described by Zeynek.[5] The product obtained had been variously described as gray, yellow, or brown and as the mono- and dihydrate. A reexamination of the procedure was undertaken and we found that the products formed by this method varied in both composition and color.

A reproducible synthetic method for 3,5-dichlorotyrosine has been developed. Significant was the ease of preparation, coupled with consistent formation of a white solid of definite composition. The compound formed only as the monohydrate and when prepared from L-tyrosine was dextrorotary.

Experimental Section

A 200-ml, three-necked, standard-taper flask was fitted with a glass thermometer, a motor-driven glass stirrer in a Teflon-sealed, gas-tight stopper in the center neck, and a "T" glass standard-taper connection in the remaining neck. One of the "T" openings connected to a chlorine gas supply tank was fitted with a pressure regulator. The remaining "T" opening was connected to a "U" type manometer containing light mineral oil.

A bath containing salt–ice–water was agitated by a magnetic stirrer, and completely surrounded the reaction flask up to the center neck. A 5-g sample of L-tyrosine powder (J. T. Baker Chemical Co.) and 125 ml of propionic acid were well mixed in the flask to obtain a fine dispersion. Both the bath fluid and the reaction mixture were stirred continuously throughout the run.

The bath temperature was dropped to −10°. Chlorine was added to flush out air in the system; this was done by raising the thermometer slightly, thus creating an exit vent, for 30 sec. The thermometer was replaced in position to again make a gas-tight system, and the chlorine regulated to give a manometer reading of about 1 cm of mineral oil. In a period of 18 min, the flask temperature rose to +1°. At this point the bath mixture was adjusted to obtain a flask temperature of 0–5° for a period of 2 hr. After about 8 min from the beginning of chlorination, the flask contents almost cleared to a single phase; only a few crystals remained. Soon thereafter crystals appeared in quantity and the mass thickened, but remained sufficiently fluid for agitation. After about 10 min from the beginning of chlorination, the manometer pressure gradually increased as the chlorine absorption rate diminished. About 3 min later, the chlorine pressure reached a maximum or constant value. The chlorine pressure in the system was kept at a positive value at all times to eliminate the possibility of air or moisture entry through leakage.

Following the 2-hr chlorination period, the "T" connection was quickly removed and replaced with a single-stem standard taper reducer. This was coupled to a large, dry glass trap in series with a water aspirator. Agitation was continued while the system was under vacuum (30 mm). When the volatiles and free chlorine were being removed, the temperature dropped and then rose again to 5°.

After agitation for one more hour at 5°, the dispersion became white in color. The flask contents were then filtered by suction, using a fritted glass, Buchner-type, jacketed, filter funnel through which ice water circulated. The residue was pressed dry to remove additional mother liquor. Filtration was continued until no more solvent was removed. The residue was washed with two 5-ml portions of propionic acid at 0° and again suction was applied until no more filtrate appeared. The filter cake weighed 12.4 g and contained an appreciable amount of mother liquor and propionic acid.

A. Salting-Out Process.—One-half of this crude residue (6.2 g) was dissolved in 62 ml of water at 15° and the small amount of insoluble material was filtered off. To the filtrate, with agitation, was added 13 ml of an aqueous solution containing 3.3 g of sodium acetate trihydrate. After stirring for 10 min, the mixture was refrigerated to 10°, and filtered through a cold fritted glass funnel. The residue was washed three times by dispersing well each time in an equal volume of water at 0°. The residue was sucked dry for 2 hr or more at room temperature to constant weight. The pure product obtained weighed 2.5 g (67.6% yield). *Anal.* Calcd for $C_9H_9NCl_2O_3 \cdot H_2O$: C, 40.30; H, 4.10; N, 5.23; Cl, 26.40. Found: C, 40.35; H, 4.16; N, 5.27; Cl, 26.34.

(5) R. Zeynek, *Z. Physiol. Chem.*, **114**, 275 (1921).

B. Neutralization Process.—The remaining half of the crude residue (6.2 g) was dissolved in 25 ml of water at 15° and filtered. The filtrate was diluted with 200 ml of water, and then kept at 5° during subsequent operations. The solution was neutralized to pH 8 with 1 *N* NaOH with good agitation and again filtered, and the filtrate was brought to pH 3 with 1 *N* hydrochloric acid. Following filtration, the residue was washed by dispersal three times in equal volumes of water and sucked dry. Suction was continued at ambient temperature to constant weight. A white product (2.3 g) was obtained (62.3% yield). *Anal.* Found: C, 40.32; H, 4.13; N, 5.21; Cl, 26.39.

Of the two general processes, the salting-out procedure with sodium acetate solution gave slightly higher yields.

The product had a melting point of 225–228° with decomposition (Nalge microscope-type, polarized melting point apparatus). Ascending chromatography on Whatman No. 1 paper revealed a single ninhydrin-reacting spot at R_f 0.59 in 4:1:1 (v/v/v) 1-butanol–acetic acid–water and at R_f 0.70 in 130:33:40 (v/v/v) 2-propanol–concentrated HCl–water. There was an ultraviolet absorbance peak at 305 mμ. A sample of 3,5-dichlorotyrosine monohydrate allowed to stand under high vacuum at normal temperature in the presence of concentrated H_2SO_4 for 33 days showed weight loss corresponding to 1 H_2O (calcd: 6.7%; found: 6.6%). The compound synthesized from L-tyrosine was dextrorotary, $[\alpha]^{25}D$ +1.16 (*c* 5, 1 *N* HCl), whereas that synthesized from D-tyrosine was levorotary $[\alpha]^{25}D$ −1.13. To confirm the purity of the optical isomers, an enzyme system was used.[6] The large change in optical density at 332 mμ in borate buffer, in the presence of L-amino acid oxidase (*Crotalus adamanteus* venom) and catalase, with the 3,5-dichlorotyrosine prepared from L-tyrosine, was indicative of the L form. The compound synthesized from D-tyrosine, under identical test conditions, was not reactive.

In place of the propionic acid, glacial acetic acid has also been used as an alternative solvent at 20° maximum temperature (care must be taken to prevent solidification of the reaction mixture by keeping the temperature above 16°). The yield and purity of compounds formed using both solvents were identical. The keys to a successful preparation are rigid temperature control and the thorough removal of excess chlorine following halogenation.

Registry No.—3,5-Dichloro-D-tyrosine, 15924-16-0; 3,5-dichloro-L-tyrosine, 15106-62-4.

Acknowledgment.—The authors are grateful to Dr. George Delpierre for the polarimetry measurements.

(6) R. P. Spencer and D. Brock, *Endocrinology*, **70**, 750 (1962).

On the Reaction of 1-Phenylcyclopentanecarbonitrile with Methylmagnesium Iodide. Formation of Bis(1-phenylcyclopentyl) Ketone[1]

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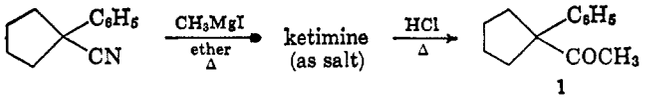
Some years ago, in connection with another problem, we had occasion to prepare 1-phenylcyclopentyl methyl ketone (**1**). We chose the method of Smith and



1

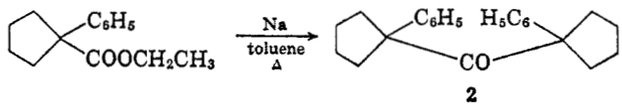
(1) This reaction was first noticed during the doctoral research of Herbert Philip, and is described in his Dissertation, pp 108–109, Loyola University (1959). No structural assignment was made at that time.

coworkers[2] wherein 1-phenylcyclopentanecarbonitrile was treated with methylmagnesium iodide in ether. The initial ketimine was hydrolyzed by these workers to obtain **1** in 57% yield. Their liquid product and its 2,4-dinitrophenylhydrazone and semicarbazone derivatives were characterized by elemental analysis. Recently, MacKenzie, *et al.*,[3] made **1** "in good yield" by the same process. Their material and its semicarbazone were apparently the same as Smith's.

However, in our hands at that time, this reaction took another course. We found that when less ether was used than that employed by Smith and coworkers,[4] a white solid **2**, mp 98.5–99.5°, was observed as the major product of the reaction after acidic work-up. Lesser quantities of recovered nitrile and **1** were also obtained, although our samples of the two aforementioned derivatives of **1** melted far from the reported values.

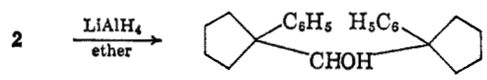
Recently we decided to unravel the apparent mystery involved in this process. First, to check the structure of **1**, its infrared and nmr spectra were determined and found to be consonant with the proposed structure. Furthermore, hypobromite oxidation of **1** led to 1-phenylcyclopentanecarboxylic acid. So the structure of **1** does seem secure. Just why the derivatives we made melted at different temperatures than those reported[2,3] is not known. 2,4-Dinitrophenylhydrazones in particular, however, often exhibit polymorphism, as well as *cis*, *trans* stereoisomerism, and we suggest such may be the situation here. Second, the effect of the concentration of reactants was checked. Under concentrated reactant conditions, **2** was formed in 42% yield while the yield of **1** was only 19%. When the more dilute reactant concentrations employed by Smith were used, however, the yield of white solid **2** fell to 4.1% while that of **1** rose to 32.3%, with 38.2% of unchanged starting nitrile being recovered. Whereas we were unable to duplicate Smith's work any better, it was at least apparent that the solid **2** could have been missed under his conditions. We then turned to the structure of the white solid **2**.

This crystalline solid was nitrogen-free and had a composition by combustion analysis best fitted to $C_{23}H_{26}O$. The oxygen was apparently carbonyl in character from a very sharp and strong absorption at 5.98 μ. The nmr spectrum was simple, with aromatic hydrogens as a sharp multiplet centered at δ 7.18 (5 H's) and two upfield multiplets, one at 2.5–1.53 (4 H's) and another at 1.53–0.92 (4 H's) relative to internal tetramethylsilane (TMS). These facts and others (see Experimental Section), plus the possible aberrations involved in the reaction of Grignard reagents with nitriles, led us eventually to formulate **2** as **bis(1-phenylcyclopentyl) ketone**. A search showed that this compound had actually been prepared in 1952 by van Heyningen[5] in an attempted acyloin condensation of ethyl 1-phenylcyclopentanecarboxylate. The ketone was reported to melt at 93–95° and to have infrared absorptions at 5.94, 9.26, and 9.67 μ. Our reaction product **2** did melt at this temperature, though purified samples melted at 98.5–99.5°, and the infrared spectral agreement was good.



2

As might be expected from its hindered nature, **2** did not form derivatives easily. It was, however, readily reduced to the carbinol **3** with lithium aluminum hydride. Attempted cleavage of **2** either by means of



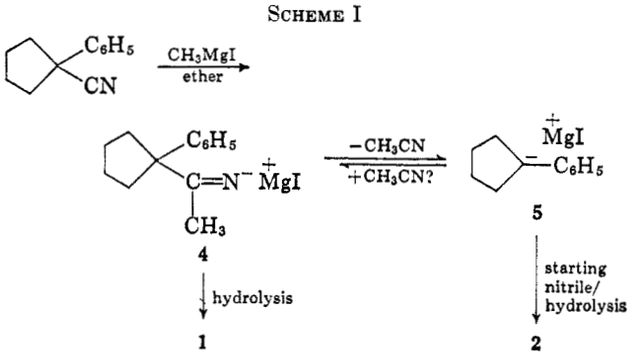
3

sodamide in refluxing toluene or by the recently described[6] use of potassium *t*-butoxide in dimethyl sulfoxide failed. The ketone was recovered unchanged in each case.

The probable initial step in the formation of **2** in this reaction represents an interesting example of what has been termed the "reductive displacement" of nitriles by Grignard reagents.[7] The intermediate imino anion **4**, undoubtedly involved in the "normal" process, can dissociate to some degree to the 1-phenylcyclopentyl anion **5**[8] with loss of acetonitrile. Reaction of **5** with the starting nitrile in the usual way would then produce **2** *via* its imine salt (the free imine was detected in the reaction, see Experimental Section). Eventual hydrolysis of undissociated **4** *via* its imine could lead to **1**, the expected product. It is possible that **1** might also result from **5** and the acetonitrile liberated from **4**. This is improbable, however, because acetonitrile is well known to behave poorly in ketone syntheses of this type because of its acidic α hydrogens.[9]

The postulated exchange of nitrile and magnesio functions in Scheme I has actually been observed on occasion, particularly with polyarylacetonitriles.[10] For instance, propionitrile has been detected in the reaction of diphenylacetonitrile and ethylmagnesium

SCHEME I



(2) P. A. S. Smith, D. R. Baer, and S. N. Ege, *J. Amer. Chem. Soc.*, **76**, 4564 (1954).

(3) S. MacKenzie, S. F. Marsocci, and H. C. Lampe, *J. Org. Chem.*, **30**, 3328 (1965).

(4) Each method used *ca.* threefold excess Grignard reagent. MacKenzie and coworkers[3] also employed threefold excess Grignard, but no other information was given.

(5) E. van Heyningen, *J. Amer. Chem. Soc.*, **74**, 4861 (1952).

(6) P. G. Gassman and F. V. Zalar, *Tetrahedron Lett.*, 3031 (1964).

(7) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954, p 779.

(8) That this carbanion is relatively easily formed may be surmised from the moderately good (50%) yield of 1-phenylcyclopentanecarboxylic acid obtained upon carbonation of the solution resulting from treatment of 1-phenylcyclopentyl methyl ether with sodium–potassium alloy: G. W. Wheland and R. D. Kleene, *J. Amer. Chem. Soc.*, **63**, 3321 (1941).

(9) P. A. S. Smith, "The Chemistry of Open-Chain Organic Nitrogen Compounds," Vol. 1, W. A. Benjamin, Inc., New York, N. Y., 1965, p 214.

(10) Reference 7, pp 779–782.

bromide.[11] Triphenylacetonitrile is another well-documented instance, its reaction with benzylmagnesium chloride affording a 70% yield of triphenylmethane.[12] In this latter case, as opposed to the present one, the intermediate trityl anion apparently was too stable to attack the reactant nitrile, so hydrolysis gave hydrocarbon instead of carbonyl product. Even with these literature precedents, the present illustration of this exchange is nonetheless interesting because it is the first monoarylacetonitrile to behave in this manner.

The effect of reactant concentration is also rationalized by the reaction scheme above. Provided that conversion of starting nitrile into **4** is not overly rapid,[13] the subsequent formation of **2** (as its imine salt) would be faster in more concentrated solutions because the possibility of reaction between **5** and the starting nitrile is increased. As more dilute solutions are employed, the formation of the imine salt of **2** would correspondingly decrease while the conversion of the starting nitrile into **4** would correspondingly increase. With the route to **2** thus impeded, the process would then take the expected path to **1**, as found.

Finally, the rates of the various processes in this reaction must be rather critically balanced, as attempts to find this exchange reaction in homologs of 1-phenylcyclopentanecarbonitrile uniformly failed.[14] Only the expected methyl ketones were observed as products here.

Experimental Section

Melting points and boiling points are uncorrected for stem exposure. The former were determined on a calibrated Fisher-Johns block. The latter were taken during short-path distillations under nonequilibrium conditions and may reflect superheating. Infrared spectra were obtained on Perkin-Elmer Model 21 and Beckman IR-5A instruments and are given in microns (μ). Nmr spectra were determined on a Varian A-60A spectrometer with internal TMS as a standard. Gas–liquid partition chromatography (glpc) was performed on an Aerograph A-90P chromatograph using helium as the carrier gas. Microanalyses were done by Micro-Tech Laboratories, Inc., Skokie, Ill.

Reaction of 1-Phenylcyclopentanecarbonitrile and Methyl Grignard Reagent (Concentrated Reactant Conditions).—1-Phenylcyclopentanecarbonitrile [5.0 g, 29 mmol, freshly prepared from phenylacetonitrile and 1,4-dibromobutane using sodamide;[15] bp 106.5° (0.3 mm); λ^{neat} 4.51 (CN); δ^{neat}_{TMS} 7.6–7.13 m (Ar–H), 2.5–1.5 m (cyclopentyl H's); homogeneous in glpc] in dry ether (6.4 ml) was added over a 5-min period to the Grignard reagent prepared from methyl iodide (12.32 g, 5.54 ml, 88 mmol), magnesium turnings[16] (2.14 g, 88 mg-atoms), and ether (39 ml). The material was then stirred and refluxed 18 hr protected from moisture. To the mixture, cooled to 0°, water (10 ml) was now added dropwise. After this decomposition of the excess Grignard reagent, the total contents were added with vigorous stirring to ice (100 g) and hydrochloric acid (concentrated, 15 ml). The material formed two phases with an interphase of a crystalline substance. The ether phase was separated and processed separately (see below). The aqueous phase, collected together with the solid interphase, was refluxed a further 18 hr, whereupon the crystals were replaced with oil globules. The cooled mixture was then extracted with benzene (thrice with 50 ml). The benzene extracts were combined, washed with aqueous sodium carbonate (10%) and then water to neutrality, dried, and stripped free of benzene. The oily residue partially crystallized on standing. The crystals (**2**) were separated from the oil and washed with cold ethanol. Further crystals were obtained by concentrating these ethanol washings.

In this way there was obtained **2**, identified as **bis(1-phenylcyclopentyl) ketone**, as glistening needles (1.94 g, 42%, mp 94–95°). Purification by recrystallization from ethanol proceeded easily and with little loss and gave **2** as snow-white needles (1.85 g, 40%): mp 98.5–99.5°; λ^{KBr} 5.98 (sharp, >C=O), 3.31, 3.42, 3.52, 6.28, 6.71, 6.92, 7.7 (broad), 8.2 8.85, 9.30, 9.46, 9.70, 10.49, 10.72, 10.93, 11.28, 13.2 (broad), 13.91, 14.33; $\delta^{CCl_4}_{TMS}$ 7.18 (sharp multiplet, Ar–H), 2.5–1.53 m (four cyclopentyl H's per ring), 1.53–0.92 m (other four cyclopentyl H's per ring) (lit.[5] mp 93–95°; λ (medium not stated) 5.94, 9.26, 9.67).

Anal. Calcd for $C_{23}H_{26}O$: C, 86.74; H, 8.23. Found: C, 86.72, 86.97; H, 8.01, 8.21.

The oily portion of the residue was distilled to afford 1.04 g (19%) of **1-phenylcyclopentyl methyl ketone** (**1**): bp 115–120° (3.0 mm); $n^{25}D$ 1.5330; λ^{neat} 5.89 and 7.4 (–$COCH_3$), 3.3, 3.4, 3.5, 6.27, 6.71, 6.92, 6.98, 8.19, 8.5, 8.69, 8.93, 9.31, 9.68, 9.98, 10.36, 10.57, 10.8, 11.0, 13.2, 14.3; δ^{neat}_{TMS} 7.32 m (sharp, Ar–H), 2.80–1.40 m (cyclopentyl H's), 1.85 s (–$COCH_3$); homogeneous by glpc (lit.[2] bp 142–148° (18 mm), 110° (3 mm); $n^{25}D$ 1.5398).

The **2,4-dinitrophenylhydrazone** of **1** was a yellow, microcrystalline solid, mp 107.5–108° from ethanol (lit.[2] mp 145.6–146.2°).

Anal. Calcd for $C_{19}H_{20}O_4N_4$: N, 15.21. Found: N, 15.45.

The **semicarbazone** of **1** was also prepared (white microcrystalline solid from aqueous alcohol, mp 211–215° dec (lit. mp 228.5–231° dec,[2] 228–230°[3]).

Anal. Calcd for $C_{14}H_{19}ON_3$: N, 17.13. Found: N, 17.55.

The ether phase from the reaction was freed of solvent and yielded an oil and a small amount of a semisolid. The latter, while not **2** because of differing spectra, nevertheless did afford **2** upon repeated recrystallization from aqueous alcohol. It was probably ketimine salt that escaped hydrolysis (or perhaps the free imine). The oil (1.21 g, bp 105° (0.5 mm, $n^{20}D$ 1.5324) was shown to be recovered starting nitrile (24.3% recovery) by spectral comparison with starting material.

Hypobromite Cleavage of 1.—Because of the discrepancies between the earlier[2,3] and present samples of **1** and its derivatives, the ketone (0.5 g) was cleaved with excess bromine and sodium hydroxide (2 hr on the steam bath). Bromoform was formed as a heavy oil which was separated. The aqueous phase was well chilled and acidified with hydrochloric acid (using sodium bisulfite to remove the excess bromine liberated). The crystalline white solid (0.2 g, 40%) that precipitated was **1-phenylcyclopentanecarboxylic acid** which had a melting point and mixture melting point with an authentic sample of 156.5–158° and identical infrared spectra (lit.[17] mp 158–159°).

Grignard Reaction under Dilute Reactant Conditions.—The reaction of 1-phenylcyclopentanecarbonitrile (2.57 g, 15 mmol) in dry ether (30 ml) with the Grignard reagent prepared from methyl iodide (6.4 g, 45 mmol), and magnesium turnings[16] (1.09 g, 45 mg-atoms) in ether (30 ml) was performed exactly as described above. From the ether phase after processing the reaction there was isolated starting nitrile (0.98 g, 38.2% recovery, bp 110–111° (0.2 mm)), identified by its infrared spectrum, contaminated slightly with ketone **1**. From the aqueous phase there was obtained ketone **1** containing a trace of starting nitrile (0.91 g, 32.3%, bp 111–112° (0.2 mm)), again identified spectrally, as well as crystalline **2** (0.10 g, 4.1%), also identified by spectral comparison with the material obtained under more concentrated conditions.

Attempted Reactions on 2.—This ketone was relatively inert. It could be recovered essentially quantitatively after treatment with hot sodium hydroxide in aqueous dioxane, bromine in methanol, hot hydrochloric acid, hot 30% sulfuric acid, cold concentrated sulfuric acid, and sodamide in refluxing toluene. Attempted cleavage of the ketone (4.6 mmol) under nitrogen with fresh potassium *t*-butoxide (35 mmol) in purified dimethyl sulfoxide (11 ml) containing water (10 mmol), a recent technique[6] of reputed value in ketone cleavage, gave over 90% recovery of

(11) F. F. Blicke and E. P. Tsao, *J. Amer. Chem. Soc.*, **75**, 5587 (1953).

(12) P. Ramart-Lucas and F. Salmon-Legagneur, *Bull. Soc. Chim. Fr.*, **43**, 321 (1928).

(13) This is a reasonable proviso in that significant nitrile is recoverable from the reaction.

(14) As a rationalization of this point, it might be pointed out that neither the 1-phenylcyclohexyl carbanion nor the 1-phenylcyclobutyl carbanion readily resulted from the same type cleavage (Na–K alloy) of the corresponding methyl ether that easily formed the 1-phenylcyclopentyl analog. *Cf.* ref 8 and J. W. Wilt, L. L. Maravetz, and J. F. Zawadzki, *J. Org. Chem.*, **31**, 3018 (1966).

(15) A. W. Weston, *J. Amer. Chem. Soc.*, **68**, 2345 (1946).

(16) Baker and Adamson Division, Allied Chemical Corp., Code 1904. This magnesium was used throughout the study on all the nitriles.

(17) F. Case, *ibid.*, **56**, 715 (1934).

2.[18] No carbonyl derivatives of **2** could be formed, although attempts in this direction were not exhaustive. All these facts were of assistance in ascribing the structure given to **2**.

Reduction of 2 to Bis(1-phenylcyclopentyl)carbinol (3).—Treatment of **2** with excess lithium aluminum hydride in ether at room temperature in the usual manner led to alcohol **3** in 85% yield: mp 97–98° from aqueous ethanol, mixture melting point with **2** depressed (69–88°); λ^{KBr} 2.92 (O–H), 9.68 and 9.81 (C–O), 3.31, 3.36, 3.45, 3.55, 6.29, 6.72, 7.27, 7.41, 7.60, 7.8–8.1 (broad), 8.32, 9.05, 9.30, 10.0, 10.38, 10.6, 11.3, 13.14, 14.40; $\delta_{TMS}^{CCl_4}$ 7.25 m (sharp, Ar–H), 4.07 s (broad, >CHOH), 1.99 s (broad, lost in D_2O, –OH), 1.83–1.0 m (all cyclopentyl H's).

Anal. Calcd for $C_{23}H_{28}O$: C, 86.20; H, 8.81. Found: C, 85.89; H, 8.80.

Reactions of Other 1-Phenylcycloalkanecarbonitriles with Methyl Grignard Reagent.—The cyclopropyl, cyclobutyl, and cyclohexyl analogs were available from earlier work.[19] Small scale (*ca.* 10 mmol) reaction of these with methylmagnesium iodide in ether under the concentrated reactant conditions described earlier for the cyclopentyl case failed to give products analogous to **2** in workable amounts, although traces of unidentified semisolid or solid material was occasionally obtained. The ketone products were collected by glpc or Hickman still distillation, so boiling points were not determined. The cyclohexyl analog gave **1-phenylcyclohexyl methyl ketone** in 26.5% yield, mp 31–33°, lit.[20] mp 33–35° (λ^{melt} 5.88, 7.40 (–$COCH_3$)), and much recovered nitrile.[21] The cyclobutyl member afforded **1-phenylcyclobutyl methyl ketone** in 31.4% yield (oil, λ^{neat} 5.90, 7.40, (–$COCH_3$), lit.[3] bp 56–57° (0.2 mm)) with some starting nitrile again being recovered. Finally, the cyclopropyl example yielded **1-phenylcyclopropyl methyl ketone** in 29.5% yield (oil, λ^{neat} 5.93, 7.40 (–$COCH_3$), 7.80, 8.70, 9.12, 9.72, 13.17, 14.25; lit.[22] bp 122° (25 mm), lit.[23] λ^{neat} *inter alia* 5.86, 7.79, 8.70, 9.12, 9.72, 13.16, 14.24) and, as usual, some starting nitrile. In this case an unidentified oil was isolated from the aqueous phase. Its properties were much unlike those of **2**, however, and its spectra suggested that it was a ring-opened derivative of the methyl ketone.

Registry No.—1-Phenylcyclopentanecarbonitrile, 77-57-6; methylmagnesium iodide, 917-64-6; **1**, 4046-09-7; **1** 2,4-dinitrophenylhydrazone, 15811-00-4; **1** semicarbazone, 15811-01-5; **2**, 15811-02-6; **3**, 15811-03-7.

(18) Whereas excellent in some less-hindered cases, this method, as reported,[6] gave only a 9% cleavage of the hindered ketone, camphenilone.

(19) J. W. Wilt and H. Philip, *J. Org. Chem.*, **24**, 616 (1959); J. W. Wilt and D. D. Roberts, *ibid.*, **27**, 3434 (1962).

(20) G. G. Lyle, R. A. Covey, and R. E. Lyle, *J. Amer. Chem. Soc.*, **76**, 2713 (1954).

(21) MacKenzie, *et al.*,[3] reported that this cyclohexyl homolog failed to react with methyl Grignard reagent under the conditions that they used for the cyclopentyl case.

(22) S. C. Bunce and J. B. Cloke, *J. Amer. Chem. Soc.*, **76**, 2244 (1954).

(23) S. E. Wiberley and S. C. Bunce, *Anal. Chem.*, **24**, 623 (1952).

7,7-Dicarbomethoxycycloheptatriene[1a]

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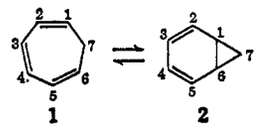
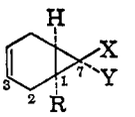
Although substitution of cyano groups at C-7 shifts the cycloheptatriene (**1**)–norcaradiene (**2**) equilibrium constant in favor of the bicyclic valency tautomer,[2] this structural feature does not seem to be required for the existence of a stable norcaradiene (*cf.* the 2,5,7-triphenyl derivative[3]). As a point on the



1 **2**

developing but still incompletely understood plot of substitution pattern *vs.* structure in this series, we record the properties of 7,7-dicarbomethoxycycloheptatriene. The syntheses of this sensitive substance and other tropilidene derivatives are carried out by methods that should be widely applicable to members of this class.

The synthetic approach to the tropilidene ring system is by cyclopropanation of a dihydrobenzene, essentially as in the method so effectively developed by Vogel and his coworkers.[4] However, the oxidation state of the resulting norcarene, which has been adjusted in previous syntheses[4] by addition of bromine to the double bond and dehydrohalogenation with amines or alcoholic alkali, involves procedures that are unsuitable to some of the cases of interest to us. For example, addition of bromine to norcarenes with a *syn*-7-carbomethoxy group leads either to complex



3a, R = H; X = Y = CO_2CH_3
b, R = CH_3; X = Y = CO_2CH_3
c, R = H; X = CN; Y = CO_2CH_3

mixtures in the case of **3a** or to a bromolactone rather than to the desired dibromide in the case of **3b**. Although a dibromide, mp 136°, can be obtained from the cyano ester **3c** with $C_5H_6N^+Br_3^-$/HOAc, dehydrohalogenation leads again to a complex mixture.

7,7-Dicarbomethoxynorcar-3-ene (**4**), prepared from the photolysis of methyl diazomalonate in 1,4-cyclohexadiene,[5] when treated with selenium dioxide in aqueous dioxane gives a mixture of the allylic alcohols **5** and **6** in the ratio 86 : 14 as determined by nuclear magnetic resonance (nmr) analysis. The same two alcohols are obtained (17 : 83 ratio) by oxidation of the isomeric diester **7**, prepared from 1,3-cyclohexadiene (see Scheme I). Although direct acid-catalyzed dehydration of these alcohols fails, conversion into bromides (PBr_3/CCl_4) and treatment with sodium methoxide gives 7,7-dicarbomethoxycycloheptatriene **8**. Dehydrogenation of **7** (with N-bromosuccinimide in CCl_4), or of **4** (with dicyanodichloroquinone in benzene), also gives **8** directly in yields of about 30%, but the substance is accompanied by unreacted starting material and aromatization product (phenylmalonic ester), from which it is difficultly separable. The method of choice in this case involves reaction of the mixture of alcohols **5** and **6** with *p*-bromobenzenesulfonyl chloride in 2,6-lutidine at 0–20°. Isolation by chromatography gives **8**, mp 45–45.5°, in yields of 25–30%. The synthesis of 3,7,7-trimethylcycloheptatriene **10**, which is much less subject than **8** to aro-

(1) (a) This work was supported in part by the National Science Foundation and the Air Force Office of Scientific Research. (b) National Institutes of Health Postdoctoral Fellow, 1966–1967.

(2) E. Ciganek, *J. Amer. Chem. Soc.*, **89**, 1454 (1967).

(3) T. Mukai, H. Kubota, T. Toda, *Tetrahedron Lett.*, 3581 (1967).

(4) E. Vogel, W. Wiedemann, H. Kiefer, and V. F. Harrison, *ibid.*, 673 (1963), and subsequent papers.

(5) For the corresponding diethyl ester, see H. Musso and U. Biethan, *Chem. Ber.*, **97**, 2282 (1964).