suspensions were dissimilar only in the region from 8 to 12 microns, possibly due to the differences in crystal structure.

Biological assays of the two forms showed no significant difference in estrogenic activity.[3]

(3) Modified Kahnt-Doisy method, by S. Margolin and M. T. Spoerlein, Biological Laboratories of this Company.

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Isomerization of Saturated Hydrocarbons. VIII.[1] The Effect of Oxygen and Light upon the Isomerization of Methylcyclopentane in the Presence of Aluminum Bromide

BY HERMAN PINES, EUGENE ARISTOFF[2] AND V. N. IPATIEFF

The promoting effect of oxygen upon the isomerization of *n*-butane and *n*-pentane in the presence of either aluminum chloride or aluminum bromide has been reported previously.[3] This study has now been extended to determine whether oxygen in the presence of aluminum bromide but in the absence of added hydrogen bromide promotes the isomerization of saturated cyclic hydrocarbons such as methylcyclopentane to cyclohexane. The experiments were conducted in either quartz or Pyrex reaction tubes.

It was noticed that in diffused light, and a Pyrex reaction tube, with methylcyclopentane, aluminum bromide and oxygen in a molal ratio of 100:2:0.2, isomerization of methylcyclopentane to cyclohexane does not occur. When the reaction tube was exposed for eighteen hours to a quartz cadmium–mercury arc lamp 6% of the methylcyclopentane was isomerized; the extent of isomerization was increased to 13% when a quartz reaction tube instead of a Pyrex one was used.

The introduction of a larger amount of oxygen into a Pyrex reaction zone, namely, 1 mole equivalent of oxygen per 100 moles of methylcyclopentane and 4 moles of aluminum bromide, caused the isomerization of 15% of methylcyclopentane; when a quartz reaction tube was used and irradiated, 42% of cyclohexane was formed.

In line with previous observations[1,4,5] it was noticed that the presence of about 0.04 mole per cent. of benzene in methylcyclopentane greatly reduces the degree of isomerization. The experimental results are summarized in Table I.

During the course of this study it was observed that aluminum bromide *per se* placed in a quartz tube and irradiated did not change coloration. It was noticed however that when aluminum bromide in the presence of oxygen was irradiated for 0.5–1 hour the tube was filled with brown vapors, which became more deeply colored as the time of irradiation increased. The mechanism by which the oxidation of aluminum bromide proceeds was not studied. It is very likely that the promoting effect of the oxygen is due to the oxidation of aluminum bromide with formation of bromine. The latter then reacts with methylcyclopentane to form bromomethylcyclopentane, which is a chain initiator for the isomerization.[6] The oxidation of aluminum bromide in solution in hydrocarbons seems to proceed even in diffused light.

The inhibiting effect of benzene upon the isomerization of methylcyclopentane is not entirely unexpected; it is most likely due to the removal of the chain initiator through the reaction with benzene, as has been shown previously.[1,5]

TABLE I

ISOMERIZATION OF METHYLCYCLOPENTANE

Expt.	Irradiation, hours	Reaction tube[b]	Methylcyclopentane used, moles × 10²	Reactant charged moles per 100 moles of methylcyclopentane: $AlBr_3$	O_2	C_6H_6	Cyclohexane produced, %
1	18[a]	P	2.22	2.01	0.18	0	0
2	18[a]	P	3.10	4.00	1.05	0	15
3	18	P	2.11	2.02	0.18	0	6
4	18	Q	1.37	1.99	.17	0	13
5	18	Q	1.04	4.02	.96	0	42
6	18	Q	2.60	2.04	.20	0.037	0
7	18	Q	1.00	3.98	.96	0.039	6

[a] In experiments 1 and 2 the reaction tubes were not irradiated. [b] P, Pyrex reaction tube; Q, quartz reaction tube.

Experimental

The high vacuum apparatus and procedure have been described previously.[1,6] Linde oxygen was introduced into the apparatus through a phosphorus pentoxide drying tube. After being measured in the calibrated portion of the Töpler pump, the oxygen was transferred to an ampoule having a thin walled break-off. The sealed ampoule was carefully placed in the reaction tube, then the latter evacuated. After the other reactants had been added, the reaction tube was sealed off then shaken, in order to break the thin bulb of the ampoule containing oxygen. The composition of the hydrocarbons obtained from the reaction was determined by means of infrared absorption spectra.

(1) For paper VII of this series see H. Pines, E. Aristoff and V. N. Ipatieff, THIS JOURNAL, **72**, 4055 (1950).

(2) Universal Oil Products Company Predoctoral Research Fellow 1947–1949.

(3) H. Pines and R. C. Wackher, THIS JOURNAL, **68**, 599 (1946).

(4) J. M. Mavity, H. Pines, R. C. Wackher and J. A. Brooks, *Ind. Eng. Chem.*, **40**, 2374 (1948).

(5) H. Pines, E. Aristoff and V. N. Ipatieff, THIS JOURNAL, **71**, 749 (1949).

(6) H. Pines, B. M. Abraham and V. N. Ipatieff, *ibid.*, **70**, 1742 (1948).

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The Structure of Methyl Acetylacrylate[1]

BY SAMUEL RAYMOND

Methyl acetylacrylate was first prepared in 1914 by Pauly, Gilmour and Will[1a] by the dehydro-

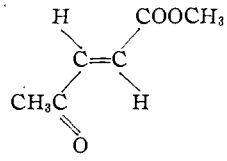
(1) This work was supported by a grant from the National Institutes of Health and from the John and Mary R. Markle Foundation.

(1a) Pauly, Gilmour and Will, *Ann.*, **403**, 119 (1914).

bromination of methyl bromolevulinate with anhydrous sodium acetate. Shaw,[2] in 1946, prepared a methyl ester (I, m. p. 60°) by the reaction of acetylacrylic acid with diazomethane. Raymond,[3] in 1949, prepared a methyl ester, which was identical with I, both by the selenium dioxide dehydrogenation of methyl levulinate, and by the dehydrobromination method. The identity of the three preparations was shown by mixed m. p., by the formation of the same semicarbazone, and by identity of the ultraviolet spectra.

Present interest in these esters arises from their structural relationship to certain antibiotics of botanical origin. Protoanemonin, for example, is the lactone of acetylacrylic acid.

Three structures must be taken into account for I if the carbon skeleton is maintained but migration of the methoxyl group is not excluded during the formation from methyl levulinate. These three are the *trans* (II), the *cis* (III) and the cyclic (IV).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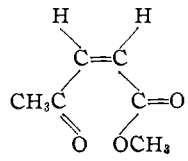
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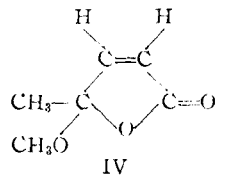
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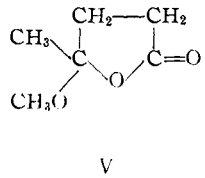
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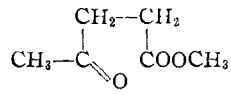
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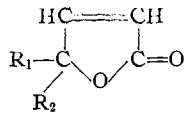
VII

Pauly[1a] formulated the product as a keto-unsaturated ester (II or III) but did not consider the *cis–trans* isomerism. Shaw, on the basis of the ultraviolet spectrum, stated that I is *probably* the methyl ester of the pseudo-acid (cyclic) form (IV).

New experimental evidence, given in this paper, and a revaluation of the spectral evidence, seems to exclude IV as the structure of I, leaving II or III for consideration.[4] In support of this statement the following evidence is cited: (1) The synthesis of I from the methyl levulinate isomer of the open-chain structure[5] by two independent methods is presumptive evidence for an open-chain structure. Nevertheless, the possibility of a migration of methoxyl group during the reaction or isolation cannot be excluded on this evidence alone.

(2) The compound I reacts with semicarbazide in the usual manner to form a semicarbazone.[6] The implication of this fact is that a true ketone group is present which must be lacking in the ring structure. It should be noted that the pseudoester of levulinic acid (V) does not react with semicarbazide.[5]

(3) Hydrogenation of I in the presence of platinum, under strictly neutral conditions and at atmospheric pressure, produces VI and not V. Unsaturated lactones of type VII (R_1, R_2 and H or alkyl), however, are known to produce saturated lactones, on hydrogenation, which are stable toward further hydrogenation.[7] The isolation of VI in the present instance was not due to an isomerization of V to VI under the reaction conditions, since a separate experiment showed that V is entirely stable under the conditions used. Raney nickel also catalyzed the hydrogenation of I to VI, but this catalyst also caused a partial isomerization of V to VI, presumably due to the acid which was found to be adsorbed on the nickel.

(4) The ultraviolet absorption spectrum of I shows features characteristic of the α,β-unsaturated ketone structure present in formulas II and III (Fig. 1). The broad band at 324 mμ (log ϵ 1.59) is the ketone band ("R-band" of Burawoy[8]) shifted by the conjugation from its

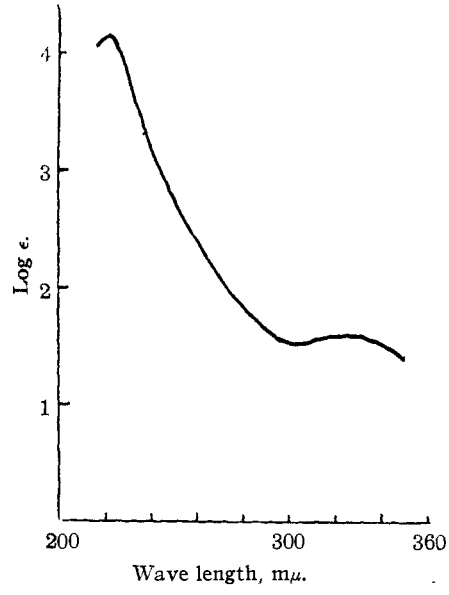

Fig. 1.—The ultraviolet absorption spectrum of methyl acetylacrylate.

(2) Shaw, THIS JOURNAL, **68**, 2510 (1946).

(3) Presented at the 115th National Meeting, American Chemical Society, San Francisco, April, 1949; THIS JOURNAL, **72**, 3296 (1950).

(4) The specific assignment to the compound of either the *trans* (II) or the *cis* (III) structure is not possible from the presently known facts.

(5) Langlois and Wolff, THIS JOURNAL, **70**, 2624 (1948).

(6) Rinkes and v. Hasselt, *Chem. Zentr.*, **87**, II, 390 (1916); *cf.* **88**, I, 208 (1917).

(7) Jacobs and Scott, *J. Biol. Chem.*, **87**, 601 (1930); **93**, 139 (1931); Hill, Salvin and O'Brien, THIS JOURNAL, **59**, 2385 (1937).

(8) Burawoy, *J. Chem. Soc.*, 1177 (1939).

unconjugated position at 275 millimicrons to a longer wave length. This feature of the spectrum is particularly valuable in distinguishing IV from II or III, since no unsaturated lactones have been reported to show a band of this type.

The sharp peak at 222 mμ (log ε 4.15) is perhaps somewhat more ambiguous in origin, since both unsaturated lactones and unsaturated ketones are reported to absorb in this region. Recent work on unsaturated lactones of type VII, however, places the maximum at or below 214 mμ[9]; Haynes and Jones specifically state that the maxima of absorption of their compounds lie at the extreme end of the usual ultraviolet range, and can be discerned in only certain cases.

α,β-Unsaturated ketones also have an absorption near the end of the ultraviolet range which has been termed the "K-band" by Burawoy.[8] This band lies at 225 ± 5 mμ in monosubstituted α,β-unsaturated ketones.[10] The peak at 222 mμ in the spectrum of I may therefore be interpreted as the K-band due to the conjugated unsaturated ketone system. The additional substitution on the ethylene group of an ester group appears to have no more effect in compounds of this type than an equal substitution of alkyl group; compare ethyl crotonate, maximum at 208 mμ (log ε 4.3),[11] with dimethyl fumarate, maximum at 209 mμ (log ε 4.5).[12]

(5) It has been established that mono-unsaturated lactones of the angelica lactone type show only a low order of antibacterial activity (minimum effective concentration 200 micrograms per ml. and above).[13] On the other hand, many unsaturated ketones show a comparatively high activity (minimum effective concentration 1–10 micrograms per ml.).[14,15] The esters of acetylacrylic acid, including I, exhibit a high antibacterial potency (minimum effective concentration 1–10 micrograms per ml.) (Table I). This activity is difficult to understand or to explain on the basis of structure IV, but appears reasonable when the compounds are formulated as unsaturated ketones.

TABLE I

MINIMUM CONCENTRATION (MICROGRAM/ML.) OF UNSATURATED KETONES WHICH WILL INHIBIT THE GROWTH OF SEVERAL MICROÖRGANISMS

Compound	*Es. coli*	*My. tuberculosis*	*Pneumococcus III*
Methyl acetylacrylate	5	2	25
Ethyl acetylacrylate	5	0.4	20
Propyl acetylacrylate	10	1	40
Butyl acetylacrylate	20	2	40
Benzyl acetylacrylate	40	4	
Diacetylethylene	2	2	20

(9) Haynes and Jones, *J. Chem. Soc.*, 954 (1946); Coker and Hornsby, *ibid.*, 1157 (1947).

(10) Woodward, THIS JOURNAL, **63**, 1123 (1941).

(11) Rusoff, Platt, Klevens and Burr, *ibid.*, **67**, 678 (1945).

(12) Sörensen, *Ann.*, **546**, 51 (1940).

(13) Baer, Holden and Seegal, *J. Biol. Chem.*, **162**, 65 (1946); Brodersen and Kjaer, *Acta Pharmacol.*, **2**, 109 (1946); Haynes, *Quart. Rev.*, 11, 46 (1948); Kuhn, Jerchel, Moewus and Moller, *Naturwiss.*, **31**, 468 (1948); McCawley, Rubin and Giacomino, *Fed. Proc.*, 191 (1946); Rubin, *Yale J. Biol. Med.*, **20**, 233 (1948).

(14) Geiger and Conn, THIS JOURNAL, **67**, 112 (1945).

(15) Including diacetylethylene, which is included in Table I as an example of an unsaturated ketone.

Experimental

Methyl Acetylacrylate (I).—The normal methyl levulinate,[5] 13 g. (0.1 mole) and 5.5 g. of selenium dioxide (0.05 mole) were triturated together and allowed to stand at room temperature for two weeks. The mixture was then extracted with dichloromethane and the extract steam distilled. Two liters of distillate was collected and extracted with dichloromethane. The solvent was evaporated and the residue, on being cooled to −20°, deposited crystals which were rapidly filtered and washed with ligroin–ether mixture. One recrystallization of the crystals from ether–ligroin gave 0.42 g. of pure methyl acetylacrylate, m. p. 59–60°, yield 3.2%. The same melting point was obtained in mixture with the methyl acetylacrylate obtained by the method of Pauly[1a] and of Shaw.[2] The three preparations all formed identical semicarbazones, m. p. 193–194°,[6] and all gave the same ultraviolet spectrum.

Hydrogenation of I.—A solution of 493 mg. of I in absolute methanol absorbed 102 ml. of hydrogen at atmospheric pressure in the presence of 20 mg. of Adams platinum catalyst. The absorption was complete in thirty minutes. The resulting solution was filtered and made up to 50 ml. with methanol. A 10-ml. sample, hydrolyzed by the method of Langlois and Wolff,[5] required 0.08 ml. of 0.1 *N* alkali. Twenty ml., treated with semicarbazide following Langlois and Wolff, gave 0.1 g. of methyl levulinate semicarbazone, m. p. 140–141°. The experiment was repeated, using 0.2 g. of Raney nickel in place of the platinum catalyst. Results were exactly the same.

Effect of Catalyst on V.—A solution of 500 mg. of V in 50 ml. of absolute methanol was prepared. A 10-ml. sample required 7.55 ml. of 0.0964 *N* NaOH in the Langlois–Wolff titration. The calculated value was 7.69 ml., indicating a 98% content of pseudo-ester. After being shaken 30 minutes with the catalyst in the presence of hydrogen, none of which was absorbed, the solution required 7.61 ml. of base for 10 ml., indicating that no isomerization had taken place. The experiment was repeated, using 0.2 g. of Raney nickel in place of the platinum catalyst. After one hour the titration value was 3.14 ml., indicating a 41% conversion to normal ester. The catalyst alone required 0.11 ml. of base.

Minimum Inhibitory Concentrations for Three Pathogenic Microörganisms.—Tests were set up according to a standard protocol in which the total concentrations of the antibiotics in suitable media ranged from 800 micrograms to 0.2 microgram per ml. Each tube was inoculated with a constant amount of the test organism. Tubes were incubated at 37° and inhibition was read when the controls showed growth. The medium, inoculum and time of incubation varied with the organism being tested.[16]

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(16) Holden, Seegal and Baer, *Proc. Soc. Exptl. Biol. Med.*, **66**, 54 (1947).