[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Condensation Products of Cyclic 1,2-Diketones with Benzylidene-bis-piperidine and their Spectral Properties

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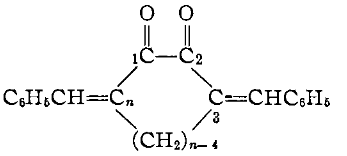
A study has been made of the products formed in the condensation of 1,2-cycloalkanediones (7-, 9-, 10-, 11-, 12-, 13- and 14-membered rings) with benzylidene-bis-piperidine, and the reaction has been utilized to obtain the corresponding dibenzylidene-1,2-cycloalkanediones Ia,c-h. The diaminodiketones VIIIc-h also isolated serve as precursors for the dibenzylidenediketones. Tricyclic dimeric condensation products Xa,d,g,h of the monocyclic 1,2-diketones were found as minor constituents. Infrared and ultraviolet spectral correlations have been made for series of dibenzylidene-1,2-cycloalkanediones, 3,10-diarylidene-1,2-cyclodecanediones and 3-arylidene-1,2-cyclodecanediones.

A partial series of dibenzylidene cyclic 1,2-diketones had been made previously in this Laboratory and subjected to ultraviolet spectral study.[2] It was desired to extend this series, to resolve certain peculiarities in the spectra of the 3,n-dibenzylidene-1,2-cycloalkanediones (I, n = ring size), and to investigate more completely the products formed in the piperidine-induced condensation of aromatic aldehydes with 1,2-cycloalkanediones (II).



I

	n		n
a	7	e	11
b	8	f	12
c	9	g	13
d	10	h	14

Piperidine or piperidinium acetate has been found to be effective in promoting aromatic aldehyde condensations with 1,2-diketones.[3-9] Not only do stronger bases encourage the self-condensation of cyclic 1,2-diketones, and other side reactions, but the dibenzylidene products are known to be unstable in the presence of strong alkalies. In syntheses directed at extending the series of 3,n-dibenzylidene-1,2-cycloalkanediones at least through the 14-membered ring compound (Ih), we found an improvement in the preformation of benzylidene-bis-piperidine (III).[10] The use of this intermediate also enabled us to resolve any uncertainty as to the purity and identity of the dibenzylidene products described previously[2] and to establish the structure of the nitrogen-containing compounds isolated from 1,2-cyclododecanedione and 1,2-cyclotridecanedione.[11,12] An efficient procedure in carrying out direct condensations of benzylidene-bis-piperidine with cyclic 1,2-diketones was to mix benzaldehyde[13] and piperidine in 1:2 molar ratio in cyclohexane and to remove the water formed with a Dean–Stark trap. Cyclohexane was removed *in vacuo* and replaced with the reaction solvent, usually absolute ethanol, followed by the cyclic 1,2-diketone.

The combination of benzylidene-bis-piperidine with the 1,2-cycloalkanediones II,a,c-h appears to be slow at room temperature, but raising the temperature led to unwanted side reactions. The mechanism of the reaction has not been examined explicitly in our study; nevertheless, logical reaction paths can be envisaged, dependent upon the formation of the enolate IV of the 1,2-cycloalkanedione in the basic medium (*e.g.*, by III) and combination of the enolate with the conjugate acid V[14] of benzylidene-bis-piperidine, more probably in the dissociated (or partly dissociated) form VI. The monosubstituted product VII thus formed would lead to the disubstituted product VIII in a repetition of the process. The diaminodiketone VIII could therefore be an intermediate[10] on the route to the dibenzylidenediketones I; however, it could also be formed by the addition of piperidine[10,15] (present in excess) to the dibenzylidenediketone resulting from some other path.

According to the reaction scheme proposed above, it might be expected that diaminodiketones of type VIII could be isolated from the combination of benzylidene-bis-piperidine with certain of the 1,2-diketones. Such compounds were actually obtained previously[11,12] from the 12- and 13-membered ring diketones II (n = 12, 13), but they were not identified. In a careful investigation of the products formed by combination of II (series) and III under comparable conditions, it was found that the dibenzylidenediketones I were obtained exclusively from 1,2-cycloheptanedione (IIa) and preferentially from the 9-, 10- and 11-membered ring diketones IIc-e, together with small quantities of the diaminodiketones VIIc-e. The diaminodiketones VIIIf-h were the major products isolated from the 12-, 13- and 14-membered ring diketones IIf-h. The stability of these intermediate diaminodiketones can be attributed in part to effects arising from variation in ring size, the larger rings tending to halt the reaction at the diaminodiketone stage. However, the main reason is more likely due to a less subtle effect, namely, the very low

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[1] National Science Foundation Fellow, 1954–1957.

[2] N. J. Leonard and G. C. Robinson, THIS JOURNAL, **75**, 2714 (1953); see also **75**, 2143 (1953).

[3] A Kötz and E. Lemien, *J. prakt. Chem.*, **90**, 382 (1914).

[4] P. Karrer and Ch. Cochand, *Helv. Chim. Acta*, **28**, 1181 (1945).

[5] P. Karrer and N. Neuss, *ibid.*, **28**, 1185 (1945).

[6] P. Karrer, Ch. Cochand and N. Neuss, *ibid.*, **29**, 1836 (1946).

[7] N. A. Sörensen, E. Samuelsen and Fr. Oxaal, *Acta Chem. Scand.*, **1**, 458 (1947).

[8] H. Schlenk, *Ber.*, **81**, 175 (1948).

[9] H. Schlenk, *ibid.*, **85**, 901 (1952).

[10] W. Dilthey and B. Stallmann, *ibid.*, **62**, 1603 (1929).

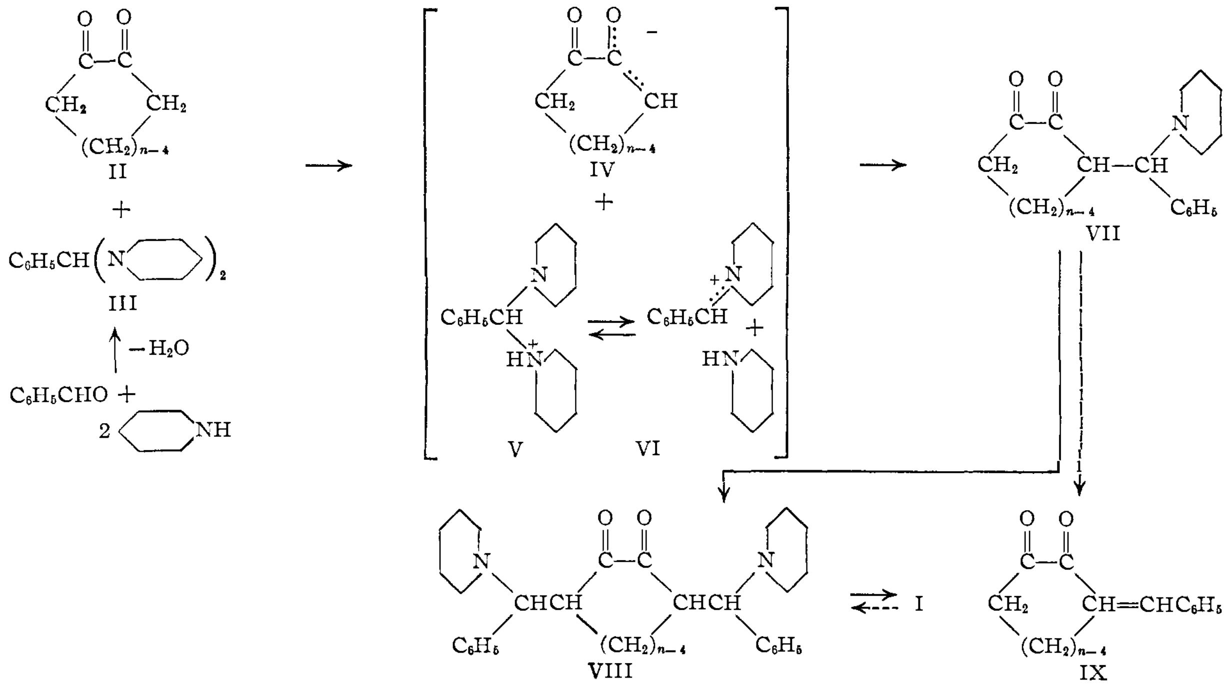
[11] G. C. Robinson, Ph.D. Thesis, University of Illinois, 1952.

[12] A. J. Kresge, Ph.D. Thesis, University of Illinois, 1953.

[13] Traces of benzoic acid not excluded.

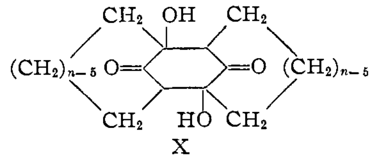
[14] E. Staple and E. C. Wagner, *J. Org. Chem.*, **14**, 559 (1949).

[15] R. Baltzly, E. Lorz, P. B. Russell and F. M. Smith, THIS JOURNAL, **77**, 624 (1955).



solubility of the larger ring diaminodiketones so that the final deamination (→ I) is not achieved.

An interesting side reaction was detected in the isolation of a small amount of colorless, highly insoluble substance from the 7-, 10-, 13- and very probably the 14-membered ring 1,2-diketones. The by-products in these four cases showed saturated ketone and non-bonded hydroxyl bands in the infrared, microanalytical values were satisfactory for the respective 1,2-diketones, while the molecular weights suggested that the compounds were dimeric formulations of the diketones. The infrared data, together with the fact that the compounds were not yellow, indicated that the 1,2-diketone grouping was not present as such. It was therefore concluded that the compounds were bis-aldols formed by base-catalyzed self-condensation of the diketones. The presence of only one unresolved band each for the ketone and the hydroxyl group was suggestive of a symmetrical molecule. Following the reported course of the dimerization of biacetyl,[16,17] the tricyclic structures (Xa,d,g,h) are proposed



X

One of the compounds, 1,10-dihydroxytricyclo-[9.7.1.1^{2,10}]cosane-19,20-dione (Xd), has been described previously,[18] and the physical properties reported agree well with the data provided in the present study. The structures of the other three compounds in this series (Xa,g,h) were assigned on the basis of analogy and also similarity in properties. It can be assumed that aldol catalysis by stronger base[18] would improve the yields of the tricyclic compounds, should these be the products desired.[19]

The Experimental section contains details on the formation of the various products (I, VIII, X) from 1,2-diketones II[20] and benzaldehyde-bis-piperidine. The case of the ten-membered ring will serve to illustrate the scope of the condensation reaction and its products. The first product which separated from the solution of sebacil (IId) and benzylidene-bis-piperidine (III) in ethanol, maintained at room temperature, was 3,10-dibenzylidene-1,2-cyclodecanedione (Id),[2] followed by 3,10-di-(phenyl-1′-piperidylmethyl)-1,2-cyclodecanedione (VIIId). The deamination of VIIId to give Id was effected readily by warming in 50% methanolic acetic acid. When the piperidine-induced condensation of benzaldehyde with sebacil was carried out in refluxing aqueous ethanol, it was possible to isolate 3-benzylidene-1,2-cyclodecanedione (IXd) along with the 3,10-dibenzylidene-1,2-cyclodecanedione. Compound Xd was a minor by-product. The lack of reactivity of the dicarbonyl system in 3,10-dibenzylidene-1,2-cyclodecanedione (Id) was demonstrated by the failure of this compound to combine with semicarbazide, phenylhydrazine and *o*-phenylenediamine. It was possible to obtain a mono-2,4-dinitrophenylhydrazone in low yield. Reduction of the olefinic double bonds in Id was effected with platinum and hydrogen, giving 3,10-dibenzyl-1,2-cyclodecanedione, which was also practically inert to carbonyl reagents and *o*-phenylenediamine. Reduction of the carbonyl double bonds in Id with lithium aluminum hydride yielded 3,10-dibenzylidene-1,2-cyclodecanediol.

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(16) H. v. Pechmann and E. Wedekind, *Ber.*, **28**, 1845 (1895).

(17) O. Diels, W. M. Blanchard and H. v. d. Heyden, *ibid.*, **47**, 2355 (1914).

(18) R. A. Raphael and A. I. Scott, *J. Chem. Soc.*, 4566 (1952).

(19) The tricyclic compounds may also serve as precursors for large-ring diametric diketones.[18]

(20) 1,2-Cycloöctanedione (IIb) was not used.

TABLE I

INFRARED ABSORPTION MAXIMA[a]

Compd.	ν_{CO} cm^{-1}	ν_{CO}, cm^{-1}	$\nu_{C=C \text{ and arom.}}$, cm^{-1}
	3,*n*-Dibenzylidene-1,2-cycloalkanediones (I)		
a	(?) 1693	1688	1605, 1578, 1497
c	*ca.* 1680	1670	1593, 1574, 1495
d	1662	[b]	1592, 1571, 1494
e	1674	1650	1609, 1594, 1574, 1495
f	1670	1650	1609, 1592, 1573, 1494
g	*ca.* 1670	1653	1608, 1592, 1568, 1494
h	*ca.* 1670	1653	1611, 1590, 1572, 1495
Cinnamil	1672	1645	1605, 1575, 1497
	3,10-Diarylidene-1,2-cyclodecanediones[c]		
Aryl group			
m-$CH_3C_6H_4$	1664		1594, *ca.* 1584, *ca.* 1482
p-$CH_3C_6H_4$	1662		1593, *ca.* 1568, 1510
p-$(CH_3)_2CHC_6H_4$	1662		1592, 1565, 1510
p-$CH_3OC_6H_4$	1662		*ca.* 1604, 1590, 1571, 1513
	3-Arylidine-1,2-cyclodecanediones		
C_6H_5 (IXd)	1697	1667	1593, 1575, 1495
p-$CH_3OC_6H_4$	1698	1662	1606, 1583, 1579, 1510, 1480
p-$(CH_3)_2NC_6H_4$	1696	1648	1606, 1557, 1516, 1474
	Model compounds		
Compound			
$CH_3COCH{=}CHC_6H_4N(CH_3)_2$		1657	1630, 1602–1575, 1549, 1522, 1482
$(CH_3)_3CCOCOCH{=}CHC_6H_5$	1701	1683, 1660	1620, 1605, 1575, 1500
IXd, with 10-$C_6H_5CH_2$[21]	1695	1666	1605, 1572, 1493

[a] Determined as 5% solutions in chloroform, except for cinnamil, which was a 2.5% solution. [b] Split in Nujol mull. [c] Compare the maxima observed for 3,7-diarylidene-1,2-cycloheptanediones (Nujol mull) (N. J. Leonard and J. W. Berry, THIS JOURNAL, **75**, 4989 (1953)).

Other aldehydes were caused to condense with sebacil IId under identical conditions which, in the case of benzaldehyde, favored the formation of the dibenzylidene derivative Id. The diarylidene compound was in fact the major product from IId and *p*-tolualdehyde, *m*-tolualdehyde and *p*-isopropylbenzaldehyde, whereas the monoarylidene compound predominated from anisaldehyde and *p*-dimethylaminobenzaldehyde.

In the 11-membered ring series, it was possible to obtain 3,11-dibenzylidene-1,2-cyclohendecanedione (Ie) and 3,11-di-(phenyl-1′-piperidylmethyl)-1,2-cyclohendecanedione (VIIIe). The former compound, m.p. 158–159°, corresponded to the high melting $C_{25}H_{26}O_2$ "isomer" previously reported in this Laboratory,[2] but the low melting "isomer" also described[2] must now be regarded as impure 3,10-dibenzylidene-1,2-cyclodecanedione (Id). The 10-membered ring impurity which persisted through many reactions and purification stages can now be traced to the original material in the reaction sequence, a commercial sample of nonamethylene dibromide which was apparently contaminated with octamethylene dibromide. For the synthesis of the 12- and 13-membered ring dibenzylidenediketones If,g, the route was the deamination of the corresponding diaminodiketones VIIIf,g by warming with methanolic acetic acid. In the case of the 14-membered ring, it was possible by varying the conditions to obtain either 3,14-dibenzylidene-1,2-cyclotetradecanedione (Ih) or 3,14-di-(phenyl-1′-piperidylmethyl)-1,2-cyclotetradecanedione (VIIIh).

The infrared absorption maxima observed for the dibenzylidenediketones I are presented in Table I. The variations in the series may be related to ring size but other factors enter into the picture, making it difficult to assign the specific causes of these variations. The lowest C=O stretching frequency is exhibited by the 10-membered ring compound, as also appears to be the case for the series of 1,2-cycoalkanediones II.[21] For all of the dibenzylidenediketones, two carbonyl bands are observed, and the higher-frequency band is generally less intense, often appearing as a shoulder. The explanation may lie in the coupling of the two carbonyl groups[22] or in their geometrical, with attendant conjugational, dissimilarity. It was noted that the band near 1600 cm.$^{-1}$ was generally the strongest band among those listed. In the 3-benzylidene-1,2-cycloalkanediones, the two carbonyl bands are logically due to the fact that one carbonyl group is conjugated with a styryl group and the other is not. By comparison (Table I) of the carbonyl maxima of 3-benzylidene-1,2-cyclodecanedione and 3,10-dibenzylidene-1,2-cyclodecanedione, 3-anisylidene-1,2-cyclodecanedione and 3,10-dianisylidene-1,2-cyclodecanedione, it will be seen that the second arylidene group lowers the carbonyl frequency by about 35 cm.$^{-1}$.

The compilation of the ultraviolet absorption maxima for the dibenzylidenediketones begun earlier[2] can now be completed (through Ih), as

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(21) J. C. Little, Ph.D. Thesis, University of Illinois, 1957.

(22) G. Herzberg, "Molecular Spectra and Molecular Structure," Vol. II, D. Van Nostrand Co., Inc., New York, N. Y., 1945, p. 215.

TABLE II

ULTRAVIOLET ABSORPTION SPECTRA[a]

Compd.	N → A_1[b]	N → V_1[c]	N → V_2[c]	N → V_3[c]	N → V_4[c]
	3,*n*-Dibenzylidene-1,2-cycloalkanediones (I)				
a	427(116)	305(30,600)	~270(16,000)[d]		
c	~403(187)	302(31,500)		231(12,900)	225(13,800)
d	408(191)	306(28,200)	~270(16,000)	231(12,000)	
e	~397(218)	301(31,500)		230(13,600)	225(14,000)
f	~403(200)	299(31,800)		~230(13,600)	225(14,200)
g	~408(200)	298(29,700)	~270(?)	~230(12,800)	225(14,000)
h	~408(180)	300(29,700)	~270(13,000)	229(13,300)	225(13,600)
Cinnamil	487(119) ~434(74)	330(33,000)			
	3,10-Diarylidene-1,2-cyclodecanediones				
Aryl group					
m-$CH_3C_6H_4$	407(214)	309(27,200)	~273(15,400)	~235(11,500)	
p-$CH_3C_6H_4$	404(273)	316(33,000)	~278(16,400)	235(12,800)	
p-$(CH_3)_2CHC_6H_4$	405(285)	318(36,800)	~278(18,200)	236(12,700)	
p-$CH_3OC_6H_4$	~421(414)	337[e]	~285[c]	237[e]	
	3-Arylidene-1,2-cyclodecanediones				
C_6H_5(IXd)	422(158)	305(12,600)	230(8700)		
p-$CH_3OC_6H_4$	419(353)	334(16,800)	239(8700)		
p-$(CH_3)_2NC_6H_4$		388(25,000)	259(9800)		
		Model compounds			
Compound					
$CH_3COCH{=}CHC_6H_4N(CH_3)_2$		360(23,400)	243(8100)		
$(CH_3)_3CCOCOCH{=}CHC_6H_4$	434(74)	305(13,800)	227(7400)		
IXd, with 10-$C_6H_5CH_2$		306(18,900)	231(11,000)		

[a] The first figure represents the wave length of the maximum in mμ; the figure in parentheses, ε. [b] ±6 mμ. Solvent, carbon tetrachloride. [c] Solvent, cyclohexane. [d] ~ Denotes inflection point. [e] Not calculated because of partial solubility. N → V_1 maximum in CCl_4 344 mμ (37,400).

shown in Table II. The longest wave length band in each spectrum, that due to excitation of the 1,2-dicarbonyl grouping (N → A_1), has been detected by the use of carbon tetrachloride as the solvent. The other values were obtained in cyclohexane. All of the spectra were determined immediately upon preparing each solution, since it was found that the conjugated 1,2-diketones and some unconjugated 1,2-diketones are unstable in solution. A marked decrease in the intensity, especially of the band near 300 mμ, was observed with aging of the solution. The values given previously[2] for the ultraviolet maxima of the 11-membered ring compound Ie must now be revised, and the correct values are listed in Table II.

The assignments of the excited states[23] have been made tentatively as indicated in Table II. The designation of the N → A_1 band as due to the dicarbonyl grouping and that of the N → V_1 band to excitations of the cinnamoyl grouping as a whole are considered reliable. The other N → V bands are probably due to excitations in less extended conjugated systems.[2,21]

Experimental[24]

Condensations of Aromatic Aldehydes with 1,2-Cycloalkanediones. 1. 1,2-Cycloheptanedione.—The method described previously[2] produced **3,7-dibenzylidene-1,2-cycloheptanedione** in 23% yield. A purified sample separated from 85% acetic acid as hexagonal yellow prisms, m.p. 188–189° (reported[2] 189–190°).

In a condensation of 1,2-cycloheptanedione[25–28] with benzylidene-bis-piperidine (prepared by adding two moles of piperidine per mole of benzaldehyde in cyclohexane, removing the water formed by azeotropic distillation and replacing the cyclohexane with the desired solvent)[10] in ether for 9 days at room temperature, **1,7-dihydroxytricyclo[6.4.1.1^{2,7}]tetradecane-13,14-dione** (8%) was formed. An analytically pure sample separated from acetic acid–ethyl acetate as tiny colorless needles, m.p. 220–221° dec.

Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.73; H, 8.01.

The infrared absorption spectrum (5% in chloroform) showed bands at 3432 (OH) and 1704 cm.$^{-1}$ (C=O).

2. **1,2-Cyclononanedione.**—To 25 ml. of absolute ethanol was added 2.07 g. (13.4 mmoles) of azelail[29–34] and 7.00 g.

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[23] G. W. Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1955, pp. 244–336.

[24] All melting points are corrected. All reagents were purified unless otherwise specified. Infrared absorption spectra were recorded on a Perkin–Elmer model 21 double beam recording instrument by Mr. James Brader and his associates. Ultraviolet spectra were determined on a Cary recording instrument by Miss Gerardine Meerman and Mr. Mou-shu Chao. All solutions were prepared immediately before running, in the solvent designated. Solutions of homologous series, etc., were of about the same concentration, and the wave lengths are reported in millimicrons (mμ). Numbers in parentheses following the wave length are molar extinction coefficients (ε) and those in brackets are log ε. Microanalyses were performed by Mr. Josef Nemeth and his associates.

[25] M. Godchot and G. Cauquil, *Compt. rend.*, **202**, 326 (1936).

[26] E. C. Rauh, G. F. Smith, C. V. Banks and H. Diehl, *J. Org. Chem.*, **10**, 199 (1945).

[27] L. W. Butz, B. L. Davis and A. M. Gaddis, *ibid.*, **12**, 122 (1947).

[28] R. W. Vander Haar, R. C. Voter and C. V. Banks, *ibid.*, **14**, 836 (1949).

[29] P. Ruggli and P. Zeller, *Helv. Chim. Acta*, **28**, 741 (1945).

[30] A. T. Blomquist, L. H. Liu and J. C. Bohrer, THIS JOURNAL, **74**, 3643 (1952).

[31] A. T. Blomquist, R. E. Burge, Jr., and A. C. Sucsy, *ibid.*, **74**, 3636 (1952).

[32] V. Prelog, K. Schenker and H. H. Günthard, *Helv. Chim. Acta*, **35**, 1598 (1952).

[33] A. T. Blomquist and L. H. Liu, THIS JOURNAL, **75**, 2153 (1953).

[34] A. T. Blomquist and A. Goldstein, *Org. Syntheses*, **36**, 77 (1956).

(27.1 mmoles) of (freshly prepared) benzylidene-bis-piperidine in 25 ml. of absolute ethanol. The mixture was allowed to stand at room temperature for 1 week and was then chilled and filtered to yield 0.53 g. (8%) of **3,9-di-(phenyl-1′-piperidylmethyl)-1,2-cyclononanedione**, clusters of light yellow needles from ethyl acetate, m.p. 177–178° dec.

Anal. Calcd. for $C_{33}H_{44}N_2O_2$: C, 79.16; H, 8.86; N, 5.60. Found: C, 78.95; H, 8.64; N, 5.62.

The infrared spectrum (5% in chloroform) showed bands at 1705 (C=O); 1164, 1099 (C-N?); 1034, 699 cm.$^{-1}$ (m.s. phenyl).

The supernatant solution from the reaction described above was heated under reflux for 3 hours, chilled and filtered to yield 1.29 g. (29%) of **3,9-dibenzylidene-1,2-cyclononanedione**, light yellow prisms from ethyl acetate, m.p. 109–110° (reported[2] 109.5–110.5°).

Anal. Calcd. for $C_{23}H_{22}O_2$: C, 83.60; H, 6.71. Found: C, 83.61; H, 6.66.

The deamination of 3,9-di-(phenyl-1′-piperidylmethyl)-1,2-cyclononanedione was carried out by heating 18 mg. (0.036 mmole) of the material with 2 ml. of 50% acetic acid in methanol at the boiling point for 3 minutes. Cooling and filtration yielded 10 mg. (83%) of the dibenzylidenediketone, m.p. 108–110°, undepressed on admixture with an authentic sample.

3. **1,2-Cyclodecanedione.**—To 110 ml. of absolute ethanol was added 7.40 g. (44 mmoles) of sebacil[35] and 23 g. (89 mmoles) of benzylidene-bis-piperidine. The mixture was allowed to stand at room temperature for 7.5 days and was then chilled and filtered to yield 12.04 g. (80%) of **3,10-dibenzylidene-1,2-cyclodecanedione**, recrystallized from ethyl acetate as light yellow platelets, m.p. 139–140° (reported[2] 139–140°).

Anal. Calcd. for $C_{24}H_{24}O_2$: C, 83.69; H, 7.02. Found: C, 83.60; H, 7.16.

The supernatant from this condensation was allowed to stand an additional two weeks and was then chilled and filtered to yield 0.16 g. of yellow crystals, m.p. (sinter 138°), 175–177° dec. Fractional crystallization from ethyl acetate yielded small, light yellow granules, m.p. 187–187.5° dec. and then a small amount of the dibenzylidenediketone, m.p. 138–139°. The first crop was purified by recrystallization from ethyl acetate to yield rectangular yellow needles, m.p. 188–188.5° dec., identified as **3,10-di-(phenyl-1′-piperidylmethyl)-1,2-cyclodecanedione.**

Anal. Calcd. for $C_{24}H_{46}N_2O_2$: C, 79.33; H, 9.01; N, 5.44. Found: C, 79.51; H, 9.16; N, 5.59.

The infrared absorption spectrum (5% in chloroform) showed bands at 1704 (C=O); 1165, 1100 (C-N?); 1033, 699 cm.$^{-1}$ (m.s. phenyl).

The deamination of this material was carried out by heating 9.8 mg. (0.019 mmole) in 1.5 ml. of 50% methanolic acetic acid under reflux for 10 minutes. Cooling and filtering yielded 4.0 mg. (61%) of the dibenzylidenecyclodecanedione, m.p. 139.5–140°, undepressed on admixture with authentic diketone.

In another condensation reaction, a mixture of 42.0 g. (0.25 mole) of sebacil, 63.6 g. (0.6 mole) of benzaldehyde and 1 ml. of piperidine in 400 ml. of 95% ethanol was heated for 23 hours under nitrogen, with stirring, at the reflux temperature. The solution was chilled and filtered to yield 39 g. of bright yellow crystals, m.p. 95–130°. Infrared analysis (5% in chloroform) showed that this was a mixture of approximately 33% 3,10-dibenzylidene-1,2-cyclodecanedione and 67% **3-benzylidene-1,2-cyclodecanedione.** A sample of the latter material was separated by fractional crystallization, and an analytical sample was recrystallized from 95% ethanol as long yellow needles, m.p. 104–105°.

Anal. Calcd. for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.65; H, 7.92.

Structure proof of this compound was accomplished by condensing 25 mg. (0.097 mmole) with 12.6 mg. (0.119 mmole) of benzaldehyde and 1 drop each (*ca.* 12 mg.) of piperidine and acetic acid in 2 ml. of absolute ethanol during two weeks. Chilling and filtration yielded 14 mg. (40%) of the dibenzylidenediketone, m.p. 136–138.5°. Recrystallization from absolute ethanol afforded yellow needles, m.p. 139–140°, undepressed on admixture with authentic diketone. The infrared absorption spectra were identical.

To check the stability of **3,10-dibenzylidene-1,2-cyclodecanedione under dealdolizing conditions**, 1.00 g. of the pure material (m.p. 139.5–140.5°) was heated under reflux for 4 hours with 10 ml. of 95% ethanol containing 1 drop each of piperidine and benzaldehyde. The mixture was chilled and filtered to yield 0.96 g (96% recovery) of pure dibenzylidenediketone, m.p. 139.5–140.5°.

There was obtained from another condensation a small amount (0.08%) of colorless material, an analytical sample of which separated from acetic acid–ethyl acetate as colorless needles of **1,10-dihydroxytricyclo[9.7.1.1^{2,10}]cosane-19,-20-dione**, m.p. 245–245.5° (reported[18] 255°).

Anal. Calcd. for $C_{20}H_{32}O_4$: C, 71.39; H, 9.59. Found: C, 71.40; H, 9.45.

The infrared spectrum (Nujol mull) showed bands at 3395 cm.$^{-1}$ (OH) and 1686 cm.$^{-1}$ (C=O).

The mono-2,4-dinitrophenylhydrazone of 3,10-dibenzylidene-1,2-cyclodecanedione was prepared by allowing the usual reagents[36] to stand in contact for 2 days. An analytical sample separated from ethyl acetate–ethanol as clusters of orange prisms, m.p. 178–179°.

Anal. Calcd. for $C_{30}H_{28}N_4O_5$: C, 68.69; H, 5.38. Found: C, 68.57; H, 5.48.

The infrared spectrum (5% in chloroform) showed maxima at 3280 (NH); 1660 (C=O), 1615 (C=C); 1596, 1573, 1505 (aromatic); 1536, 1520, 1341, 1314 cm.$^{-1}$ (NO_2). The ultraviolet spectrum in cyclohexane showed peaks at 359 [4.28], 306 [4.26] and 258 [4.43] mμ.

The preparation of **3,10-dibenzyl-1,2-cyclodecanedione** was effected by hydrogenation of 2.0 g. (5.8 mmoles) of 3,10-dibenzylidene-1,2-cyclodecanedione in ethyl acetate at 25° and 3 atm. using 0.05 g. of platinum oxide. The ethyl acetate was then replaced by methanol as a solvent, and cooling with seeding yielded 0.60 g. (30%) of yellow needles, m.p. 88–91°. The pure dibenzyldiketone crystallized from methanol as light yellow needles, m.p. 93–94°.

Anal. Calcd. for $C_{24}H_{28}O_2$: C, 82.72; H, 8.10. Found: C, 82.76; H, 8.24.

The infrared spectrum (5% in chloroform) showed bands at 1705 (C=O); 1612, 1505 and 700 cm.$^{-1}$ (aromatic). The ultraviolet absorption spectrum showed maxima at (cyclohexane) 240 [3.24] and shoulders at 258 [3.13], 265 [3.00] and 268 [2.90]; (carbon tetrachloride) 425 (39) mμ.

Reduction of 1.0 g. (2.91 mmoles) of 3,10-dibenzylidene-1,2-cyclodecanedione with 225 mg. (5.9 mmoles) of lithium aluminum hydride in ether yielded 0.76 g. (75%) of **3,10-dibenzylidene-1,2-cyclodecanediol**, m.p. 136.5–137.5°, which was chromatographically (alumina) homogeneous.

Anal. Calcd. for $C_{24}H_{28}O_2$: C, 82.72; H, 8.10. Found: C, 82.58; H, 8.02.

The infrared absorption spectrum (5% in chloroform) showed bands at 3570 (free OH); *ca.* 3400 (bonded OH); *ca.* 1640 (C=C); 1600, 1575, 1496, 698 cm.$^{-1}$; 5% in carbon disulfide) 3520 and *ca.* 3380 (OH); 780 (olefinic CH) and 699 cm.$^{-1}$ (aromatic). The ultraviolet absorption spectrum (cyclohexane) showed a maximum at 247 [4.33] mμ.

Sebacoin 3,5-dinitrobenzoate was prepared in 75% yield according to the general method of Brewster and Ciotti[37] and recrystallized from methanol–water as ivory prisms, m.p. 98–99°.

Anal. Calcd. for $C_{17}H_{20}N_2O_7$: C, 56.04; H, 5.53; N, 7.64. Found: C, 55.95; H, 5.29; N, 7.62.

The condensation of various other aldehydes with sebacil was accomplished by allowing 1.0 g. (5.95 mmoles) of the diketone to stand in 10 ml. of absolute ethanol with 12.5 mmoles of the aldehyde and 0.1 ml. each of piperidine and acetic acid at room temperature for 10 days. The results are summarized below.

Anisaldehyde.—The product was a mixture of the mono- and dibenzylidene derivatives, m.p. 127–150°. Fractional crystallization yielded **3,10-dianisylidene-1,2-cyclodecanedione**, yellow prisms from ethyl acetate, m.p. 179–180°, as the more insoluble species.

Anal. Calcd. for $C_{26}H_{28}O_4$: C, 77.20; H, 6.98. Found: C, 77.41; H, 7.09.

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(35) N. J. Allinger, *Org. Syntheses*, **36**, 79 (1956).

(36) R. L. Shriner, R. C. Fuson and D. Y. Curtin, "The Systematic Identification of Organic Compounds," fourth edition, John Wiley and Sons, Inc., New York, N. Y., 1956, p. 219.

(37) J. H. Brewster and C. J. Ciotti, Jr., THIS JOURNAL, **77**, 6214 (1955).

The more soluble fraction of the above material yielded **3-anisylidene-1,2-cyclodecanedione**, small yellow platelets from ethanol, m.p. 100–101°.

Anal. Calcd. for $C_{18}H_{22}O_3$: C, 75.49; H, 7.88. Found: C, 75.29; H, 7.88.

p-Isopropylbenzaldehyde.—The product was 1.20 g. (47%) of yellow solid, m.p. 139–142°. A pure sample of **3,10-di-(p-isopropylbenzylidene)-1,2-cyclodecanedione** separated from ethyl acetate as thin yellow platelets, m.p. 148–149°.

Anal. Calcd. for $C_{30}H_{36}O_2$: C, 84.07; H, 8.47. Found: C, 84.18; H, 8.59.

m-Tolualdehyde.—The product was 1.05 g. (47%) of a yellow solid, m.p. 115–119°. An analytically pure sample of **3,10-di-(m-methylbenzylidene)-1,2-cyclodecanedione** was crystallized from ethyl acetate as yellow platelets, m.p. 134.5–136.5°.

Anal. Calcd. for $C_{26}H_{28}O_2$: C, 83.83; H, 7.58. Found: C, 84.02; H, 7.50.

p-Dimethylaminobenzaldehyde.—The product consisted of 0.66 g. (37%) of orange crystals, m.p. 118–122°. The analytically pure sample of **3-(p-dimethylaminobenzylidene)-1,2-cyclodecanedione** separated from ethanol as light-orange platelets, m.p. 126–127°.

Anal. Calcd. for $C_{19}H_{25}NO_2$: C, 76.22; H, 8.42; N, 4.68. Found: C, 75.91; H, 8.39; N, 4.82.

p-Tolualdehyde.—The product was 8.59 g. (77%) of the dibenzylidene derivative, m.p. 150–154°. A pure sample of **3,10-di-(p-methylbenzylidene)-1,2-cyclodecanedione** was recrystallized from ethyl acetate–ethanol as yellow platelets, m.p. 161–162°.

Anal. Calcd. for $C_{26}H_{28}O_2$: C, 83.83; H, 7.58. Found: C, 83.66; H, 7.73.

4. 1,2-Cyclohendecanedione.—To 15 ml. of absolute ethanol was added 1.71 g. (9.4 mmoles) of the diketone, 6.25 g. (24.2 mmoles) of benzylidene-bis-piperidine and 0.5 ml. of piperidine. The mixture was heated under reflux for 15 hours and then chilled and filtered to yield 2.22 g. of yellow solid, m.p. 145–180°. The supernatant was treated with 0.6 ml. of acetic acid and 1.1 g. (0.96 mmole) additional benzaldehyde and then heated for 12 hours. The cooled mixture was extracted with ether, and the extracts were washed with water, sodium bisulfite and sodium carbonate solutions, and then dried over anhydrous magnesium sulfate. The solvent was removed to yield an additional 0.50 g. of yellow solid, m.p. 151–158°, which was combined with the solid previously obtained and refluxed with 50% acetic acid in methanol for 10 minutes. Chilling and filtration yielded 2.01 g. (60%) of the dibenzylidenediketone, m.p. 157–158°. An analytical sample of **3,11-dibenzylidene-1,2-cyclohendecanedione** separated from ethyl acetate as large yellow prisms, m.p. 158–159° (reported[2] 150°).

Anal. Calcd. for $C_{25}H_{26}O_2$: C, 83.76; H, 7.31. Found: C, 83.62; H, 7.20.

In another condensation, a solution of 1.66 g. (9.12 mmoles) of the diketone, 6.45 g. (25 mmoles) of benzylidene-bis-piperidine and 0.5 ml. of piperidine in 25 ml. of absolute ethanol was heated at reflux under nitrogen for 6 hours. The mixture was chilled and filtered to yield 1.04 g. (22%) of yellow crystals, m.p. 187–188°. The analytically pure sample of **3,11-di-(phenyl-1′-piperidylmethyl)-1,2-cyclohendecanedione** crystallized from ethyl acetate as clusters of yellow needles, m.p. 195.5–196° dec.

Anal. Calcd. for $C_{35}H_{48}N_2O_2$: C, 79.50; H, 9.15. Found: C, 79.51; H, 9.05.

The infrared spectrum (5% in chloroform) showed absorption maxima at 1706 (C=O); 1165, 1099 (C–N?); 1037, 699 cm.$^{-1}$ (m.s. phenyl).

This diaminodiketone was deaminated by warming 0.20 g. of material, m.p. 193–194° dec. to 80° for ten minutes. Chilling and filtration yielded 0.12 g. of yellow solid, m.p. 134–159°. Fractional crystallization from absolute ethanol showed that the material was a mixture of 3,11-dibenzylidene-1,2-cyclohendecanedione and 3,10-dibenzylidene-1,2-cyclodecanedione, indicating that the latter material was present as an impurity.

5. 1,2-Cyclododecanedione.—The yellow solid, m.p. 199–200° dec. obtained[11,12] from the condensation of 1,2-cyclododecanedione with benzaldehyde and piperidine was identified as **3,12-di-(phenyl-1′-piperidylmethyl)-1,2-cyclodecanedione**, crystallizing from ethyl acetate as small yellow needles, m.p. 202–203° dec.

Anal. Calcd. for $C_{36}H_{50}N_2O_2$: C, 79.66; H, 9.29; N, 5.16. Found: C, 79.80; H, 9.54; N, 5.07.

The infrared absorption spectrum (5% in chloroform) showed absorption maxima at 1706 (C=O); 1163, 1099 (C–N?); 1036, 698 cm.$^{-1}$ (m.s. phenyl).

One gram (1.85 mmoles) of this material was heated in 25 ml.. of 1:1 acetic acid–methanol for 15 minutes at the reflux temperature. The mixture was diluted with methanol, chilled and filtered to yield 0.48 g. (70%) of the yellow dibenzylidenediketone, m.p. 93.5–94.5°. A pure sample of **3,12-dibenzylidene-1,2-cyclododecanedione** separated from absolute ethanol as yellow rhombohedral prisms, m.p. 93.5–94.5°.

Anal. Calcd. for $C_{26}H_{28}O_2$: C, 83.83; H, 7.79. Found: C, 83.70; H, 7.79.

6. 1,2-Cyclotridecanedione.—To 1.67 g. (7.95 mmoles) of brassil in 30 ml. of absolute ethanol was added 4.1 g. (24.4 mmoles) of benzylidene-bis-piperidine, and the mixture was allowed to stand at room temperature for 9 days. Chilling and filtration yielded 2.26 g. (51%) of yellow aminoketone. An analytically pure sample of **3,13-di-(phenyl-1′-piperidylmethyl)-1,2-cyclotridecanedione** crystallized from ethyl acetate as flat yellow needles, m.p. 188–189° dec. (reported[12] 191–192°).

Anal. Calcd. for $C_{37}H_{52}N_2O_2$: C, 79.81; H, 9.68; N, 5.03. Found: C, 79.83; H, 9.68; N, 4.95.

The infrared absorption spectrum (5% in chloroform) showed absorption maxima at 1706 (C=O); 1163, 1098 C–N?); 1037, 699 cm.$^{-1}$ (m.s. phenyl). Ultraviolet absorption maxima were observed (cyclohexane) at 440(52) and 320(655) mμ.

The deamination of this compound (0.27 g., 0.49 mmole) was carried out in refluxing 50% methanolic acetic acid (3 ml.) during 10 minutes. The mixture was chilled and seeded to yield 0.12 g. (64%) of **3,13-dibenzylidene-1,2-cyclotridecanedione**, m.p. 79–80°. An analytical sample was obtained from methanol as long, faint yellow needles, m.p. 81–81.5°.

Anal. Calcd. for $C_{27}H_{30}O_2$: C, 83.90; H, 7.82. Found: C, 83.88; H, 7.82.

A by-product obtained from the deamination was purified and characterized tentatively as **1,12-dihydroxytricyclo-[12.10.1.1^{2,13}]hexacosane-25,26-dione**, tiny colorless needles from ethyl acetate, m.p. 259–261°.

Anal. Calcd. for $C_{26}H_{44}O_4$: C, 74.24; H, 10.54. Found: C, 74.20; H, 10.66.

The infrared absorption spectrum (2.5% in chloroform) showed bands at 3474 (OH) and 1709 cm.$^{-1}$ (C=O).

7. 1,2-Cyclotetradecanedione.—To 35 ml. of absolute ethanol was added 1.0 g. (4.45 mmoles) of 1,2-cyclotetradecanedione, 4.4 g. (17.0 mmoles) of benzylidene-bis-piperidine and 0.5 ml. of piperidine. The mixture was heated at reflux under nitrogen for one day, cooled and extracted with ether. The ether extracts were washed with water and sodium bisulfite solution and dried over anhydrous magnesium sulfate. Removal of the solvent yielded a dark yellow residue which was crystallized from ethyl acetate to yield 0.79 g. (44%) of **3,14-dibenzylidene-1,2-cyclotetradecanedione**, fine, faint yellow needles, m.p. 109.5–110.5°.

Anal. Calcd. for $C_{28}H_{32}O_2$: C, 83.96; H, 8.05. Found: C, 83.80; H, 8.02.

In another condensation reaction, 1.0 g. (4.45 mmoles) of diketone and 5.4 g. (19.4 mmoles) of benzylidene-bis-piperidine in 30 ml. of absolute ethanol was heated at reflux for 22 hours under nitrogen. Cooling and filtration yielded 1.72 g. (68%) of the diaminodiketone. A purified sample of **3,14-di-(phenyl-1′-piperidylmethyl)-1,2-cyclotetradecanedione** separated from acetone as faint yellow microcrystalline needles, m.p. 185–185.5° dec. (reported[11] 165–166°—impure).

Anal. Calcd. for $C_{38}H_{54}N_2O_2$: C, 79.95; H, 9.54; N, 4.91. Found: C, 79.73; H, 9.53; N, 4.96.

The infrared spectrum (4.5% in chloroform) showed maxima at 1707 (C=O), 1163, 1100 (C–N?) and 699 cm.$^{-1}$ (m.s. phenyl).

Deamination of the above material to form the dibenzylidenediketone was accomplished by recrystallization from ethyl acetate containing about 5% of acetic acid.

There was isolated from another condensation reaction a small amount of material which crystallized from ethyl acetate as tiny colorless needles, m.p. 288.5–289°. Satisfactory purification was not possible because of the small quantity obtained, but the material appeared to be mainly 1,14-**dihydroxytricyclo[13.11.1.$1^{2,4}$]octacosane-27,28-dione.**

Anal. Calcd. for $C_{28}H_{48}O_4$: C, 74.95; H, 10.78. Found: C, 74.54, 74.22; H, 10.90, 10.54.

The infrared absorption spectrum (1% in chloroform) showed maxima at 3456 (OH), 1706 (C=O) and a weak band at 1605 cm.$^{-1}$ (C=C?).

Preparation of 3-Benzyl-1,2-cyclotridecanedione.—Diethyl α-benzylbrassylate was prepared *via* a malonic ester synthesis, using ethyl 11-bromohendecanoate and diethyl benzylmalonate, in 51% yield, b.p. 176–178° (0.2 mm.), n^{19}D 1.4802, infrared C=O maximum at 1737 cm.$^{-1}$.

Anal. Calcd. for $C_{24}H_{36}O_4$: C, 73.80; H, 9.81. Found: C, 73.77; H, 9.84.

The dianilide of α-benzylbrassylic acid formed colorless crystals from methanol, m.p. 145–146°.

Anal. Calcd. for $C_{32}H_{40}N_2O_2$: C, 79.30; H, 8.32; N, 5.78. Found: C, 79.26; H, 8.22; N, 5.91.

The acyloin condensation of diethyl α-benzylbrassylate was carried out in the usual manner and the crude product was oxidized directly with cupric acetate in acetic acid[29] to **3-benzyl-1,2-cyclotridecanedione,** b.p. 139–140°, n^{20}D 1.5244; infrared C=O maximum (5% chloroform) at 1708 cm.$^{-1}$; ultraviolet maximum (cyclohexane) at 448 (43) mμ.

Anal. Calcd. for $C_{20}H_{28}O_2$: C, 79.95; H, 9.39. Found: C, 79.70; H, 9.44.

The quinoxaline of 3-benzyl-1,2-cyclotridecanedione was obtained by heating the diketone with 10% molar excess of *o*-phenylenediamine in absolute ethanol under reflux for 2 hours and was purified by recrystallization from 95% ethanol, light yellow crystals, m.p. 80.5–82°.

Anal. Calcd. for $C_{26}H_{32}N_2$: C, 83.82; H, 8.66; N, 7.52. Found: C, 83.71; H, 8.68; N, 7.61.

Preparation of 4,4-Dimethyl-2,3-pentanedione. 4-Isonitroso-2,2-dimethyl-3-pentanone.—An ether solution (100 g.) containing 0.55 mole of hydrogen chloride was added to a solution of 57 g. (0.5 mole) of 2,2-dimethyl-3-pentanone[38] in 570 g. of anhydrous benzene. The resulting solution was stirred and cooled externally. When the internal temperature was −8°, a solution of 57 g. (0.55 mole) of *n*-butyl nitrite[39] in 280 g. of absolute ether was added during 1.5 hours while stirring and maintaining at −8 to −10°. The deep red solution was kept in a refrigerator for 2.5 days, after which the color was light orange. The reaction mixture was washed with three 500-ml. portions of ice-water. The organic layer was extracted with two 500-ml. portions of cold 1 *N* sodium hydroxide. The combined cold alkaline extracts were carefully neutralized to *p*H 7 with cold dilute sulfuric acid. The precipitated product was collected, dried and recrystallized from hexane as colorless needles, m.p. 110.5–111.5°, yield 59 g. (82%); infrared maxima at 3370 (OH), 1672 (conj. C=O) and 1632 cm.$^{-1}$ (C=N).

Anal. Calcd. for $C_7H_{13}NO_2$: C, 58.72; H, 9.15; N, 9.78. Found: C, 58.88; H, 8.97; N, 9.62.

4,4-Dimethyl-2,3-pentanedione dioxime was prepared from the isonitrosoketone and hydroxylamine hydrochloride in ethanol–pyridine and recrystallized from aqueous ethanol as colorless needles, m.p. 183.5–184° (reported[40] 182.5°).

Anal. Calcd. for $C_7H_{14}N_2O_2$: C, 53.14; H, 8.92; N, 17.71. Found: C, 53.44; H, 9.22; N, 17.58.

4,4-Dimethyl-2,3-pentanedione was obtained from 4-isonitroso-2,2-dimethyl-3-pentanone by the method of Fréon and Ser,[41] using concentrated hydrochloric acid, with formalin as the hydroxylamine acceptor; yield 26%, b.p. 125–126°, n^{20}D 1.4047; infrared C=O band centered at 1710 cm.$^{-1}$.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.97; H, 9.54.

The dioxime was identical with the hydroxylamine condensation product from 4-isonitroso-2,2-dimethyl-3-pentanone. The **bis-2,4-dinitrophenylhydrazone** was obtained as yellow-orange crystals from aqueous dimethylformamide, m.p. 220.5–221.5° (reported[40] 214–215°).

Condensation of Benzaldehyde with 4,4-Dimethyl-2,3-pentanedione.—The condensation of 4,4-dimethyl-2,3-pentanedione and benzaldehyde was carried out in the presence of a trace of piperidine in refluxing ethanol solution to give **1-phenyl-5,5-dimethyl-1-hexene-3,4-dione** in 34% yield, b.p. 66° (0.03 mm.), n^{19}D 1.5641.

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 78.01; H, 7.36.

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(38) F. C. Whitmore, C. I. Noll and V. C. Meunier, This Journal, **61**, 683 (1939).

(39) E. Karg, *Arch. Pharm.*, **282**, 49 (1944).

(40) E. B. Reid and R. B. Fortenbaugh, *J. Org. Chem.*, **16**, 33 (1951).

(41) P. Fréon and S. Ser, *Compt. rend.*, **222**, 447 (1946).

URBANA, ILLINOIS

[Contribution from the George Herbert Jones Laboratory, University of Chicago]

Some Reactions of Amino Acid N-Carboxy Anhydrides

By Kenneth D. Kopple

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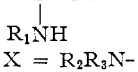
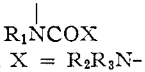
Primary amino acid N-carboxy anhydrides (NCA's) react with amines and sodium methoxide to yield carbamic acid derivatives. It is suggested that these derivatives arise *via* intermediate α-isocyanato acids. Evidence is adduced to demonstrate that under basic conditions NCA's can be converted to such intermediates and that isocyanato acids are likely intermediates in certain NCA polymerization reactions. An approximate equilibrium constant for base-catalyzed dissociation in dioxane of *p*-nitrophenyl N-phenylcarbamate into the corresponding phenol and phenyl isocyanate has been determined.

In a recent paper, it was reported that amino acid N-carboxy anhydrides (NCA's) react with excess of primary and secondary amines, yielding


$$\begin{array}{c}\mathrm{RCHCOX}\\ |\\ \mathrm{R_1NH}\end{array}$$

Ia, X = R_2R_3N-
Ib, X = CH_3O-


$$\begin{array}{c}\mathrm{RCHCOOH}\\ |\\ \mathrm{R_1NCOX}\end{array}$$

IIa, X = R_2R_3N-
IIb, X = CH_3O-

both α-amino amides (Ia) and α-ureido acids (IIa). With a given anhydride, the ratio of the two products is dependent on the amine.[1] Extension of this study to include reaction with sodium methoxide has led to the results which are cited in Table I.

It was suggested previously that Ia and IIa are products of nucleophilic addition to the 5- and 2-carbonyl groups, respectively, of the anhydride.[1]

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(1) K. D. Kopple, This Journal, **79**, 662 (1957).