9 g. (89%) of V, m.p. 84–88° (identified), and 0.4 g. (7%) of oil which could not be crystallized and was presumed to be, but not actually identified as, IV.

Aluminum isopropoxide reduction of *trans*-chalcone proceeded according to the method of Truett and Moulton,[8] but in our hands required 2.5 hr. of refluxing for completion; 10 g. of I gave 9.5 g. (94%) of fluffy crystals of VI, m.p. 55–56° (ref. 8, 57–59°). Ultraviolet absorption: $\lambda_{\max.}$ 253 mμ (ϵ 21,000) and shoulder at 284 mμ (ϵ 1,700); infrared bands at 2.79, 2.97 and 6.30 μ, and none at 6.0–6.2μ.

Anal. Calcd. for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.44; H, 6.53.

Similar **reduction** of *cis*-chalcone (2 g.) gave 1.85 g. (92.5%) of an oil from which no crystals were obtained; fractional evaporation at reduced pressure onto a cold-finger condenser, and repetition of the procedure on the middle cut to obtain another middle cut, gave a product which was characterized as VII[9], n^{25}_{D} 1.6111 (ref. 9, gave n^{20}_{D} 1.5821 for the product of Raney nickel partial hydrogenation of 1,3-diphenyl-3-hydroxypropyne-1). Ultraviolet absorption: $\lambda_{\max.}$ 2.47 mμ (ϵ 12,900) and 280–295 mμ (ϵ 2,000); infrared bands at 2.78, 2.95 (broad), 6.08 (medium) and 6.27 μ.

Anal. Calcd. for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 86.28; H, 6.56.

The Relative Rates of Reduction of *cis*- and *trans*-Chalcones by Aluminum Isopropoxide.—A solution of 1 g. of *cis*- or *trans*-chalcone in 12.5 ml. of isopropyl alcohol was added to a boiling solution of 5.5 g. of aluminum isopropoxide. The mixture was refluxed for 30 min., poured into water, treated with excess sodium hydroxide and extracted with ether. After drying over sodium sulfate and evaporation under reduced pressure, the residual oil was kept under reduced pressure at 50–70° for several hours to eliminate last traces of solvent (almost quantitative) and was analyzed by ultraviolet absorptivity as compared with the absorptivity of pure *cis*- or *trans*-chalcone at the long wave length $\lambda_{\max.}$ of 295 and 298 mμ, respectively, assuming the absorptivity to be zero when reduction was complete. In the case of the *trans* isomer this oil was found to be 97% reduction product, and in the case of the *cis*, 31%.

***trans*-Benzalacetomesitylene[5] (VIII)** under similar reducing conditions but with 12 hr. refluxing time was recovered unchanged; 91% identified. Infrared: no absorption at 2.6–2.8 μ; band at 6.17 μ (inflections at 6.09 and 6.27 μ; shoulder at 6.38 μ).

Lithium aluminum hydride reduction of *trans*-chalcone was carried out by the method of Hochstein and Brown[17] for the reduction of cinnamaldehyde, except that inverse order of addition was not used; temperature −10°, time 12 min. The product (oil) crystallized from ligroin, 8.92 g. (88.3%), m.p. 50–54° (recrystallized, m.p. 55–56°, and identified as VI).

Corresponding **reduction of** *cis*-chalcone (2 g.) gave 1.9 g. (95%) of oil from which no crystals were obtained. After purification this oil was shown to be identical with the above sample of VII by analysis: n^{25}_{D} 1.6094; $\lambda_{\max.}$ 244 mμ (ϵ 12,500) and 280–300 mμ (ϵ 600); infrared bands at 2.79 μ (shoulder at 2.94 μ) and 6.28 μ; a weak plateau at 6.0–6.2 μ.

Anal. Calcd. for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.27; H, 6.58.

A similar **reduction of *trans*-benzalacetomesitylene (VIII)** (3 g.) gave 2.9 g. (97%) of oil which was purified by two fractional evaporations under reduced pressure and collection of the several cuts in succession on a cold-finger condenser. It was identified as benzylacetomesitylene (XI) by analysis and the following properties: n^{25}_{D} 1.5568; $\lambda_{\max.}$ 235 mμ (ϵ 770); 248 mμ (ϵ 1,590); infrared: no absorption at 2.6–2.8 μ; bands at 5.97 (carbonyl) and 6.24 μ.

Anal. Calcd. for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.44; H, 8.63.

1-Mesityl-3-phenylpropanol-1 (X).—Lithium aluminum hydride reduction of the saturated ketone XI under the conditions applied to the unsaturated ketone VIII gave the saturated carbinol X, n^{25}_{D} 1.5625; infrared absorption bands at 2.66, 2.80 and 6.20 μ; none at 5.8–6.1 μ.

Anal. Calcd. for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 84.81; H, 8.63.

Sodium borohydride reduction of *trans*-chalcone was patterned somewhat after the method of Chaikin and Brown,[18] using 0.57 g. of reagent, 10 g. of I and 200 ml. of methanol, under reflux for 5 hr. (the reaction had gone only about half way in 1.5 hr.); yield 7.9 g. (78%), m.p. 55–56.5° (identified as VI).

Similar reduction of *cis*-chalcone (1.0 g.) by 0.14 g. of sodium borohydride in 25 ml. of boiling methanol (refluxing time 6.5 hr.) gave 0.72 g. (72%) of oil which was identified as the *cis* unsaturated alcohol VII by identity of its ultraviolet absorption spectrum with that of the sample obtained by aluminum isopropoxide reduction (above).

Application of similar reducing conditions to benzalacetomesitylene (VIII) resulted in 83% recovery of starting material.

Relative Rates of Sodium Borohydride Reductions of *cis*- and *trans*-Chalcones.—A solution of 1 g. of *cis*- or *trans*-chalcone in 12.5 ml. of absolute methanol was added to a boiling solution of 0.07 g. of sodium borohydride in 12.5 ml. of methanol. The mixture was refluxed for one hour, poured into 150 ml. of cold water and immediately extracted with ether; the ether was dried over sodium sulfate overnight, evaporated under reduced pressure and kept under reduced pressure at 50–70° for several hours. The resulting oils (89–92% yield), from duplicate runs on each isomer,

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[15] Prepared according to C. F. H. Allen and S. Converse, "Organic Syntheses," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932, p. 226.

[16] Prepared according to H. Gilman and Miller, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 353.

[17] F. A. Hochstein and W. G. Brown, THIS JOURNAL, **70**, 3484 (1948).

[18] S. W. Chaikin and W. G. Brown, *ibid.*, **71**, 122 (1949).

were analyzed by determination of the long wave length ultraviolet absorption maxima (as above in the case of the aluminum isopropoxide reductions) and comparison with those of the pure chalcones, and in the case of the *trans*-chalcone consisted of 68–71.5% of reduction product and largely unchanged material in the case of the *cis* isomer.

Attempted sodium bisulfite addition was unsuccessful under the conditions employed successfully with dimesitoylethylene.[19] The method of Morisse[18] succeeded on both isomers but long refluxing time was required (10 hr.); yield 99%. (Reaction in neither case was complete after 8 hr. of refluxing time.) Upon addition to hot sodium hydroxide solution the addition compound gave *trans*-chalcone.

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(19) R. E. Lutz and W. G. Reveley, THIS JOURNAL, **61**, 1859 (1939).

CHARLOTTESVILLE, VIRGINIA

[CONTRIBUTION FROM AVERY LABORATORY OF THE UNIVERSITY OF NEBRASKA]

Some Methylphenanthrolines and Corresponding Aldehydes

BY ROBERT L. EIFERT[1] AND CLIFF S. HAMILTON

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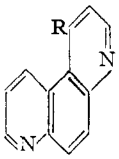
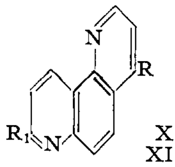
The synthesis of three new phenanthroline aldehydes by selenium dioxide oxidation of the appropriate methylphenanthroline is described. Two previously unknown methylphenanthrolines have been synthesized by a new route. An improved synthesis of 4-methyl-1,10-phenanthroline is presented.

Only a few mono-methylphenanthrolines have been described in the literature. For the most part these substances have been prepared from an aminoquinaldine[2] or an aminolepidine[3] by means of a Skraup reaction and have been obtained in very poor yields.

In the present investigation, an adaptation of a method studied by Campbell and Schaffner[4] for the preparation of some 4-methylquinolines was applied successfully to the synthesis of 1-methyl-4,7-phenanthroline (X) and 4-methyl-1,7-phenanthroline (XII).



X, R = CH_3
XI, R = CHO



XII, R = CH_3, R_1 = H
XIII, R = CHO, R_1 = H
XIV, R = H, R_1 = CH_3
XV, R = H, R_1 = CHO

The reaction was carried out by the dropwise addition of methyl vinyl ketone to an alcoholic solution of an aminoquinoline or its hydrochloride and ferric chloride. The two previously unknown methylphenanthrolines were obtained as white needles from benzene–petroleum ether and were soluble in ether, ethanol and hot water.

Although this method was successful for the preparation of X and XII, it failed in the case of 4-methyl-1,10-phenanthroline (XVI). This failure was due to the formation of the extremely stable ferrous complex salt of XVI from which only a small amount of XVI could be isolated. This difficulty was circumvented by applying a modification of the Skraup reaction described by Yale and Bernstein.[5] The formation of XVI proceeded in 26–30% yield when methyl vinyl ketone was added to a solution of 8-aminoquinoline (VI) and arsenic pentoxide in 85% phosphoric acid. This yield was somewhat better than the 14.9% obtained by Case[3] from 8-aminolepidine by means of the Skraup reaction.

The reaction of 5-aminoquinaldine (IX) with glycerol under the conditions of the Skraup reaction gave a 25% yield of 8-methyl-1,7-phenanthroline (XIV). This compound was first described by Gerdeissen[2] and was erroneously named 2-methyl-1,7-phenanthroline. It should be noted that only one substance was isolated in this investigation although Gerdeissen reported the formation of a second substance having the same empirical formula as XIV.

Many quinoline aldehydes have been prepared by the oxidizing action of selenium dioxide on methylquinolines,[6] but the extension of this useful reaction to the analogous methylphenanthrolines is not recorded in the literature.

Oxidation of X, XII and XIV with freshly prepared selenium dioxide proceeded readily in boiling xylene. The aldehydes crystallized from benzene as white needles after being isolated from the xylene solution as their bisulfite addition products. All of the aldehydes reduced Tollens reagent and formed high melting thiosemicarbazones which were insoluble in most solvents. The infrared absorption spectra of the aldehydes revealed a carbonyl stretching frequency of 1680 cm.$^{-1}$ for 4,7-phenanthroline-1-carboxaldehyde (XI) and 1690 cm.$^{-1}$ for 1,7-phenanthroline-8-carboxaldehyde (XV).

The oxidation of XVI proceeded with the precipitation of selenium, but no aldehyde could be isolated from the reaction mixture.

Experimental

6-Nitroquinoline (I).—This compound was prepared from *p*-nitroaniline in 48% yield as described by Capps and Hamilton.[7]

5-Nitro- (II) and 8-Nitroquinoline (III).—Nitration of quinoline by the method of Fieser and Hershberg[8] gave II (35%) and III (43%).

Aminoquinolines.—5-Nitro-, 6-nitro- and 8-nitroquinoline were reduced with iron and acetic acid as described by Linsker and Evans[9] for the synthesis of 6-aminoquinoline. The yields were: 5-amino- (IV) (71%), 6-amino- (V) (88%), 8-amino- (VI) (40.7%).

5-Nitro- (VII) and 8-Nitroquinaldine (VIII).—Quinaldine

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(1) Parke, Davis and Company Fellow 1952–1953; E. I. du Pont Fellow 1953–1954.

(2) Gerdeissen, *Ber.*, **22**, 244 (1889).

(3) F. H. Case, THIS JOURNAL, **70**, 3994 (1948).

(4) K. N. Campbell and I. J. Schaffner, *ibid.*, **67**, 86 (1945).

(5) H. L. Yale and J. Bernstein, *ibid.*, **70**, 254 (1948).

(6) R. Adams, "Organic Reactions," Vol. 5, John Wiley and Sons, Inc., New York, N. Y., 1949, Chap. 8.

(7) J. Capps and C. S. Hamilton, THIS JOURNAL, **60**, 2104 (1938).

(8) L. F. Fieser and E. B. Hershberg, *ibid.*, **62**, 1640 (1940).

(9) F. Linsker and R. L. Evans, *ibid.*, **68**, 874 (1946).