TABLE I

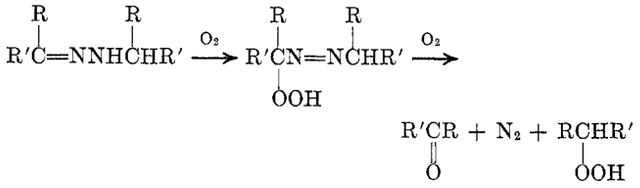
RATE CONSTANT RATIOS AND PRODUCT BALANCES FROM THE DECOMPOSITIONS OF COMPOUNDS 1a AND 1b[a]

Azo compound ArCHN=NCHAr (CH3, CH3)	Solvent	No. of samples[b]	k_d/k_c[c]	Yield[d] of combination + disproportionation products, %	Yield of ketone, %
Ar = C_6H_5 (1a)	C_6H_6	8	0.097 ± 0.002	95 ± 2	0
1a	o-$C_6H_4Cl_2$	16	0.090 ± 0.006	80 ± 3	21–54[e]
1a	C_6H_6/C_6H_5N	2	*f*	*f*	0[g]
Ar = p-ClC_6H_4 (1b)	C_6H_6	8	0.176 ± 0.009	50 ± 2	48.6 ± 2.2[h]
1b	C_6H_6/C_6H_5N	4	0.182 ± 0.008	96.9 ± 2.4	0

[a] From decomposition of the appropriate azo compounds at 118° in sealed ampoules degassed three times. [b] Each sample analyzed in duplicate by glpc. [c] Relative rates of disproportionation to combination as moles α-arylethane/mole 2,3-diarylbutane. [d] From standard plots using 0.1 *M* biphenyl as internal standard. [e] The yield is given as a range since it increases with time up to the value 54%, after which time it remains constant. [f] No values given since pyridine obscured the disproportionation product peak in the glpc trace. [g] Acetophenone was added and the solution rechecked to prove pyridine was not obscuring that peak also, which it was not. [h] The only analysis on this solution was 4 days after opening.

vestigators[3–5] have shown that hydrazones are readily autoxidized to azo hydroperoxides.

The azo hydroperoxide could decompose to ketone, nitrogen, and a secondary alkyl hydroperoxide *via* a homolytic scission and reaction with oxygen. The resultant phenylalkyl hydroperoxide would slowly decompose to a second mole of ketone, with ample precedent.[6]



Chloroazo compound **1b** had been found by Cohen, *et al.*,[7] to yield only about 60% of the theoretical amount of N_2, and Peterson and Ross[8] also obtained approximately 60% of the theoretical N_2 in their study of induced decomposition of azo compound **1a** in the presence of chloranil. Both groups postulated hydrazone formation.

In both these and the study reported here the abnormal decomposition was found when a reactant or solvent contained chlorine. Ioffe and Stopskii[9] have determined that the hydrazone is the more stable tautomer for a series of alkyl azo compounds, in agreement with the observations here. Care must be exercised in analyzing the results of studies of free radicals in halogenated aromatic solvents.

Experimental Section

A more detailed description of synthesis, solvent purification, analytical equipment, techniques, and experimental errors has been presented elsewhere.[2] Benzene, *o*-dichlorobenzene, and pyridine were dried and carefully distilled.

The azo decompositions were performed in sealed ampoules after three freeze–thaw degassings at 10^{-6} mm. Half-lives of the azo compounds studied were approximately 3 hr[7] at 118° and typical reaction times were 24–48 hr (8–16 half-lives).

For the nmr studies, three nmr tubes connected to 10/30 standard taper joints were degassed, sealed, and thermolyzed as above. Tube A contained 49.1 mg of **1a** and 0.5 ml of benzene, tube B 50 mg of **1a** and 0.5 ml of *o*-dichlorobenzene, and tube C 65 mg of **1b** and 0.5 ml of benzene.

Registry No.—**1a**, 5661-68-7; **1b**, 32234-17-6.

(3) A. J. Bellamy and R. D. Guthrie, *J. Chem. Soc.*, 3528 (1965).
(4) H. C. Yao and P. Resnick, *J. Org. Chem.*, **30**, 2832 (1965).
(5) G. J. Karabatsos and R. A. Taller, *J. Amer. Chem. Soc.*, **85**, 3624 (1963).
(6) A. G. Davies, "Organic Peroxides," Butterworths, London, 1961, Chapters 9 and 10.
(7) S. G. Cohen, S. J. Groscos, and D. B. Sparrow, *J. Amer. Chem. Soc.*, **72**, 3947 (1950).
(8) R. Peterson and R. Ross, *Tetrahedron Lett.*, 18 (1960).
(9) B. V. Ioffe and V. S. Stopskii, *ibid.*, 1333 (1968).

Transannular Alkylations of Cyclooctanones

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Intramolecular alkylation reactions have recently enjoyed considerable popularity as a method for the synthesis of complex polycyclic compounds.[2] In the present report we examine three suitably substituted cyclooctanones for which transannular effects might be expected to play an important role.

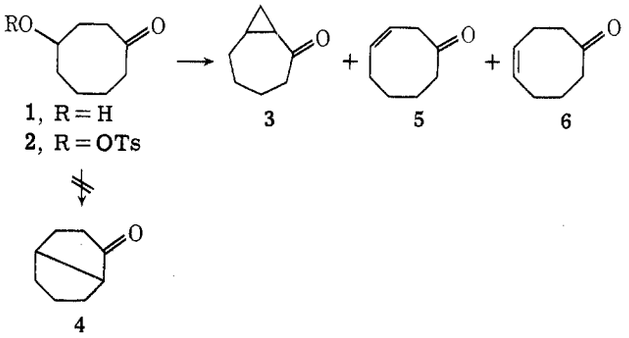
Derivatives of 4-hydroxycyclooctanone (**1**) were examined first. In this instance base treatment should promote enolate formation by proton removal at either side of the carbonyl group with roughly equal facility. The conformational constraints of the carbocyclic system might be expected to enhance the formation of a cyclopentane ring at the expense of the normally favored three-membered ring.[3] In fact, treatment of tosylate **2** with NaH–DMSO, KO-*t*-Bu in ether, or potassium carbonate in DMF all gave bicyclo[5.1.0]cyclooctan-2-one (**3**) cleanly. None of the isomeric ketone **4** was detected. Heating alcohol **1** with dicyclohexylcarbodiimide[4] led to **3** in a more direct synthetic approach.

The acetolysis of certain sulfonate esters has been described as proceeding by participation of a preformed enol derived from a neighboring ketone group.[5] A similar process could occur with **2**. Treatment of **2**

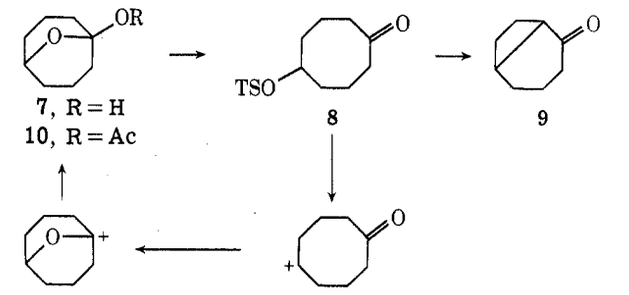
(1) (a) Alfred P. Sloan Fellow, 1968–1970; John Simon Guggenheim Fellow, 1970–1971. (b) NSF Undergraduate Summer Research Participant, 1970–1971. (c) NSF Undergraduate Summer Research Participant, 1967.
(2 See, for example, C. H. Heathcock, *J. Amer. Chem. Soc.*, **88**, 4110 (1966); **89**, 4133 (1967); J. E. McMurry, *ibid.*, **90**, 6821 (1968); H. W. Whitlock, *ibid.*, **84**, 3412 (1962).
(3) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 198.
(4) C. Alexandre and F. Ronessac, *Tetrahedron Lett.*, 1011 (1970).
(5) J. L. Marshall, *Tetrahedron Lett.*, 753 (1971).

with acetic acid containing sodium acetate gave **3** as the major product; but the simple elimination products 3-cyclooctenone (**5**) and 4-cyclooctenone (**6**) were also formed. Interestingly, increasing the concentration of sodium acetate increased the percentage of **3**. Heating **2** in pyridine also gave unsaturated ketones in addition to **3**.

Thus, intramolecular alkylation in **2** proceeds with a kinetic preference for cyclopropane formation. In agreement with these results a model of the enolate precursor of **4** does not indicate an exceptionally favorable stereoelectronic situation despite the enforced proximity of the potentially interacting carbon centers. Transannular bond formation is also observed under the acidic conditions of the acetolysis of **2**.

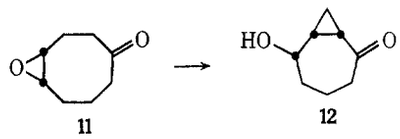


Only one cyclization mode is possible for derivatives of 5-hydroxycyclooctanone (which exists in the hemiketal form **7**), although this process leads to a cyclobutane derivative, normally not a facile cyclization. Nonetheless, reaction of tosylate **8** with either NaH–DMSO or KO-*t*-Bu in ether generated bicyclo[4.2.0]-octan-2-one (**9**) cleanly. Potassium carbonate in DMF



gave no reaction with **8** and heating **7** with dicyclohexylcarbodiimide did not yield a volatile product. Acetolysis of **8** gave mainly 4-cyclooctenone along with small amounts of **10**, probably formed by the indicated cationic cyclization. Thus, intramolecular alkylation of cyclooctanone **8** proceeds readily under strongly basic conditions but not otherwise.

The final ketone examined was 4,5-epoxycyclooctanone (**11**). This compound can react at either of the transannular functional carbons from two possible enolate positions. Furthermore, the fused epoxide ring perturbs the conformational situation. Finally, from a synthetic point of view the generation of a hydroxy group in the potential bicyclic products is of interest. Reaction of **11** with KO-*t*-Bu in ether or potassium carbonate in DMF gave only one of the possible alkylation products, *endo*-6-hydroxybicyclo[5.1.0]octanone (**12**). Thus, three-membered ring cyclization is again favored. The assigned stereochemistry of **12** follows from the presumed SN2 alkylation mechanism.



Experimental Section

General.—Nuclear magnetic resonance (nmr) spectra were taken in carbon tetrachloride solution with Varian A-60 or HR-220 spectrometers. Infrared spectra (ir) were obtained with Perkin-Elmer Model 137 Infracord spectrophotometers on neat samples. Gas chromatography (glpc) was performed on Aerograph A600 (analytical, hydrogen flame detctor), and A700 (preparative) instruments. Analytical columns were 10 ft × 0.125 in. 30% Carbowax 20 M or 10 ft × 0.375 in. SE-30 on Chromosorb W; preparative columns were 10 ft × 0.375 in. 30% Carbowax or 5 ft × 0.375 in. 15% SE-30 on 60–80 Chromosorb W. Percentage composition data were estimated by peak areas and are uncorrected for compound response. Anhydrous magnesium sulfate was used for all drying operations. Microanalyses were performed by Midwest Microlabs, Inc., Indianapolis, Ind.

4-Hydroxycyclooctanone *p*-Toluenesulfonate.—To an ice-cold solution of 10 g of **1** in 50 ml of pyridine was added 15 g of *p*-toluenesulfonyl chloride. The mixture was stirred at 0° for 24 hr and then poured into an ice–10% hydrochloric acid mixture. The crystalline mass was collected, washed with a small amount of ether, and recrystallized from hexane to give 10 g (50%) of **2**: mp 83–85°; ir 5.9, 7.5, 8.6, and 11.2 μ; nmr δ 7.6 (AA'BB' multiplet, 4, aromatic protons), 4.6 (m, 1, CHOTs), 2.45 (s, 3, CH_3), and 2.6–1.5 (m, 12).

Anal. Calcd for $C_{15}H_{20}O_4S$: C, 60.79; H, 6.80. Found: C, 60.52; H, 6.63.

5-Hydroxycyclooctanone *p*-Toluenesulfonate.—To an ice-cold solution of 10 g of **7**[6] in 50 ml of pyridine was added 21 g of *p*-toluenesulfonyl chloride. The mixture was stirred at 0° for 68 hr. The solid material was removed by filtration, water (2 ml) was added, and the solution was stirred for an additional 5 hr before pouring into an ice–10% hydrochloric acid mixture. The crystalline mass was removed by filtration to give 12.8 g (61%) of **8**: mp 77–79°; ir 5.88, 7.4, 8.58, and 11.10 μ; nmr δ 7.5 (AA'BB' multiplet, 4, aromatic protons), 4.2 (m, 1, CHOTs), 2.4 (s, 3, CH_3), and 2.6–1.7 (m, 12). An analytical sample was prepared by recrystallization from hexane.

Anal. Calcd for $C_{15}H_{20}O_4S$: C, 60.79; H, 6.80. Found: C, 60.54; H, 6.79.

Reaction of 2 with Pyridine.—To 25 ml of pyridine was added 1 g of **2**. The solution was heated on a steam bath for 6 hr, poured into 150 ml of an ice–10% hydrochloric acid solution, and extracted with ether. The ether extracts were washed with 10% hydrochloric acid, saturated sodium carbonate, and water, then dried and concentrated to give 0.32 g (76%) of a crude oil. Glpc showed two products in the ratio 89:11.

The major product was identified as **3** by comparison of its ir spectrum with that of an authentic sample.[7] The minor product was **6**, as shown by comparison.[8]

Acetolysis of 2.—To a stirred solution of 1 g of **2** in 40 ml of acetic acid was added 58 mg of anhydrous sodium acetate. The reaction was refluxed for 6 hr, poured into ice–water, and extracted with pentane. The extracts were combined, washed with saturated sodium carbonate solution and water, and then dried and concentrated to give 0.38 g (94%) of a crude oil. Glpc showed two products in the ratio 91:9. The mixture was separated by glpc. The major product was **3**. The second peak was a mixture of **5** (direct comparison[8]) and **6** in the ratio 20:80 as determined from comparison of the nmr integral for the olefin protons of both compounds at δ 5.65 with the protons characteristic of **5** at δ 3.05.

(6) Badische Anilin- und Soda-Fabrik Akt.-Ges., British Patent 823,007 (1959); *Chem. Abstr.*, **54**, 8675 (1960).

(7) W. G. Dauben and G. H. Berezin, *J. Amer. Chem. Soc.*, **89**, 3449 (1967). Professor Dauben kindly supplied us with an ir spectrum for comparison purposes.

(8) N. Heap and G. H. Whitham, *J. Chem. Soc. B*, 164 (1966).

To three separate stirred solutions of 0.1 g of **2** in 4 ml of acetic acid were added 2.9, 5.8, and 14.5 mg, respectively, of anhydrous sodium acetate. The reaction mixtures were refluxed for 6 hr, poured into 20 ml of ice–water, and extracted with pentane. Samples were analyzed by glpc. One equivalent of sodium acetate gave a **3**:**5** plus **6** ratio of 81:19; 2 equiv gave 90:10, and 5 equiv gave 92:8.

Reaction of 1 with Dicyclohexylcarbodiimide.—To 0.61 g of dicyclohexylcarbodiimide was added 0.42 g of **1**. Stirring was begun and a trace of freshly prepared CuCl was added to the flask. The flask was heated to 150° for 20 min, at which time the material in the flask had solidified. The volatile components were removed by distillation at 150° (10 mm) to give 0.28 g (76%) of **3**.

Reaction of 2 with NaH–DMSO.—In a flask was placed 0.3 g of sodium hydride–mineral oil dispersion. After the solution was washed three times with pentane, 10 ml of dimethyl sulfoxide was added by syringe and the mixture was heated under nitrogen at 70–80° for 45 min. After cooling, 1 g of **2** in 10 ml of dimethyl sulfoxide was added and the mixture was allowed to stir at room temperature for 6 hr. The product was extracted with pentane and concentrated to give 0.34 g (78%) of **3**.

Reaction of 2 with KO-*t*-Bu.—To 1 g of **2** in 50 ml of anhydrous ether under a nitrogen atmosphere was added 1 g of KO-*t*-Bu. The reaction was stirred for 6 hr at room temperature, at which time the solid material was removed by filtration and washed with ether. The ether extracts were washed with water and concentrated to yield 0.42 g (90%) of **3**.

Reaction of 2 with K_2CO_3–DMF.—To 1 g of **2** in 30 ml of DMF was added 1.0 g of anhydrous K_2CO_3. The mixture was heated to 85° for 4 hr. Water was added and the mixture was extracted with pentane. The extracts were washed with distilled water, dried, and concentrated to give 0.24 g (50%) of **3**.

Acetolysis of 8.—Reaction as described above for **2** gave 0.37 g (87%) of an oil containing two products in the ratio 94:6. The major product was **6**; the minor one was **10**.[9]

Reaction of 7 with Dicyclohexylcarbodiimide.—To 0.61 g of dicyclohexylcarbodiimide was added 0.42 g of **7**. Stirring was begun and a trace of freshly prepared CuCl was added to the flask. The flask was heated to 150° for 5 hr, at which time it was observed that no precipitate had formed. The reaction was then heated to 200° for 8 hr and cooled to 150°, and the volatile components were removed by distillation. Only small amounts of starting material were recovered.

Reaction of 8 with K_2CO_3–DMF.—Reaction as described for **2** gave only starting material.

Reaction of 8 with NaH–DMSO.—Reaction as described for **2** gave 0.3 g (71%) of an oil identified as **9**:[10] ir 5.85 μ; nmr δ 2.5–3.2 (m, 2) and 1.2–2.5 (m, 10); 2,4-DNP, mp 178–179.5° (lit.[11] mp 179.5–180°).

Reaction of 8 with KO-*t*-Bu.—Reaction as described for **2** gave 0.39 g (90%) of **9**.

Reaction of 11 with K_2CO_3–DMF.—To 2 g of **11**[12] dissolved in 60 ml of DMF was added 4 g of anhydrous K_2CO_3. The mixture was heated to 140° for 72 hr with stirring. The solid materials were removed by filtration and the DMF was removed by distillation at reduced pressure. The solid residue was removed by filtration and washed with ether. The filtrate was concentrated to give 1.8 g (89%) of **12**: ir 3.0, 3.45, 6.0, 8.75, 10.35, and 12.6 μ; nmr δ 4.1 (s, 1), 3.4 (s, 1), 2.15–1.15 (m, 8), 0.8 (m, 1), and 0.4 (m, 1).

Anal. Calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.82; H, 8.75.

Reaction of 11 with KO-*t*-Bu.—A slurry of 1 g of **11**, 2 g of KO-*t*-Bu, and 30 ml of anhydrous ether was stirred under nitrogen at room temperature for 12 hr, poured into saturated NH_4Cl solution, and extracted with ether. The ether extract was washed with water, dried, and concentrated to give 0.9 g (90%) of **12**.

Registry No.—**2**, 34958-36-6; **8**, 34958-37-7; **11**, 34958-38-8; **12**, 34958-39-9.

(9) C. Ganter and J. F. Moser, *Helv. Chim. Acta*, **52** (3), 735 (1969).
(10) A. C. Cope and R. W. Gleason, *J. Amer. Chem. Soc.*, **84**, 1933 (1962).
(11) H. O. House and T. O. Cronin, *J. Org. Chem.*, **30**, 1069 (1965).
(12) J. K. Crandall, J. P. Arrington, and C. F. Mayer, *J. Org. Chem.*, **36**, 1428 (1971).

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2,3-Annelations on Quinoline and Pyridine 1-Oxides

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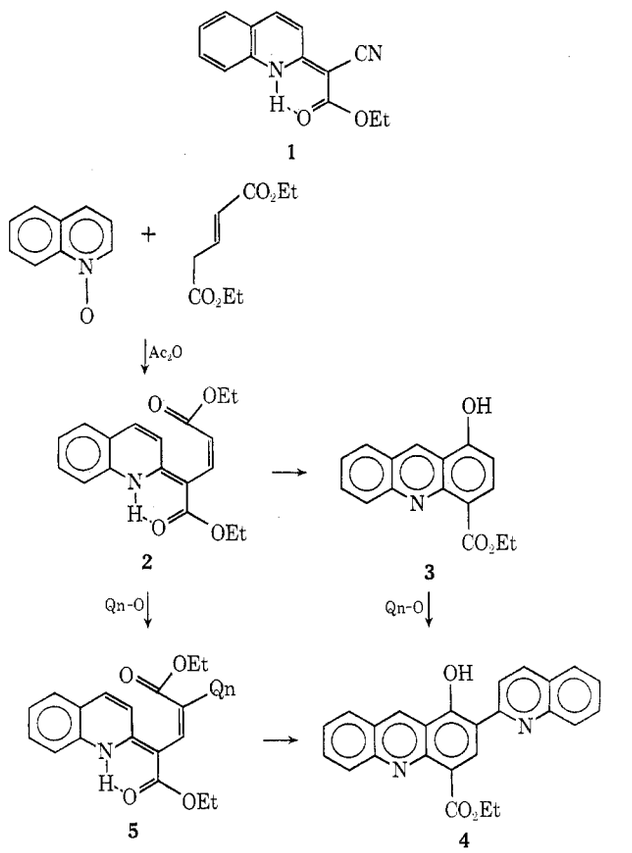
Ethyl α-(2-quinolyl)cyanoacetate, the product of the reaction of quinoline 1-oxide with ethyl cyanoacetate in the presence of acetic anhydride,[1] exists exclusively in the tautomeric form **1**.[2] This finding prompted us



to study the possibilities of achieving 2,3-annelations on the quinoline nucleus *via* intermediates having the salient structural features of **1**. We chose to investigate the reaction of diethyl glutaconate with quinoline 1-oxide, with the idea that if intermediate **2** were formed,[3] its geometry should be such as to permit nucleophilic attack by C-3 on the terminal ester function to yield the acridinol **3**.

The product of the reaction proved to be 4-ethoxycarbonyl-2-(2′-quinolyl)-1-acridinol (**4**) rather than **3**.

(1) M. Hamana and M. Yamazaki, *Chem. Pharm. Bull.*, **11**, 415 (1963).
(2) J. E. Douglass and J. M. Wesolosky, *J. Org. Chem.*, **36**, 1165 (1971).
(3) The cis geometry shown about the terminal carbon–carbon double bond in **2** is not unreasonable in view of the expected rotational lability of this grouping.