that in II, V, and VI the methoxy group is attached to the C_6. The fact that *IV* was obtained both by the addition of 2,3-dihydro-4*H*-pyran to *III*, as well as by the addition of tetrahydro-2-hydroxypyran to *I*, is additional evidence for the type of link shown in *IV*.

I has been obtained by Whetstone and Ballard[3] by the oxidation of 3,4-dihydro-2*H*-pyran-2-carboxaldehyde with silver oxide followed by treatment of the silver salt with ethyl iodide.

EXPERIMENTAL

Preparation of ethyl 3,4-dihydro-2H-pyran-2-carboxylate (I). Ethyl acrylate (160 ml.), acrolein (92 ml.), and hydroquinone (2.52 g.) were heated in a closed vessel (initial pressure 13.5 atm.) to 189° and kept at this temperature for 78 min. The products were crudely distilled. Fractional redistillation yielded ethyl 3,4-dihydro-2*H*-pyran-2-carboxylate (I) b.p. 73.5–76°/7 mm. (7 ml.). Infrared analysis showed the presence of an ester (doublet) and an isolated double bond (1650 cm.$^{-1}$).

Anal. Calcd. for $C_8H_{12}O_3$: C, 61.54; H, 7.69. Found: C, 61.50; H, 8.21.

The derived 3,4-dihydro-2*H*-pyran-2-carboxamide (VII) had a m.p. of 114–114.5° (hot stage, sublimation).

Preparation of ethyl tetrahydro-6-methoxypyran-2-carboxylate (II). Ice cold *I* (6 ml.) was mixed with ice cold methanol (2.5 ml.) and concd. aqueous hydrochloric acid was added (1 drop). After 5 hr. (3 hr. at room temperature) the mixture was neutralized (sodium bicarbonate), filtered, and distilled. The ethyl tetrahydro-6-methoxypyran-2-carboxylate (II) boiled at 81°–81.5°/2.5 mm., n_D^{25} 1.4422; yield, approximately 6 ml.

The infrared spectrum retained the ester doublet, and showed the absence of the double bond.

Anal. Calcd. for $C_9H_{16}O_4$: C, 57.45; H, 8.52. Found: C, 57.25; H, 8.76.

The derived tetrahydro-6-methoxypyran-2-carboxamide (VIII) had a m.p. of 161–162° (hot stage). Profound sublimation started around 130°, the sublimed crystals melting at 159°–160°.

Preparation of ethyl tetrahydro-6-hydroxypyran-2-carboxylate (III). Compound *I* (8 ml.) was mixed with water (14 ml.), acetone (10 ml.), tetrahydrofuran (30 ml.), and concd. aqueous hydrochloric acid (1.7 ml.). It was stirred for 1 hr. and deionized by Dowex 1X-4 anion exchange resin (bicarbonate form). Concentration *in vacuo* gave an oil. Distillation yielded ethyl tetrahydro-6-hydroxypyran-2-carboxylate (III) b.p. 114–115.7°/1 mm. (1.3 ml.), n_D^{24} 1.4586. The infrared spectrum showed hydroxyl, no water, no double bond.

Anal. Calcd. for $C_8H_{14}O_4$: C, 55.20; H, 8.05. Found: C, 54.89; H, 8.17% H.

Preparation of ethyl tetrahydro-6-[tetrahydropyran-2-oxy]-pyran-2-carboxylate (IV). Compound *III* (1.1 ml.) was mixed with 2,3 dihydro-4*H*-pyran (1.3 ml.) and concd. aqueous hydrochloric acid was added (1 drop). The mixture was left at room temperature for 3 hr., neutralized with aqueous sodium bicarbonate, and distilled to yield ethyl tetrahydro-6-[tetrahydropyran-2-oxy]pyran-2-carboxylate (IV) b.p. 142–144°/1 mm., n_D^{25} 1.4650; yield: approximately 1 ml.

Anal. Calcd. for $C_{13}H_{22}O_5$: C, 60.48; H, 8.53. Found: C, 60.25; H, 8.32% H.

The infrared spectrum showed no hydroxyl, no double bond, and an ester (doublet). When *I* was allowed to react with tetrahydro-2-hydroxypyran (acid catalysis), a product was obtained with boiling point 145–148°/2 mm., which had an infrared spectrum identical with that of *IV*, n_D^{25} 1.4648.

Preparation of tetrahydro-6-methoxypyran-2-carboxylic acid (V). Saponification of *II* (1 ml.) with sodium hydroxide (0.25 g.) in ethanol water (3 ml., 50/50 v./v.) for 1 hr., followed by acidification (6*N* hydrochloric acid), dilution with water (25 ml.), extraction by ether, and concentration of the dried (with sodium sulfate) ether layer, yielded an oil. Paper chromatography of the product, tetrahydro-6-methoxypyran-2-carboxylic acid, in ethyl acetate–acetic acid–formic acid–water (18:3:1:4) followed by spraying with an aqueous solution of Chlorophenol Red (0.8%), showed a bright yellow spot, $R_f = 0.80$.

Preparation of tetrahydro-6-methoxypyran-2-methanol (VI). Compound *II* (6 ml.) dissolved in absolute tetrahydrofuran (10 ml.) was added dropwise to a solution-suspension of lithium aluminum hydride (10 g.) in absolute tetrahydrofuran (160 ml.) while stirring. Stirring was continued overnight, and the mixture was refluxed for 6 hr. The hydride was decomposed by the dropwise addition of ethyl acetate followed by aqueous tetrahydrofuran to the reaction mixture at room temperature. Water was added (total of 450 ml.) and the slurry was filtered. Tetrahydrofuran was removed *in vacuo* and the aqueous solution was adjusted to 2*N* with sodium hydroxide, left for 2 hr. and continuously extracted with ether (4 days). The dried extract was concentrated *in vacuo* and the residual oil was distilled to yield tetrahydro-6-methoxypyran-2-methanol (VI). b.p. 70–75°/1.8 mm. (1.25 ml.), n_D^{25} 1.4535.

Anal. Calcd. for $C_7H_{14}O_3$: C, 56.55; H, 9.58. Found: C, 56.53; H, 9.53.

The infrared spectrum showed a hydroxyl peak, no water and no carbonyl.

When VI was heated on the steambath with aqueous sulfuric acid (1*N*) for 2 hr., the resulting hydrolysate had a positive Fehling reaction.

Acknowledgment. Technical assistance by Messrs. E. H. Hicks and G. F. Goodley is gratefully acknowledged.

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[3] R. R. Whetstone and S. A. Ballard, *J. Am. Chem. Soc.*, **73**, 5280 (1951).

Cyclization of 1,5-Diphenyl-1,3,5-pentanetrione with Ethyl Oxalate. 3,5-Dibenzoyl-1,2,4-cyclopentanetrione and Its Quinoxaline[1]

ROBLEY J. LIGHT[2] AND CHARLES R. HAUSER

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Recently,[3,4] the terminal methyl group of benzoylacetone was benzoylated to form triketone I. This triketone has now been cyclized with ethyl oxalate by sodium ethoxide in refluxing ethanol to

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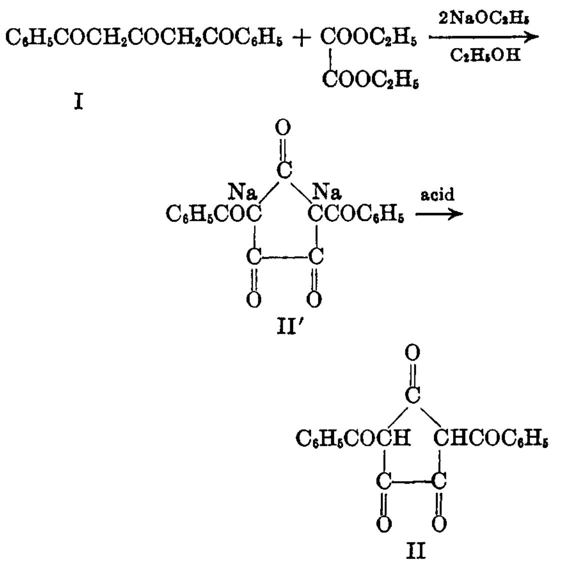
[1] Supported in part by Grant CY-4455 from the National Institutes of Health.

[2] National Science Foundation Predoctoral Fellow, 1958–60.

[3] C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, **80**, 6360 (1958).

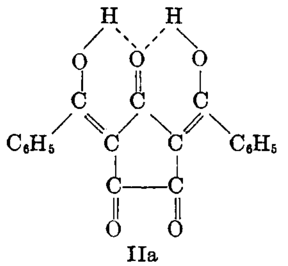
[4] R. J. Light and C. R. Hauser, *J. Org. Chem.*, **25**, 538 (1960).

give II. The reaction presumably involves a two-fold Claisen type of acylation to produce the disodio salt II′, from which II is liberated by acid (Equation 1).

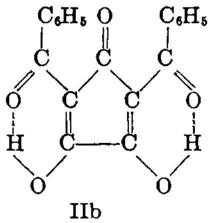


(1)

The infrared spectrum of II indicated an enol-chelate type of structure similar to that proposed for ordinary β-diketones[5] and for 1,3,5-triketones.[4] Two possible tautomers would be IIa and IIb. The compound showed strong infrared bands at 6.29 μ and 6.51 μ, characteristic of such an enol-chelate ring,[4,5] and a strong band at 5.82 μ containing a shoulder at 5.76 μ. It is not clear whether this last absorption would arise from the α-diketone structure shown in IIa or the single free carbonyl shown in IIb, either of which are conjugated with the enol-chelate rings. Five-membered ring ketones absorb in the region 5.71–5.75 μ, but are shifted to 5.83 μ on conjugation with a double bond.[6] Some cyclic α-diketones were observed to produce a double band near 5.65 μ, in contrast to a single absorption band found at 5.78–5.85 μ for other α-diketones,[7] but none of these diketones were conjugated.



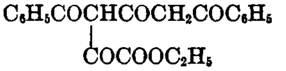
IIa



IIb

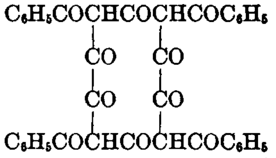
That the compound isolated was the cyclic product II (or a tautomer) was supported by its analysis, molecular weight, and neutralization equivalent. The last determination gave a value of one half of the molecular weight indicating that the dilute sodium hydroxide employed converted II to its disodio salt II′ (see equation 1). The acidity of II was also demonstrated by its solubility in sodium bicarbonate, in which triketone I was insoluble.

These data were not in agreement with the possible monoacylation product III, the anion of which was presumably formed as an intermediate, or with the unlikely ten-membered cyclic product IV which would have the same calculated analysis as II but twice the molecular weight. Neither were the data in agreement with products that might have arisen from two molecules of I and one of ethyl oxalate or from one molecule of I and two of the ester.



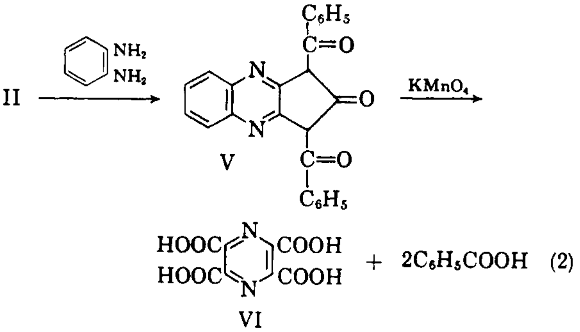
$C_6H_5COCH(COCOOC_2H_5)COCH_2COC_6H_5$

III



IV

The structure of the product was confirmed as II by further cyclization with o-phenylenediamine to form quinoxaline V, which was oxidized to give pyrazinetetracarboxylic acid (VI) and benzoic acid (Equation 2).



The tetracarboxylic acid VI was shown to be identical with an authentic sample of this compound prepared by the oxidation of phenazine.

A cyclization similar to that shown in Equation 1 has previously been realized with dicarbethoxyacetone and ethyl oxalate by sodium ethoxide to form the ditriacyl derivative VII.[8] Also certain ketones have been condensed with excess ethyl oxalate to form glyoxalates of 1,2,4-cyclopentanetriones.[9]

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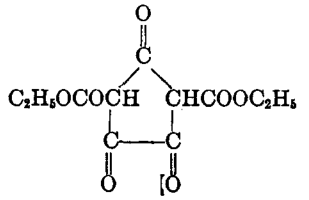
[5] See L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, 2nd ed., John Wiley and Sons, New York, N. Y., 1958, p. 142.

[6] See ref. (5), pp. 148–9.

[7] K. Alder, H. K. Schäfer, H. Esser, H. Krieger, and R. Reubke, *Ann.*, **593**, 23 (1955). See also ref. (5), p. 141.

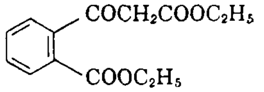
[8] E. Rimini, *Gazz. chim. ital.*, **26**, **2**, 374 (1896); W. Wislicenus and F. Melms, *Ann.*, **436**, 101 (1924); J. H. Boothe, R. G. Wilkinson, S. Kushner, and J. H. Williams, *J. Am. Chem. Soc.* **75**, 1732 (1953).

[9] See C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. Reactions*, **8**, 84 (1954).

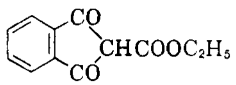


VII

A related acylation not involving ethyl oxalate is the intramolecular cyclization of VIII by sodium ethoxide to form IX.[10]

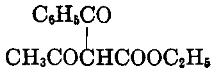


VIII



IX

Such acylations of carbanions of dicarbonyl compounds with ethyl ester groups to form triacyl derivatives are of interest, since the equilibrium between most open chain di- and triacyl carbanions in the presence of ordinary ethyl esters, sodium ethoxide, and ethanol is generally on the side of the diacyl anion. For example, triacyl compound X, which may be prepared by the benzoylation of the anion of acetoacetic ester with benzoyl chloride, undergoes cleavage with ethanolic sodium ethoxide to form the anion of ethyl benzoylacetate and ethyl acetate.[11]



$\mathrm{CH_3CO\overset{C_6H_5CO}{C}HCOOC_2H_5}$

X

EXPERIMENTAL[12]

3,5-Dibenzoyl-1,2,4-cyclopentanetrione (II). A solution of 0.15 mole of sodium ethoxide was prepared by adding 3.5 g. (0.15 g.-atom) of sodium to 250 ml. of absolute ethanol in a 500-ml. three-necked flask equipped with a stirrer, a water condenser, and a Drierite drying tube. To this stirred solution was added 10 g. (0.0375 mole) of 1,5-diphenyl-1,3,5-pentanetrione (I) as a solid through a powder funnel, followed by 5.5 g. (0.0375 mole) of ethyl oxalate. The reaction mixture was refluxed for 5 hr., and most (about 200 ml.) of the ethanol was then removed by distillation. The residual slurry was poured into 500 ml. of ice and water containing 20 ml. of concd. hydrochloric acid, and the resulting suspension was shaken with ether in a separatory funnel. The undissolved solid was then removed by filtration and was combined with the ether layer from the filtrate. This suspension was shaken with aqueous sodium bicarbonate, dissolving all the solid. The bicarbonate layer was separated and washed with ether, and the ethereal layers were combined and dried over Drierite. The solvent was removed and the residue was recrystallized from 95% ethanol to yield 2.8 g. (28%) of recovered I, m.p. 110–114° (recorded[4] m.p. 106–110° and 110–115°). The aqueous bicarbonate layer was acidified and the precipitate collected on a Büchner funnel and dried in a vacuum desiccator to yield 5.4 g. (45%) of crude II, m.p. 140–150°. Recrystallization from acetone produced 4.1 g. (34%) of II, m.p. 154–156°. Essentially the same recovery was obtained by recrystallization of the crude product from 95% ethanol, but decomposition occurred slowly in hot ethanol. Further recrystallization did not raise the melting point.

Anal. Calcd. for $C_{19}H_{12}O_5$: C, 71.25; H, 3.78; mol. wt., 320; neut. equiv., 160.2. Found: C, 71.34; H, 3.90; mol. wt., 279, 280, 317, 333, av. 302 (Rast); neut. equiv., 160.5, 160.1.

The infrared spectrum in the carbonyl and enol-chelate region[5] showed strong bands at 5.82 μ, 6.29 μ, and 6.51 μ, and a shoulder at 5.76 μ. Only a weak band was present at 2.82 μ, attributable to moisture in the potassium bromide. Ultraviolet spectrum: λ_{max} = 241 mμ, 298 mμ, 351 mμ; log ε = 4.33, 4.07, 4.22; λ_{min} = 267 mμ, 315 mμ; log ε = 3.98, 4.05. A red color was produced with ethanolic ferric nitrate.

Approximately the same yield of II was obtained when the reaction was repeated employing 0.113 mole of sodium ethoxide. The yield was not improved by removing the ethanol as an azeotrope with benzene before acidification. The usual forcing conditions employing excess of the ester were not studied.

1,3-Dibenzoyl-2-oxo-cyclopenteno[4,5-b]quinoxaline (V). A 1.5-g. (0.0047 mole) sample of 2,5-dibenzoyl-1,3,4-cyclopentanetrione (II) was dissolved in 45 ml. of hot 95% ethanol. To this solution was added rapidly a solution of 0.6 g. (0.006 mole) of *o*-phenylenediamine in 30 ml. of hot 95% ethanol. The reaction mixture was heated on the steam bath for several minutes, allowed to cool slowly to room temperature, and stored in the refrigerator overnight. The solution was filtered, and the solid was recrystallized from benzene to give 0.6 g. (32%) of V, m.p. 268–271°. An analytical sample melted at 271–274°.

Anal. Calcd. for $C_{25}H_{16}N_2O_3$: C, 76.52; H, 4.11; N, 7.14. Found: C, 76.40; H, 4.38; N, 7.15.

The infrared spectrum in the carbonyl and enol-chelate region[5] showed a medium band at 5.97 μ, and strong bands at 6.15 μ and 6.34 μ. Only a weak band was present at 2.85 μ, attributable to moisture in the potassium bromide. Ultraviolet spectrum: λ_{max} = 301 mμ; log ε = 4.44; λ_{min} = 265 mμ; log ε = 4.23.

Oxidation of quinoxaline V. A hot solution of 5.2 g. (0.033 mole) of potassium permanganate in 25 ml. of water was added dropwise to a slurry of 1.2 g. (0.003 mole) of V in 20 ml. of hot aqueous 5% potassium hydroxide. The last of the permanganate was rinsed in with 20 ml. of water, and the mixture was heated on the steam bath for 2 hr. After adding a few drops of ethanol to destroy the excess permanganate, the mixture was filtered and the solid manganese dioxide was washed with two 20-ml. portions of water. The filtrate was concentrated to 15 ml. on the hot plate, cooled, and acidified dropwise with concentrated hydrochloric acid. The precipitate, which consisted of a mixture of benzoic acid and the dipotassio salt of VI,[13] was collected on a filter funnel and washed with water. The benzoic acid was removed by suspending the solid in hot 95% ethanol and filtering. The solvent was removed from the ethanol filtrate leaving 0.65 g. (90%) of crude benzoic acid, m.p. 116–121°. One recrystallization from water raised the melting point to 120–121°, which was not depressed by mixing with an authentic sample of benzoic acid.

The solid that was not dissolved in hot ethanol was recrystallized from 10 ml. of 20% hydrochloric acid to yield 0.15 g. (20%) of pyrazinetetracarboxylic acid (VI), m.p. 195–

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(10) W. Wislicenus, *Ann.*, **246**, 349 (1888).

(11) See C. R. Hauser and B. E. Hudson, Jr., *Org. Reactions*, I, 298 (1942).

(12) Melting points were taken on a Fisher-Johns melting point apparatus which had been calibrated with melting point standards. Infrared spectra were determined with a Perkin-Elmer Infracord by the potassium bromide pellet method. Ultraviolet spectra were determined with a Warren Spectracord spectrophotometer using 2×10^{-5} *M* solutions in 95% ethanol with a 1-cm. sample cell. Elemental analyses were by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

(13) F. D. Chattaway and W. G. Humphrey, *J. Chem. Soc.*, 645 (1929).

199° dec. (reported[13] m.p. 205° dec.). The melting point was not depressed on admixture with an authentic sample of the acid prepared as described below, and the infrared spectra of the two samples were identical.

Independent synthesis of pyrazinetetracarboxylic acid (VI). A hot solution of 20.6 g. (0.13 mole) of potassium permanganate in 100 ml. of water was added dropwise to a slurry of 1.8 g. (0.01 mole) of phenazine in 20 ml. of hot water containing one pellet of potassium hydroxide. The reaction and work up were carried out as described above for the oxidation of V, except that the filtrate and washings from the manganese dioxide were concentrated to only 50 ml. before acidification. The crude precipitate was washed with ethanol and recrystallized from 25 ml. of 20% hydrochloric acid to yield 0.7 g. (27%) of VI, m.p. 199–202° dec. (reported[13] m.p. 205° dec.).

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The Synthesis of Substituted Indanes by the Cyclialkylation Reaction

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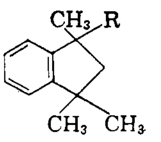
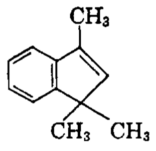
The cyclialkylation reaction of Bruson and coworkers has recently provided a unique approach to the synthesis of highly substituted β-tetralones.[1] In this manner, 1,1,4,4-tetramethyltetralone has been prepared by the alkylation of benzene with 2,2,5,5-tetramethyltetrahydrofuranone. We have been interested in the synthesis of *ortho*-substituted ditertiaryalkylbenzenes from the oxidative cleavage products of compounds of this type. In this connection, it was of interest to determine whether the isomeric ketone of unknown structure also formed in the above condensation could provide an additional source of starting material for the preparation of these substituted benzenes. To this end, we have obtained evidence which, together with the data previously presented, confirms the formulation of this compound as 1,3,3-trimethyl-1-acetylindane (I).



I. R = $COCH_3$
II. R = $COOH$
III. R = $OCOCH_3$
IV. R = OH



V

$C_6H_5C(CH_3)_2CH_2COC(CH_3)_2OH$
VI

$C_6H_5C(CH_3)_2CH_2C(CH_3)(OH)COCH_3$
VII

The basic permanganate oxidation of the isomeric ketone has been reported to result in a crystalline monocarboxylic acid—$C_{13}H_{16}O_2$.[1] We have synthesized 1,3,3-trimethyl-1-indanecarboxylic acid (II) and demonstrated its identity with this oxidation product. The sequence of reactions leading to this acid are as follows. Neophylmagnesium chloride was carbonated to yield β-phenylisovaleric acid. Treatment with thionyl chloride and ring closure with aluminum chloride resulted in 3,3-dimethylindan-1-one, which added methylmagnesium iodide to give, after dehydration, 1,1,3-trimethylindene (V). Treatment of V with formic acid in sulfuric acid, following the procedure of Koch and Haaf,[2] resulted in the desired acid. The latter reaction appears to be the first application of this method to the carboxylation of an aryl-substituted double bond.

Additional support for structure I for the isomeric ketone came from the perbenzoic acid oxidation of this material. The acetate (III) was detected in the infrared spectrum of the crude oxidation mixture but was not isolated. 1,1,3-Trimethylindene (V), the dehydration product of the intermediate tertiary alcohol (IV), was isolated and identified as a product of the saponification of the oxidation mixture.

The origin of the isomeric ketone can be rationalized by a rearrangement and cyclization of the ketol (VI) which has previously been isolated and identified as a product of the cyclialkylation reaction and which is the logical precursor of the 1,1,4,4-tetramethyltetralone. Rearrangement of the type VI to VII has been described in a closely related system.[3]

EXPERIMENTAL[4]

β-Phenylisovaleric acid. The Grignard reagent prepared from 338 g. (2.0 moles) of neophyl chloride (b.p. 93°–94°/10 mm.) and 50.0 g. (2.0 moles) of magnesium turnings in 750 cc. of anhydrous ether was poured onto an excess of Dry Ice. The acid was isolated and recrystallized from 1:1 benzene-petroleum ether (b.p. 30–60°) yielding 144.3 g. (41%) of β-phenylisovaleric acid, m.p. 57°–58° (lit.,[5] m.p. 58°–58.5°).

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.14; H, 7.92. Found: C, 74.84; H, 7.93.

3,3-Dimethylindan-1-one. The acid chloride derived by heating at reflux for 3 hr., 125 g. (0.70 mole) of β-phenylisovaleric acid and 100 g. (0.84 mole) of thionyl chloride, followed by removal of the excess thionyl chloride, was heated at reflux for 15 hr. with 93.3 g. (0.70 mole) of anhydrous aluminum chloride in 200 cc. of 3:1 petroleum ether (b.p. 30°–60°)-carbon disulfide. Water was added and the neutral material isolated and fractionally distilled. A 53% yield (59.0 g.) of 3,3-dimethylindanone, b.p. 86°–89°/1.7 mm., was obtained. The semicarbazone melted at 205°–206° (lit.,[6] m.p. 205°–207°).

Anal. Calcd. for $C_{12}H_{15}N_3O$: N, 19.34. Found: N, 19.58.

1,1,3-Trimethylindene. A dry ethereal solution of 48.0 g. (0.30 mole) of 3,3-dimethylindan-1-one was added dropwise with stirring to the Grignard reagent prepared from 56 g. (0.40 mole) of methyl iodide and 9.7 g. (0.40 mole) of mag-

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[1] H. A. Bruson, F. W. Grant, and E. Bobko, *J. Am. Chem. Soc.*, **80**, 3633 (1958).

[2] H. Koch and W. Haaf, *Angew. Chem.*, **70**, 311 (1958).

[3] A. M. Khaletskii, *J. Gen. Chem.* (*U.S.S.R.*) **15**, 524 (1945), *Chem. Abstr.*, **40**, 4696 (1946).

[4] All melting and boiling points are uncorrected.

[5] A. Hoffman, *J. Am. Chem. Soc.*, **51**, 2545 (1929).

[6] K. v. Auwers, *Ber.*, **54**, 994 (1921).