our belief, however, that the evidence favors an anionic mechanism. Urry, Juveland and Stacey[10] found that piperidine reacts with olefins in the presence of light or free radical initiators to give 2-alkylpiperidines, not 1-alkylpiperidines, by a chain reaction. Furthermore, the fact that propylene adds ammonia or amines in the presence of sodium to give the corresponding isopropylamines, not *n*-propylamines, favors an anionic mechanism. Catalysis by sodium hydride seems best interpreted as proceeding through hydride anions, and although sodium amide did not catalyze the amination reaction at 1000 atm., it did catalyze the addition of ammonia to cyclohexene and the addition of *n*-butylamine to 1-hexene at 8000 atm., presumably through amide anions. At all pressures in the temperature range tested, free radical initiators were inactive. These facts favor, but do not prove, an anionic rather than a free radical mechanism for the reaction.

Experimental

Apparatus and General Procedure.[11]—A stainless steel-lined pressure vessel of 400-ml. capacity was purged with nitrogen and charged with the catalyst (usually 5 g. of the freshly-cut alkali metal or 7.5–10 g. of the metal hydride). If an inert diluent was used, it also was added at this time. The vessel was closed, evacuated, chilled in a Dry Ice–methanol cooling bath, charged with anhydrous ammonia (usually 50 g.), and connected to a reservoir of the olefin being employed. Olefin at about 200 atm. pressure was introduced, and the vessel and its contents were heated and agitated. During a reaction time of 9–10 hours, the temperature was maintained at a predetermined level and the pressure was maintained by periodic additions of more olefin. When the reaction was complete, as evidenced by the lack of further gas absorption, the vessel was cooled to room temperature and the pressure released by passing the excess gases through traps immersed in a Dry Ice–methanol cooling mixture. The condensed material was distilled through a vacuum-jacketed low-temperature still, and any liquid remaining in the pressure vessel was filtered and distilled through a precision still.

When anhydrous ammonia was used to maintain the desired pressure during the reaction, the same general procedure was followed but the order of addition of the olefin and ammonia was reversed.

This procedure was quite flexible, permitting a series of reactions to be carried out under different conditions of pressure and temperature with various ratios of reactants in order to determine the effects of these variables.

Conditions of experiments and results for amination of ethylene are given in Table I, those for amination of higher olefins are shown in Table II.

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[11] W. F. Gresham, R. E. Brooks and W. M. Bruner, U. S. Patent 2,501,509 (1950); G. M. Whitman, U. S. Patent 2,501,556 (1950).

[CONTRIBUTION FROM THE ROLLIN H. STEVENS MEMORIAL LABORATORY OF THE DETROIT INSTITUTE OF CANCER RESEARCH AND FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE UNIVERSITY]

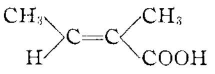
The Carboxylation of *cis*- and *trans*-2-Butenyl-2-lithium. A Stereospecific Synthesis of Angelic Acid[1]

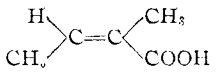
BY ANDRE S. DREIDING AND RICHARD J. PRATT

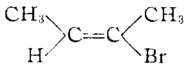
RECEIVED DECEMBER 4, 1953

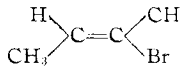
The carboxylation of the lithium derivative prepared from *trans*-2-bromo-2-butene resulted in a 64–74% yield of angelic acid; a small amount (5–6%) of tiglic acid was also formed. The same reactions with *cis*-2-bromo-2-butene afforded 21–24% of tiglic acid along with 8–10% of angelic acid. The neutral by-product in these carboxylations was non-ketonic acid and was more prevalent in the reaction with *cis*-2-bromo-2-butene than with the *trans*-isomer. These reactions confirm structure I for tiglic and structure II for angelic acid.

The possibility of stereomutation in the angelic–tiglic acid system and the greater stability of tiglic acid[2] obviate the necessity for the synthetic procedures of tiglic acid[3–8] to be stereospecific as long as the conditions of isolation are conducive to isomerization. In selecting a suitable method for the preparation of angelic acid, however, attention must be paid both to the stereospecificity of the reaction(s) and to the mildness of isolation conditions. Of the two methods,[3,6,8,9] available at present, only one[3,9] meets these requirements; it uses tiglic acid as the starting material in a three-step 33% yield[3] process.


I, tiglic acid


II, angelic acid


III, *cis*-2-bromo-2-butene


IV, *trans*-2-bromo-2-butene

A synthesis of angelic acid and of tiglic acid would be available if the bromine atom in the two isomeric 2-bromo-2-butenes (III and IV) could be replaced by a carboxyl group without changing the arrangement of the methyl groups. Efforts in this direction, which resulted in a good synthesis of angelic acid and methyl angelate from *trans*-2-bromo-2-butene (IV), will be described in this paper.

A number of alkenyl halides have been transformed into alkenyl lithium compounds either by

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[1] (a) Abstracted from a dissertation submitted by Richard J. Pratt in partial fulfillment of the requirements for the Ph.D. degree at Wayne University. (b) This work was supported in part by the American Cancer Society, Southeastern Michigan Division, the American Cancer Society, Inc., and The Kresge Foundation.

[2] For a comprehensive review of several of the stereochemical problems discussed in this paper see L. Crombie, *Quart. Rev.*, **6**, 101 (1952).

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[4] R. Adams and B. L. Van Duuren, THIS JOURNAL, **75**, 4631 (1953).

[5] A. Michael and J. Ross, *ibid.*, **55**, 3684 (1933).

[6] W. G. Young, R. T. Dillon and H. J. Lucas, *ibid.*, **51**, 2528 (1929).

[7] M. Naster and A. Gavriloff, *Bull. soc. chim. Belg.*, **42**, 519 (1933).

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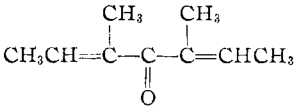
halogen–lithium exchange reactions[10–12] or by the direct interaction with lithium metal,[13,14] and the products have been shown to condense with carbonyl compounds like Grignard reagents. The available evidence indicates that the over-all process results in retention of the configuration at the trigonal carbon and that each step probably proceeds likewise.[12,15a] Several carboxylations of alkenyl lithium compounds have been described.[11–13,15,16] It is of interest that, in those cases where the alkenyl lithium solution was added to the solid carbon dioxide, the yields of α,β-olefinic acids were fair to good,[11–13] whereas the reverse procedure resulted in little[16] or no[15a] such product.[15b]

The isomeric 2-bromo-2-butenes (III and IV) were studied by Wislicenus and co-workers,[17] who assigned the *cis*-configuration to the lower boiling isomer on the basis of the concept of *cis*-elimination.[18] Later Pfeiffer[19] and Frankland[20] proposed the theory of *trans*-elimination and therefore assigned the presently accepted *trans*-configuration to the lower boiling IV and the *cis*-configuration to the higher boiling III isomer.[19] In a careful study, Lepingle[21] prepared the 2-bromo-2-butenes by heating 2,3-dibromobutane with sodium phenoxide and separating the isomers (III and IV) by fractional distillation of the azeotropic mixtures with ethanol.

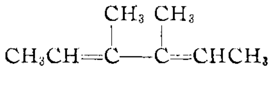
In the present work, it was found that 2,3-dibromobutane can be dehydrobrominated with a slight excess of potassium hydroxide in ethylene glycol in 70% yield if the 2-bromo-2-butenes are distilled out of the reaction mixture as they are formed. The isomers (III and IV) can then be separated by direct fractionation through an efficient column. In this way it was shown that the dehydrobromination of commercially available[22] 2,3-dibromobutane yielded III and IV in a ratio of nearly one. Samples of almost pure III and IV were fairly stable in the dark but, on exposure to light, both isomerized to an equilibrium mixture, which had been previously shown[21] to consist of 83% of *trans*-2-bromo-2-butene (IV) and 17% of the *cis*-isomer. The ready photo-stereomutation was also demonstrated with the help of infrared absorption spectra. A medium intensity absorption band at 12.18 μ exhibited by the *cis*-isomer (III) is absent in the *trans*-form (IV), while a peak at 12.54 μ is more intense in IV than in III. When samples of III and of IV were allowed to stand in sunlight for a day, the spectra were identical and the intensities of the two above-mentioned bands were roughly in agreement with an 8:2 ratio of IV:III. Refractometric measurements of redistilled commercially available[23] 2-bromo-2-butene indicated that it consisted of the equilibrium mixture. Thus it is seen that *trans*-2-bromo-2-butene (IV), which has the methyl groups in the same arrangement as angelic acid, is the more readily available isomer.

The 2-bromo-2-butenes were treated with an excess of lithium in ether at −10 to −25° under an atmosphere of nitrogen and the solution of the butenyllithium was forced on to an excess of solid carbon dioxide particles covered with ether. The product was separated into neutral and acid fractions and the angelic and tiglic acids were separated by crystallization, fractional crystallization of the calcium salts,[24] fractional distillation of the acids[6] or of their methyl esters. The methyl esters were prepared by the action of methyl iodide and potassium carbonate, which does not isomerize angelic acid.[7] The neutral fraction obtained in all experiments had a wide boiling range, showed an absorption maximum at 235 mμ, and gave a negative test with 2,4-dinitrophenylhydrazine reagent. Apparently it did not contain any dibutenyl ketone (V), which might have been expected to be formed.[15] The spectrum indicated the presence of a component with a conjugated diene chromophore.[25] These observations are consistent with the interpretation that the neutral fraction consisted of a mixture of 1,2,3,4-tetramethylbutadiene (VI), which could have arisen from a Wurtz type reaction,[10,14] and its self-condensation product(s).[26]



$CH_3CH{=}\overset{CH_3}{\overset{|}{C}}{-}\underset{\underset{O}{\|}}{C}{-}\overset{CH_3}{\overset{|}{C}}{=}CHCH_3$

V



$CH_3CH{=}\overset{CH_3}{\overset{|}{C}}{-}\overset{CH_3}{\overset{|}{C}}{=}CHCH_3$

VI

The results of the carboxylation experiments are summarized in Tables I and II. They show that the formation of the lithium salt and the carboxylation are, on the whole, stereospecific reactions, the *trans*-2-bromo-2-butene (IV) leading primarily to angelic acid (II) and the *cis*-isomer (III) forming preferentially tiglic acid. Apparently there are two side reactions: the Wurtz reaction and the isomerization, both of which compete more successfully with the carboxylation of *cis*-2-bromo-2-butene (III) than with that of the *trans*-isomer. This is reflected in the smaller yield of acidic material (and correspondingly more neutral product) as well as the smaller ratio of predominant to minor acid obtained from the *cis*- (III) than from the *trans*-isomer (IV).

These results could be explained if it is assumed that *cis*-2-butenyl-2-lithium and *cis*-2-bromo-2-butene (III) undergo the Wurtz reaction more rapidly

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TABLE I

PREPARATION OF ANGELIC AND TIGLIC ACIDS

Starting material 2-bromo-2-butene composition *trans*:*cis*	Reaction temp., °C.	Yield of total acids, %	Yield of angelic acid, %	Yield of tiglic acid, %	Ratio of angelic to tiglic acid	Neutral products yield,[a] %
50:50	25	55.4	9.0	8.2	52:48	36.4
Almost all *trans*	−10	79.8	64.6	5.5	91:9	17
Almost all *cis*	−10	37.1	8.6	24.0	26:74	32

TABLE II

PREPARATION OF METHYL ANGELATE AND METHYL TIGLATE

		Acidic products				
Starting material 2-bromo-2-butene composition *trans*:*cis*	Reaction temp., °C.	Yield of total acid, %	Yield of methyl angelate, %	Yield of methyl tiglate, %	Ratio of methyl angelate to tiglate	Neutral products Yield,[a] %
Equil. mixt. 83% *trans*	−25	52.5	33.4	7.4	82:18	25.5
Almost all *trans*	−15	82.6	73.9	6.1	92:8	7.3
Almost all *cis*	−15	36.8	10.8	20.7	30:70	52

[a] This yield is calculated on the basis of 1,2,3,4-tetramethylbutadiene.

than the corresponding *trans*-compounds. This appears reasonable from an inspection of molecular models, which shows a greater steric interference of the methyl groups when two *trans*-2-butenyl moieties approach each other in a co-planar conformation, than when the *cis*-isomers do the same.

The amount of tiglic acid formed in the carboxylation of *trans*-2-bromo-2-butene (IV), and particularly the amount of angelic acid produced in this reaction of the *cis*-isomer (III), is too large to be ascribed to contamination of IV and III with the other isomer, not removed by the distillation. It is possible that the 2-bromo-2-butenes were slowly isomerized in the interval between purification and lithium salt formation, with the *cis*-isomer (III) approaching the more distant equilibrium faster than the *trans*-isomer (IV). Attempts at keeping this effect at a minimum involved storing the distilled samples of III and IV in the dark and conducting the carboxylations as soon after purification as possible. Alternatively it should be considered that the two isomers of 2-butenyl-2-lithium are also capable of undergoing slow stereomutation toward an equilibrium mixture which favors the *trans*-isomer.

The configurations of tiglic and angelic acids have been deduced from several considerations.[19,27–30] Because of the demonstrated stereospecificity of the carboxylation *via* lithium alkenyls,[2,12,15a] the present results may be used to confirm structure I for tiglic and II for angelic acid. In further agreement with these structure assignments is the observation that tiglic acid forms an insoluble derivative with S-benzylisothiuronium chloride while angelic acid does not under the same conditions. The screening of the carboxyl group by the adjacent methyl group in angelic acid may be the cause for this effect, in the same way as it has been suggested to influence the esterification rates of I and II.[27]

Several of the interesting differences in the ultraviolet and infrared absorption spectra of tiglic and angelic acids have been mentioned recently.[4] To these can be added that the infrared spectra of tiglic (I) and angelic acid (II) differ in a band at 9.84 μ, which is present in I but not in II, and in a band at 9.57 μ, present in II but not in I. The methyl esters of I and II exhibit similar differences.

We wish to thank Dr. J. M. Vandenbelt and Mr. Bruce Scott of Parke, Davis and Co. for several of the ultraviolet and infrared absorption spectra reported in this paper. Preliminary experiments in the separation by fractional distillation of the isomeric 2-bromo-2-butenes were performed in the Research Laboratories of the Ethyl Corporation by Dr. G. G. Ecke, to whom we are grateful.

Experimental[31]

***cis*- and *trans*-2-Bromo-2-butene (III and IV).**—To a heated, well-stirred mixture of 432 g. (2.0 moles) of 2,3-dibromobutane[22] and 300 cc. of ethylene glycol in a flask, equipped with a 6-inch Vigreux column, was added slowly a solution of 137 g. (2.4 moles) of 85% potassium hydroxide in 500 cc. of ethylene glycol. The temperature of the reaction mixture was raised (to approximately 115°) until the 2-bromo-2-butenes, along with some water, distilled. The vapor temperature was maintained near 90° by controlling the rate of addition of the base. The addition took about one hour, after which time heating was continued until no more of the same distillate was obtained. The crude 2-bromo-2-butenes were separated from the water, dried over anhydrous calcium chloride, and distilled through a Fenske packed column, which had an efficiency of 25 to 30 plates under total reflux. The dried distillate weighed 242 g. The following fractions were collected at 740 mm.: (a) 17.7 g. of a forerun, b.p. 78.7–82.2°; (b) 61.4 g., b.p. 82.2–83.2°, n^{25}D 1.4561; (c) 50 g., b.p. 83.2–89.7°, n^{25}D 1.4582; (d) 76 g., b.p. 90.2–91.2° (the reflux ratio was changed), n^{25}D 1.4606.

Fraction (b) was almost pure *trans*-2-bromo-2-butene (IV), yield 22.8% (reported[21] b.p. 85.5°, n^{20}D 1.4579); *$\lambda_{\max}^{\text{liqu. film}}$ 3.34(s), 5.78(w), 5.99(m), 6.13(w), 6.91(m), 7.00(s), 7.26(m), 7.77(s), 8.79(s), 9.22(w), 9.44(w), 9.77(m), 11.12(s), 11.60(m), 12.54(s) μ. When a portion of this sample was exposed to sunlight for a day, the infrared absorption spectrum was: *$\lambda_{\max}^{\text{liqu. film}}$ 3.34(s), 5.79(w), 6.00(m), 6.14(w), 6.92(m), 7.01(s), 7.26(m), 7.77(s), 8.80(s), 9.23(w), 9.45(w), 9.78(m), 10.68(w), 11.13(s), 11.62(m), 12.15(w,infl.), 12.54(s) μ.

Fraction (d) was almost pure *cis*-2-bromo-2-butene (III), yield 28.5% (reported[21] b.p. 93.9°, n^{20}D 1.4620); *$\lambda_{\max}^{\text{liqu. film}}$ 3.34(s), 5.78(w), 6.00(m), 6.14(w), 6.92(m), 7.00(s), 7.26(m), 7.77(s), 8.80(s), 9.23(w), 9.44(m), 9.78(m), 10.67(w), 11.11(s), 11.60(m), 12.18(m-s), 12.54(s) μ. When this sample was exposed to sunlight for a day, the infrared absorption spectrum was: *$\lambda_{\max}^{\text{liqu. film}}$ 3.34(s), 5.79(w), 6.00(m), 6.14(w), 6.92(m), 7.01(s), 7.26(m), 7.77(s), 8.80(s), 9.23(w), 9.45(w), 9.78(m), 10.68(w), 11.13(s), 11.62(m), 12.13(w, infl.), 12.54(s) μ.

Fraction (c) was a mixture of III and IV. From the refractive index it can be calculated that it consisted of about 27.3 g. (10.1%) of *trans*-2-bromo-2-butene (IV) and 22.7 g. (8.4%) of *cis*-2-bromo-2-butene (III). Thus the apparent total yield of IV was 32.2% and that of III was 36.9%.

In another experiment, 240 g. of 2,3-dibromobutane (1.11 moles) was added at a moderate rate to maintain gentle reflux to a solution of 80 g. (1.2 moles) of 85% potassium hydroxide in 370 cc. of methanol. Stirring was continued for a few minutes and the mixture was cooled, diluted with four liters of distilled water, and acidified with concentrated hydrochloric acid. The organic layer was separated and the aqueous layer was extracted with ether. The organic layers were dried over calcium chloride and, after removal of the

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(30) See reference 2, pp. 111, 112, 120, 124, 130 and 131.

(31) The melting points are uncorrected. The analyses are by Micro-Tech Laboratories, Skokie, Illinois. The infrared spectra marked* were measured in a Beckman IR2T and the others on a Baird double beam instrument.

ether, the mixture of *cis*- and *trans*-2-bromo-2-butene was distilled through a 14.5 × 1.3 cm. column, packed with $^3/_{32}$ inch Fenske rings, at 82–92° (740 mm.), yield 116.5 g. (78%), n^{25}_{D} 1.4584. Judging from the refractive index, this was a 1:1 mixture of III and IV.

Carboxylations. Experiment 1.—A freshly prepared 1:1 mixture of *cis*- and *trans*-2-bromo-2-butene (III and IV), b.p. 82–92° (740 mm.), n^{25}_{D} 1.4584, weighing 27 g. (0.2 mole), was added over a period of one hour to a well stirred mixture of 2.80 g. (0.4 mole) of small pieces of lithium wire and 450 cc. of dry ether under an atmosphere of dry nitrogen at room temperature. After the addition, the mixture was stirred for 20 minutes and then forced through a tube into a large excess of crushed Dry Ice covered with 200 cc. of dry ether. The resulting mixture was allowed to stand at room temperature for several hours, a few unreacted lithium particles were removed mechanically, and the mixture was acidified with 10% hydrochloric acid. The ethereal solution was separated, washed well with sodium bicarbonate solution, dried and concentrated. The residual neutral material was distilled at 25–90° (15 mm.) to give 4 g. (40%)[32] of what may be a mixture of 1,2,3,4-tetramethylbutadiene (VI), and products of its self-condensation[26] (reported for VI,[26] b.p. 71–73° at 100 mm.), $\lambda^{\mathrm{alc}}_{\mathrm{max}}$ 235 mμ (ϵ 6,350).[32] The distillate did not give a precipitate when treated with 2,4-dinitrophenylhydrazine in aqueous alcoholic sulfuric acid.

The sodium bicarbonate extract, mentioned above, was washed once with ether, saturated with sodium chloride, and acidified with concentrated hydrochloric acid. The oily material was extracted with ether, the extract was dried and distilled through a 14.5 × 1.3 cm. column packed with $^3/_{32}$ inch glass helices with the following results: Fractions (a) (b) and (c), b.p. 88.5–92.0° (15 mm.), yield 6.28 g., gave 1.80 g. of angelic acid (9%), m.p. 42–44° (reported[3] 45°), on crystallization from petroleum ether. Fractions (d) and (e), b.p. 92.0–94.0° (15 mm.), yield 1.67 g., did not crystallize. Fraction (f), 2.50 g., b.p. 94.0–96.0° (15 mm.) and the residue (0.63 g.) crystallized from petroleum ether to give 1.63 g. (8.2%) of tiglic acid, m.p. 62–63.5° (reported[3] 65°). The total weight of acid material was 11.08 g. (55.4%).

Experiment 2.—The reaction was run in the same way as described in the preceding experiment with 3.45 g. (0.51 mole) of lithium, 500 cc. of dry ether and 32 g. (0.237 mole) of almost pure *trans*-2-bromo-2-butene (IV), b.p. 82.2–83.5° (740 mm.), n^{25}_{D} 1.4561, except that the temperature during the lithium salt formation was kept at −10 to −5°.

The neutral material was distilled at 15 mm. to afford 0.3 g. of a light yellow oil at 25–81°, 0.4 g. at 81–88°, n^{25}_{D} 1.4540, and 0.4 g. at 88–92°, n^{25}_{D} 1.4674, with 1.1 g. of pot residue. These fractions gave no solid 2,4-dinitrophenylhydrazone. Fraction 3 showed $\lambda^{\mathrm{alc}}_{\mathrm{max}}$ 235 mμ (ϵ 5,100),[32] and absorbed 1.7 moles[32] of hydrogen with Adams catalyst in acetic acid.

The semisolid acidic material weighed 18.5 g. (78%) from which 13.2 g. of angelic acid, m.p. 44–47°, was obtained by direct crystallization from petroleum ether. By fractional crystallization of the calcium salts[24] an additional 2.1 g. of angelic acid, m.p. 46–47° (total yield 64.6%) and 1.3 g. (5.5%) of tiglic acid, m.p. 58–61°, were isolated. When portions of these samples of the different acids were mixed, an oil was produced.

Experiment 3.—In the same manner as described in the preceding experiment, 5.55 g. (0.80 mole) of lithium and 50 g. (0.37 mole) of *cis*-2-bromo-2-butene (III), b.p. 91.0–91.2° (735 mm.), n^{25}_{D} 1.4606, yielded 8.9 g. (24.0%) of tiglic acid, m.p. 61–63°, and 3.2 g. (8.6%) of angelic acid, m.p. 44.46°. The neutral material distilled at 25–87° and 70–15 mm., yield 6.5 g. (with residue 32%),[32] n^{25}_{D} 1.4788, $\lambda^{\mathrm{alc}}_{\mathrm{max}}$ 236 mμ (ϵ 8,215).[32] In glacial acetic acid, this neutral material absorbed 1.8 moles[32] of hydrogen in the presence of Adams catalyst.

Experiment 4.—By conducting the same reaction at −20 to −25° with 90 g. (0.666 mole) of an equilibrium mixture of *cis*- and *trans*-2-bromo-2-butene (III and IV) (17:83), b.p. 82–86°, n^{25}_{D} 1.4568, 10.5 g. (1.5 moles) of lithium and 1 liter of dry ether, there were obtained 9.4 g. (25.5%)[32] of neutral and 35 g. (52.5%) of crude acidic material. The latter was esterified by stirring at room temperature for 30 hours with 50 g. (0.35 mole) of methyl iodide, 100 g. of powdered anhydrous potassium carbonate in 1 liter of reagent acetone. An additional 50 g. (0.35 mole) of methyl iodide was added and stirring was continued for 20 hours more. The solids were removed by filtration and the filtrate was concentrated to about 50 cc. After the addition of 25 g. of mesitylene, the ester was distilled at 740 mm. through a column of 25–30 plates efficiency to give the following fractions: (a) 2.5 g., b.p. 124.0–124.4°, n^{25}_{D} 1.4286; (b) 16.3 g., b.p. 124.4–124.8°, n^{25}_{D} 1.4303; (c) 6.0 g., b.p. 124.8–125.4°, n^{25}_{D} 1.4303; (d) 1.8 g., b.p. 125.4–128.8°, n^{25}_{D} 1.4313; (e) 2.0 g., b.p. 128.8–133.0°, n^{25}_{D} 1.4325; (f) 2.0 g., b.p. 133.0–134.4°, n^{25}_{D} 1.4335; (g) 3.0 g., b.p. 134.4–136.0°, n^{25}_{D} 1.4351; residue 28.5 g. (mostly mesitylene).

Fractions (b) and (c) were almost pure methyl angelate (29.2% yield) (reported[7] b.p. 127.6–127.8° at 764 mm., n^{20}_{D} 1.4330), $\lambda^{\mathrm{alc}}_{\mathrm{max}}$ 216 mμ (ϵ 9,350), *$\lambda^{\text{liqu. film}}_{\mathrm{max}}$ 3.34(m), 5.79(s), 6.05(w), 6.86(m), 6.96(m), 7.24(w), 7.38(m), 7.92(m), 8.08(s), 8.38(m), 8.83(s), 9.19(w), 9.52(m) (typical for methyl angelate), 10.08(w), 10.90(w), 11.75(m), 12.16(w), 13.16(w) μ. The saponification of 1.0 g. of fraction (b) was accomplished by shaking with 30 cc. of saturated barium hydroxide solution at room temperature for 24 hours, saturating with sodium chloride, acidifying, and cooling to give 0.88 g. (100%) of angelic acid, m.p. 43–44°.

Fractions (d), (e) and (f) consisted of a mixture of methyl tiglate and methyl angelate to the extent of 2.6 g. (3.5%) and 3.2 g. (4.2%) as calculated from the refractive indices.

Fraction (g) was almost pure methyl tiglate (3.9%) (reported[7] b.p. 139–139.6°, n^{20}_{D} 1.4370), $\lambda^{\mathrm{alc}}_{\mathrm{max}}$ 214 mμ (ϵ 11,300) (for the infrared spectrum of methyl tiglate, see below). The saponification of a 1.0-g. sample of fraction (g) by the procedure described above yielded 0.85 g. (97%) of tiglic acid, m.p. 62–64°.

Thus the total yield of methyl angelate in this reaction is 33.4%, of methyl tiglate 7.4%.

Experiment 5.—The lithium salt formation and the carboxylation of 101.2 g. (0.75 mole) of almost pure *trans*-2-bromo-2-butene (IV), b.p. 82.0–82.1° at 740 mm., n^{20}_{D} 1.4561, with 11.2 g. (1.6 moles) of lithium in 1 liter of ether was conducted at −15° as described in the previous experiments. The total acidic material amounted to 62 g. (82.6%) and the neutral material to 3 g. (7.3%).[32] The crude acids were esterified as described in the preceding experiment and the esters fractionated at 740 mm. to give the following fractions: (a) 58.5 g. (68.4%) of methyl angelate, b.p. 124.3–124.8°, n^{25}_{D} 1.4303; (b) 6.4 g. of a mixture, b.p. 124.8–133°, n^{25}_{D} 1.4316, consisting (from the refractive index) of 4.7 g. (5.5%) of methyl angelate and 1.7 g. (2.0%) of methyl tiglate; (c) 3.5 g. (4.1%) of methyl tiglate, b.p. 133.0–134.0°, n^{25}_{D} 1.4352. The saponification of 1.0-g. samples of fractions (a) and (c) by the procedure described above yielded 0.87 g. (99%) and 0.75 g. (85%) of angelic acid, m.p. 43–44°, and tiglic acid, m.p. 62–64°, respectively.

Experiment 6.—The carboxylation, as described above, of 96.0 g. (0.71 mole) of almost pure *cis*-2-bromo-2-butene (III), b.p. 90.0–91.0° at 740 mm., n^{25}_{D} 1.4602, with 11.2 g. (1.6 moles) of lithium in 1 liter of ether afforded 26.0 g. (36.8%) of crude acidic and 20.4 g. (52%)[32] of neutral material. After esterification of the acids, the distillation at 740 mm. through a column of 25–30 plates efficiency yielded: (a) 1.6 g. of a forerun, b.p. 124–124.2°, n^{25}_{D} 1.4266; (b) 4.5 g. of methyl angelate (5.6%), b.p. 124.2°, n^{25}_{D} 1.4303; (c) 9.0 g. of a mixture, b.p. 124.2–134.3°, n^{25}_{D} 1.4328, consisting (calculated from refractive index) of 4.8 g. (5.9%) of methyl tiglate and 4.2 g. (5.2%) of methyl angelate; (d) 12.0 g. of methyl tiglate (14.8%), b.p. 134.3–135.0°, n^{25}_{D} 1.4350, $\lambda^{\mathrm{alc}}_{\mathrm{max}}$ 214 mμ (ϵ 11,300), *$\lambda^{\text{liqu. film}}_{\mathrm{max}}$ 3.34(m), 5.79(s), 6.01(m-s), 6.89(m), 7.24(w), 7.39(w), 7.80(w), 8.10(s), 8.41(m), 8.85(s), 9.22(m) (typical for methyl tiglate), 10.24(w), 10.70(m), 11.70(m), 13.50(m) μ. Thus the total yield of methyl angelate was 10.8% and that of methyl tiglate was 20.7%. The saponification of fractions (b) and (d) with barium hydroxide (see above) gave almost quantitative yields of angelic (m.p. 42–44°) and tiglic (m.p. 62–65°) acids, respectively.

Properties of Tiglic and Angelic Acids.—The tiglic acid, obtained by the method described in this paper, had the following properties: m.p. 64.5–65.5°; $\lambda^{\mathrm{alc}}_{\mathrm{max}}$ 212.5 mμ (ϵ

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(32) The calculations of yield, absorption intensity, and hydrogen uptake of the neutral material were based on the molecular weight of 1,2,3,4-tetramethylbutadiene (VI).

12,500); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 3.4 (m,broad), 3.8(w), 3.96(w), 5.94(s), 6.07(m-s), 7.02(m), 7.22(m-w), 7.41(w), 7.81(s), 8.22 (shoulder), 8.60(m), 8.91(w), 9.21(m), 9.84 (m, typical for tiglic acid), 10.65(m, broad), 11.55(m) μ. When the sodium salt of 100 mg. (1.0 mmole) of tiglic acid in 5 cc. of methanol and 1 cc. of water was treated with 500 mg. (2.5 mmole) of S-benzylisothiuronium chloride in 2 cc. of water an immediate precipitation of the S-benzylisothiuronium salt of tiglic acid took place, yield 260 mg. (97%), m.p. 158–159°. Recrystallization from 95% ethanol afforded an analytical sample as colorless needles, m.p. 161.5–162.5°.

Anal. Calcd. for $C_{13}H_{18}N_2O_2S$: C, 58.62; H, 6.81; N, 10.52; S, 12.04. Found: C, 58.88; H, 6.85; N, 10.54; S, 12.25.

The angelic acid obtained in this work had the following properties: m.p. 44.5–46°; $\lambda_{\max}^{\mathrm{alc}}$ 215.5 mμ (ϵ 9,360); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 3.41(m), 3.8(w, shoulder), 5.92(s), 6.08(m), 6.81(m), 7.0(m, broad), 7.25(w), 7.41(w), 7.93(s, broad), 8.22 (shoulder), 8.45(w), 8.59(m), 8.80(w), 9.20(m), 9.57(m, typical for angelic acid), 10.69(m, broad), 11.68(m) μ. When the sodium salt of angelic acid was treated with S-benzylisothiouronium chloride as described above for tiglic acid, no precipitation was observed.

The treatment of a mixture of the sodium salts of 50 mg. of tiglic acid and 50 mg. of angelic acid in 5 cc. of methanol and 1 cc. of water with 500 mg. of S-benzylisothiuronium chloride in 2 cc. of water yielded 131 mg. (98%) of the derivative of tiglic acid, m.p. 153–154°. Recrystallization from 95% ethanol raised the m.p. to 159–160°, undepressed when mixed with the sample obtained from pure tiglic acid.

DETROIT, MICHIGAN

[CONTRIBUTION FROM THE CALIFORNIA RESEARCH CORPORATION]

Distribution of Isomers in the Acetylation of *t*-Butylbenzene

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m-t-Butylacetophenone has been identified as a product in the conventional Friedel–Crafts acetylation of *t*-butylbenzene. Using infrared spectrometric methods, the ratio of *o*-:*m*-:*p-t*-butylacetophenone was found to be 0:1.8:98.2. Minor amounts of acetophenone, *m*-di-*t*-butylbenzene and di-*t*-butylacetophenone are formed.

It has been assumed that only *para* derivatives are formed in Friedel–Crafts acylations of monosubstituted benzenes.[1] Work by Papa, *et al.*,[2] and others,[3,4] has shown that *meta* orientation does occur in the acylations of α-substituted toluenes in which the α-substituents are strongly *meta* directing. However, no examples of *meta* acylation are reported for simple alkyl benzenes.

The synthesis of *p-t*-butylacetophenone by Friedel–Crafts acylation of *t*-butylbenzene with acetyl chloride has been reported previously[5–10] but the isomer distribution was not given. In the current work, the isomer distribution and the minor products were determined by a careful fractional distillation of the reaction products and physical and chemical analyses of various fractions. The identification of *m-t*-butylacetophenone, the first reported formation of a *meta* isomer in the acylation of an alkyl benzene, is important in view of the current interest in orientation in aromatic substitution.[11,12]

Discussion of Results

The *t*-butylacetophenone was prepared by the conventional means of acetylation[13] of *t*-butylbenzene; 93.5% of the calculated weight yield was isolated in the various cuts of a fractional distillation (Table I, Fig. 1). The 6.5 weight per cent. loss may be attributed to the loss of low molecular weight material during the reaction (*i.e.*, isobutane), the loss of slightly water-soluble materials in the separation of the reaction mixture, and the loss of portions of the low boiling fractions during distillation. However, it may be assumed that the compositions of the various fractions represent a close approximation to the compositions prior to any loss.

The infrared spectra of *p-t*-butylacetophenone, purified by crystallization to a constant freezing point (Fig. 2), acetophenone and *t*-butylbenzene were used as criteria for determining the percentage of these compounds present in any fraction and for determining the percentage of other compounds by difference.

Tabulation of the distillation data gives the following mole per cent. conversions based on *t*-butylbenzene charged: *t*-butylbenzene (recovered), 1.9; *p-t*-butylacetophenone, 85.9; *m-t*-butylacetophenone, 1.55; acetophenone, 3.05; *m*-di-*t*-butylbenzene, 0.1; di-*t*-butylacetophenone, 2.5 (all high boiling miscellaneous materials are included in this percentage). A total of 94.1 mole per cent. is accounted for. The *para* to *meta* ratio of *t*-butylacetophenones is 98.2/1.8. There is no evidence for an ortho isomer.

This work does not afford a basis for assigning a mechanism for the formation of *m-t*-butylacetophenone, that is, whether it is formed by acetylation in the *meta* position or by some more devious route. There is considerable evidence for migrations of both alkyl and acetyl groups[7,10,14,15] in aromatic ketones in the presence of aluminum

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