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STUDIES ON QUINOLIZONES—II

BROMINATION AND ACETYLATION OF 4H-QUINOLIZIN-4-ONE

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Abstract—Bromination of 4H-quinolizin-4-one under different conditions results in mono and dibromination, The position of entry of the bromine atoms is established by brominative decarboxylation of the corresponding quinolizone carboxylic acids, comparable to the behaviour of salicylic acid or *p*-hydroxybenzoic acid. Direct acetylation of quinolizone under a variety of conditions failed. Acetylquinolizones were prepared by direct synthesis. The facile replacement of the acetyl groups by nitro groups in the quinolizones is also demonstrated, providing thereby a synthesis of 1-nitro-4H-quinolizin-4-one.

BROMINATION of 4H-quinolizin-4-one in acetic acid medium results in facile entry of two bromine atoms by substitution. It was not possible to interrupt this reaction at the monobromination stage, but the use of ethyl bromide in dimethyl sulphoxide results in monobromination, the bromine entering the 3-position. Further bromination of this with bromine in acetic acid produces the same dibromo derivative as was obtained in one step. The position of entry of the bromine atoms was established as described in the sequel.

It had earlier been demonstrated[1] that carboxyl groups in 4H-quinolizin-4-one were easily displaced by the nitro group. The elegant work of Grovenstein *et al.*,[2,3] has shown that aromatic acids carrying an *o*- or *p*-hydroxy group undergo ready displacement by bromine by way of an electrophilic substitution. The quinolizone carboxylic acids exhibit parallel behaviour. Thus, 1,3-dicarboxy-4H-quinolizin-4-one affords by brominative decarboxylation, the same dibromo derivative as was obtained by direct bromination of the unsubstituted quinolizone. In a parallel study* of 2-methyl-3-5-dicarboxy-6-pyridone, the pyridone is unaffected over a period of 6 hr while the quinolizone carboxylic acids lose carbon dioxide in a matter of minutes. Once again, this emphasizes the greater aromaticity in quinolizone over the pyridone system.

However, esters of the same quinolizone acids do not undergo simple bromination at other reactive sites in the molecule. Attempted reaction of 1,3-dicarbethoxy-4H-quinolizin-4-one with bromine in refluxing acetic acid affords 1-carbethoxy-3-bromo-4H-quinolizin-4-one, presumably through the 3-carboxy compound. It is well known

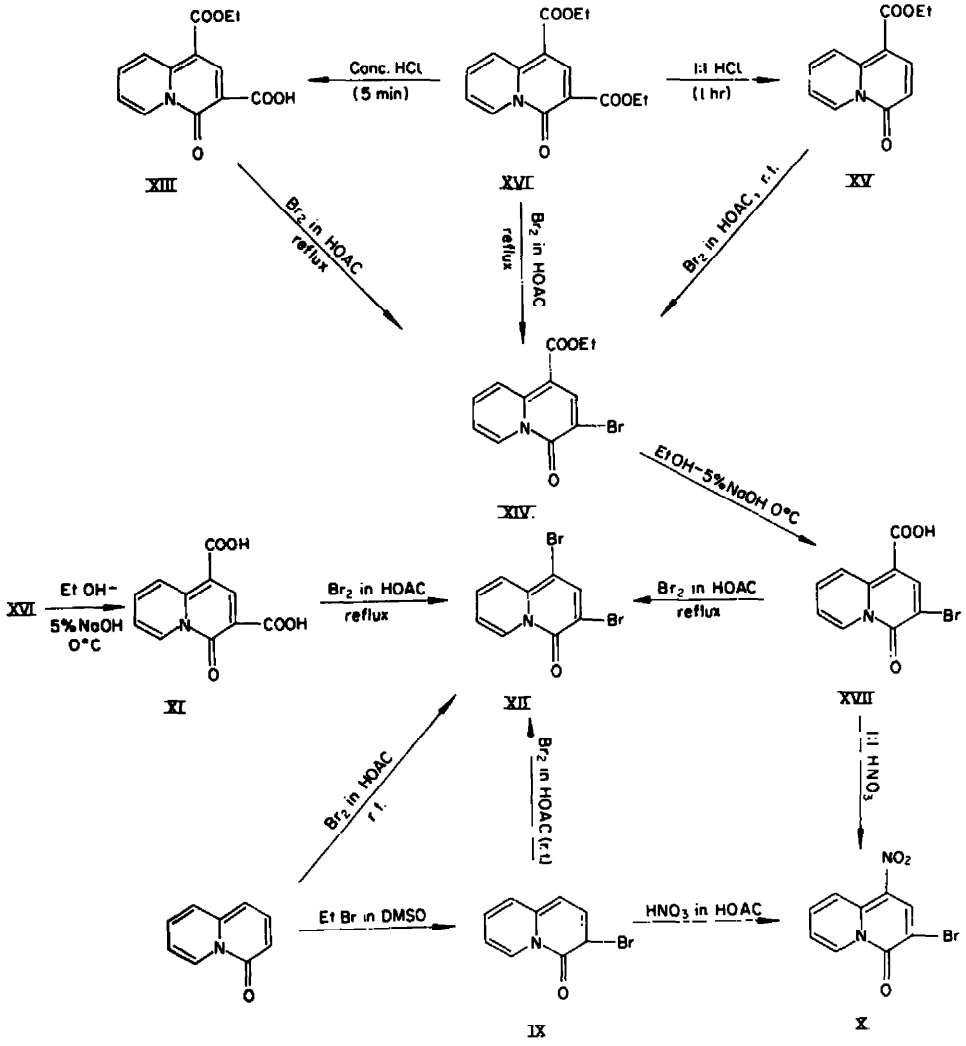
* K. Rajagopalan, unpublished results.

[1] B. S. Thyagarajan and P. V. Gopalakrishnan, *Tetrahedron* **20**, 1051 (1964).
[2] E. Grovenstein Jr. and U.V. Henderson Jr., *J. Amer. Chem. Soc.* **78**, 569 (1956).
[3] E. Grovenstein Jr. and U.V. Henderson Jr., *J. Amer. Chem. Soc.* **78**, 2560 (1956).

that the 3-carbethoxy group is easily hydrolysed. The same bromo derivative was also obtainable by simple bromination of 1-carbethoxy-4H-quinolizin-4-one, or by brominative decarboxylation of 1-carbethoxy-3-carboxy-4H-quinolizin-4-one. Dimethyl sulfoxide and ethyl bromide did not effect any bromination when the 1 and 3 positions were blocked by carbalkoxy groups.

The sequence of reactions leading to the different bromo derivatives starting from 1,3-dicarbethoxy-4H-quinolizin-4-one is illustrated in Chart I.

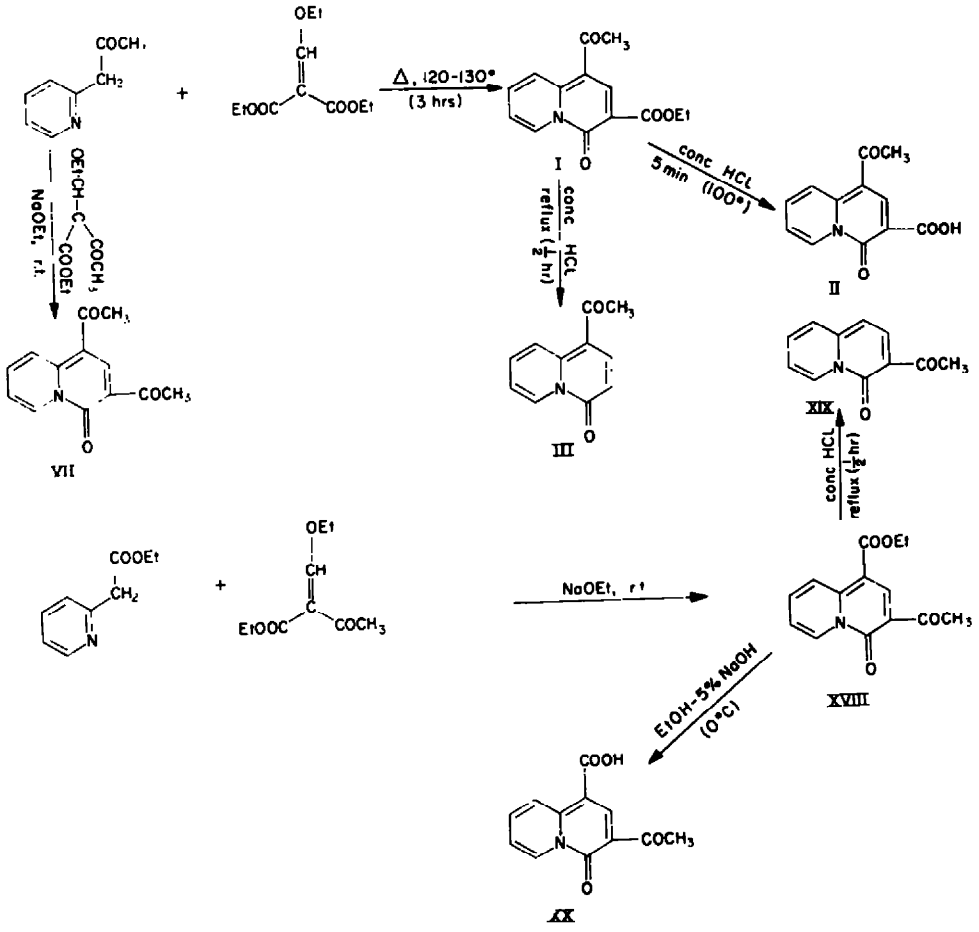
Chart I



Acetylation of 4H-quinolizin-4-one under a wide variety of conditions did not lead to the acetyl derivatives. In most instances the starting quinolizone was recovered

unchanged while in others only intractable tarry materials were formed. Consequently, the acetylquinolizones were prepared by direct synthesis as outlined in Chart II.

Chart II



In a manner similar to the displacement of the carboxyl groups in the quinolizone, the acetyl groups undergo facile displacement by nitro groups. Thus, 1,3-diacetyl-4H-quinolizin-4-one affords the corresponding 1,3-dinitro derivative and similarly 1-nitro-4H-quinolizin-4-one (Chart III) was prepared.

The present study, once again, demonstrates the lack of anionic activation of the non-oxygenated ring of the quinolizone system. An explanation for this may partly be found in the fact that once a bromine or a nitro group enters the 3-position, the opposing dipoles of the nitro and carbonyl suppress the full development of the anionic charge on the quinolizone oxygen, leading thereby to lack of reactivity towards further electrophilic substitution. Studies are in progress to evaluate other possible electrophilic substitutions which will avoid this difficulty.

Chart III

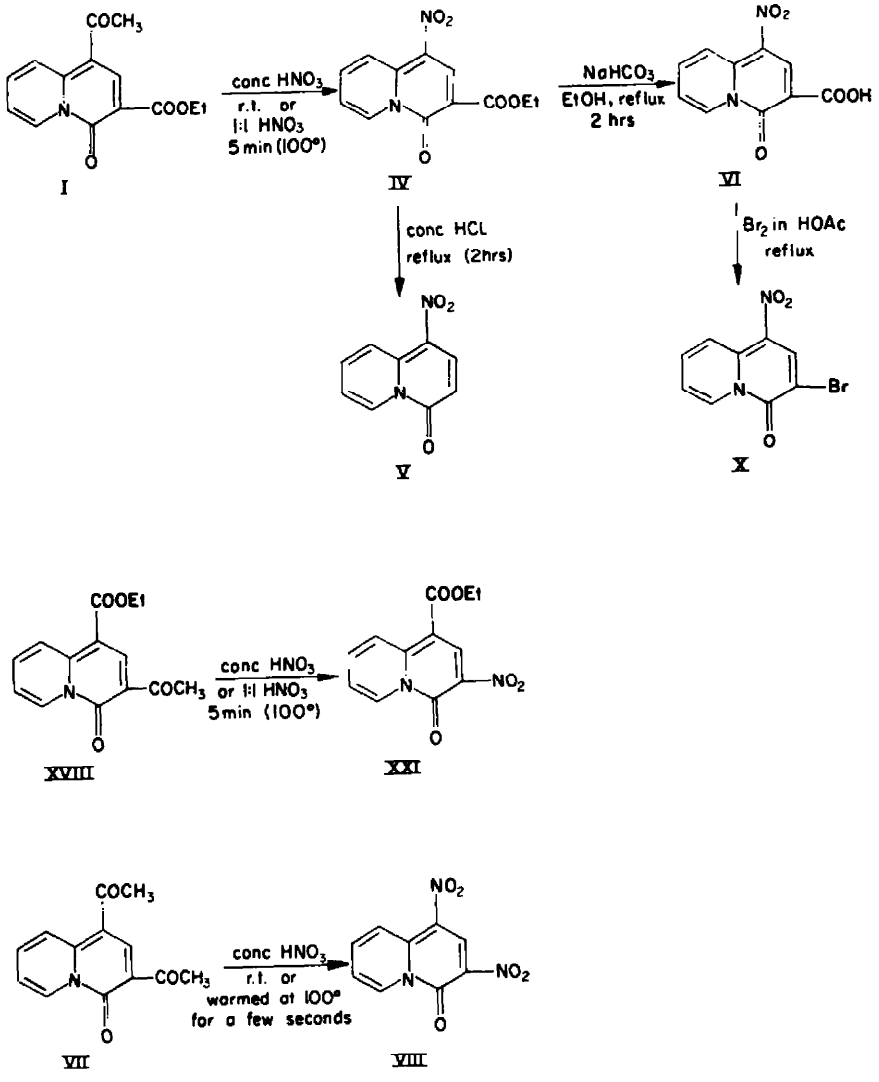

COCH3
COOEt
I
conc HNO3
r.t. or
1:1 HNO3
5 min (100°)
NO2
COOEt
IV
NaHCO3
EtOH, reflux
2 hrs
NO2
COOH
VI
conc HCL
reflux (2hrs)
NO2
V
Br2 in HOAc
reflux
NO2
Br
X
COOEt
COCH3
XVIII
conc HNO3
or 1:1 HNO3
5min (100°)
COOEt
NO2
XXI
COCH3
COCH3
VII
conc HNO3
r.t. or
warmed at 100°
for a few seconds
NO2
NO2
VIII

TABLE 1. ATTEMPTED ACETYLATION OF 4H-QUINOLIZIN-4-ONE

S. no.	Condition	Method of working	Ref.
1	Treated with Ac_2O and $AlCl_3$ at room temp in CS_2	[a]	
2	Refluxed for 5 hr with Ac_2O and $AlCl_3$	[e]	
3	Ac_2O and $ZnCl_2$ sealed tube at 140°–150°—2 hr	[c]	
4	NaAc and Ac_2O refluxed for 6 hr in N_2 refluxed for 10 hr	[b]	[4] Y. Arata, T. Ohashi and K. Uwai, *J. Pharm. Soc., Japan* **75**, 265 (1955).
5	AcCl, Dichloroethane and Fe refluxed for 7 hr	[d]	[5] I. P. Tsukervanik, Kh. Kim and A. S. Kurbatova, *J. Gen. Chem.* **33**, 227 (1963).
6	Dimethylacetamide + $POCl_3$ on water bath for 2 hr	[e]	[6] William C. Anthony, *J. Org. Chem.* **25**, 2049 (1960).
7	Ac_2O, $AlCl_3$ in nitrobenzene refluxed for 4 hr	[c]	
8	Anhydrous $SnCl_4$ and tetrachloroethane–3 days at room temp	[e]	[7] R. J. Windgassen Jr., W. H. Saunders Jr., and Boeklheide, *J. Amer. Chem. Soc.* **81**, 1459 (1959)
9	Acetic acid, polyphosphoric acid on water bath for 2 hr	[e]	[8] S. Dev, *J. Indian. Chem. Soc.* **33**, 703 (1956).
10	Ac_2O and BF_3-etherate, overnight at room temp	[d]	[9] J. P. Collmann, R. L. Marshall, W. C. Young III and C. T. Sears Jr. *J. Org. Chem.* **28**, 1449 (1963).
11	Ac_2O, AcOH and $HClO_4$	[d]	
12	Pyridine and AcCl	[c]	

The quantity of 4H-quinolizin-4-one used was about 500 mg–1 gm. The acetylquinolizones reported herein are solids, sparingly soluble in water whereas 4H-quinolizin-4-one is a low melting deliquescent solid. The following methods were used to see whether the oil obtained after the reaction was only the recovered starting material or a mixture of starting material and the acetylated product.

[a] Picric acid was added to the oil and the picrate formed compared with an authentic sample of 4H-quinolizin-4-one picrate.
[b] The oil chromatographed.
[c] Only tarry material was obtained.
[d] Some white solids were formed initially, probably salts of 4H-quinolizin-4-one with AcCl, BF_3, $HClO_4$ and $SnCl_4$. In the first three cases, the salts dissolved in water to give oil, which was worked by method *e*.
[e] The oil was treated with 2,4-DNP to see whether a solid derivative of acetylated product could be formed.

EXPERIMENTAL

Synthesis of 1-*acetyl*-4H-*quinolizin*-4-*one* (III)

(a) 2-*Pyridylacetone* was prepared by the method of Büchi *et al.*[10]

(b) 1-*Acetyl*-3-*carbethoxy*-4H-*quinolizin*-4-*one* (I) was prepared by heating 2-pyridylacetone (10 g) with ethyl ethoxymethylenemalonate (18 g) at 120°–130° for 3 hr, cooling, washing the solidified mass with ice-cold acetone and recrystallizing from benzene–pet. ether (yield 10 g; 50%) m.p. 162·8°–163·8°. (Found: C, 64·76; H, 5·49. $C_{14}H_{13}NO_4$ requires: C, 64·86; H, 5·00%.) λ_{max}^{EtOH} 240, 265, 280, 345 and 400 mμ (log ε 3·673, 4·008, 3·972, 4·206 and 4·206). $\lambda_{max}^{CHCl_3}$ 3·35 (m), 5·8 (s), 5·925 (s), 6·1 (vs) 6·375 (s), 6·65 (m), 6·75 (vs), 7·325 (m), 7·6 (w), 7·8 (w), 8·00 (s), 8·2 (vs), 8·35 (s), 8·55 (w), 8·8 (m) and 9·0 (m) μ.

(c) 1-*Acetyl*-4H-*quinolizin*-4-*one* (III). Compound I (8 g) in conc. HCl (200 ml) was heated under

[10] J. Büchi, F. Kracher and G. Schmidt, *Helv. Chim. Acta* **45**, 729 (1962).

reflux for ½ hr and cooled. It was neutralized with solid Na_2CO_3, extracted with benzene, the benzene layer was dried, and distilled to yield III (5g; 73%). After crystallization from benzene–pet. ether, it melted at 143·2°–144·2°. (Found: C, 70·52; H, 5·28. $C_{11}H_9NO_2$ requires: C, 70·58; H, 4·8%.) λ_{max}^{EtOH} 258, 288, 340 and 370 mμ (log ε 3·89, 3·898, 4·127 and 4·106). $\lambda_{max}^{CHCl_3}$ 3·35 (m), 5·975 (s), 6·15 (vs), 6·375 (s), 6·6 (w), 6·8 (s), 7·1 (w), 7·3 (m), 7·45 (v.w), 7·825 (s), 8·2 (vs), 8·35 (vs), 8·725 (m), 9·075 (m), 9·725 (w), 10·925 (m), and 12·275 (m) μ.

1-*Acetyl*-3-*carboxy*-4H-*quinolizin*-4-*one* (II)

Mild hydrolysis of I (500 mg) by conc. HCl (2·5 ml) at 100° for 5 min yielded II (370 mg; 84%) as a water insoluble solid, m.p. 224°–227° from ethyl acetate. (Found: C, 62·27; H, 3·97; N, 6·06. $C_{12}H_9NO_4$ requires: C, 62·34; H, 3·90; N, 6·06%.) λ_{max}^{EtOH} 265, 350 and 395 mμ (log ε 3·939, 4·022 and 4·041). λ_{max}^{KBr} 3·0 (m), 3·3 (m), 5·825 (vs), 6·025 (s) 6·125 (s), 6·2 (vs), 6·375 (s), 6·63 (vs), 6·7 (vs), 7·0 (s), 7·175 (vs), 7·375 (vs), 7·65 (vs), 8·2 (vs), 8·4 (m), 8·9 (w), 9·225 (m), 9·525 (m), 9·9 (w), 10·6 (w), 11·2 (m), 11·45 (m), 12·045 (m), 12·8 (s), and 14·5 (w) μ.

Synthesis of 1-*nitro*-4H-*quinolizin*-4-*one* (V)

(a) 1-*Nitro*-3-*carbethoxy*-4H-*quinolizin*-4-*one* (IV). Conc. HNO_3 (30 ml) was added slowly to I (10 g). The reaction became exothermic and brown fumes evolved. The flask was cooled under the tap and the contents poured onto ice. The precipitated solid was filtered, and washed with EtOH to yield IV (6·2 g; 62%). It was recrystallized from ethyl acetate. m.p. 165·4°–166·4°. (Found: C, 55·34; H, 3·83; N, 10·55. $C_{12}H_{10}N_2O_6$ requires: C, 54·96; H, 3·83; N, 11·04%.) λ_{max}^{EtOH} 385 mμ (log ε 4·309). λ_{max}^{KBr} (up to 9 μ) 3·3 (m), 5·75 (vs), 5·825 (s), 6·15 (m), 6·325 (vs), 6·525 (s), 6·65 (vs), 6·75 (m), 7·00 (m), 7·325 (m), 7·45 (m), 7·55 (vs), 7·626 (vs), 7·725 (s), 8·1 (m), 8·4 (s) and 8·7 (m) μ.

(b) 1-*Nitro*-4H-*quinolizin*-4-*one* (V). Compound IV (400 mg) was refluxed with conc. HCl (20 ml) for 2 hr, the mixture was cooled, neutralized with solid Na_2CO_3, extracted with benzene (500 ml); the volume of benzene reduced to ca. 10 ml, the gummy portion removed and pet. ether was added to yield V (150 mg; 50%). After crystallization from benzene–pet. ether, the IR spectrum was identical with an authentic sample.*

Synthesis of 1,3-*diacetyl*-4H-*quinolizin*-4-*one* (VII)

A mixture of 2-pyridylacetone (6·65 g), freshly distilled ethyl ethoxymethyleneacetoacetate (9·3 g) and EtOH (20 ml) containing Na (100 mg) was kept overnight at room temp. The precipitated solid was filtered and recrystallized from EtOH, yield (4·5 g; 39%) m.p. 201·2°–202°. (Found: C, 68·46; H, 4·87; N, 6·13. $C_{13}H_{11}NO_3$ requires C, 68·10; H, 4·80; N, 6·1%.) λ_{max}^{EtOH} 270, 350 and 410 mμ (log ε 4·062, 4·164 and 4·326). $\lambda_{max}^{CHCl_3}$ 3·35 (m), 5·95 (s), 6·1 (vs), 6·675 (s), 6·75 (vs), 7·0 (w), 7·2 (w), 7·325 (s), 7·5 (m), 7·6 (w), 8·0 (m), 8·2 (m), 9·05 (w), 10·3 (w) and 10·85 (w) μ.

1,3-*Dinitro*-4H-*quinolizin*-4-*one* (VIII)

Compound VII (180 mg) was warmed for a few sec on a steam bath with conc. HNO_3 (*d* 1·42; 1 ml) with vigorous evolution of oxides of N_2. The solution was poured onto ice, the precipitated solid filtered, washed well with ice water and recrystallized from EtOH. The IR spectrum was identical with the earlier synthesized 1,3-dinitro-4H-quinolizin-4-one.

Synthesis of 3-*acetyl*-4H-*quinolizin*-4-*one* (XIX)

(a) 3-*Acetyl*-1-*carbethoxy*-4H-*quinolizin*-4-*one* (XVIII). Ethyl 2-pyridylacetate[11] (10 g) was mixed with a solution of freshly distilled ethyl ethoxymethyleneacetoacetate (18 g) in EtOH (20 ml) containing Na (280 mg). After a few min, a red solid began to form. After keeping the mixture overnight, the red solid was filtered off washed well with ice water and then with EtOH to yield a crystalline yellow material (13·5 g; 86%) which was recrystallized from benzene–pet. ether, m.p. 173·8°–174·2°. (Found: C, 65·06; H, 5·29. $C_{14}H_{13}NO_4$ requires: C, 64·86; H, 5·00%.) λ_{max}^{EtOH} 270, 345 and 410 mμ (log ε 4·214, 3·948 and 4·226). $\lambda_{max}^{CHCl_3}$ 3·35 (m), 5·9 (s), 6·05 (vs), 6·15 (s), 6·35 (s), 6·75 (vs), 7·0 (w), 7·15 (w),

* B. S. Thyagarajan and P. V. Gopalakrishnan (loc. cit.)

[11] N. N. Goldberg, B. M. Perfetti and R. Levine, *J. Amer. Chem. Soc.* **75**, 3843 (1953).

7.325 (s), 7·375 (s), 7·475 (s), 7·6 (m), 7·75 (s), 8·0 (m), 8·2 (broad), 8·8 (m), 9·1 (w), 9·55 (w) and 9·85 (s) μ.

(b) 3-*Acetyl*-4H-*quinolizin*-4-*one* (XIX). Compound XVIII (1 g) in conc. HCl (25 ml) was refluxed for ½ hr, the mixture cooled, neutralized with solid Na_2CO_3, extracted with benzene and the solvent removed to yield 600 mg of crude substance, m.p. 157°–167°. After two sublimations *in vacuo* (4 mm), 400 mg pure XIV was obtained, m.p. 184°–185°. It did not depress the m.p. of an authentic sample[12] and had an identical IR spectrum. λ_{max}^{EtOH} 260, 350 and 420 mμ (log ε 4·006, 3·599 and 4·33). λ_{max}^{KBr} 2·9 (m), 3·2 (m), 3·3 (m), 3·4 (m), 3·425 (m), 5·925 (vs), 5·975 (vs), 6·1 (vs), 6·15 (vs), 6·3 (vs), 6·525 (s), 6·625 (vs), 6·8 (vs), 6·9 (vs), 7·125 (s), 7·35 (vs), 7·7 (vs), 8·0 (s), 8·1 (m), 8·525 (w), 8·674 (s), 8·85 (s), 9·05 (s), 9·45 (s), 9·775 (s), 10.375 (vs), 11·5 (m), 12·1 (vs), 12·375 (s), 13·05 (vs) and 13·41 (w) μ.

3-*Acetyl*-1-*carboxy*-4H-*quinolizin*-4-*one* (XX)

To the warm alcoholic solution (10 ml) of XVIII (1 g), 5% NaOH aq (10 ml) was added. The solution was kept overnight in the refrigerator then acidified to congo red and the amorphous solid was filtered off washed with water and dried, yield (420 mg; 47%). It was recrystallized from EtOH, m.p. 252° with dec and gas evolution. (Found: C, 62·15; H, 4·09. $C_{12}H_9NO_4$ requires: C, 62·34; H, 3·9%.) λ_{max}^{EtOH} 260, 345 and 420 mμ (log ε 4·095, 3·645 and 4·112). λ_{max}^{KBr} (up to 9 μ) 2·9 (s), 3·2 (m), 3·3 (m), 5·85 (vs), 5·95 (vs), 6·15 (vs), 6·325 (s), 6·65 (vs), 6·95 (s), 7·1 (w), 7·25 (s), 7·4 (m), 7·5 (m), 7·75 (vs), 7·95 (vs), 8·1 (s) and 8·3 (s) μ.

3-*Nitro*-1-*carbethoxy*-4H-*quinolizin*-4-*one* (XXI)

Compound XIII (1 g) was warmed for a few sec on a steam bath with conc. HNO_3 (5 ml) or 1:1 HNO_3 (20 ml) for 5 min, cooled and poured onto ice. The precipitated solid was filtered off washed with ice water and dried, yield (700 mg; 70%). After recrystallization from acetone, it did not depress the m.p. of the earlier synthesized material.

1-*Nitro*-3-*carboxy*-4H-*quinolizin*-4-*one* (VI)

Compound IV (6 g) was suspended in EtOH (40 ml) and a solution of $NaHCO_3$ (6 g) in water (60 ml) was added. The mixture was kept on the water bath for 2 hr, the sodium salt of VI formed was dissolved in water and acidified to yield the free acid (4 g; 76%). It was recrystallized from EtOH m.p. 234°–235°. (Found: C, 50·91; H, 2·8. $C_{10}H_6N_2O_5$ requires: C, 51·24; H, 2·56%.) λ_{max}^{EtOH} 258 and 380 mμ (log ε 3·859 and 4·238). λ_{max}^{KBr} (up to 9 μ) 2·9, 3·2 (w), 5·775 (vs), 6·05 (s), 6·175 (vs), 6·325 (vs), 6·525 (vs), 6·625 (vs), 6·75 (m), 7·0 (vs), 7·1 (s), 7·45 (s), 7·65 (vs), 7·775 (s), 8·05 (s), 8·45 (m) 8·7 (s) μ.

1-*Nitro*-3-*bromo*-4H-*quinolizin*-4-*one* (X)

Compound VI (4 g) was suspended in acetic acid (20 ml) and liquid Br_2 (1 ml) added and the mixture gently heated to reflux. The course of the reaction was followed by the CO_2 evolved and collected. Actually, the theoretical amount of CO_2 evolved within 15 min. After heating for 15 min more, the green solution was poured onto ice pieces and the precipitated solid filtered off and recrystallized from EtOH, yield 1·5 g, m.p. 192°–193°. (Found: C, 40·15; H, 2·16. $C_9H_5N_2O_3Br$ requires: C, 40·15; H, 1·86%.) λ_{max}^{EtOH} 258 and 380 mμ (log ε 3·995 and 3·798). $\lambda_{max}^{CHCl_3}$ (up to 9 μ) 3·3 (w), 5·9 (s), 6·15 (m), 6·35 (s), 6·5 (s), 6·65 (s), 6·775 (m), 7·45 (m), 7·65 (vs), 7·8 (s), 7·975 (m), 8·7 (s) μ.

3-*Bromo*-1-*carbethoxy*-4H-*quinolizin*-4-*one* (XIV)

(a) *From* XIII *by brominative decarboxylation.* Compound XIII (4 g) was treated as for X with acetic acid (25 ml) and liquid Br_2 (1 ml). The mixture was refluxed for ½ hr, poured onto ice and the precipitated solid filtered off, yield 4 g; 87% and recrystallized from benzene, m.p. 148°–149°. (Found: C, 49·4; H, 3·45. $C_{12}H_{10}NO_3Br$ requires: C, 48·97; H, 3·39%.) λ_{max}^{EtOH} 263, 283, and 385 mμ (log ε 4·133, 3·904 and 4·244). $\lambda_{max}^{CHCl_3}$ (up to 9 μ) 3·3 (w), 5·875 (m), 5·987 (vs), 6·0375 (vs), 6·1375 (m), 6·35 (m), 6·575 (m), 6·775 (s), 7·3125 (m), 7·85 (s), 8·125 (s), 8·75 (m) μ.

[12] D. Leaver, W. K. Gibson and J. D. R. Vass, *J. Chem. Soc.* 6053 (1963). We are thankful to Dr. Leaver for authentic sample, for comparison.

(b) *From* XV. Treatment of XV with Br_2 in acetic acid at room temp yielded XIV.

(c) *From* XVI. Compound XVI (500 mg) was refluxed with a solution of liquid Br_2 (0·5 ml) in glacial acetic acid (5 ml) for 1 hr (as in the case of X). The mixture was poured onto ice, neutralized and extracted with benzene. The volume of benzene was reduced to a small amount and pet. ether added. The tarry material was decanted, more pet. ether added, the precipitated solid filtered off and recrystallized from benzene. This did not depress the m.p. of XIV obtained by method (a).

3-*Bromo*-1-*carboxy*-4H-*quinolizin*-4-*one* XVII

To a warm suspension of XIV (1 g) in EtOH was added 5% NaOH aq (10 ml) and the mixture kept overnight in the refrigerator. It was then acidified, the amorphous solid was filtered off and dried, yield quantitative, m.p. 225° from EtOH. (Found: C, 44·23; H, 2·18; N, 5·09, 5·13. $C_{10}H_6NO_3Br$ requires: C, 44·77; H, 2·24; N, 5·26%.) λ_{max}^{KBr} (up to 9 μ) 2·85, 3·2 (s), 5·925 (s), 6·0 (vs), 6·075 (vs) 6·15 (vs), 6·2 (s), 6·375 (s), 6·6 (s), 6·775 (s), 6·9 (m), 7·15 (m), 7·275 (s), 7·475 (m), 7·775 (m), 7·9 (m), 8·45 (vs), 8·75 (s) μ.

3-*Bromo*-1-*nitro*-4H-*quinolizin*-4-*one* (X) *from* XVII

Warming XVII (500 mg) with 1:1 HNO_3 (6 ml) on a water bath for a few sec and pouring onto ice yielded a crystalline solid (250 mg). After recrystallization from EtOH, it did not depress the m.p. of X.

1,3-*Dibromo*-4H-*quinolizin*-4-*one* (XII)

Compound XI (750 mg) was dissolved in acetic acid (20 ml) and liquid Br_2 (0·4 ml) added. The solution was gently refluxed for 1 hr, poured onto ice, neutralized with soda, the solid filtered, washed with water to remove the inorganic material and recrystallized from benzene–pet. ether to yield XII (350 mg), m.p. 161°–161·8°. (Found: C, 36·18; H, 1·35; N, 4·92. $C_9H_5NOBr_2$ requires: C, 35·64; H, 1·60; N, 4·62%.) λ_{max}^{EtOH} 255 and 415 mμ (log ε 4·418 and 4·392). $\lambda_{max}^{CH_2Cl_2}$ 6·02 (vs), 6·15 (vs), 6·45 (w), 6·6 (m), 6·85 (m), 7·52 (s), 8·3 (w), 9·09 (s), 9·43 (w), 9·76 (w), 10·85 (w), 12·2 (w) μ.

Bromination of 4H-*quinolizin*-4-*one*

(a) *With* Br_2 *in acetic acid.* To 4H-quinolizin-4-one (1·5 g) dissolved in glacial acetic acid (5 ml), a solution of Br_2 (0·8 ml) in acetic acid (5 ml) was added dropwise during 10 min at room temp. The mixture was poured onto ice and the solid filtered off washed and dried, to yield 1·9 g (70%). After recrystallization from benzene–pet. ether, this did not depress the m.p. of XII. The IR spectra were also superimposable.

(b) *With ethyl bromide in DMSO.*[18] A mixture of 4H-quinolizin-4-one (1·5 g), ethyl bromide (1·5 ml) and DMSO (15 ml) was kept overnight at room temp and then in an oil-bath at 110°–120° for 1½ hr. It was then poured onto ice, neutralized and extracted with benzene. The volume of benzene was reduced and pet. ether added till just turbid and left overnight in the refrigerator. The crystalline solid formed weighed 0·9 g, m.p. 132°–134°. It was once again recrystallized from benzene–pet. ether, m.p. 138·6°–139·6°. (Found: C, 48·73; H, 2·99; N, 6·37. C_9H_6NOBr requires: C, 48·21; H, 2·68; N, 6·25%.) λ_{max}^{EtOH} 250 and 400 mμ (log ε 4·794 and 4·94). λ_{max}^{KBr} 6·056 (s), 6·186 (s), 6·49 (m), 6·83 (s), 6·9 (m), 6·92 (m), 7·69 (s), 7·97 (m), 8·05 (w), 8·77 (w), 8·97 (m), 9·09 (s), 9·43 (w), 11·44 (w), 11·83 (w), 12·2 (w), 12·74 (s), 13·5 (m) and 14·5 (m) μ.

Nitration of IX

Compound IX (1·3 g) was dissolved in acetic acid (5 ml) and conc. HNO_3 (d 1·42; 4 ml) added slowly at room temp. It was then shaken for a few sec and poured onto ice. The precipitated solid (650 mg) was filtered, recrystallized twice from EtOH m.p. 192°–193°. This did not depress the m.p. of X and the IR Spectra were identical.

Reaction of 1,3-*dicarbethoxy*-4H-*quinolizin*-4-*one with ethyl-bromide in DMSO*

Treatment of XVI (1 g) with ethyl bromide (0·6 ml) in DMSO (10 ml) at 110°–120° for 1½ hr yielded quantitatively the starting material.

[18] [a] T. L. Fletcher and H. L. Pan, *J. Amer. Chem. Soc.* **78**, 4812 (1956);
[b] T. L. Fletcher, M. J. Namkung and H. L. Pan, *Chem. & Ind.* 660 (1957).

Conversion of 3-bromo-1-carboxy-4H-quinolizin-4-one to XII

Compound XVII (750 mg) was suspended in acetic acid (20 ml) and liquid Br_2 (0·2 ml) added. The solution was refluxed for ½ hr and poured onto ice. The greenish solid formed was filtered off and dried (350 mg). After recrystallization from pet. ether–benzene yielded 1,3-dibromo-4H-quinolizin-4-one identical with that obtained by bromination of 4H-quinolizin-4-one by Br_2 in acetic acid.

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