from acetone; m.p. 198° (dec.). Rotation: 0.0175 g. made up to 1.59 ml. with chloroform at 28° gave α_D −0.130°, *l* 1, $[\alpha]^{28}_D$ −11.81° (±0.5°).

Anal. Calcd. for $C_{29}H_{36}O_9N_2$: C, 62.59; H, 6.47; N, 5.03. Found: C, 62.67; H, 6.67; N, 5.07.

Acetyldicrotalic Anhydride.—A solution of 0.50 g. of dicrotalic acid in 10 ml. of benzene and 5 ml. of acetic anhydride was boiled under reflux for 2 hours in the presence of a few drops of acetyl chloride. The excess solvent and reagent was removed under reduced pressure. On addition of ether to the residual oil, a colorless crystalline solid separated; 0.35 g. The substance was recrystallized from ether; transparent prisms, m.p. 85°.

Anal. Calcd. for $C_8H_{10}O_5$: C, 51.61; H, 5.37. Found: C, 51.85; H, 5.58.

Anhydrodicrotalic Anhydride.—Acetyldicrotalic anhydride, 0.25 g., was heated at 100° for 12 hours. The resultant oil crystallized as fine needles on standing in a vacuum desiccator. The product was purified by crystallization from ether; m.p. 85°.

Anal. Calcd. for $C_6H_6O_3$: C, 57.14; H, 4.76. Found: C, 56.88; H, 4.99.

Anhydrodicrotalic Acid.—Anhydrodicrotalic anhydride, 0.10 g., was treated with a slight excess of 10% aqueous sodium hydroxide on a steam-cone for 0.5 hours. The solution was acidified and extracted with ether (6 × 10 ml.). The ether solution was dried over anhydrous sodium sulfate. Removal of the solvent left a crystalline solid; 0.06 g. (60%). The product was recrystallized from ether; m.p. 149–150°.

Anal. Calcd. for $C_6H_8O_4$: C, 50.00; H, 5.55. Found: C, 50.17; H, 5.78.

***trans*-α-Methylglutaconic Acid.**—Diethyl malonate and chloroform were condensed in presence of sodium ethoxide using the procedure of Conrad and Guthzeit.[7] The yellow sodium salt was treated with methyl iodide in ethanol by the method of Thole and Thorpe.[8] Diethyl α-methyl-α,γ-dicarbethoxyglutaconate was obtained in 70% yield, b.p. 205–206.5° (15 mm.) (reported b.p. 211° (21 mm.)).[8] This ester gave on alkaline hydrolysis and recrystallization from ether *trans*-α-methylglutaconic acid, m.p. 145–146° (reported m.p. 145–146°).[8]

Anal. Calcd. for $C_6H_8O_4$: C, 50.00; H, 5.55. Found: C, 50.21; H, 5.50.

***cis*-β-Methylglutaconic Acid.**—Ethyl isodehydroacetate[9] was hydrolyzed with 10% aqueous alkali and pure *cis*-β-methylglutaconic acid, m.p. 149–150°, obtained by repeated crystallization from ether (reported m.p. 147°).[9] This acid gave no depression of melting point on admixture with anhydrodicrotalic acid.

β-Methylglutaconic Anhydride.—The anhydride was prepared from a mixture of *cis*- and *trans*-β-methylglutaconic acids by boiling with acetyl chloride. The product was recrystallized from ether, m.p. 85° (reported m.p. 86°).[10] This substance gave no depression of melting point on admixture with anhydrodicrotalic anhydride.

Diethyl β-Methyl-β-hydroxyglutarate.—A mixture of 170 g. of ethyl acetoacetate and 220 g. of ethyl bromoacetate in 800 ml. of benzene was added to 70 g. of zinc at such a rate that the benzene refluxed gently. The mixture was stirred during the addition. After addition was complete the mixture was refluxed for 2 hours, acidified with cold 10% sulfuric acid and the benzene layer separated. The aqueous solution was extracted with benzene (2 × 100 ml.) and the combined benzene extract washed first with aqueous sodium bicarbonate and then with water. The extract was dried with anhydrous magnesium sulfate and the solvent removed under reduced pressure. Distillation of the product yielded 30 g. (13.7%) of a colorless liquid, b.p. 143.5° (16 mm.). The product was redistilled without change in boiling point; n^{20}_D 1.4348.

Anal. Calcd. for $C_{10}H_{18}O_5$: C, 55.04; H, 8.25. Found: C, 54.80; H, 7.94.

β-Methyl-β-hydroxyglutaric Acid.—Hydrolysis with 10% aqueous alkali of the ester described above yielded an acid which was extracted with ether from the acidified aqueous solution. It was purified by recrystallization from ether–petroleum ether (b.p. 30–60°); colorless flakes, m.p. 109°. This acid gave no depression of melting point on admixture with dicrotalic acid.

Anal. Calcd. for $C_6H_{10}O_5$: C, 44.44; H, 6.17. Found: C, 44.70: H, 6.22.

URBANA, ILLINOIS

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[7] M. Conrad and M. Guthzeit, *Ann.*, **222**, 249 (1884).

[8] F. B. Thole and J. C. Thorpe, *J. Chem. Soc.*, **99**, 2187 (1911).

[9] F. Feist, *Ann.*, **345**, 60 (1906).

[10] H. Rogerson and J. F. Thorpe, *J. Chem. Soc.*, **87**, 1685 (1905).

[CONTRIBUTION NO. 1705 FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY]

On the Stereochemistry of Azines: Cinnamalazine and Phenylpentadienalazine*

BY JOHANNES DALE† AND L. ZECHMEISTER

RECEIVED NOVEMBER 3, 1952

Either of the azines mentioned can be partially converted by thermic or photochemical treatments and by iodine catalysis into two *cis* forms. Interconversions of the respective stereoisomers cause typical shifts in the spectral curves. On the basis of the respective thermo- and photostabilities and of spectroscopic phenomena, including the *cis*-peak effect, and behavior toward iodine, tentative configurations are proposed for the new *cis*-azines.

In the last few years some studies have been carried out in this Laboratory on the *cis–trans* isomerization of aliphatic conjugated carbon–carbon double bond systems such as carotenoid pigments, phytofluene and diphenylpolyenes.[1] In the present paper we wish to report on an extension of this work to symmetrical azines containing the =N—N= group located in the center of the chromophore, according to the general formula, $C_6H_5\cdot(CH{=}CH)_n\cdot CH{=}N{-}N{=}CH\cdot(CH{=}CH)_n\cdot C_6H_5$. The calculated number of stereoisomers is 10 for cinnamalazine (n = 1) and 36 for phenylpentadienalazine (n = 2) which figures may have to be reduced by the probable effect of steric hindrance.[2]

As in corresponding carbon–carbon sets, a pure sample of ordinary (all-*trans*) azine forms a single zone on the chromatographic column, but a partial *trans* → *cis* rearrangement becomes manifest by the appearance of more complex chromatograms. It was advantageous, and in many instances indeed necessary, to inspect such chromatograms in ultra-

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* Presented at the Meeting of the American Chemical Society, March 19, 1953, in Los Angeles, Calif.

† Norwegian Defence Research Establishment, Lilleström, Norway.

[1] L. Zechmeister, *Chem. Revs.*, **34**, 267 (1944); L. Zechmeister and A. Sandoval, THIS JOURNAL, **68**, 197 (1946); F. J. Petracek and L. Zechmeister, *ibid.*, **74**, 184 (1952); A. Sandoval and L. Zechmeister, *ibid.*, **69**, 553 (1947); J. H. Pinckard, B. Wille and L. Zechmeister, *ibid.*, **70**, 1938 (1948).

[2] L. Zechmeister and A. L. LeRosen, *ibid.*, **64**, 2755 (1942).

violet light which showed the presence of dull-red zones, although phenylpentadienalazine zones displayed visible color.

Although the lower homolog, benzalazine ($n = 0$) has given negative results so far, cinnamalazine and phenylpentadienalazine can be converted into *cis* isomers by the same methods as used in the field of the carotenoids; the *cis* forms can be reconverted to the all-*trans* compound which cannot be separated in the mixed-chromatogram test from a corresponding sample obtained by direct synthesis.

Cinnamalazine (*cf.* also Table I).—The following treatments converted this azine partially into a stereoisomer termed *cis*-I: Standing in solution at room temperature, overnight; refluxing in dim light for an hour; and exposure of solutions to a daylight lamp or to sunshine ("insolation"). When all-*trans* crystals were melted or when dilute solutions were subjected to prolonged, intense insolation, marked quantities of another stereoisomer termed *cis*-II also appeared. In contrast to carotenoid pigments, all-*trans*-cinnamalazine suffers only slight steric change when catalyzed with iodine in light, due to the predominance of the *trans* form in this stereoisomeric equilibrium. However, iodine is a powerful stereoisomerizing agent when acting on the *cis*-II compound (see below).

TABLE I

THE COMPOSITION OF STEREOISOMERIC MIXTURES OF CINNAMALAZINES OBTAINED FROM THE ALL-*trans* FORM

Treatment	Relative amounts of the stereoisomers (% of recovered material)[a]			Irreversible losses (% of starting material)
	All-*trans*	*cis*-I	*cis*-II	
Sunshine,[b] 1 hr.	75	23	1–2	Negligible
Sunshine, 3 hr.	72	24	4	Negligible
Sunshine, 6 hr.	68	26	6	Negligible
Sunshine, iodine, 1 hr.	74	23	3	Negligible
Sunshine, iodine, 3 hr.	69	24	6	Negligible
Sunshine, iodine, 6 hr.	67	25	8	Negligible
Daylight lamp, 1 hr.	80	18	1–2	Negligible
Daylight lamp, 6 hr.	80	19	1–2	Negligible
Daylight lamp, iodine, 1 hr.	81	17	1–2	Negligible
Daylight lamp, iodine, 6 hr.	82	17	1–2	Negligible
Refluxing in hexane,[c] 3 hr.	78	20	1–2	Negligible
Refluxing in hexane, 6 hr.	78	19	1–2	Negligible
Melt,[d] 175°, 2 min.	73	23	4	20
Melt, 175°, 10 min.	70	24	6	55
Melt, 190°, 2 min.	75	21	5	40
Melt, 190°, 10 min.	70	21	8	75

[a] The hexane solution of each mixture was resolved by developing with hexane + 5% acetone on zinc carbonate. Upon elution with ethanol and dilution with the same solvent to 100 ml., the extinction values were taken at 350 mμ. [b] All illuminations were carried out in Pyrex volumetric flasks, each containing 2 mg. of substance in 100 ml. of hexane. The insolation took place in intense sunshine at noontime. "Daylight lamp" means exposure from 60 cm. distance to two 3500° Mazda lamps, white and yellowish, length 120 cm., 40 watt. For the chromatographic resolution samples of the solution each containing 0.5 mg. of substance were used. [c] Refluxing of solutions containing 2 mg. of azine in 100 ml. of hexane, was carried out in dim light. [d] Two mg. of azine was sealed *in vacuo* in a thin-walled Pyrex tube (diam., 6 mm.). After immersion in an oil-bath the tube was removed and rapidly cooled with ice-water.

Neither of the two *cis* compounds could be obtained in crystalline form. Although crystals do appear in the absence of solvents when *cis*-I-cinnamalazine is kept in darkness at 4° for several days or is exposed to sunshine for a few minutes, such crystals are those of the newly formed all-*trans* compound. This behavior is identical with that of mono-*cis*-diphenylbutadiene.[1]

The two *cis*-cinnamalazines belong to different spatial types. When a zinc carbonate chromatogram is developed with hexane containing 2 to 5% acetone, *cis*-I appears considerably above but *cis*-II just below the all-*trans* zone. While a hexane solution of *cis*-II remains practically unchanged during 2–3 hours refluxing, corresponding solutions of *cis*-I rearrange to a large extent when kept at room temperature for a few hours. When solutions are illuminated with a daylight lamp or by sunshine, *cis*-I is by far more photosensitive than *cis*-II and rearranges to the all-*trans* form. These relative photosensitivities are, however, inverted in the presence of iodine when the difference in the behavior of the two *cis* forms becomes more striking. The moderate rates of stereoisomerization shown by *cis*-I are not markedly increased by the catalyst and the daylight lamp; however, the otherwise rather photostable *cis*-II is converted into the *trans* form much more rapidly than is *cis*-I. With some oversimplification, *cis*-I-cinnamalazine may be designated as being iodine-catalysis resistant and *cis*-II as sensitive.

When a hexane solution of the all-*trans*-azine is exposed to a daylight lamp, the extinction in the main band slowly decreases while a new maximum grows out at 277 mμ (Fig. 1). In sunshine the latter is higher and appears sooner; thus, within 10 min. a stereoisomeric quasi-equilibrium is reached. Such a "*cis*-peak effect" was first observed and interpreted in the field of the carotenoids.[3]

The isomer mainly responsible for the *cis*-peak effect (Fig. 1) is the photochemically formed *cis*-I-cinnamalazine whose spectral curve shows a very high *cis*-peak. Upon illumination (especially insolation) the *cis*-peak decreases rapidly while the height of the main band increases (Fig. 2). Much weaker is the spectral shift observed upon refluxing all-*trans*-cinnamalazine, indicating a quasi-equilibrium mixture that contains more of the all-*trans* form than that obtained by illumination. Accordingly, when *cis*-I is refluxed, the flattening out of the *cis*-peak, and hence the formation of the all-*trans* azine, is more complete than in photochemical experiments (Fig. 3).

The spectroscopic behavior of *cis*-II-cinnamalazine is shown in Fig. 4. This curve differs conspicuously from those of the *trans*- and *cis*-I forms by the absence of fine structures in both the main band and *cis*-peak regions. In this respect the pair, all-*trans*- and *cis*-II-cinnamalazine, parallels the pair, all-*trans*- and a *cis*-diphenylbutadiene.[1]

cis-II-Cinnamalazine while stable when refluxed

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(3) L. Zechmeister and A. Polgár, THIS JOURNAL, **65**, 1222 (1943); L. Zechmeister, A. L. LeRosen, W. A. Schroeder, A. Polgár and L. Pauling, *ibid.*, **65**, 1940 (1943). In the case of cinnamalazine it is interesting to note that the *cis*-peak appears at about the same wave length (277 mμ) as the main maximum of cinnamaldehyde (279 mμ).

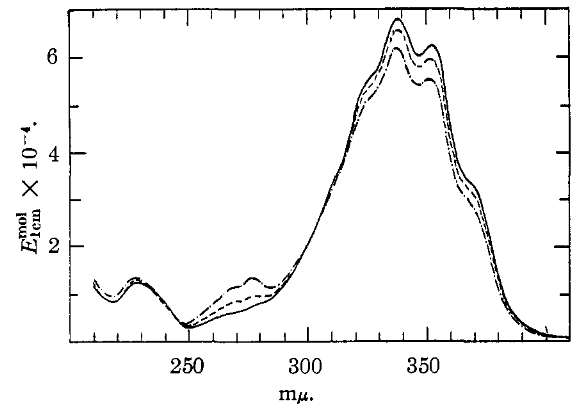

Fig. 1.—Molecular extinction curves of cinnamalazine in hexane: —, fresh solution of the all-*trans* form; – – –, mixture of stereoisomers upon exposure to daylight lamp for 150 min. (no equilibrium was reached at this point; the same curve was obtained in the presence of iodine; approximately the same curve was also obtained upon refluxing in dim light for 6 hr.); and –·–·–, mixture of stereoisomers after 10 min. insolation (constant after 30 min.).

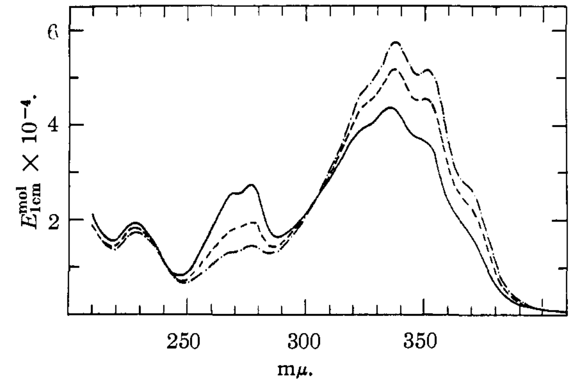

Fig. 2.—Molecular extinction curves of *cis*-I-cinnamalazine in hexane: —, fresh solution of *cis*-I; – – –, mixture of stereoisomers after exposure to daylight lamp for 150 min. (no equilibrium was reached at this point; the same curve was obtained in the presence of iodine); and –·–·–, mixture of stereoisomers after 10 min. insolation of *cis*-I (constant after 15 min.).

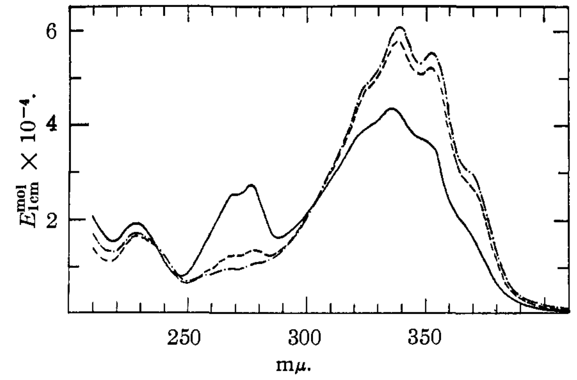

Fig. 3.—Molecular extinction curves of *cis*-I-cinnamalazine in hexane: —, fresh solution of *cis*-I; – – –, mixture of stereoisomers after refluxing in dim light for 60 min.; and –·–·–, after 120 min. (practically constant after 180 min.).

or exposed to a daylight lamp, stereoisomerizes in the presence of iodine (Fig. 4). During a brief illumination the *cis* peak flattens out and the main maximum increases, demonstrating the almost exclusive formation of the all-*trans* compound. However, in the course of prolonged illumination with the daylight lamp or subsequent exposure to sunshine a *cis*-peak develops anew and the main band is lowered because marked amounts of *cis*-I also appear, originating from a secondary (partial) rearrangement of the all-*trans* isomer formed during the first stage of the experiment. Likewise, in the presence of iodine, insolation of a fresh *cis*-II solution yields the corresponding curve directly within a few minutes (Fig. 4, dashed line). In the absence of the catalyst this rearrangement proceeds more slowly and is accompanied by substantial destruction as shown by the depressed height of the resulting extinction curve.

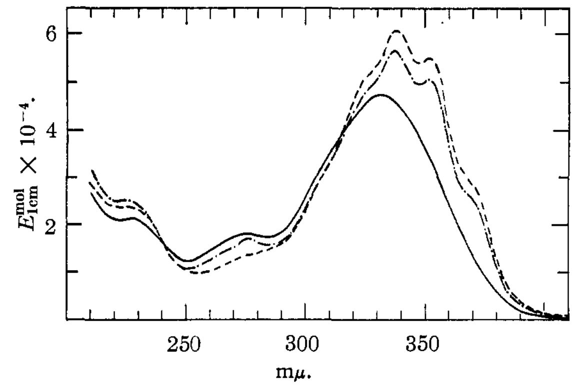

Fig. 4.—Molecular extinction curves of *cis*-II-cinnamalazine in hexane: —, fresh solution of *cis*-II (this curve remained unchanged when illuminated with a daylight lamp for 150 min.); –·–·–, mixture of stereoisomers after exposure to daylight lamp in the presence of iodine for 5 min. (a prolonged exposure for 150 min. caused only a slight decrease in the main band and a slight increase in the *cis*-peak region); and –·–•–, mixture of stereoisomers after insolation for 5 min. either of the solutions illuminated with daylight lamp or of a fresh solution, in the presence of iodine. (In the absence of the catalyst more than 1 hr. of insolation was required for obtaining a curve of approximately the same shape; then a general decrease in the extinction indicated substantial destruction.)

All these spectroscopic phenomena were confirmed by chromatographic resolutions.

On the basis of the presented data we propose for the two *cis*-cinnamalazines the configurations shown in Fig. 5. To *cis*-I we assign a *cis* configuration at a C=N bond, *i.e.*, in the nearest possible position to the center of the conjugated system, in accordance with the high *cis*-peak.[3] Furthermore, the behavior of *cis*-I in the iodine catalysis test, quite different from that of *cis*-C=C bonds in carotene, phytofluene or diphenylbutadiene, is indicative for a special steric feature. Finally, the small wave length difference (2–3 mμ in hexane) between the main maxima of all-*trans*- and *cis*-I-cinnamalazine points to a mono-*cis* and excludes a tri-*cis* configuration. On the other hand, *cis*-I cannot be a di-*cis* compound, since, according to the models, two of the four possible di-*cis* isomers can possess only very low *cis*-peaks and the two others none at all.

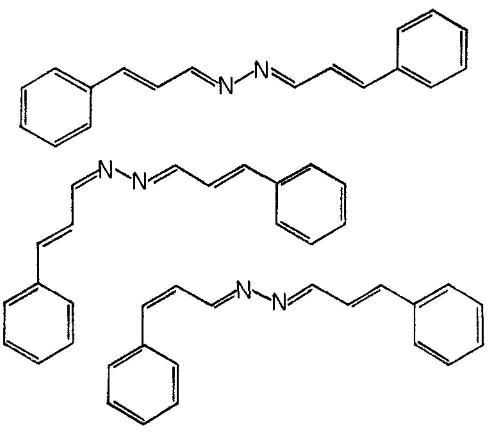

Fig. 5.—Skeleton models of three spatial forms of cinnamalazine; top, all-*trans* form; middle, assumed configuration of *cis*-I; and bottom, of *cis*-II.

The configuration proposed for *cis*-II (Fig. 5, bottom) represents the other one of the two possible mono-*cis* forms, in accordance with the moderately high *cis*-peak and the "normal" behavior in iodine catalysis. As Fig. 4 shows, the outstanding features of the *cis*-II curve are, the lack of fine structure and the considerable wave length difference (7 mμ) at $\lambda_{max.}$ from the all-*trans* compound. A di-*cis* configuration is not possible because of the considerable *cis*-peak. A tri-*cis* configuration is not suggested for the following reasons. As mentioned the illumination of *cis*-II yields first the all-*trans* and later (in part) the *cis*-I form. It would not be understandable why a tri-*cis* isomer should not yield *cis*-I directly, *i.e.*, not *via* the all-*trans* form. Instead of assuming a tri-*cis* configuration, we explain the lack of fine structure (which parallels that in *cis*-diphenylbutadienes) and the location of $\lambda_{max.}$ by the circumstance that a H-atom of the benzene ring in opposition to the side chain is sterically hindered by one of the H-atoms of the latter in case of *cis* configuration; thus an approximately planar configuration becomes impossible.[2]

Phenylpentadienalazine (*cf.* also Table II).—When this azine was submitted to the treatments mentioned above, it rearranged reversibly and assumed (in part) in each instance the same two preferred *cis* configurations, termed *cis*-I- and *cis*-II-phenylpentadienalazines. The weight ratio of these oily stereoisomers is subject to broad variations, depending on the nature of the treatment. The composition of some of the stereoisomeric mixtures obtained is listed in Table II which shows that iodine catalysis when applied to the ordinary (all-*trans*) compound under a daylight lamp, converts a much smaller fraction of the substance into *cis* isomers than in corresponding experiments carried out with carotenoids. Under the conditions just mentioned the formation of the *cis*-II configuration is markedly favored; thus, after 3 hours treatment the ratio, *cis*-I:*cis*-II, was 9:1 in the absence but 3:1 in the presence of the catalyst.

When developed on an activated zinc carbonate column with hexane containing 5 to 8% acetone, the *cis*-I zone appears much above the all-*trans* form. This sequence is, however, inverted on weak zinc carbonate where *cis*-I is located just below the all-*trans* zone. On the same adsorbent of medium activity no separation takes place. *cis*-II-Phenylpentadienalazine separates from the all-*trans* compound easily on any brand of zinc carbonate or on alumina, when adsorbed from hexane and developed with benzene, and occupies a lower position than the all-*trans* zone.

TABLE II

THE COMPOSITION OF STEREOISOMERIC MIXTURES OF PHENYLPENTADIENALAZINES OBTAINED FROM THE ALL-*trans* FORM

Treatment	Relative amounts of the stereoisomers (% of recovered material)[a] All-*trans*	*cis*-I	*cis*-II	Irreversible loss (% of starting material)
Sunshine,[b] 1 hr.	67	24	9	8
Sunshine, 6 hr.	68	24	8	13
Sunshine, iodine, 1 hr.	70	21	9	9
Sunshine, iodine, 6 hr.	73	20	7	13
Daylight lamp,[b] 1 hr.	85	13	2	8
Daylight lamp, 3 hr.	80	18	2	8
Daylight lamp, 6 hr.	75	23	2	8
Daylight lamp, iodine, 1 hr.	83	12	5	7
Daylight lamp, iodine, 3 hr.	77	17	6	9
Daylight lamp, iodine, 6 hr.	75	19	6	11
Refluxing in hexane,[c] 1 hr.	84	14	2	10
Refluxing in hexane, 3 hr.	78	20	2	18
Refluxing in hexane, 6 hr.	73	24	3	20
Naphthalene melt,[d] 160°, 2 min.	76	21	3	30
Naphthalene melt, 160°, 10 min.	74	22	4	40
Naphthalene melt, 180°, 10 min.	73	19	8	65

[a] The hexane solution of each stereoisomeric mixture was resolved by developing with hexane + 8% acetone on zinc carbonate. Upon elution with ethanol and dilution with the same solvent to 100 ml., the extinction values were taken at 390 mμ. [b] All illuminations were carried out in Pyrex volumetric flasks containing 1 mg. substance in 100 ml. of hexane. The insolation took place in intense sunshine at noon time. "Daylight lamp" means exposure from 60 cm. distance, to two 3500° Mazda lamps, white and yellowish, length 120 cm., 40 watt. For the chromatographic resolution samples of the solution each containing 0.25 mg. substance were used. [c] The refluxing of solutions containing 1 mg. of azine in 100 ml. of hexane was carried out in dim light. [d] 0.5 mg. of azine was mixed with 50 mg. of naphthalene, in a thin-walled Pyrex tube (diam., 6 mm.) and sealed *in vacuo*. After immersion in an oil-bath the tube containing the melt was removed rapidly and cooled with ice-water.

Like *cis*-I-cinnamalazine, *cis*-I-phenylpentadienalazine rearranges easily in the absence of solvents and yields all-*trans* crystals. This process was found to be practically complete within 1–2 weeks in the cold room and in darkness but took place almost instantaneously in bright sunshine. No crystals appeared when *cis*-II was kept in darkness; and in sunshine several minutes were required for crystallization.

Under the influence of sunshine a solution of either *cis* isomer or of the all-*trans* form rearranged rapidly and yielded within 10 min. the same stereoisomeric mixture in which the all-*trans* form was preponderant. No significant destruction took place. More sharply dependent on the configuration is the spatial rearrangement induced by the daylight lamp. Thus, under the conditions given in the footnotes to Table II such exposure of either the all-*trans* or the *cis*-I form caused marked stereoisomerization while *cis*-II remained almost unaltered during 3 hours. However, under the influence of iodine most of *cis*-II was converted to the *trans* form within 5 min., while the two other isomers were much less affected. This is explained by the composition of the resulting mixture (Table II). When a hexane solution is refluxed in dim light for 1–2 hours, *cis*-I-phenylpentadienalazine undergoes extensive rearrangement and also some irreversible destruction which becomes the main process in the case of *cis*-II.

The extinction curve of all-*trans*-phenylpentadienalazine (Fig. 6) is remarkably similar to that of octatrienalazine and one of its end-substituted derivatives.[4] Evidently, the addition of a phenyl group to similar conjugated systems exerts no stronger influence on the spectrum than the lengthening of the system by an aliphatic conjugated double bond.

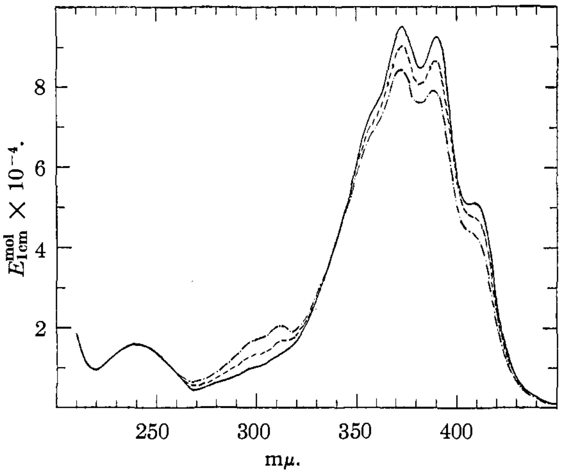

Fig. 6.—Molecular extinction curves of phenylpentadienalazine in hexane: —, fresh solution of the all-*trans* form; - - -, mixture of stereoisomers upon exposure to daylight lamp, after 10 min.; and —·—·—, after 150 min. The same values were also observed in the presence of iodine. A curve very similar to the dashed one was also obtained by 10 min. insolation (no further change was noticed after 30 min.).

Upon illumination with a daylight lamp in the absence or presence of iodine the main spectral maxima of all-*trans*-phenylpentadienalazine decrease and at the same time a *cis*-peak[3] grows out (maximum at 311 mμ in hexane, Fig. 6). A similar change is observed in sunshine which does not involve any marked destruction, while refluxing a solution results in a less pronounced spectral effect which is accompanied by a considerable irreversible cleavage (*cf.* Fig. 7 and Table II).

The extinction maxima of the two *cis* forms are considerably lower than those of the all-*trans* form, and they are located at 2–3 mμ shorter wave lengths (in hexane). The curves of *cis*-I and *cis*-II are sharply differentiated from the *trans* isomer by their *cis* peaks. The respective extinguished areas in the *cis*-peak region are not very different for the two *cis* forms. Under the influence of a daylight lamp the *cis*-peak of *cis*-I decreased, the main band increased, and this shift was not influenced by iodine (Fig. 8). In contrast, such an exposure had almost no effect on *cis*-II within 2 hours; however, a trace of iodine induced rapid stereoisomerization and gave within 5 min. a curve that included a low *cis*-peak. As in the case of *cis*-II-cinnamalazine, this decrease in the *cis*-peak was followed, upon prolonged illumination, by a distinct increase as a result of a secondary process, *viz.*, all-*trans* → *cis*-I (Fig. 9).

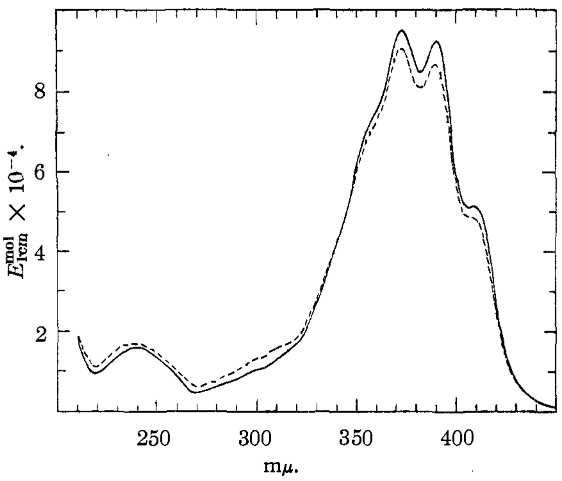

Fig. 7.—Molecular extinction curves of phenylpentadienalazine in hexane: —, fresh solution of the all-*trans* form; – – –, mixture of stereoisomers after refluxing in dim light for 180 min. (after 30 min. and 60 min. refluxing intermediate values were obtained).

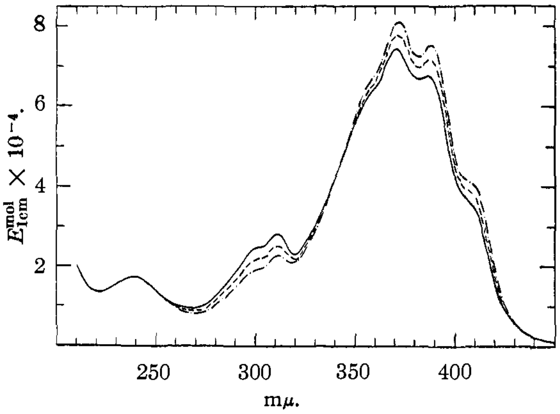

Fig. 8.—Molecular extinction curve of *cis*-I-phenylpentadienalazine in hexane: —, fresh solution; - - -, after exposure to daylight lamp for 10 min.; and —·—·—, after 30 min. (The values remained practically constant after 150 min.) Identical curves were also obtained in the presence of iodine. A curve very similar to —·—·— was obtained upon 10 min. insolation and was practically constant after 30 min.

In brief insolation experiments the two *cis* forms behaved similarly and reached within 10 min. practically identical spectral curves of the equilibrium mixture (*cf.* Fig. 10).

We believe that *cis*-I-phenylpentadienalazine is an analog of *cis*-I-cinnamalazine and represents that mono-*cis* form in which a C=N bond has assumed *cis* configuration (Fig. 11, middle). This is in

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[4] E. R. Blout and M. Fields, THIS JOURNAL, **70**, 18 (1948); H. H. Inhoffen and G. Leibner, *Ann.*, **575**, 105 (1952).

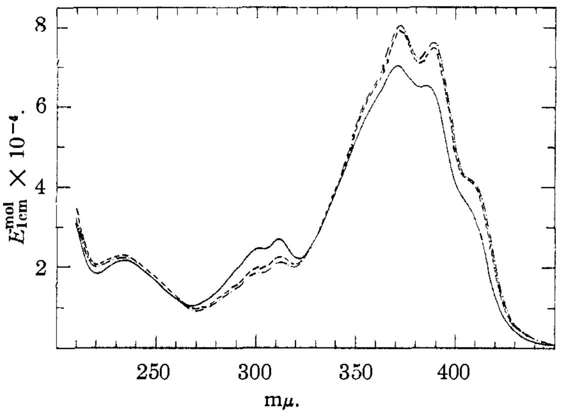

Fig. 9.—Molecular extinction curves of *cis*-II-phenylpentadienalazine in hexane: —, fresh solution (this curve remained practically constant during a 30 min. illumination with the daylight lamp, in the absence of iodine; only a slight change was observed upon 150 min. illumination); - - -, after illumination, in the presence of iodine, for 5 min.; and -.-.-, for 10 min. After 150 min. the extinction in the $\lambda_{max.}$ region decreased by 5% while in the *cis*-peak region a slight increase (up to the 5-min. curve) was observed.

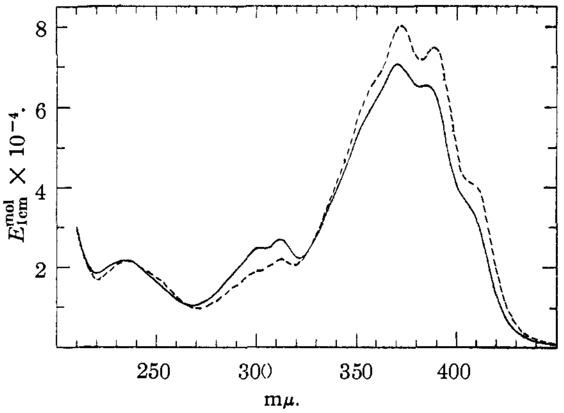

Fig. 10.—Molecular extinction curves of *cis*-II-phenylpentadienalazine in hexane: —, fresh solution; and - - -, after insolation for 10 min. (practically constant after 30 min.).

accordance with the observed wave length position of the main maxima, the high *cis*-peak and the "anormal" behavior in iodine catalysis.

cis-II-Phenylpentadienalazine must possess a C=C mono-*cis* configuration. The considerable height of its *cis*-peak and the degree of fine structure in the main band (similar to that of the corresponding all-*trans* band but very different from the *cis*-II-cinnamalazine band) do not indicate a peripheral location in the conjugated system for this *cis* double bond. Hence, the configuration shown in Fig. 11 (bottom) is proposed for *cis*-II-phenylpentadienalazine.

Acknowledgment.—We are indebted to Dr. Chr. Burckhardt for the preparation of the two azine samples used in the present study. Some improvements in the synthesis of polyene azines made by Dr. Burckhardt will be reported later.

Experimental

The best adsorbents used for the resolution of stereoisomeric cinnamalazine mixtures are, zinc carbonate (Merck

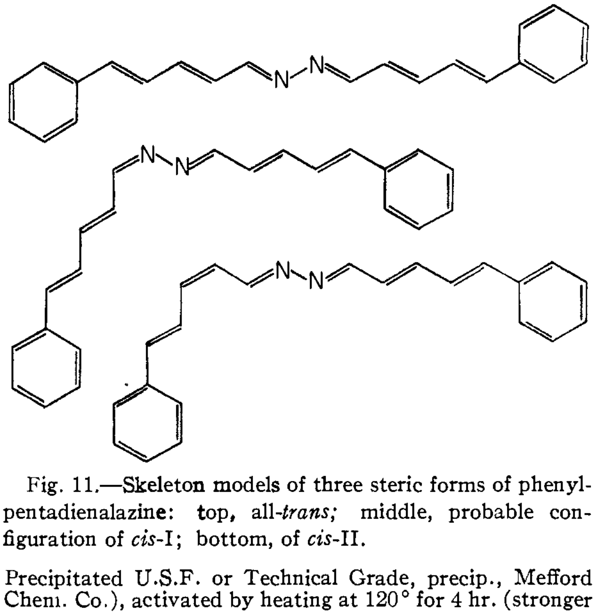

Fig. 11.—Skeleton models of three steric forms of phenylpentadienalazine: top, all-*trans;* middle, probable configuration of *cis*-I; bottom, of *cis*-II.

Precipitated U.S.F. or Technical Grade, precip., Mefford Chem. Co.), activated by heating at 120° for 4 hr. (stronger heating is undesirable because of the dark appearance of such materials in ultraviolet light). For phenylpentadienalazines the Technical Grade was used. Activated carbonate samples were kept in closed containers. For the final purification of some *cis* isomers aluminum oxide (Merck, Reagent Grade, ignited) was applied. Mostly hexane solutions were poured onto the column, whereupon the substance adsorbed at the top was developed with hexane containing acetone (2–5% for cinnamalazines and 8% for phenylpentadienalazines). In both instances lengthy adsorption experiments gave rise to a new bottom zone, which, although similar to the azine zones, showed a different spectrum. Very probably such zones contain, respectively, cinnamalacetone $C_6H_5\cdot CH{=}CH{-}CH{=}CH\cdot CO\cdot CH_3$ or phenylpentadienalacetone, $C_6H_5\cdot CH{=}CH{-}CH{=}CH{-}CH{=}CH\cdot CO\cdot CH_3$; the maximum of the latter (340 mμ in hexane) corresponds to that (341 mμ) of phenylheptatrienal. Consequently, it is advantageous to carry out the resolutions as rapidly as possible. Furthermore, when small amounts of a *cis* form are to be separated from much larger quantities of the corresponding all-*trans* isomer, it is recommended to concentrate the solution *in vacuo* until most of the *trans*-azine has crystallized and chromatograph the filtrate rapidly, on a smaller scale. All chromatograms were inspected using a Photoflood bulb No. 1 and a molded Corning light filter No. 5840.

Illumination with a daylight lamp means exposure, from 60 cm. distance, to the light emitted by two parallel 3500° Mazda lamps, 40 watt, white and yellowish, length 120 cm. In stereoisomerizations requiring strong light sources, sunshine was found to be far superior to the beam of a 1000 watt projection lamp (with or without light filters). When insolating all-*trans*-azines, the influence of the temperature was negligible between 10 and 60°. Such exposures were carried out in Pyrex volumetric flasks since quartz or amber glass did not improve the result. Spectral observations were made in the Beckman spectrophotometer.

Cinnamalazine.—**All-*trans*-cinnamalazine**[5] was prepared from cinnamaldehyde and hydrazine hydrate; thin, yellow needles, m.p. 168–169°, cor.; extinction maxima: $E^{mol.}_{1\,cm.}$ (hexane) 6.24×10^4 at 353 mμ, 6.80×10^4 at *338* mμ.

***cis*-I-Cinnamalazine** is best obtained by exposure to sunshine. A solution of 500 mg. of the *trans* form in 2 liters of hexane, divided into twenty-five portions, was insolated in 100-ml. volumetric flasks for 4 hr., then adsorbed on three activated zinc carbonate columns (Merck, 30 × 8 cm.) and developed with hexane +5% acetone (the figures on the left designate thickness of zones in mm.; observations in ultraviolet light):

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[5] L. N. Ferguson and G. E. K. Branch, THIS JOURNAL, **66**, 1467 (1944); for the spectrum in polar solvents, *cf.* also E. R. Blout and R. M. Gofstein, *ibid.*, **67**, 13 (1945); M. P. Grammaticakis, *Bull. soc. chim. France*, 973 (1948); D. Rădulescu and V. Alexa, *Ber.*, **64**, 2230 (1931).

6	yellow (in daylight), irreversible
20	empty interzone
15	dark dull red: *cis*-I
40	interzone, traces of contaminant (maxima, 371 and 356 mμ)
60	dark dull red: unchanged all-*trans* form
20	empty interzone
13	dark dull red (does not give the HCl color reaction), spectrum indicative for cinnamalacetone
42	empty interzone
6	a dark and a light fluorescent zone

The *cis*-I zone was cut out, eluted with alcohol, transferred with water into hexane, washed, dried with sodium sulfate and rechromatographed twice. A bright-grayish fluorescent impurity which still adsorbed at the top of the *cis*-I zone was eliminated by developing on alumina (21 × 3.8 cm.) with benzene which left the contaminant near the top. By means of a rechromatographing on zinc carbonate some all-*trans* compound was removed that had been formed by stereoisomerization during the operations described; yield, a few mg.; maxima of *cis*-I-cinnamalazine: $E_{1\,\mathrm{cm.}}^{\mathrm{mol.}}$ (hexane) 4.37×10^4 at *336* mμ, 2.73×10^4 at 277 mμ (*cis*-peak).

Two by-products should be discussed briefly at this point. (a) Cinnamalacetone appears in larger quantities when the elution is carried out with acetone, instead of ethanol (any replacement of acetone in the developing mixture results in less satisfactory separations). (b) Another contaminant which in repeated elutions would decrease the *cis*-I yields, is acetone-azine $(CH_3)_2{\cdot}C{=}N{-}N{=}C(CH_3)_2$, whose spectral curve (max., 227 mμ in hexane) is very similar to those of higher azines. Since this compound is volatile, it does not contaminate *cis*-I samples isolated by evaporation. Its presence can be detected on displacing the hexane–acetone developer by washing the column with optical hexane, whereupon any cinnamalazine zone when eluted with acetone and transferred into optical hexane shows, besides its own spectral curve, a second curve including a maximum at 227 mμ.

***cis*-II-Cinnamalazine** was prepared by fusion of all-*trans* crystals. Five thin-walled Pyrex tubes (diam., 6 mm.) containing 100 mg. of substance each, were sealed *in vacuo*, immersed in a bath at 175° for 10 min., then rapidly cooled in ice-water and crushed in a mortar. A hexane solution prepared at room temperature was poured onto a zinc carbonate column (12 × 13 cm.) built up on a fritted glass buchner funnel in order to reduce the time of contact with the adsorbent in the presence of acetone; developer, hexane +5% acetone:

12	partly distinct colored zones (in daylight): contaminants
6	empty interzone
4	bright yellowish fluorescence: irreversible
7	dark dull red: *cis*-I
10	empty interzone
30	dark dull red: unchanged all-*trans* form
3	empty interzone
15	moderately dark red: *cis*-II
7	bright fluorescent (max. around 255 mμ)
15	empty interzone
3	intense blue fluorescence: unidentified

Each of the two *cis* zones was cut out, eluted with ethanol and rechromatographed as described (21 × 3.8 cm.). In the *cis*-II chromatogram the latter formed the main zone, and the rest of the chromatogram contained only some all-*trans* isomer above, and a bright fluorescent substance below the *cis*-II zone. While it was easy to cut out and eliminate the former, the latter contaminant required rechromatographing, *viz.*, developing on alumina (18 × 1.9 cm.) with hexane (a slow process). In that system the original sequence was inverted and the brightly fluorescent compound remained near the top. In contrast to *cis*-I, the *cis*-II form did not rearrange to the all-*trans* compound during the purification described; yield, a few mg.; maxima of *cis*-II-cinnamalazine: $E_{1\,\mathrm{cm.}}^{\mathrm{mol.}}$ (hexane) 4.75×10^4 at *331* mμ, 1.80×10^4 at 276 mμ (*cis*-peak).

Phenylpentadienalazine.—All-*trans* - phenylpentadienalazine was prepared from phenylpentadienal and hydrazine hydrate and recrystallized from ethyl acetate, m.p. 211°, cor. In spite of its low solubility in hexane (less than 20 mg./l.), this solvent had to be used for an initial adsorption on columns and for spectral readings; extinction maxima in hexane: $E_{1\,\mathrm{cm.}}^{\mathrm{mol.}}$ (hexane) 9.25×10^4 at *390* mμ, 9.50×10^4 at *373* mμ.

Anal. Calcd. for $C_{22}H_{20}N_2$: C, 84.56; H, 6.46; N, 8.98. Found: C, 84.75; H, 6.58; N, 8.97.

Isolation of Crude *cis*-I- and *cis*-II-Phenylpentadienalazine Samples.—For this purpose (a) insolation of solutions or (b) melting crystals mixed with naphthalene can be used. Method (a) has the advantage of little destruction but it requires the handling of large volumes; (b) can be carried out more rapidly, especially when the resolidified melt is treated with a volume of hexane so small that the easily soluble *cis* isomers are removed while most of the unchanged all-*trans* form is left behind. Hence, further operations can be carried out on a small scale. The extent of irreversible changes taking place in fusion experiments amounts to 30–65% of the starting material (Table II).

(a) A solution of 100 mg. of all-*trans*-phenylpentadienalazine in 5 liters of hexane was divided into ten portions, exposed in volumetric flasks to intense sunshine for 3 hr., then evaporated *in vacuo* to 1 liter, in a bath at 30–40°, while nitrogen bubbled through the capillary. Upon cooling, a large quantity of all-*trans* crystals appeared within a few hours; they were filtered off and washed with a little cold solvent. The filtrate was poured onto a zinc carbonate column (12 × 14 cm.) built up on a fritted glass buchner funnel, and developed with hexane + 8% acetone. Within about 15 min. the following chromatogram appeared:

20	empty top zone
10	yellow; dark red in ultraviolet light: *cis*-I
20	empty interzone
20	yellow; dark red in ultraviolet light; unchanged all-*trans*
35	empty interzone
15	yellow; dark red in ultraviolet light: *cis*-II

Filtrate: yellow (before it passed through, a faint yellow zone with a non-typical spectrum appeared; it did not belong to the set).

The column was removed from the inverted funnel by blowing into the stem and tapping on the glass walls. The two *cis* zones were cut out, eluted with ethanol, each transferred with water into hexane, washed, dried and kept in a dark and cold room.

(b) A mixture of 100 mg. of all-*trans*-phenylpentadienalazine and 3 g. of naphthalene[6] was divided into five portions and each was filled into a thin-walled Pyrex tube (diam. 6 mm.), then sealed *in vacuo*. The tubes were immersed in an oil-bath at 180° for 10 min., then cooled rapidly in ice-water, crushed and extracted with 50–100 ml. of hexane at 20°. The insoluble residue, which was filtered off, consisted mainly of unchanged all-*trans* compound. The filtrate gave about the same chromatogram as described under (a) with the sole difference that the all-*trans* zone also contained a bright yellowish-gray fluorescent destruction product.

Purification of *cis*-I-Phenylpentadienalazine.—Marked amounts of the all-*trans* form were eliminated from the crude solution by developing with hexane +8% acetone on a 12 × 4.8 cm. zinc carbonate column, whereupon acetone derivatives were washed into the filtrate with benzene, followed by optical hexane. The *cis*-I zone was cut out, eluted with ethanol, transferred into optical hexane, washed, dried and evaporated completely *in vacuo*. The solution of the yellow oily residue (a few mg.) served for the optical investigation, $E_{1\,\mathrm{cm.}}^{\mathrm{mol.}}$ (max. hexane) 6.75×10^4 at 387 mμ, 7.45×10^4 at *371* mμ, 2.80×10^4 at 311 mμ (*cis*-peak).

Purification of *cis*-II-Phenylpentadienalazine.—It was easy to free this isomer from some all-*trans* compound by rechromatographing it once or twice on zinc carbonate (12 × 4.8 cm.; hexane +5% acetone). However, as indicated by the extinction curve such treatment did not eliminate a foreign contaminant. This was achieved by developing with hexane +30% benzene on alumina (21 × 3.8 cm.) showing a grayish fluorescent zone which was retained near the top while the *cis*-II zone migrated downwards. When

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(6) Because of the high melting point (211°) most of the material is destroyed in similar fusion experiments in the absence of naphthalene.

the two zones had become separated by a 5–6 cm. clear interzone, the column was extruded and the oily *cis*-II compound (a few mg.) isolated as described for *cis*-I; $E^{\text{mol.}}_{1\text{ cm.}}$ (max. hexane) 6.53×10^4 at 385 mμ, 7.05×10^4 at 370 mμ, 2.68×10^4 at 311–312 mμ (*cis*-peak).

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[CONTRIBUTION FROM HAVEMEYER LABORATORY, COLUMBIA UNIVERSITY]

Two-Step Synthesis of Azulene

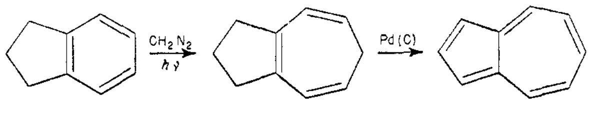
BY W. VON E. DOERING,[1] J. RICHARD MAYER[1] AND C. H. DEPUY[1]

RECEIVED NOVEMBER 8, 1952

Azulene is prepared from indane by irradiating with diazomethane and dehydrogenating the resulting trimethylenetropilidene.

Among the various syntheses of azulene,[2] the most satisfactory is that of Plattner and St. Pfau[2a] as improved by Anderson and Nelson[2c] in which four steps and an over-all yield 5.8% of theory are involved. In this paper a shorter, more convenient synthesis is reported.

Application of the method of preparing tropilidenes from benzenes and diazomethane by irradiation[3] to indane yields a mixture of hydrocarbons from which crude trimethylenetropilidenes are separated by distillation. Catalytic dehydrogenation affords azulene in 18.3% of the theoretical yield or 6.7% over-all based on the amount of indane consumed. Purified with very small loss by solution in ice-cold 7.5 *M* sulfuric acid, precipitation and sublimation, the azulene had the same m.p.[2a] and absorption spectra[4,2a,5] as reported in the literature.



Experimental

Trimethylenetropilidene.—To a stirred mixture of 322 g. of indane, b.p. 72–74° at 20 mm., and 60 ml. of 50% aqueous potassium hydroxide in a 1-l. erlenmeyer flask surrounded by an ice-bath, 21 g. of nitrosomethylurea was added in several portions over the course of 1 hr. After being stirred for another hour, the yellow organic layer was separated, dried over potassium hydroxide, and transferred to a Pyrex, 500-ml., water-jacketed, round-bottom flask. The solution was then irradiated with two General Electric Reflector Sunlamps on opposite sides of the flask for 24 hr. by which time the initially rapid evolution of nitrogen had ceased and the solution was pale yellow. Distillation through a one-foot Widmer column yielded a higher boiling residue which was saved and 267 g. of indane, b.p. 72–75° at 20 mm., which was retreated with diazomethane. The second and third irradiations were performed using 267 g. and 235 g. of indane, respectively, and the same quantity of diazomethane. In each case, the higher boiling residue was separated from the recovered indane which was used for the subsequent irradiation. From the third irradiation there was recovered 189 g. of indane. The combined higher boiling residues were fractionated under nitrogen through a one-foot, helix-packed column at 20 mm. yielding 98 g. of indane, b.p. 70–75°, and 14.2 g. of a colorless liquid, b.p. 80–81°, $n^{25}\text{D}$ 1.5174.

Azulene.—The dehydrogenation apparatus was a Pyrex tube 25 cm. long and 18 mm. wide, fitted at the top with an addition funnel and at the bottom with a small side-arm flask. The tube was charged with *ca.* 5 g. of a catalyst consisting of 5% palladium-on-coconut charcoal prepared by procedure of Linstead and Thomas.[6] The column was heated electrically to 340°. The dehydrogenation was effected by adding trimethylenetropilidene dropwise at the top of the column at 20 mm. pressure. The addition was completed in about one hour. Slower addition did not affect the yield. The cooled column and the receiver were washed with pentane to dissolve all azulene. Analysis of this solution spectroscopically indicated the presence of 2.52 g. of azulene. The pentane solution was extracted with 100 ml. of ice-cold 7.5 *M* sulfuric acid and then with a 50-ml. portion of acid. The red acid solutions were extracted once with pentane and poured slowly into 200 ml. of ice-cold water in a separatory funnel. The pentane extract of the liberated azulene was dried over anhydrous potassium carbonate, concentrated in a sublimator tube by heating gently over a steam-bath, the last vapors of pentane being "poured" off. Sublimation at 0.5 mm. and about 40° yielded 2.27 g. of purple crystals, m.p. 98–99°; reported[2a] m.p. 98.5–99°. The absorption spectra of this sample in the ultraviolet, visible and infrared were identical with those reported.[4,2a,5]

Based on a total consumption of 35 g. of indane in the three irradiations, the yield of azulene (2.52 g.) was 6.7%.

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(1) Sterling Chemistry Laboratory, Yale University, New Haven, Connecticut.

(2) (a) Pl. A. Plattner and A. St. Pfau, *Helv. Chim. Acta*, **20**, 224 (1937); (b) W. Reppe, O. Schlichting and H. Meister, *Ann.*, **560**, 93 (1948); (c) A. G. Anderson and J. A. Nelson, THIS JOURNAL, **73**, 232 (1951); (d) Hs. H. Günthard, R. Süess, L. Marti, A. Fürst and Pl. A. Plattner, *Helv. Chim. Acta*, **34**, 959 (1951); (e) E. A. Braude and W. F. Forbes, *Nature*, **168**, 874 (1951).

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