Registry No.—**1a**, 24499-89-6; **1b**, 34440-84-1; **2a**, 24496-61-5; **2b**, 34440-86-3; **3a**, 24496-65-9; **3b**, 34440-88-5; **6**, 34440-89-6; **12a**, 34440-90-9; **12b**, 34440-91-0; **13c**, 34440-94-3; **13d**, 34440-92-1; **14c**, 34440-93-2; **14d**, 34440-95-4; **15b**, 34440-96-5; **15c**, 34440-97-6; **15d**, 34440-98-7; **15e**, 34440-99-8; **15f**, 34441-00-4.

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Notes

Cycloalkanones. I. The Stereochemistry of α,α'-Dibenzylcycloalkanones

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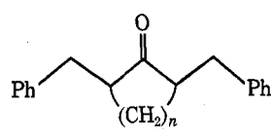
In the course of investigation of cycloalkanones for possible drug uses,[2] it became necessary to establish the stereochemistry of the series of α,α'-dibenzylcycloalkanones **1**–**4**. The *cis*- (**2a**) and *trans*- (**2b**) cyclo-



1, $n = 2$ **3**, $n = 4$
2, $n = 3$ **4**, $n = 5$

hexanones are known in the literature.[3,4] Both *cis*- (**1a**) and *trans*- (**1b**) cyclopentanone have been reported,[5] but the sterochemistry has not been established. A liquid dibenzylcycloheptanone has been reported[6] as well as its oxime.[7] The cis (**3a**) and trans (**3b**) isomers have not been isolated previously. Neither *cis*- (**4a**) nor *trans*- (**4b**) dibenzylcyclooctanone is known. In the present work, all four pairs of isomers were isolated and their configurations established.

The configurations of the isomeric ketones were established by lithium aluminum hydride reduction. Analysis for the number of alcohols obtained in each case was by vpc. The results are given in Table I. The assignment of the cyclohexanone isomers was consistent with the literature.[3] As a further check on the analysis, samples of the alcohols from both isomers of the cyclohexanone and cyclooctanone compounds were isolated by preparative vpc and used for mass spectral analysis. All showed the correct molecular ion peak. The molecular ion peak was small in all cases, but each had a large P − 18 peak, confirming that the compounds seen by vpc were the alcohols.

TABLE I
NUMBERS OF ALCOHOLS PRODUCED ON $LiAlH_4$ REDUCTION OF α,α'-DIBENZYLCYCLOALKANONES

Compd	Mp, °C	No. of alcohols[a]	Assigned configuration
1a	39–40	2	cis
1b	54–55	1	trans
2a	119–122	2	cis
2b	55	1	trans
3a	*b*	2	cis
3b	*c*	1	trans
4a	84–85	2	cis
4b	82–83	1	trans

[a] From $LiAlH_4$ reduction. [b] First ketone isolated during column chromatography. [c] Second ketone isolated during column chromatography.

As it was necessary for biological correlation to know which isomer predominated in an equilibrating system, one isomer of each pair of ketones was equilibrated in 0.1 *M* NaOEt, in ethanol. Samples were taken at 24-hr intervals until no change was seen. The cyclohexanones and cyclooctanones were separable as the ketones, but the cycloheptanones had to be reduced to the alcohols with $NaBH_4$. The equilibrium concentration of the cyclopentanones was not obtained owing to the inability to separate either the ketones or the alcohols on a variety of columns. The two alcohols from the cis ketone could be separated, but one of them overlapped the alcohol from the trans ketone. The equilibrium concentrations are given in Table II.

TABLE II
EQUILIBRIUM CONCENTRATIONS OF α,α'-DIBENZYLCYCLOALKANONES IN 0.1 *M* NaOEt IN ETHANOL

Compd	cis, %	trans, %
2	88	12
3	35	65
4	40	60

Experimental Section

All melting points are uncorrected and were obtained on a Mel-Temp apparatus. Analytical vpc utilized a Packard model 800 and preparative vpc utilized a Varian Aerograph Model 202. The α,α'-dibenzylidenecycloalkanones were prepared by base-catalyzed condensations of benzaldehyde with the appropriate

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cyclic ketone.[2] Elemental analysis was made of all compounds.[2]

cis-**2,5-Dibenzylcyclopentanone.**—Hydrogenation of 2,5-dibenzylidenecyclopentanone[2] in EtOAc over 10% Pd/C gave a mixture of saturated ketone and alcohol (ir). Chromatography on silica gel gave an oil which later crystallized on standing in an open dish, mp 39–40° (lit.[5] mp 39°).

trans-**2,5-Dibenzylcyclopentanone.**—Isomerization of the cis isomer in methanolic KOH after Cornubert, *et al.*,[5] gave the trans isomer, mp 54–55° (lit.[5] mp 58°). By tlc (C_6H_6/$CHCl_3$, 95:5) this material was free of the cis isomer.

cis-**2,6-Dibenzylcyclohexanone.**—Crystallization of the crude mixture from hydrogenation (10% Pd/C in EtOAc) of 2,6-dibenzylidenecyclohexanone[2] from MeOH gave the cis isomer, mp 119–122° (lit.[3] mp 122°).

trans-**2,6-Dibenzylcyclohexanone.**—The trans isomer was isolated from the mother liquor from crystallization of the cis isomer, after several batches of cis isomer were removed, mp 55° (lit.[3] mp 55°).

cis- **and** *trans*-**2,7-Dibenzylcycloheptanone.**—Hydrogenation of 2,7-dibenzylidenecycloheptanone[2] (10% Pd/C in EtOAc) gave an oil which failed to crystallize. Chromatography of 1 g of the oil on a 2-cm column using 60 g of 75–325 mesh silica gel and C_6H_6 eluent gave first the cis isomer, followed by the trans. Neither isomer was ever obtained as a solid.

trans-**2,8-Dibenzylcyclooctanone.**—Crystallization of the crude mixture from hydrogenation (10% Pd/C in EtOAc) of 2,8-dibenzylidenecyclooctanone[2] from MeOH gave the trans isomer, mp 82–83°.

cis-**2,8-Dibenzylcyclooctanone.**—Isomerization of trans isomer was carried out using 0.1 *M* NaOEt in EtOH,[2] yielding cis isomer, mp 84–85°. These were not the same compounds by mixture melting point, ir, and nmr.

Lithium Aluminum Hydride Reductions.—Each isomeric ketone (50 mg) was reduced with 50 mg of $LiAlH_4$ in anhydrous Et_2O by standard procedures.

Equilibration of Isomers.—One gram of one isomer of each pair was dissolved in 0.1 *M* NaOEt in EtOH and stirred at room temperature. Samples were analyzed at 24-hr intervals until no change in concentration was seen. The samples of the cycloheptanones had to be reduced to the alcohols with $NaBH_4$ before analysis. This was done by adding 50 mg of $NaBH_4$ to the aliquot, allowing it to stand overnight, and extracting into Et_2O after acidifying with 1 *N* HCl.

Vapor Phase Chromatography.—The cyclooctanones were separated on a 5 ft × 0.25 in. o.d. glass column packed with 3% OV-225 on Chromosorb W-AW-DMCS. The cyclohexanones were separated on a 5 ft × 0.25 in. o.d. glass column packed with 3% OV-17 on Chromosorb W-AW-DMCS. The alcohols obtained from the ketones were separated on the OV-225 column. The two alcohols from the *cis*-2,5-dibenzylcyclopentanone were separable but the alcohol from the trans isomer had the same retention time as one of the alcohols from the cis ketone.

Registry No.—**1a**, 34403-27-5; **1b**, 34403-28-6; **2a**, 7382-09-4; **2b**, 7382-10-7; **3a**, 34403-31-1; **3b**, 34410-06-5; **4a**, 34403-32-2; **4b**, 34403-33-3.

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Noble Metal Catalysis. I. Synthesis of Succinates from Olefins

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Dialkyl succinates[1] can be prepared in good yields by the oxidative carbonylation of olefins in the presence of alcohols with a palladium redox system, according to eq 1.

$$C_2H_4 + 2CO + {}^1/_2O_2 + 2ROH \longrightarrow RO_2CCH_2CH_2CO_2R + H_2O \quad (1)$$

The palladium redox system is somewhat similar to the one used in acetaldehyde synthesis[2] but optimum results are achieved by restricting both the amounts of excess hydrogen ion and chloride ion. Both iron and copper chlorides were shown to be useful as redox reagents for palladium, according to the following equations (for copper).

$$PdCl_2 + 2CO + CH_2{=}CH_2 + 2ROH \longrightarrow RO_2CCH_2CH_2CO_2R + Pd^0 + 2HCl \quad (2)$$

$$2CuCl_2 + Pd^0 \longrightarrow Cu_2Cl_2 + PdCl_2 \quad (3)$$

$$Cu_2Cl_2 + 2HCl + {}^1/_2O_2 \longrightarrow 2CuCl_2 + H_2O \quad (4)$$

However, it was quickly found that palladium chloride with either cupric chloride or ferric chloride alone gave a very poor catalyst system for succinate synthesis. The problem was found to be due to the presence of hydrogen chloride generated by eq 2. To the extent that eq 2 and 3 are faster than 4, then large amounts of cupric chloride give large amounts of hydrogen chloride. It was found that, when cuprous chloride was added, the excess chloride ion could be tied up. In the iron system, ferrous chloride was more effective than even a mixture of ferrous and ferric chlorides.

The oxidation of ferrous chloride by air was already known to be much faster in alcohols than in water and to increase in rate with increasing molecular weight of the alcohol.[3] The presence of water or small amounts of mineral acid in the solution reduced the rate of oxidation considerably. The rate of oxidation was related to the square of the concentration of ferrous chloride. The reaction was thought to be eq 5. Some oxidation

$$2FeCl_2 + {}^1/_2O_2 \longrightarrow FeCl_3 + FeOCl \quad (5)$$

of the ethanol solvent to acetaldehyde and ethyl acetate was also observed.

The acid–base effect is illustrated in Table I, where

TABLE I

EFFECT OF ACID AND BASE[a]

Acid or base	Wt, of acid or base, g	Mol of product produced: Methyl succinate	Carbon dioxide	Other
	0	0.17	0.17	Methyl formate, 0.02
Sodium acetate	3	0.22	0.10	
37% Hydrochloric acid	1	0.04	0.26	Methyl formate, 0.02 Methylal, 0.1

[a] At 300 psig CO, 700 psig C_2H_4, methanol to 400 ml in a 0.5-gal stirred titanium autoclave with 1 g of $PdCl_2$, 10 g of $FeCl_2 \cdot 4H_2O$, and oxygen addition to 125–175 psig in increments at 85°.

it is seen that in the synthesis of methyl succinate the addition of small amounts of sodium acetate (organic bases such as pyridine are also effective) increases the yield of succinate and decreases the yield of carbon dioxide, the chief by-product. On the other hand, hydrogen chloride has just the opposite effect.

The other product produced along with the succinate

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