39. Photolytic Closure of 4,5-Diphenyl-oxazol-2-ones to Phenanthro[9,10-d]oxazol-2-ones and an Improved Synthesis of Benzoins

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Summary

The synthesis of phenathrenes substituted by nitrogen and oxygen atoms in position 9 and 10 by photolysis of 4,5-diphenyl-oxazol-2-ones (cf. *Scheme 4*) is described. Moreover an improved general procedure for the synthesis of benzoins in aprotic solvent (tetra-*t*-butylammonium cyanide in DMF/DMSO) is developed.

Phenanthrenes substituted by nitrogen and oxygen atoms in position 9 and 10 are important synthetic intermediates in the synthesis of many natural products containing a phenanthrene moiety, such as terpenes, steroids and some alkaloids, as well as of a variety of synthetic pharmaceuticals.

The photolysis of stilbenes to obtain phenanthrenes was first studied by *Mallory et al.* [1]. *Collins & Hobbs* [2] examined the effect of copper(II) ion on the course of photolysis of the stilbenes: the yield was improved using iodine and copper(II) chloride in the presence of air. Apparently iodine is a more efficient catalyst for the oxidation of dihydrophenanthrene than copper(II) chloride, but it is not as efficient in preventing peroxide formation [3–5].

An interesting photolysis of the stilbene system of 4,5-diphenyl-oxazoles in ethanolic solution in the absence of copper(II) chloride, but in the presence of iodine and air, has been observed by *Cooper & Wassermann* [6] (*Scheme 1*).

Scheme 1
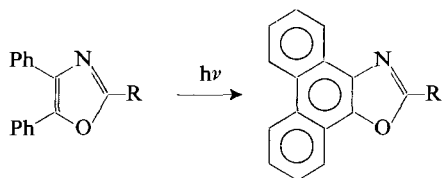

In this paper we report the synthesis of differently substituted phenanthro[9,10-*d*]-oxazol-2-ones by photolysis of the corresponding 4,5-diphenyl-oxazol-2-ones. The oxazolones [7] were obtained from the corresponding benzoins which in turn were synthesized from readily available aromatic aldehydes. It became necessary to develop an improved general procedure for the synthesis of benzoins.

Results and Discussion. – *Synthesis of Benzoins.* The benzoin condensation is usually done in a protic solvent (methods a [8] and b [9], see exper. part). However, cyanide ion is strongly solvated in these solvents, thereby reducing the ions potential, nucleophilicity and basicity by distributing its charge over a larger volume. The use of aprotic solvents would prevent this. However, the effects of the use of an aprotic solvent to decrease the effective charge density on large anions such as the oxygen anion and carbanion intermediates of the benzoin condensation would be expected to be considerably less. Furthermore, the increased basicity of the cyanide ion might be expected to increase the formation of enolate ion A, thereby removing the benzoin formed from the reaction mixture.

Scheme 2
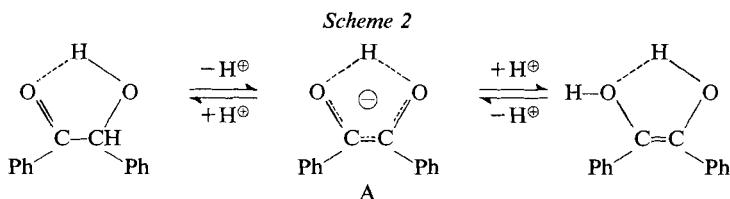
With these considerations in mind we hoped that the use of aprotic solvents would result in improved conditions for the benzoin condensation. When we used KCN in DMF or DMSO at room temperature (c_1 or c_2, see exper. part), we were able to obtain the desired products in much higher yields. For some syntheses the mixture DMF/DMSO 2:1 gave the best yield (method c_3), and for some it was better to substitute tetra-*t*-butylammonium cyanide for potassium cyanide (method c_4).

Synthesis of Oxazolones. Oxazolones [7] were obtained from benzoins by reaction with ethyl carbamate in the presence of a catalytic amount of pyridine at 150° (*Scheme 3*).

Scheme 3
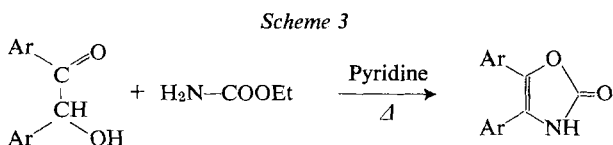
Since the photolysis of N-unsubstituted oxazolones usually failed to yield phenanthrenes, N-substituted oxazolones were prepared from N-unsubstituted oxazolones in usual way[1]). The N-benzyl-oxazolone gave the highest yield of phenanthrene derivative on photolysis.

Synthesis of phenanthrenes. Photolysis of N-unsubstituted diphenyl-oxazolone (*Scheme 4*,I) in methanol in the presence of copper(II) chloride, iodine and air according to *Collins & Hobbs* [2] gave the corresponding phenanthrene II in 4% yield, besides some starting material, and mainly unidentifiable oil.

When the photolysis time was decreased from 24 h to 16, 8 and 4 h, the yield of II increased to 4.8, 5 and 8% respectively. The amount of starting material increased, whereas the amount of oily compounds decreased.

However in the photolysis of 3-acetyl-4,5-diphenyl-oxazol-2-one the acetyl group was removed to give the phenanthrene II in 5% yield. II could be acetylated to 3-acetyl-phenanthro[9,10-*d*]oxazol-2-one (IV).

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[1]) For experimental details see exper. part.

Scheme 4

R^1, R^2, R^3

R^2
R^3 — R^1

R^4 — R^6R
R^5

$\xrightarrow[\text{Methanol/CuCl}_2]{h\nu}$

R^4, R^5, R^6
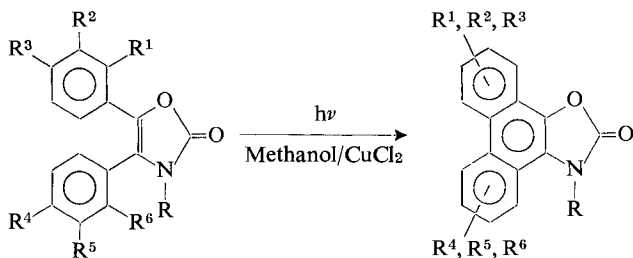
I $R = R^1 = R^2 = R^3 = R^4 = R^5 = H$	II $R = R^1 = R^2 = R^3 = R^4 = R^5 = H$
III $R = CH_3CO$, $R^1 = R^2 = R^3 = R^4 = R^5 = H$	IV $R = CH_3CO$, $R^1 = R^2 = R^3 = R^4 = R^5 = H$
V $R = CH_3$, $R^1 = R^2 = R^3 = R^4 = R^5 = H$	VI $R = CH_3$, $R^1 = R^2 = R^3 = R^4 = R^5 = H$
VII $R = C_6H_5$–CH_2, R^1 to $R^5 = H$	VIII $R = C_5H_5$–CH_2, R^1 to $R^5 = H$

When 3-methyl-4,5-diphenyl-oxazol-2-one (V) was photolysed under the same conditions for 4 h the 3-methyl-phenanthro[9,10-d]oxazol-2-one (VI) precipitated in 37% yield; recycling raised the yield to 65%.

Since an easily removable protecting group was desired at the N-atom the 3-benzyl-4,5-diphenyl-oxazol-2-one (VII) was prepared and photolysed at 40° to 3-benzyl-phenanthro[9,10-d]oxazol-2-one (VIII) (yield: 70%). At more than 40° the yield decreased to 58%, at less than 40° it increased to 80%.

Table 1

R^1	R^2	R^3	R^4	R^5	Oxazolone $R = H$	$R = CH_2C_6H_5$	Phenanthrene $R = CH_2C_6H_5$
H	H	OCH₃	OCH₃	H	IX	X	XI
H	H	OCH₃	H	H	XII[a]	XIII[a]	XIV[a]
H	H	CH₃	CH₃	H	XV	XVI	XVII
H	OCH₂O	OCH₂O	OCH₂O	OCH₂O	XVIII	XIX	XX
Cl	H	H	OCH₂O	OCH₂O	XXI[a]	XXII[a]	XXIII[a]
H	H	H	OCH₂O	OCH₂O	XXIV[a]	XXV[a]	XXVI[a]
H	H	CH₃	H	H	XXVII[a]	XXVIII[a]	
H	H	H	OCH₃	OCH₃	XXX[a]		

[a]   These compounds are presumably mixtures of isomers.

Other oxazolones, their N-benzyl derivatives and the product of photolysis of the latter (see *Scheme 4*), all obtained in a similar way, are summarized in Table 1.

Experimental Part

General. All the starting materials pure grade were obtained from *Fluka AG*, Switzerland. All melting points were determined with an *Ernest Leitz* melting point apparatus, and are uncorrected. Infrared spectra in cm⁻¹ were measured on a *Beckman* IR 8 spectrophotometer and ultraviolet spectra (λ_{max} (log ε)) on a *Beckman* DK-24 model. Mass spectra were obtained by a 'CH_5' mass spectrophotometer. All elemental analysis were performed at *Northeastern University* by the aid of Dr. *Boyce*.

Photolysis apparatus: the UV. source made by breaking the outer bulb of a *Philips* mercury 1000 W/220 V lamp and separating its tungsten connection operated in a typical run at 2.5 amperes (stabilized) and 115 volts. This source was lowered into a quartz tube (63 mm internal diameter,

1.6 mm wall thickness) which was fixed in the centre of a 2-l-pyrex beaker. During irradiation the contents of the beaker were kept at 30–40° by an ice-water bath.

Benzoin Condensation. – *Method a*: Aqueous alcoholic KCN was used as described in [10]. Benzoin (m.p. 130–131°), anisoin (m.p. 106–107°), and 4-methoxy-benzoin (m.p. 103–104°) were prepared by this method in 42, 52 and 28.9% yield, respectively.

Method b: To a solution of 21.2 g (0.2 mol) of benzaldehyde in a mixture of 25 ml of water and 25 ml of methanol were added 6.6 g (0.017 mol) of tetra-*t*-butylammonium iodide and 1.7 g (0.34 mol) of NaCN. The solution was stirred for 15 h. Then the mixture was filtered, the precipitate washed with ether and recrystallized from methanol to give 24.8 g (99%) of benzoin, m.p. 130–131° (Lit. [10] m.p. 134°). – MS. (m/e): 212 (M^+).

Method c_1: To a solution of 4-methyl-benzaldehyde (24 g, 0.2 mol) in 120 ml of DMF were added 4 g (0.06 mol) of KCN. The solution was stirred at RT. for 20 h. The mixture was poured in water, and the precipitate was filtered off, washed with ether and recrystallized from methanol to give 23 g (90%) of 4,4'-dimethyl-benzoin, m.p. 76–75° (Lit. [10] m.p. 88°). – MS. (m/e): 240 (M^+).

Other benzoins prepared by method c_1 are given in Table 2.

Table 2

Benzoin	m.p. (°)[a]	Yield %[b]	Reaction time h	m/e (M^+)
Anisoin	106–107 (110)	23 (160)	20	272
3,4,3',4'-dimethylenedioxy-benzoin	(120)	90 (80)	30	300
3,4-dimethoxy-benzoin	Oil	20	30	271
3,4-methylene-dioxy-benzoin	112–113 (120)	60 (32)	9	256
2'-chloro-3,4-methylenedioxy-benzoin	108–110 (116)	90 (50)	5	292
4-methyl-benzoin[c]	80–83	79	24	
4'-methyl-benzoin	(109)	(42)		

[a]) In parentheses m.p. of Lit. [10].
[b]) In parentheses yield of Lit. [10].
[c]) The NMR. shows 10–20% 4'-methyl- and 80–90% 4-methyl-benzoin.

$C_{15}H_{14}O_2$ Calc. C 79.22 H 5.70%   Found C 79.45 H 5.64%

Method c_2: As method c_1, but DMSO was used instead of DMF. The yield of anisoin (m.p. 106–107°) was 89%.

Method c_3: As method c_1, but a mixture of 40 ml DMSO and 80 ml DMF was used instead of DMF. The yield of 4-methoxy-benzoin after 30 h was 80%, m.p. 103–105° (Lit. [10] m.p. 105°). – MS. (m/e): 242 (M^+).

The yield of 3,4,4'-trimethoxy-benzoin after 20 h was 80%, m.p. 110–111°.

$C_{17}H_{18}O_5$ Calc. C 67.54 H 6.00%   Found C 67.28 H 5.93%

Method c_4: As method c_1 but a mixture of 6.6 g (0.017 mol) of tetra-*t*-butylammonium iodide and 3 g (0.04 mol) of KCN was used instead of KCN. The yield of 4-methoxy-benzoin after 5 h was 78%, m.p. 103–104°.

Oxazolone Synthesis. – *4,5-Diphenyl-oxazol-2-one* (**1**). Benzoin (53 g, 0.5 mol), ethyl carbamate (114 g, 1.28 mol) and 20 ml of pyridine were heated for 24 h at 150–160°. The solution was cooled and 300 ml of cold water were added. The precipitate was filtered off, dried and washed with ether to give 60 g of crude diphenyl-oxazolone, m.p. 203–206°. Recrystallization from ethyl acetate gave 55 g (92%) of white crystals, m.p. 205–206° (Lit. [7] m.p. 210°). – MS. (m/e): 237 (M^+).

Table 3 shows the melting points, yields and analytical data of different oxazolones synthesized by this method.

3-Acetyl-4,5-diphenyl-oxazol-2-one (*III*). 4,5-diphenyl-oxazol-2-one (12 g, 0.05 mol) was dissolved in 100 ml of acetic anhydride and refluxed for 8 h. The mixture was then poured in cold water and left overnight. The precipitate was filtered off, washed with water and dried to give 12 g (98%) of III,

Table 3

Oxazolone	m.p. (°)	Yield %	Calc. %			Found %		
			C	H	N	C	H	N
IX	203–205	84	68.67	5.08	4.71	68.51	5.10	4.72
XII	180–182	93	71.90	4.90	5.25	71.62	4.85	5.30
XV	188–190	94	76.96	5.70	5.28	76.64	5.73	5.28
XVIII	218–220	95	62.77	3.41	4.31	62.45	3.42	4.32
XXI	200–201	90	60.86	3.19	4.43	61.00	3.20	4.44
XXIV	182–184	88	68.32	3.94	4.94	68.18	3.98	5.01
XXVII	158–160	87	76.47	5.22	5.57	76.04	5.21	5.55
XXX	190–192	68	68.67	5.08	4.71	67.26	5.07	4.73

m.p. 134–136°. Recrystallization from methanol yielded 11 g (90%) of the N-acetyl derivative as white crystals, m.p. 135–136° (Lit. [7] m.p. 139°). – MS. (*m/e*): 279 (M^+).

3-Methyl-4,5-diphenyl-oxazol-2-one (V). To a stirred solution of 12 g (0.05 mol) of 4,5-diphenyl-oxazol-2-one in 80 ml DMF cooled in an ice bath were added 75 g (0.58 mol) of dimethylsulfate, slowly 1.4 g (0.058 mol) of NaH as an 80% dispersion in oil. After stirring for 1 h at RT. water was added gradually until the product precipitated: 11 g (90%) V, m.p. 93°. Recrystallization from methanol yielded 10 g (81%) of product, m.p. 94–96° (Lit. [7] m.p. 96°). – MS. (*m/e*): 251 (M^+).

3-Benzyl-4,5-diphenyl-oxazol-2-one (VII). Treatment of 12 g (0.05 mol) of 4,5-diphenyl-oxazol-2-one with 7.5 g (0.057 mol) of benzyl chloride (or bromide) and 1.4 g (0.058 mol) of NaH as above gave 15.6 g (93%) VII, m.p. 90–93°. Recrystallized from methanol: 15 g (90%) N-benzyl derivative, m.p. 92–93° (Lit. [7] m.p. 100°). – MS. (*m/e*): 327 (M^+).

Table 4 shows the melting points, yields and analytical data of different N-benzyl substituted oxazolones synthesized by this method.

Table 4

Oxazolone	m.p.(°)	Yield %	Calc. %			Found %		
			C	H	N	C	H	N
X	144–146	80	74.40	5.46	3.62	74.33	5.44	3.63
XIII	110–111	85	77.29	5.36	3.92	77.36	5.37	3.93
XVI	115–116	77	81.10	5.96	3.94	80.93	5.98	3.94
XIX	150–152	98	69.39	4.13	3.37	69.46	4.15	3.37
XXII	130–132	75	68.06	3.97	3.45	68.10	3.99	3.41
XXV	96– 97	50	74.38	4.61	3.77	74.16	4.69	3.76
XXVIII	100–102	55	81.10	5.96	3.94	81.22	5.94	3.96

Synthesis of Phenanthrenes. – *Photolysis of 4,5-diphenyl-oxazol-2-one* (I). A mixture of I (12 g, 40 mmol), copper(II) chloride (2 g, 14 mmol) and iodine (0.3 g, 0.12 mmol) in 1 l of methanol was irradiated at 30–35° in the presence of air for 4 h. Then the methanol was evaporated and the resulting oil dissolved in ethylacetate and filtered to separate inorganic materials. Then 1 g of a crystalline product separated from the filtrate. The mother liquor gave on evaporation 9 g of oil with no desirable characteristic. The crystalline material II (4%) had m.p. 305–307°. – IR. (KBr): 1730*s*, 1336*m*, 101*m*. – UV. (Ethanol): 263 (4.20), 202 (4.20), 314 (4.30).

$C_{15}H_9NO_2$ (235)   Calc. C 76.58   H 3.86   N 5.96%   Found C 76.70   H 3.88   N 5.98%

Photolysis of 3-acetyl-4,5-diphenyl-oxazol-2-one (III) by a procedure similar to the above resulted in the formation of compound II. Treatment of II with acetic anhydride yielded 85% of 3-acetyl-phenanthro[9,10-*d*]oxazol-2-one (IV), m.p. 184–185°.

$C_{17}H_{11}NO_3$ (277)   Calc. C 73.69   H 4.00   N 5.05%   Found C 73.79   H 4.03   N 5.03%

Photolysis of 3-methyl-4,5-diphenyl-oxazol-2-one (V). Photolysis (5 h) by the procedure described below afforded after recrystallization from methanol the 3-methyl-phenanthro[9,10-*d*]oxazol-2-one (VI), m.p. 210–211°, in 65% yield. – IR. (KBr): 1730*s*, 1335*m*, 1010*m*. – UV. (Ethanol): 261 (4.30), 300 (4.00), 311 (4.47).

$C_{16}H_{11}NO_2$ (249)   Calc. C 77.09 H 4.45 N 5.62%   Found C 76.90 H 4.46 N 5.65%

Photolysis of 3-benzyl-4,5-diphenyl-oxazol-2-one (VII). A solution of VII (16 g, 50 mmol) in methanol (1 l) mixed with copper(II) chloride (2 g, 14 mmol) and iodine (3 g, mmol) was irradiated for 4 h at 30–35°. The resulting precipitate was filtered off and the filtrate was irradiated for 3 h. Again, the precipitate was filtered off. The amount collected was 13.5 g (90%) of crude product m.p. 206–210°. Recrystallization from DMF/water gave 13 g (80%) of 3-benzyl-phenanthro[9,10-*d*]oxazol-2-one (VIII), m.p. 207–210°. – IR. (KBr): 1730*s*, 1338*m*, 1020*m*. – UV. (Ethanol): 261 (4.31), 300 (4.00), 312 (4.46).

$C_{22}H_{15}NO_2$ (325)   Calc. C 81.21 H 4.65 N 4.31%   Found C 81.19 H 4.66 N 4.32%

Melting points, yields, elemental analysis and spectroscopic data of different 3-benzyl-phenanthro-[9,10-*d*]oxazol-2-ones synthesized by this method are presented in Tables 5 and 6.

Table 5

Phenanthrene	m.p. °	Yield %	Calc. %			Found %		
			C	H	N	C	H	N
XI	208–210	90	74.79	4.97	3.63	74.84	4.96	3.64
XIV	205–208	86	77.73	4.82	3.94	77.64	4.82	3.93
XVII	215–217	84	81.56	5.42	3.96	81.45	5.43	4.66
XX	265–267	83	69.73	3.66	3.39	69.63	3.65	3.41
XXIII	275–277	85	68.40	3.49	3.47	68.50	3.49	3.48
XXVI	240–243	66.6	74.79	4.09	3.79	74.45	4.07	3.76

Table 6

Phenanthrene	IR. (KBr)	UV. (Ethanol)
XI	1730*s*, 1340*m*, 1260*w*, 1150*w*, 1010*m*	263 (4.34), 304 (4.30), 314 (4.64)
XIV	1730*s*, 1340*m*, 1240*w*, 1120*w*, 1025*m*	261 (4.30), 300 (4.12), 312 (4.47)
XVII	1730*s*, 1340*m*, 1030*m*	262 (4.29), 301 (4.00), 311 (4.46)
XX	1730*s*, 1345*m*, 1260*w*, 1220*w*, 1020*m*	263 (4.34), 304 (4.10), 315 (4.47)
XXIII	1730*s*, 1335*m*, 1240 (sh), 1030*m*	262 (4.20), 302 (4.00), 314 (4.47)
XXVI	1730*s*, 1340*m*, 1241 (sh), 1200*w*, 1025*m*	261 (4.27), 301 (4.06), 313 (4.45)

REFERENCES

[1] *C. S. Wood & F. B. Mallory*, J. org. Chemistry *29*, 3373 (1964), and references therein.
[2] *D. J. Collins & J. J. Hobbs*, Austral. J. Chemistry *20*, 1905.
[3] *M. S. Kharasch & G. Sosnovsky*, J. Amer. chem. Soc. *80*, 750 (1958).
[4] *A. L. J. Keckwith & G. W. Evans*, Proc. chem. Soc. *1962*, 63.
[5] *J. K. Kochi & H. E. Mains*, J. org. Chemistry *30*, 1862 (1965).
[6] *J. L. Cooper & H. H. Wasserman*, Chem. Commun. *1969*, 200.
[7] *R. Compper*, Chem. Ber. *89*, 1748 (1956); *R. Gompper & H. Herlinger*, ibid. *89*, 2816 (1956).
[8] *W. S. Ide & J. S. Buck*, in 'Organic Reactions', ed. R. Adams, John Wiley & Sons, Inc., New York 1948, Vol. IV, p. 269.
[9] *J. Solodar*, Tetrahedron Letters *1971*, 287.
[10] *T. van Es & O. G. Backeberg*, J. chem. Soc. *1963*, 1379.