Nonformation of a dibromide from ethyl p-t-butyl-β-cyano-α-ethoxycinnamate. Dry bromine (1.0 cc.) was added dropwise with stirring to a solution of 5.1 g. of the ester in 20 cc. cc. of carbon tetrachloride protected from moisture in the Mini Lab. After standing 7 days there was no evidence of reaction. The mixture was distilled under diminished pressure to give 4.3 g. of starting material, b.p. 156–159° (0.26 mm.); n_D^{25} 1.5320. No bromide could be isolated.

NEWARK, DEL.

[CONTRIBUTION FROM LABORATORY OF CHEMISTRY, RAMNARAIN RUIA COLLEGE, UNIVERSITY OF BOMBAY]

β-Arylglutaconic Acids. IV.[1] Synthesis of Crotono- and Valerolactones of β-Arylglutaconic and Glutaric Acids

J. J. NERURKAR,[2] R. N. JOSHI, V. N. MARATHE, G. S. PHADKE, AND V. M. BHAVE

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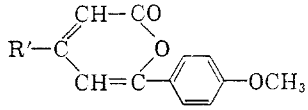
Through the condensation of β-arylglutaconic anhydrides with phenolic ethers in the presence of anhydrous aluminum chloride, a series of β-aryl-γ-benzoylcrotonic acids and their lactones were prepared. In addition, a general method for the synthesis of β,γ-substituted benzoylbutyric acids has been developed. These acids after reduction and lactonization gave the corresponding β,δ-substituted valerolactones. The crotono- and valerolactones are being tested for their anthelmintic activity and for their perfumery properties.

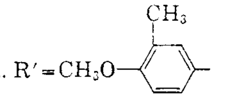
Though the relationship between chemical constitution and anthelmintic effect has not been fully elucidated, a number of the anthelmintics have been found which possess a lactonic group.[3] A detailed study by Rosenmund[4] and Nargund[5] has indicated that some arylbutyrolactones possess good anthelmintic effect. Moreover, unsaturation in the lactone ring has been shown to enhance the anthelmintic activity.[6]

These findings have led us to prepare a number of unsaturated lactones with different aryl substituents (Type I) for testing their anthelmintic effects.

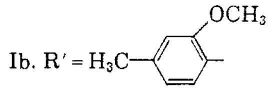


I

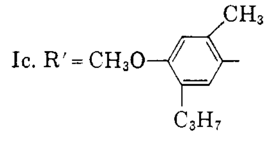
Ia.



Ib.



Ic.



Since 1926, the chemistry of lactones has assumed a great importance in the field of perfumery. Many naturally occurring lactones and their synthetic substitutes have been extensively studied in the light of their perfumery values.[7–9] The variation in odor of lactone has been studied as a function of the substituents attached to the lactone and, accordingly, a series of α and γ-substituted γ-butyrolactones were prepared.[10] Even the variation in intensity of odor with increase in the size of the lactonic ring was studied.[11] However, as yet, no definite relationship between the structure of a lactone and the intensity of its odor has been determined. It was therefore thought interesting to study the lactones (I) from the perfumery value point of view and attempt to gain some knowledge concerning the relationship between structure and odor intensity.

In the present work, condensation of (1) β-(4-methoxy-3-methylphenyl)-, (2) β-(2-methoxy-4-methylphenyl)- and (3) β-(4-methoxy-2-methyl-5-isopropylphenyl(glutaconic anhydrides in nitrobenzene with an equimolar quantity of anisole in the presence of anhydrous aluminum chloride was effected following the observation of Bhave.[12] From this reaction, two distinct products were isolated. The predominant product (80% yield) was a neutral compound and by analogy with

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(1) (a) Prior publications, *J. Org. Chem.*, **24**, 520 (1959); (b) *J. Org. Chem.*, **24**, 2055 (1959); (c) *J. Org. Chem.*, in press.

(2) Present address: Laboratory of Pharmaceutical Chemistry, The University of Kansas, Lawrence, Kan.

(3) P. Trendelenburg, *Arch. exp. Pathol. Pharmacol.*, **79**, 190 (1926).

(4) K. W. Rosenmund and D. Shapiro, *Arch. pharm.*, **272**, 313 (1934).

(5) (a) V. A. Vyas, K. V. Bokil, and K. S. Nargund, *J. Univ. Bombay*, **9**, 145 (1940). (b) J. J. Trivedi and K. S. Nargund, *J. Univ. Bombay*, **10**, 99 (1941).

(c) C. K. Paranjpe, N. L. Phalnikar, and K. S. Nargund, *J. Univ. Bombay*, **11**, 124 (1941).

(6) W. F. Ottingen, *J. Am. Chem. Soc.*, **52**, 2024 (1930); *J. Pharmacol. Exptl. Therap.*, **36**, 335 (1929).

(7) M. Kerschbaum, *Ber.*, **60**, 902 (1927).

(8) L. Ruzicka and M. Stoll, *Helv. Chim. Acta*, **11**, 1159 (1928).

(9) J. W. Hill and W. H. Carothers, *J. Am. Chem. Soc.*, **55**, 5039 (1933).

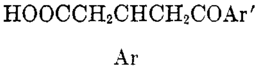
(10) B. Rothstein, *Bull. soc. chim.*, [5], 2, 80, 1936 (1935).

(11) M. Stoll and P. Bolle, *Helv. Chim. Acta*, **21**, 1547 (1938).

(12) V. M. Bhave, *Rasayanam*, I, 224 (1941) [*Chem. Abstr.*, **36**, 1032 (1942)].

TABLE I

3-Aryl-4-aroylbutyric Acids



$HOOCCH_2\underset{Ar}{CH}CH_2COAr'$

IV

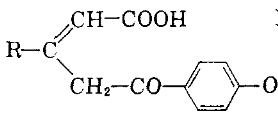
						Analysis: Carbon		Hydrogen		Neut. Equiv.	
No.	Ar	Ar′	Yield, %	M.P. °	Formula	Calcd.	Found	Calcd.	Found	Calcd.	Found
1	4-Methoxyphenyl[a,b]	Anisyl	55[c]	126	$C_{19}H_{20}O_3$	69.50	69.60	6.14	6.13	328.30	327.80
	Methyl ester[d]			65	$C_{20}H_{22}O_5$	70.16	69.95	6.48	6.45		
	Ethyl ester[e]			58	$C_{21}H_{24}O_5$	70.76	70.62	6.79	6.91		
	Phenylhydrazone[f]			176	$C_{25}H_{26}N_2O_4$					418.47	418.00
	Semicarbazone[g]			218	$C_{20}H_{23}N_3O_5$					385.41	384.60
	Oxime[h]			173	$C_{19}H_{21}NO_5$					343.37	344.80
2	4-Methoxy-3-methylphenyl[i]	Anisyl	53[j]	109	$C_{20}H_{22}O_5$	70.16	70.31	6.48	6.50	342.40	344.80
	Methyl ester[k]			66	$C_{21}H_{24}O_5$	70.76	71.06	6.79	6.45		
	Ethyl ester[l]			72	$C_{22}H_{26}O_5$	71.33	71.47	7.08	6.99		
	Phenylhydrazone[m]			184	$C_{26}H_{28}N_2O_4$					432.50	434.80
	Semicarbazone[n]			218	$C_{21}H_{25}N_3O_5$					399.40	400.00
	Oxime[o]			168	$C_{20}H_{23}NO_5$					357.40	360.40
3	2-Methoxy-5-methylphenyl[p]	Anisyl	61	112	$C_{20}H_{22}O_5$	70.16	68.98	6.48	6.76	342.40	343.90
	Phenylhydrazone[q]			182	$C_{26}H_{28}N_2O_4$					432.50	435.20
	Semicarbazone[r]			203 dec.	$C_{21}H_{25}N_3O_5$					399.43	398.20
	Oxime[s]			163	$C_{20}H_{23}NO_5$					357.39	358.40
4	4-Methoxyphenyl[t]	*o*-Cresylmethyl ether	64	124	$C_{20}H_{22}O_5$	70.16	70.38	6.48	6.58	342.4	344.2
	Methyl ester[u]			79	$C_{21}H_{24}O_5$	70.76	70.54	6.79	6.92		
	Phenylhydrazone[u]			171	$C_{26}H_{28}N_2O_4$					432.50	435.90
	Semicarbazone[u]			208	$C_{21}H_{25}N_3O_5$					399.43	397.42
	Oxime[u]			150	$C_{20}H_{23}NO_5$					357.39	354.30
5	2-Methoxy-5-methylphenyl[p]	*o*-Cresylmethyl ether	58	95	$C_{21}H_{24}O_5$	70.76	70.57	6.79	6.63		
	Methyl ester[u]			89	$C_{22}H_{26}O_5$	71.33	71.56	7.08	7.31		
	Phenylhydrazone[u]			158	$C_{27}H_{30}N_2O_4$					446.53	445.50
	Semicarbazone[u]			197 dec.	$C_{22}H_{27}N_3O_5$					413.46	415.30
	Oxime[u]			133	$C_{21}H_{25}NO_5$					371.42	369.60
6	4-Methoxyphenyl[t]	*m*-Cresylmethyl ether	64	101	$C_{20}H_{22}O_5$	70.16	70.41	6.48	6.36		
7	2-Methoxy-5-methylphenyl	*m*-Cresylmethyl ether	45	104	$C_{21}H_{24}O_5$	70.76	70.44	6.79	6.51	356.40	355.00
	Phenylhydrazone[q]			120	$C_{27}H_{30}N_2O_4$					446.53	443.80
8	4-Methoxyphenyl[t]	*p*-Cresylmethyl ether	59	122	$C_{20}H_{22}O_5$	70.16	70.43	6.48	6.42		
	Semicarbazone[v]			152	$C_{21}H_{25}N_3O_5$					405.40	399.43
9	2-Methoxy-5-methylphenyl[w]			108	$C_{21}H_{24}O_5$	70.76	70.94	6.79	6.37	356.40	355.00
	Semicarbazone			202 dec.	$C_{22}H_{27}N_3O_5$					413.46	416.38
10	4-Methoxyphenyl[t]	Thymolmethyl ether	67	117	$C_{23}H_{28}O_5$	71.85	71.78	7.34	7.37		
	Phenylhydrazone[u]			171	$C_{29}H_{34}N_2O_4$					474.58	471.30
11	2-Methoxy-5-methylphenyl[t]	Thymolmethyl ether	59	102	$C_{24}H_{30}O_5$	72.33	72.21	7.51	7.35		
12	4-Methoxyphenyl[t]	Resorcinyldimethyl ether	56	135	$C_{20}H_{22}O_6$	67.02	66.93	6.19	6.24	358.40	357.10
	Methyl ester[x]			78	$C_{21}H_{24}O_6$	67.73	67.40	6.50	6.49		
	Semicarbazone[v]			156	$C_{21}H_{25}N_3O_6$					417.40	415.43
	Oxime[v]			171	$C_{20}H_{23}NO_6$					375.60	373.39
13	2-Methoxy-5-methylphenyl[t]	Resorcinyldimethyl ether	60	89	$C_{21}H_{24}O_6$	67.73	67.90	6.50	6.47		
	Semicarbazone[v]			198 dec.	$C_{22}H_{27}N_3O_6$					429.46	431.58
	Oxime[x]			145	$C_{21}H_{25}NO_6$					387.42	391.45
14	4-Methoxyphenyl[y]	Hydroquinone dimethyl ether	68	130	$C_{20}H_{22}O_6$	67.02	66.74	6.19	6.23		
	Methyl ester[r]			45	$C_{21}H_{24}O_6$	67.73	68.01	6.50	6.36		
	Semicarbazone[q]			165	$C_{21}H_{25}N_3O_6$					419.70	415.43

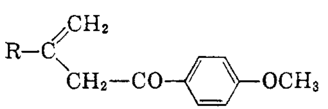
TABLE I (*Continued*)

						Analysis					
			Yield,			Carbon		Hydrogen		Neut. Equiv.	
No.	Ar	Ar′	%	M.P. °	Formula	Calcd.	Found	Calcd.	Found	Calcd.	Found
15	2-Methoxy-5-methylphenyl[s]	Hydroquinone dimethyl ether	63	117	$C_{21}H_{24}O_6$	67.73	67.32	6.50	6.20	372.40	368.90
	Semicarbazone[r]			196 dec.	$C_{22}H_{27}N_3O_6$					429.46	426.00
	Oxime[r]			201	$C_{21}H_{25}NO_6$					387.42	383.80
16	4-Methoxyphenyl[t]	Biphenyloxide	69	140	$C_{24}H_{22}O_5$	73.83	74.19	5.68	5.66		
	Methyl ester[x]			81	$C_{25}H_{24}O_5$	74.24	73.95	5.98	5.83		
	Semicarbazone[q]			221	$C_{25}H_{25}N_3O_5$					446.20	447.47
17	2-Methoxy-5-methylphenyl[x]	Biphenyloxide	71	104	$C_{25}H_{24}O_5$	74.24	73.92	5.98	5.79		
	Semicarbazone[u]			197 dec.	$C_{26}H_{27}N_3O_5$					461.50	461.00
18	4-Methoxy-2-methyl-5-isopropylphenyl[aa]	Anisyl	68	125	$C_{23}H_{28}O_5$	71.85	71.64	7.34	7.58		
	Oxime[u]			160	$C_{23}H_{29}NO_5$					399.47	402.04

[a] The intermediate, 4-methoxyphenylglutaric anhydride was prepared following the procedure of D. B. Limaye and R. G. Chitre, *J. Univ. Bombay*, **4,** 96 (1935). [b] White-needles from 50% acetic acid. [c] The yield was 61% when tetrachloroethane was used as solvent in place of nitrobenzene and 46% when carbon disulfide was used as solvent. [d] The ester was made using the Fischer Spier method, E. Fischer and A. Spier, *Ber.*, **28,** 3252 (1895); white crystals from methanol. [e] Prepared using Fischer Spier method, white crystals from ethanol. [f] White crystals from ethanol. [g] Colorless crystals from ethanol. [h] Shining needles from ethanol. [i] The intermediate glutaric anhydride was prepared following the procedure of Limaye and Chitre[a]; colorless needles from 50% acetic acid or a large quantity of water. [j] The yield was 65% using tetrachloroethane and 44% using carbon disulfide. [k] Dull white needles from methanol. [l] Shining white needles from ethanol. [m] White flakes from ethanol. [n] Colorless needles from ethanol. [o] Pale yellow needles from ethanol. [p] The intermediate glutaric anhydride was prepared following the procedure of Limaye and Chitre[a]; dull white crystals from 25% acetic acid. [q] White flakes from ethanol. [r] White needles from ethanol. [s] White shining flakes from ethanol. [t] White crystals from 50% acetic acid. [u] White crystals from ethanol. [v] White crystals from dilute ethanol. [w] Colorless needles from ethanol. [x] White needles from methanol. [y] White crystals from 50% methanol. [z] Dull white crystals from 10% acetic acid. [aa] See Experimental for the preparation of the intermediate β-(4-methoxy-2-methyl-5-isopropylphenyl)glutaric acid and its anhydride.

earlier work in our laboratory[12,13] was the β-aryl-γ-4-methoxybenzoylcrotonolactone (I). From the mother liquor of I, an acid product (10% yield) was isolated by treatment with dilute hydrochloric acid. It proved to be a monobasic acid by titration and it was shown to be ketonic in nature as evidenced through the formation of a semicarbazone and a phenylhydrazone. Its elementary analysis was also indicative of the structure II.


II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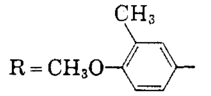
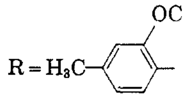
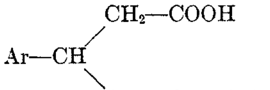
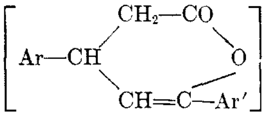
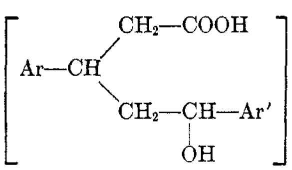

IIa & IIIa

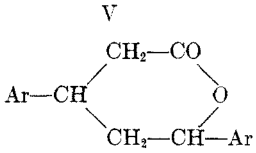

IIb & IIIb

In an attempt to open the lactonic ring of I to produce II, I was treated with sodium ethoxide in ethanol. The resulting product was, however, a neutral ketone (III) which gave a crystalline phenylhydrazone. The same product (III) was obtained by decarboxylation of II, suggesting that probably under the conditions of the experiment, sodium ethoxide brought about hydrolysis and subsequent decarboxylation. Hydrolysis of I in alcoholic alkali, however, resulted predominantly in the formation of II (70–75% yield) and a small percentage (6–8%) of III. The keto acid (II) could be reconverted to the starting lactone I by treatment with mineral acid or acetic anhydride.


IV (Table I)


V


VI


VII (Table II)

This reaction was extended by condensing several β-arylglutaric anhydrides with various phenolic ethers. Suprisingly, however, unlike the β-arylglutaconic anhydrides, β-aryl-γ-benzoylbutyric acids (IV, Table I) and not the lactones (V) were the only products isolated from the reaction. These acids were characterized through elementary analysis and through the formation of the usual ketonic derivatives. When IV was oxidized using alkaline potassium permanganate, free as well as substituted anisic acids were recovered as the products of reaction, supporting the assigned structure for

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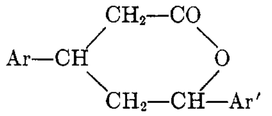
(13) V. M. Bhave and R. V. Bhagwat, *J. Indian Chem. Soc.*, **25,** 425 (1948).

TABLE II

3-ARYL-5-ARYLVALEROLACTONES



VII

						Analysis			
						Carbon		Hydrogen	
No.	Ar	Ar′	Yield, %	M.P. °	Formula	Calcd.	Found	Calcd.	Found
1	4-Methoxyphenyl[a]	Anisyl	45	83	$C_{19}H_{20}O_4$	73.06	72.70	6.45	6.26
2	4-Methoxy-3-methylphenyl[a,b]	Anisyl	40	80	$C_{20}H_{22}O_4$	73.60	73.31	6.79	6.50
3	2-Methoxy-5-methylphenyl[c]	Anisyl	42	202	$C_{20}H_{22}O_4$	73.60	73.41	6.79	6.34
4	4-Methoxyphenyl[c]	*o*-Cresylmethyl ether	51	87	$C_{20}H_{22}O_4$	73.60	73.84	6.79	6.86
5	2-Methoxy-5-methylphenyl	*o*-Cresylmethyl ether	47	212	$C_{21}H_{24}O_4$	74.09	73.96	7.11	6.95
6	4-Methoxyphenyl[d]	Resorcinyldimethyl ether	39	106	$C_{20}H_{22}O_5$	70.16	70.41	6.48	6.76

[a] Plates from 50% ethanol, pleasant balsamic odor on melting but no odor in solid state. [b] No odor in solid state but faint aromatic odor on melting. [c] White crystals from ethanol, pleasant aromatic odor in liquid state. [d] Purified by vacuum distillation, balsamic odor.

IV. When IV was reduced in the presence of sodium amalgam in an attempt to obtain the corresponding hydroxy acid (VI), the latter proved to be very unstable, and it immediately lactonized to the corresponding β-aryl-δ-arylvalerolactone (VII, Table II) upon treatment with acetic anhydride.

EXPERIMENTAL[14]

3-(4-Methoxy-3-methylphenyl)-5-anisyl-5-oxo-2-pentenoic acid-eno-lactone (Ia). The general procedure of Bhave[13] was followed. To a well stirred solution of 2.3 g. (0.01 mole) of β-(4-methoxy-3-methylphenyl)glutaconic anhydride[15] and 1.1 g. (0.01 mole) of anisole in 10 ml. of freshly distilled nitrobenzene, in a dry flask equipped with an air condenser carrying a calcium chloride tube, 3 g. of freshly powdered anhydrous aluminum chloride was added in portions during a period of about 30 min. The reaction was exothermic and the temperature was controlled (15–20°) by immersing the reaction flask in a cold water bath. The mixture was stirred at room temperature for 4 hr., and then the resulting dark red mixture was poured slowly into 100 ml. of ice-cold water containing 10 ml. of concd. hydrochloric acid. The solvent nitrobenzene was removed by distillation and the residue collected, washed with water, and then treated with 10% sodium carbonate solution. From the alkaline filtrate 0.15 g. (5% yield) of the acid (IIa) was isolated. The neutral residue on the filter was well washed with water and upon drying, it was crystallized from alcohol to give 2.6 g. (80% yield) of Ia as yellow needles, m.p. 169–170.5°.

Anal. Calcd. for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63. Found: C, 74.69; H, 5.79.

3-(4-Methoxy-3-methylphenyl)-5-anisyl-5-oxo-2-pentenoic acid (IIa). To a yellow solution of 1 g. of Ia in 100 ml. of boiling alcohol, a solution of 1.5 g. sodium hydroxide in 4 ml. of water was added. The resulting dark red solution was heated at reflux temperature for 15 min. After a portion of 25 ml. of water was added, the solvent alcohol was removed under water pressure vacuum. The alkaline solution was filtered, and the filtrate neutralized with dilute hydrochloric acid at ice bath temperature. The gummy solid which separated solidified upon standing. It was recrystallized from alcohol to afford 0.4 g. (43% yield) of IIa, m.p. 148–149.5° dec.

Anal. Calcd. for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92; neut. equiv., 340.4. Found: C, 70.54; H, 5.76; neut. equiv., 341.9.

The residue collected after filtering the alkaline solution was washed thoroughly with water, dried, and recrystallized from alcohol to give 0.14 g. (15% yield) of IIIa, m.p. 87–88°.

2-(4-Methoxy-3-methylphenyl)-4-anisyl-4-oxo-butene-1 (IIIa). *Method A.* One gram of acid (IIa) was heated in a hard glass test tube at about 148–152° until no more carbon dioxide was evolved (tested by lime water). The brown gummy mass, which separated after chilling the contents of the tube, solidified upon trituration with alcohol. It was treated with dilute sodium bicarbonate solution and water. The dry solid was then recrystallized from alcohol giving 0.35 g. (38% yield) of IIIa, as faintly yellow crystals, m.p. 87–88°.

Method B. To a solution of 3.2 g. (0.01 mole) of Ia in 200 ml. of alcohol, a solution of sodium ethoxide, prepared from 0.46 g. of sodium and 25 ml. of alcohol, was added. The mixture was heated at reflux temperature for 15 min. Removal of the solvent left a residue, which after washing with water and drying, was recrystallized from alcohol to give 1.7 g. (60% yield) of IIIa, as faint yellow flakes, m.p. 87–88.5°. The melting point of a mixture of the samples prepared by methods *A* and *B* showed no depression.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 77.01; H, 6.80. Found: C, 76.74; H, 6.73.

3-(2-Methoxy-4-methylphenyl)-5-anisyl-5-oxo-2-pentenoic acid-eno-lactone (Ib). This lactone was prepared following the procedure for Ia. From 2.3 g. (0.01 mole) of β-(2-methoxy-4-methylphenyl)glutaconic anhydride,[16] 2.5 g. (78% yield) of Ib was obtained, m.p. 127.5–128°.

Anal. Calcd. for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63. Found: C, 74.63; H, 5.67.

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(14) All melting points are uncorrected.

(15) D. B. Limaye and V. M. Dixit, *Proc. Indian Sci. Congr.*, 167 (1930).

(16) D. B. Limaye and G. R. Gogte, *J. Univ. Bombay*, **3**, 135 (1934).

3-(2-Methoxy-4-methylphenyl)-5-anisyl-5-oxo-2-pentenoic acid (IIb). Following the procedure used in making IIa, this acid was obtained in 72% yield from Ib, m.p. 128–128.5° dec.

Anal. Calcd. for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92; neut. equiv., 340.4. Found: C, 70.54; H, 5.76; neut. equiv., 343.7.

A phenylhydrazone of IIb was prepared by treating equimolar quantities of IIb and phenylhydrazine in acetic acid solvent. It was recrystallized from alcohol to give white crystals, m.p. 164–165.5° dec.

Anal. Calcd. for $C_{26}H_{26}N_4O_2$: Neut. equiv., 426.5. Found: Neut. equiv., 430.2.

A semicarbazone of IIb was also prepared, m.p. 178–179.5° dec.

Anal. Calcd. for $C_{21}H_{23}N_3O_5$: Neut. equiv., 397.4. Found: Neut. equiv., 399.4.

2-(2-Methoxy-4-methylphenyl)-4-anisyl-4-oxo-butene-1 (IIIb). This ketone was prepared from Ib in 46% yield and from IIb in 56% yield following the procedures used for IIIa. It was obtained as faint yellow crystals from alcohol, m.p. 83–84°.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 77.18; H, 6.82.

3-(4-Methoxy-2-methyl-5-isopropylphenyl)-5-anisyl-5-oxo-pentenoic acid-eno-lactone (Ic). This lactone was obtained in about 53% yield from β-(4-methoxy-2-methyl-5-isopropylphenyl)glutaconic anhydride[17] following the general procedure outlined for making Ia; m.p. 158–159°.

Anal. Calcd. for $C_{23}H_{24}O_4$: C, 75.80; H, 6.64. Found: C, 75.82; H, 6.40.

3-Aryl-5-aryl-5-oxo-pentanoic acids (IV, *Table* I). *General procedure.* These substituted butyric acids were prepared from the corresponding β-arylglutaric anhydrides by adopting the general procedure used in making Ia, b, and c. The sticky solid left after removal of the solvent nitrobenzene was washed with water and then treated with 10% sodium bicarbonate solution. The clear solution was treated with active charcoal and then filtered. Upon neutralization of this filtrate, there was obtained a gum which solidified on standing. Two to three recrystallizations usually gave a pure sample of the acid.

The use of tetrachloroethane as a solvent in place of nitrobenzene improved the yield but with carbon disulfide as a substitute for nitrobenzene, the yield was poorer.

Oxidation of 3-aryl-5-aryl-5-oxo-pentanoic acids (from Table I). To a solution of 1 g. of acid in 40 ml. of 2.5% sodium carbonate solution, 3 g. of finely powdered potassium permanganate was added in portions with vigorous stirring. After two hours' stirring at room temperature, the hydrated manganese dioxide was removed by filtration. The clear filtrate upon concentration to a small volume (about 10 ml.) was neutralized with concd. hydrochloric acid at ice bath temperature. Usually one of the substituted anisic acids was recovered as an insoluble precipitate, and the mother liquor contained water soluble oxidation products obtained from the other part of the molecule. The latter was subjected to continuous ether extraction and to the oily residue left after evaporation of the ether, 2 ml. of glacial acetic acid and 6 ml. of 0.3*N* hydrogen peroxide solution was added. Upon concentration of this solution at room temperature, there was left a solid which was characterized as the other substituted anisic acid by a melting point determination of a mixture with an authentic sample.

In some cases, both the oxidation products (anisic acids) were recovered as a mixture during potassium permanganate oxidation. They were separated by fractional crystallization and then identified by determining mixed melting points of a mixture with authentic samples. Two recrystallizations were usually necessary before a pure sample was obtained.

2-Oxo-4-aryl-6-aryl-tetrahydropyran (VII, *Table* II). *General procedure.* A solution of 2 g. of the butyric acid (Table I) in 1*N* sodium hydroxide solution sufficient for neutralization was shaken vigorously for about 45 min. in a stoppered bottle with 10 g. of 4% sodium-amalgam (prepared from 10 g. of mercury and 0.4 g. of sodium). After the evolution of hydrogen had ceased (about 2 hr.), the alkaline solution was filtered. Neutralization of the filtrate with hydrochloric acid at ice bath temperature gave a solid melting over a wide range (5–10°). All attempts to obtain a pure sample of the solid failed. To the crude dry solid in a flask, 3 ml. of acetic anhydride was added and the entire mixture was heated at 100° for 15 min. and then poured into 50 ml. of water. The solid which separated was washed with several portions of dilute sodium bicarbonate solution and then water. After drying, it was recrystallized several times to give a pure sample of the lactone.

β-(4-Methoxy-2-methyl-5-isopropylphenyl)glutaric acid. A solution of 5 g. of β-(4-methoxy-2-methyl-5-isopropylphenyl)glutaconic acid[17] in 1*N* sodium hydroxide solution sufficient for neutralization was taken in a stoppered bottle. A portion of 40 g. of 4% sodium amalgam (from 40 g. of mercury and 1.6 g. of sodium metal) was slowly added to this solution and the reaction mixture was vigorously shaken for 45 min. After the evolution of hydrogen had ceased (about 2 hr.), it was filtered and the filtrate was neutralized with concd. hydrochloric acid at ice bath temperature. A sticky and dull white mass which separated solidified after standing. It was collected on a filter and the dry solid was recrystallized twice from boiling water to give 4.1 g. (81% yield) of the reduced acid as white needles, m.p. 148–149°.

Anal. Calcd. for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53; neut. equiv., 147.17. Found: C, 65.40; H, 7.42; neut. equiv., 147.12.

β-(4-Methoxy-2-methyl-5-isopropylphenyl)glutaric anhydride. A mixture of 5 g. of the glutaric acid and 10 ml. of acetic anhydride was heated at reflux temperature for 5 min. The resulting gummy mass was washed with ether when it solidified. Recrystallization from benzene gave 4.1 g. (86% yield) of the anhydride as shining plates, m.p. 135–136.5°.

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.78; H, 7.22.

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[17] V. M. Bhave, *J. Indian Chem. Soc.*, 29, 275 (1952).