the brown solution into 100 cc. of water and crystallizing the precipitated product from aqueous methanol, 4.15 g. (76% yield) of β-phthalimidopropionamide was obtained, melting at 204–206°, as did an admixture with the amide obtained on hydrolyzing the β-phthalimidopropionitrile previously described.

Anal. Calcd. for $C_{11}H_{10}O_3N_2$: C, 60.50; H, 4.58; N, 12.84. Found: C, 60.40; H, 4.80; N, 13.00.

β-Alanine.—Hydrolysis of β-phthalimidopropionitrile and β-phthalimidopropionic acid with 20% hydrochloric acid requires four and one-half hours,[3,15] whereas conversion of the nitrile with 30% sulfuric acid is complete in three hours. The crude β-phthalimidopropionitrile (20 g.) was heated for ten minutes with 20 cc. of 96% sulfuric acid on the steam-bath for conversion to the amide and, following dilution of the cooled solution with 40 cc. of water, the mixture was boiled for one hour to redissolve precipitated solids and for an additional two hours following the crystallization of phthalic acid. The precipitated acid (slightly yellow, m. p. 200°, 16.1 g. or 97%) was filtered from the cooled solution and washed with two 20-cc. portions of cold water, the filtrate was diluted to 400 cc. and treated with barium hydroxide equivalent to the sulfuric acid initially used and after removal and lixiviation of the precipitated sulfate, the combined filtrates were concentrated to a sirup prior to trituration with methanol, which deposited crystalline β-alanine, melting at 197° (with decomposition) after being washed with methanol and dried at 60°; yield 8.2 g.; 92%.

The authors are indebted to Mr. J. F. Alicino of the Squibb Institute, New Brunswick, N. J., for the analyses.

Summary

A convenient method has been described for preparing β-alanine from β,β′-iminodipropionic acid and its derivatives, involving conversion with phthalic anhydride to the corresponding β-phthalimido compounds and a subsequent hydrolysis.

HARRISON, N. J. RECEIVED JULY 11, 1946

---

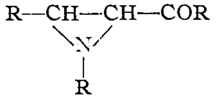
[15] Gabriel, *Ber.*, **38**, 633 (1905).

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

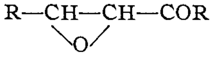
Ethylene Imine Ketones.[1] Reaction with Grignard Reagents[2]

BY NORMAN H. CROMWELL

The unique combination of functional groups present in the ethylene imine ketones (A) suggests that an extensive investigation of reactions likely to lead to combination with the carbonyl group and/or opening of the ethylene imine ring should prove to be quite interesting.



(A)



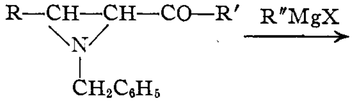
(B)

The structural relationship between the ethylene imine ketones (A) and the epoxy ketones (B) suggests a comparison of the properties of the two series. Several investigations of the latter series are to be found in the literature. The present communication is concerned with the reaction of ethylene imine ketones with Grignard reagents, a reaction which was extensively investigated with epoxy ketones several years ago by E. P. Kohler and his students.[3]

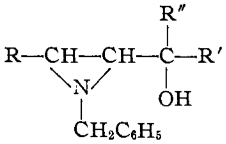
Three new ethylene imine ketones, 1-benzyl-2-(*m*-nitrophenyl)-3-benzoylethylenimine (I), 1-benzyl-2-phenyl-3-(*p*-methylbenzoyl)-ethylenimine (II) and 1-benzyl-2-(*p*-tolyl)-3-benzoylethylenimine (III) have been prepared from benzylamine and the corresponding α,β-dibromobenzylacetophenones by the method described in the previous papers dealing with ethylene imine ketones.[1,4]

1-Benzyl-2-phenyl-3-benzoylethylenimine[4] was treated with an excess of methylmagnesium iodide, phenylmagnesium bromide and *p*-tolylmagnesium bromide, respectively, while the ethylene imine ketones (II) and (III) were each allowed to react with an excess of phenylmagnesium bromide.

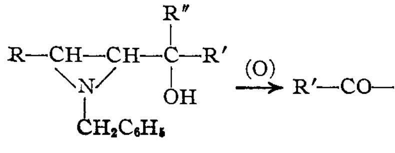
The crystalline product in each case corresponded to the reaction of the ethylene imine ketone with one equivalent of Grignard reagent. Oxidative cleavage experiments indicated these compounds to be the enimine carbinols (IV), (V), (VI), (VII) and (VIII), respectively.



(I) R, $m\text{-}NO_2C_6H_4$; R′, C_6H_5
(II) R, C_6H_5; R′, $p\text{-}CH_3C_6H_4$
(III) R, $p\text{-}CH_3C_6H_4$; R′, C_6H_5



(IV) R and R′, C_6H_5; R″, CH_3
(V) R, R′ and R″, C_6H_5
(VI) R and R′, C_6H_5; R″, $p\text{-}CH_3C_6H_4$
(VII) R and R″, C_6H_5; R′, $p\text{-}CH_3C_6H_4$
(VIII) R′ and R″, C_6H_5; R, $p\text{-}CH_3C_6H_4$



---

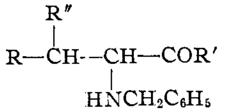
[1] For the previous paper in this series see Cromwell and Caughlan, THIS JOURNAL, **67**, 2235 (1945).

[2] Presented before a session of the Division of Organic Chemistry, 110th Meeting of the American Chemical Society, Chicago, Illinois, September 12, 1946.

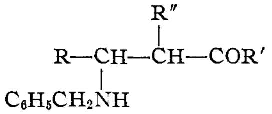
[3] Kohler, Richtmyer and Hester, THIS JOURNAL, **53**, 205 (1931).

[4] Cromwell, Babson and Harris, THIS JOURNAL, **65**, 312 (1943).

Such proof of the structures of these Grignard addition products was necessary since it was conceivable that the reagent might open the ethylene imine ring, as does hydrogen bromide,[1] in either of the alternative ways to give the isomeric amino ketones (C) and (D). It was necessary that the groups R and R′ be different, because (C) on oxidative cleavage would be expected to give the ketone, R—CO—R″.


$\mathrm{R{-}\overset{R''}{CH}{-}\underset{HNCH_2C_6H_5}{CH}{-}COR'}$

(C)


$\mathrm{R{-}\underset{C_6H_5CH_2NH}{CH}{-}\overset{R''}{CH}{-}COR'}$

(D)

Compounds of structure (D) might also be expected to yield the ketone R″—CO—R′ under the conditions of oxidative cleavage and steam distillation of the alkaline reaction mixture as applied here.

$$\text{(D)} \xrightarrow[\mathrm{H_2O}]{\text{(O)}} \mathrm{R''{-}CO{-}COR'} \xrightarrow{\mathrm{NaOH}} \mathrm{R''R'C(OH)\,COOH} \xrightarrow{\text{(O)}} \mathrm{R''{-}CO{-}R'}$$

However, Zincke[5] reported that benzil or benzoin gives benzaldehyde and benzoic acid on vigorous oxidation, while Müller and v. Pechmann[6] showed that acetyl benzoyl reacts in the presence of alkali to form 2,5-diphenylquinone.

On submitting benzoin to the oxidizing conditions as applied in these structure proof experiments, only benzil, benzoic acid and benzilic acid were obtained. Thus it would not seem that compounds of structure (D) would be expected to give the ketones, R″ COR′ on oxidation.

The enimine carbinols (VI) and (VII) which might have been expected to be identical, actually had different physical properties. Since (VI) and (VII) behaved identically in the oxidative cleavage experiments, and since the structures of the Grignard reaction products (VII) and (VIII) seem to be established beyond reasonable doubt, it is highly probable that all of these crystalline products have the enimine carbinol structures that have been written for them. The differences in the physical properties of (VI) and (VII) may be the result of a difference in racemic mixture composition.

These enimine carbinols were obtained in excellent yields and the addition reactions were quite rapid, indicating that the presence of the ethylene imine ring offers very little hindrance to the carbonyl group in these ketones. Moreover, the ethylene imine ring is not readily opened, nor the aliphatic chain cleaved by the Grignard reagent. In an investigation to be published soon it was found that the carbonyl group in certain of the α,β-diaminoketones is hindered, and that the Grignard reagent cleaves the aliphatic chain in a manner similar to that shown by Kohler for the epoxy ketones[3] and 1,3-diketones.[7]

It is important to recall that Kohler and Bruce[8] found that α-amino-α,β-unsaturated ketones add the Grignard reagent in the 1,4-position in the usual way for α,β-unsaturated ketones. The fact that these reaction products of α,β-dibromobenzylacetophenones and a primary amine gave only the carbinols on reaction with Grignard reagents is further evidence that they possess ethylene imine ketone structures.

The author appreciates a grant from the Research Council of the University of Nebraska which aided in the completion of this investigation.

Experimental

Ethylene Imine Ketones.—The corresponding α,β-dibromobenzylacetophenone (0.1 mole) was mixed with 0.32 mole of benzylamine in 40 ml. of absolute alcohol. As the reaction proceeded the dibromide dissolved, the solution turned yellow and heat was generated. The temperature of the solution was not allowed to rise above 40°. After the reaction had subsided the reaction mixture was allowed to stand at room temperature for twelve hours and in the ice chest for five hours. The solution was filtered and the precipitate washed with cold 80% alcohol, then water and again with cold 80% alcohol. The colorless products were recrystallized once from 95% alcohol and again from a mixture of benzene and petroleum ether.

In this way the ethylene imine ketones, (I), (II) and (III) were prepared from α,β-dibromo-*m*-nitrobenzylacetophenone,[9] α,β-dibromobenzyl-*p*-methylacetophenone[10] and α,β-dibromo-*p*-methylbenzylacetophenone,[11] respectively (see Table I). The isolation of other products from these reactions was not attempted.

Reactions of Ethylene Imine Ketones with Grignard Reagents.—A dry ether solution containing four equivalents of the Grignard reagent was prepared and to this solution was added rapidly one equivalent of the ethylene imine ketone dissolved in the minimum amount of a 50% mixture of dry benzene and dry ether. A white precipitate formed in five to thirty minutes. The reaction mixtures were stirred and refluxed for one hour and then decomposed by pouring into a slight excess of ammonium chloride and ice.

The benzene–ether layer was washed several times with water and dried over anhydrous calcium sulfate. Evaporation of the solvent caused the products to crystallize out. These colorless compounds were recrystallized from boiling petroleum ether (b. p. 60–70°) which contained a small amount of benzene.

In this way (IV) was prepared by allowing methylmagnesium iodide to react with 1-benzyl-2-phenyl-3-benzoylethylenimine.[2] Phenylmagnesium bromide was added to 1-benzyl-2-phenyl-3-benzoylethylenimine giving (V), to (II) forming (VII), and to (III) to give (VIII). When *p*-tolylmagnesium bromide was added to 1-benzyl-2-phenyl-3-benzoylethylenimine, (VI) resulted which might have been expected to be identical with (VII). Various mixtures of (VI) and (VII) melted over a range of 105–130° while mixtures of (VI) and (VIII) melted over the range of 118–139° (see Table I).

Oxidative Cleavage of Enimine Carbinols.—A 2-g. sample of the enimine carbinol was mixed with 5.0 g. of sodium dichromate dissolved in 46 ml. of 33% sulfuric acid. After the vigorous initial reaction had subsided the dark-red reaction mixture was heated on the steam-bath

---

(5) Zincke, *Ber.*, **4**, 836 (1871).

(6) Müller and v. Pechmann, *ibid.*, **22**, 2127 (1889).

(7) Kohler and Erickson, THIS JOURNAL, **53**, 2301 (1931).

(8) Kohler and Bruce, *ibid.*, **53**, 1994 (1931).

(9) Sorge, *Ber.*, **35**, 1068 (1902).

(10) Weygand, *ibid.*, **57**, 416 (1924).

(11) Hanzlik and Bianchi, *ibid.*, **32**, 2283 (1899).

TABLE I

PHYSICAL AND ANALYTICAL DATA OF ENIMINES

Ethylenimines	No.	M. p., °C.	Yield, %	Formula	Percentage composition			
					Calcd.		Found	
					C	H	C	H
1-Benzyl-2-(*m*-nitrophenyl)-3-benzoyl	(I)	106	20	$C_{22}H_{18}N_2O_3$	73.72	5.06	73.80	5.24
1-Benzoyl-2-phenyl-3-(*p*-methylbenzoyl)	(II)	116	20	$C_{23}H_{21}NO$	84.37	6.47	84.11	6.78
1-Benzyl-2-(*p*-tolyl)-3-benzoyl	(III)	122	25	$C_{23}H_{21}NO$	84.37	6.47	84.20	6.61
α-Butylenimines								
1-Benzyl-2,4-diphenyl-4-hydroxy-	(IV)	93	85	$C_{23}H_{23}NO$	83.85	7.04	83.77	7.14
Propylenimines								
1-Benzyl-2,4,4-triphenyl-4-hydroxy-[a]	(V)	137	90	$C_{28}H_{25}NO$	85.90	6.44	85.51	6.68
1-Benzyl-2,4-diphenyl-4-(*p*-tolyl)-4-hydroxy-	(VI)	138	85	$C_{29}H_{27}NO$	85.89	6.71	85.67	6.81
	(VII)	117	80				85.69	6.84
1-Benzyl-2-(*p*-tolyl)-4,4-diphenyl-4-hydroxy-	(VIII)	143	95	$C_{29}H_{27}NO$	85.89	6.71	85.77	6.88

[a] Calcd.: N, 3.57. Found: N, 3.54.

for one hour. The reaction mixture was then poured into about 100 ml. of water and the solution made basic with dilute sodium hydroxide. This basic mixture was steam distilled until the distillate became clear (about one liter of distillate). The distillate was extracted with three 100-ml. portions of ether. The ether solution was washed several times with water and once with 0.1 *N* hydrochloric acid. After drying, the ether solution was evaporated to leave an oily residue.

The oily residue obtained from the oxidation of (IV) was dissolved in dilute alcohol and treated with phenylhydrazine to give 0.40 g. of the phenylhydrazone of acetophenone, m. p. 102°. When the oily residues resulting from the other experiments were touched with authentic crystals of the corresponding benzophenones they solidified and it was found that the enimine carbinol (V) gave 0.6 g. of benzophenone, (VI) gave 0.6 g. of phenyl *p*-tolyl ketone, (VII) gave 0.7 g. of phenyl *p*-tolyl ketone and (VIII) gave 0.8 g. of benzophenone. When about equal amounts of benzophenone and phenyl *p*-tolyl ketone are pressed together an oil results. These benzophenones were further identified by converting them to their corresponding phenylhydrazones.

When 2.0 g. of benzoin was oxidized in the same way, the steam-distillation distillate gave only 0.2 g. of benzil, m. p. 96°. The alkaline residue from the distillation step was acidified to precipitate 1.0 g. of solid acids which on several recrystallizations proved to be a mixture of benzoic acid and benzilic acid.

Miscellaneous Properties of Enimine Carbinols.—Carbinol (IV) was heated with phenylhydrazine in a mixture of 95% alcohol and acetic acid for thirty minutes. On cooling, the reaction mixture precipitated 75% of the starting material (IV).

When (V) was heated for ten minutes with an equivalent amount of benzoyl chloride in a pyridine solution, or in a benzene solution for two hours no reaction took place and the enimine carbinol was recovered unchanged.

These carbinols do not possess the unpleasant odor of the ketones from which they are derived. They are only slightly soluble in dilute mineral acids. When 1.0 g. of (V) was boiled for twenty minutes with 15% sulfuric acid only a small amount was changed (odor of benzaldehyde) and 0.6 g. of the starting material was recovered.

Summary

Ethylene imine ketones add the Grignard reagent to the carbonyl group to give a new class of compounds, enimine carbinols. These results may be taken as further evidence for the structures of the ethylene imine ketones, and as an indication of the stability of the ethylene imine ring and its inability to hinder the carbonyl reactions in such compounds.

LINCOLN, NEBRASKA RECEIVED OCTOBER 5, 1946

[CONTRIBUTION FROM THE LABORATORY OF LADY ESTHER, LTD.]

Derivatives of Phenanthrene. The Preparation of 9-Amino-, 9-Iodo- and 9-Fluorophenanthrene

BY M. A. GOLDBERG,[1] E. P. ORDAS[2] AND G. CARSCH[3]

In the course of our work on the synthesis of various halogenated phenanthryl amino alcohols as potential antimalarials,[4,5,6,7] it appeared desirable to prepare 9-iodo- and 9-fluorophenanthrene. 9-Fluorophenanthrene has not been previously described, and since the only previous preparation of 9-iodophenanthrene was not very satisfactory (reaction of 9-phenanthrylmagnesium bromide with iodine[8]), it seemed desirable to prepare these halogenated compounds from 9-phenanthrylamine.

However, the preparation of large quantities of 9-phenanthrylamine presented some difficulty. The best reported methods are those of Bachmann and Boatner[9] as modified by Krueger and Mosettig,[10] involving Beckmann rearrangement of the oxime of 9-acetylphenanthrene, and that of

---

[1] Present address: Pepsodent Division, Lever Bros. Co., Chicago, Illinois.

[2] Present address: The Velsicol Corporation, Chicago, Illinois.

[3] Present address: 600 S. Michigan Avenue, Chicago, Illinois.

[4] Schultz, Goldberg, Ordas and Carsch, *J. Org. Chem.*, **11**, 307 (1946).

[5] Schultz, Goldberg, Ordas and Carsch, *ibid.*, **11**, 314 (1946).

[6] Schultz, Goldberg, Ordas and Carsch, *ibid.*, 320 (1946).

[7] Schultz, Goldberg, Ordas and Carsch, *ibid.*, 329 (1946).

[8] Zalkind and Lubinskaia, *Ber.*, **61B**, 269 (1928).

[9] Bachmann and Boatner, THIS JOURNAL, **58**, 2097 (1936).

[10] Krueger and Mosettig, *J. Org. Chem.*, **5**, 313 (1940).