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3H-AZEPINES AND RELATED SYSTEMS. PART 4.[1] PREPARATION OF 3H-AZEPIN-2-ONES AND 6H-AZEPINO[2,1-b]QUINAZOLIN-12-ONES BY PHOTO-INDUCED RING EXPANSIONS OF ARYL AZIDES

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Summary: *Photolysis of a series of p-substituted phenyl azides (p-X-$C_6H_4N_3$; X= CO_2Me, CO_2Et, CN, CF_3, SO_2NH_2, CO_2CHPh_2, COMe, CHO, and NO_2) in 1:1 (v/v) THF-water solution produces, in the majority of cases, a 5-substituted-3H-azepine-2-one. In a like manner, 3H-azepin-2-one-3-carboxylates can be prepared from 5-substituted-2-azidobenzoates, providing the 5-substituent is electron-withdrawing.*

3H-Azepin-2-one mono- and di-carboxylic acids, the former in admixture with decarboxylated material, and 6H-azepino[2,1-b]quinazolin-12-ones, are obtained by irradiation of 2-azidobenzoic acid and of 5-azidoisophthalic acid, respectively. The mode of formation of the azepino-quinazolinones is discussed.

Photo-induced ring-expansion of aryl azides in amine solution is a well-established preparative route to 2-amino-3H-azepines (4).[2] Attempts to extend this photolytic process to the synthesis of other 2-substituted 3H-azepines have, in general, been unsuccessful.* For example, irradiation of aryl azides in THF-ammonia, THF-hydrogen sulphide,[7] and in thiols,[8] yield only triplet nitrene derived products i.e. amines and/or azo-compounds.[9]

However, in THF-alcohol (1:1; v/v) solution, aryl azides bearing an electron-withdrawing group (e.g. CO_2R, CONHR, CN), particularly at the ortho-position to the azide function, undergo photo-induced ring-expansion readily and in high yield to 2-alkoxy-3H-azepines.[10] Preliminary results[7] also indicate that photolytic ring-expansion to 3H-azepin-2-ones can be effected in aqueous-THF. Methyl 2-azidobenzoate, for example, under these conditions gives methyl 3H-azepin-2-one-3-carboxylate in 59% yield.

In this paper, we describe further examples of 3H-azepin-2-one formation, and also our attempts to prepare the little known 3H-azepine carboxylic acids, work which has led to a new synthesis of azepino-[2,1-b]quinazolin-12-ones.

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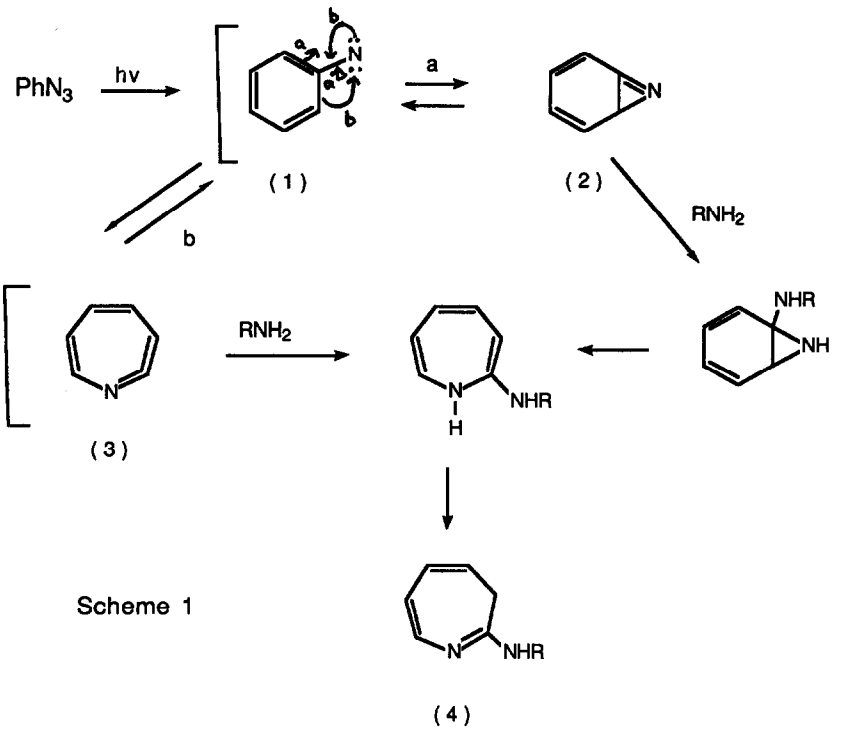
*Ring-expansions of aryl and heteroaryl azides by photolysis in strongly basic media (KOMe-MeOH-dioxan)[3] have been used extensively to prepare bicyclic azepines,[4] and more recently, di-,[5] and tri-[6] azepines.

Introduction

3H-Azepines (4) are thought[9] to be produced by addition of a nucleophile to the reactive imine bond of either a benzazirine (2) or a didehydroazepine (azacycloheptatetraene) (3) intermediate, which is in equilibrium with the initially formed singlet nitrene (1) (Scheme 1).



Scheme 1

(4)

Scheme 1

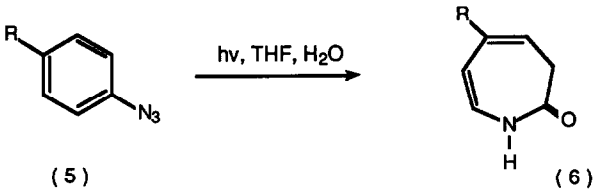
There is convincing spectroscopic evidence for the traditionally accepted benzazirine,[11] and for the 1,2-didehydroazepine, from low temperature matrix studies.[12,13] In addition, equally compelling spectroscopic evidence is available,[14] from gas-phase thermolysis studies on aryl azides, for the intermediacy of the seven-membered azacumulene (3). Much debate, however, has taken place over which of these two equally viable transient species is responsible for azepine formation under more moderate reaction conditions.

In a previous paper[7] we suggested that an electron-withdrawing group ortho- or para- to the azide is necessary for efficient azepine formation as it can stabilise a 1,2-didehydroazepine intermediate. Moreover, we also pointed out that this intermediate offers a more rational explanation for those isolated cases[7,15] in which 7- rather than 3-substituted 3H-azepines are formed. Subsequently, unequivocal evidence in support of didehydroazepines as the sole precursors of 3H-azepines during the photolysis of monocyclic aryl azides in the presence of diethylamine at ambient temperatures has been presented,[16] and the efficacy of an electron-withdrawing group on azepine production demonstrated. In accord with our previous work,[7] and with these

recent findings, we now report that the formation of 3H-azepin-2-ones by photolysis of aryl azides in aqueous-THF is also influenced by the nature of substituent groups and that best yields of azepinones are obtained when electron-withdrawing group are present at the ortho- and/or para position to the azide.

Results

Thus photolysis of a series of p-substituted azides (5a-j) in water-THF (1:1; v/v) over a period of hours (Table 1) furnished, in the majority of cases, a 5-substituted 3H-azepin-2-one (6).

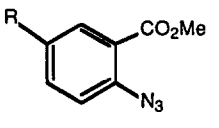


(5) (6)

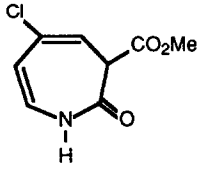
a) R = CO_2Me; b) R = CO_2Et; c) R = CN; d) R = CF_3; e) R = SO_2NH_2; f) R = CO_2CHPh_2; g) R = CO_2H; h) R = COMe; i) R = CHO; j) R = NO_2

Exceptions were the 4-acetyl (5h) and 4-formyl (5i) derivatives, which gave mainly amines and some tar (the usual indicators of triplet nitrene participation), and the p-nitro-azide (5j). The formation of azo-compound, rather than azepinone, from the nitro-azide was not surprising as nitro-azides are notorious in their resistance to ring-expansion to azepines. In fact, it is only recently that nitro-3H-azepines have been detected at low temperatures during the photolysis of p-nitrophenylazide in diethylamine,[16] and actually isolated in the case of m-nitrophenylazide.[17]

The detrimental effects on 3H-azepin-2-one formation of an electron-donating group para- to the azide function is emphasised by our results with 5-substituted 2-azidobenzoates (7). Whereas the unsubstituted azido-esters (5a,b) and the o-azido-ester described previously[7] gave 3H-azepin-2-ones in practicable yields, photolysis, in aqueous-THF, of the 5-acetamido- (7a), 5-morpholinyl- (7b), 5-methyl- (7c), and 5-methoxy- (7d) methyl esters gave only amines and/or azo-compounds along with some tar.

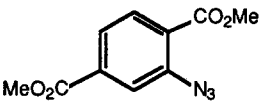


(7) a) R = NHAc
b) R = N-morpholinyl
c) R = Me
d) R = MeO
e) R = Cl



(8)

In contrast, the 5-chloro-derivative (7e) furnished the azepinone-3-carboxylate (8) in 45% yield, while irradiation of dimethyl 2-azidoterephthalate (9) (two-electron withdrawing groups) gave azepinone-dicarboxylate (10) in excellent yield (84%).



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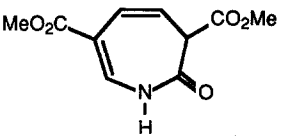
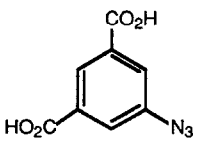


(10)

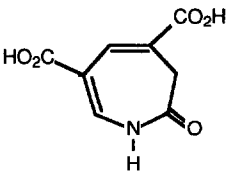
Of particular interest, were the photolyses of 2- and 4-azidobenzoic acid since previous attempts[10] to produce an azepine-carboxylic acid had failed. In fact, unlike their esters[10] and amides,[18] 3H-azepine-carboxylic acids are rare derivatives. 4-Methoxy-3H-azepin-2-one-5-carboxylic acid has been prepared by hydrolysis of the corresponding 2-methoxy-3H-azepine-5-carboxylate,[19] but as far as we are aware there is only one example of their production by ring-expansion of an azidoarene carboxylic acid.[16]

Unlike in our previous studies[10] on the photolysis of azido-acids in THF-alcohol solution, irradiation of p-azidobenzoic acid in water-THF was successful and gave 3H-azepin-2-one-5-carboxylic acid (6g) (36%). Its structure was confirmed by spectroscopic data (i.r., n.m.r., mass), and also by its conversion into the (diphenylmethyl) ester (6f), which was identical to the product obtained by photolysing p-azido-ester (5f) in aqueous-THF.

Interestingly, irradiation, in aqueous THF of 5-azidoisophthalic acid (11), in which the electron withdrawing groups are meta- to the azide function, was also successful and yielded the azepin-2-one dicarboxylic acid (12) (32%).



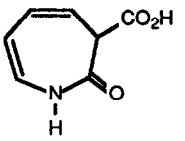
(11)



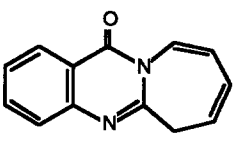
(12)

A more complex reaction was observed, however, on irradiating 2-azidobenzoic acid in THF-water. Flash chromatographic separation of the photolysate yielded three products, the major one of which (36%) proved to be 3H-azepin-2-one-3-carboxylic acid (13). Also isolated and characterised was the known[20]

decarboxylated material, 3H-azepin-2-one (6; R = H) (5%). The structure of the third, and minor product, was assigned, on the basis of mass and ^{1}H n.m.r. data, as the 6H-azepino[2,1-b]quinazolin-12-one (14). Derivatives of this tricyclic ring-system having a saturated azepine-ring are well known[21] and possess potent bronchodilatory activity.[22] However, we are aware of only one report,[23] on the synthesis of the parent unsaturated system (14).



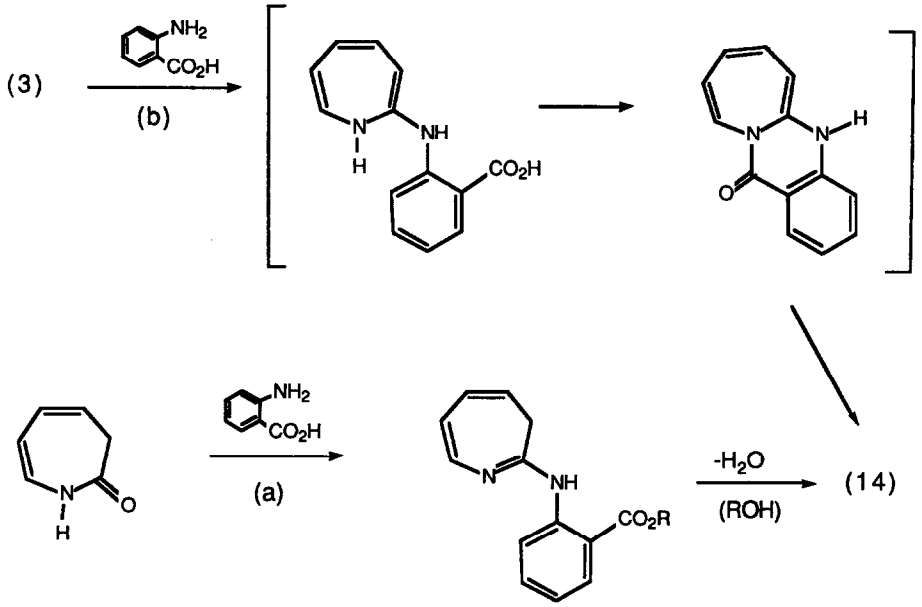
(13)



(14)

The formation of azepinoquinazolinone (14) must involve anthranilic acid, which is formed as by-product in the photolysis presumably as a result of hydrogen abstraction by the triplet nitrene derived from o-azidobenzoic acid.

The obvious route to tricycle (14) is that the anthranilic acid so-formed condenses directly with 3H-azepin-2-one (6; R = H) (or the azepinone-3-carboxylic acid followed by decarboxylation) (Scheme 2 - path a). An analogous condensation of anthranilic acid with 2-(n-butoxy)-3H-azepine is employed by Gompper and his coworkers[23] in their synthesis of azepino-quinazolinone (14).



(15) a) R = H; b) R = Me

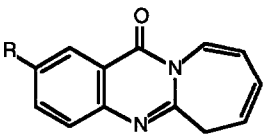
Scheme 2.

This route, was discounted, however, when all attempts to condense anthranilic acid with 3H-azepin-2-one, either under photolytic or thermal conditions, failed. Curiously, efforts to prepare azepinoquinazolinone (14), or its precursor the 2-amino-3H-azepine (15), by thermolysis of phenyl azide in methyl 2-aminobenzoate, were also unsuccessful.

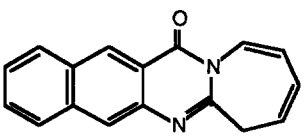
An alternative route to tricycle (14) (Scheme 2 - path b) is that anthranilic acid, formed at an early stage in the photolysis, competes successfully, as a nucleophile, with water for the didehydroazepine intermediate (3). Supporting evidence for this reaction pathway was obtained by irradiating 2-azidobenzoic acid in aqueous-THF containing added amounts of anthranilic acid. Increasing the molar ratio of anthranilic acid to 2-azidobenzoic acid brought about an increase in the yield of azepino-quinazolinone accompanied by a corresponding decrease in the amount of 3H-azepin-2-one-3-carboxylic acid. In fact with 2 equivalents of amino acid no 3H-azepinone or its acid derivative could be detected. Irradiation of o-azidobenzoic acid in THF with added anthranilic acid also gave the azepinoquinazoline (14) but the reaction was much less clean and resulted in some tarry by-products.

Subsequently, the generality of this procedure for preparing substituted azepinoquinazolinones has been demonstrated by irradiating, in aqueous-THF, not only o-azidobenzoic acid, but also other aryl azides bearing electron-withdrawing groups, in the presence of aromatic o-amino acids or -esters.

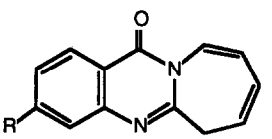
Thus, o-azidobenzoic acid in aqueous-THF containing 5-methyl-2-aminobenzoic acid, 4-nitro-2-aminobenzoic acid, dimethyl 2-aminoterephthalate or 3-amino-2-naphthoic acid, yielded the azepinoquinazolinones (16a), (18a,c), and (17), respectively. The reaction, however, failed with 5-nitro-2-aminobenzoic acid, presumably on account of the reduced nucleophilicity of this p-nitroamine.



(16) a) R = Me
b) R = Cl

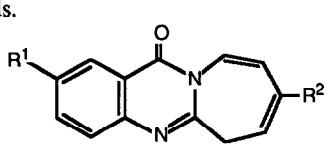


(17)

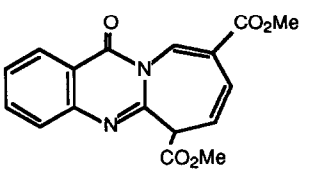


(18) a R = NO_2
b R = Cl
c R = CO_2Me

Likewise successful were the photolyses of 4-cyanophenyl azide and of dimethyl 2-azidoterephthalate in aqueous-THF containing anthranilic acid, which afforded azepino-quinazolinones (19a) and (20) respectively, albeit in low yields.



(19) a) R^1 = H, R^2 = CN
b) R^1 = H, R^2 = Cl
c) R^1 = Me, R^2 = Cl



(20)

The irradiation of 2-azidobenzoic acid in the presence of either 4-chloro-, or 5-chloro-2-aminobenzoic acid was odd in that, in both cases, unsubstituted azepinoquinazolinone (14) was obtained (10% and 25% yield) along with the expected chloro-derivatives (16b) (15%) and (8b) (5%) respectively. Presumably, anthranilic acid formed *in situ* from the triplet nitrene, is competing successfully as a nucleophile with the chloroamino-acids for intermediate (3).

More intriguing, are the results from the photolysis of 5-chloro-2-azidobenzoic in the presence of 2-amino- and 5-methyl-2-amino- benzoic acid. In each case, the expected chloroazepinoquinazolinones (19b,c) were formed but as minor products (4% and 8%), the major products being the dechlorinated derivatives (14; 25%) and (16a; 28%) respectively.

The loss of chlorine during azepine formation from aryl azides under thermal conditions has been noted previously,[24] and, more recently,[25] during the photolysis of fluoroazidobenzoates in diethylamine.

Attempts to extend these photo-reactions to the synthesis of other fused azepines so far have failed. For example, photolysis of o-azidobenzoic acid in the presence of ethyl β-aminocrotonate, 2-aminopyridine-3-carboxylic acid, or 2-aminobenzenesulphonic acid have yielded only parent azepino-quinazolinone (14) and much tar.

Experimental

I.r., mass, and ^{1}H n.m.r. spectra were measured on a Perkin-Elmer 1710 Fourier Transform Infrared spectrometer, a Finnegan 4000 mass spectrometer, and a Brucker AC 300 MHz n.m.r. spectrometer, respectively. I.r. spectra were recorded as nujol mulls, and ^{1}H n.m.r. spectra in $CDCl_3$ solution, unless stated otherwise. T.l.c. was conducted on Camlab. Polygram silica G/UV_{254} or alumina N/UV_{254} plates. Flash chromatography was carried out on silica gel 60 (Merck 9385), medium pressure column chromatography on silica gel 60 H (Merck 7736), and alumina column chromatography on neutral alumina Type H (B.D.H. Ltd.). Unless stated otherwise light petrol refers to the fraction of b.p. 60-80°C.

All m.p.'s are uncorrected.

Preparation of aryl azides: General method - In all cases, other than those described separately, the azides listed below were prepared by diazotisation of the corresponding commercially available amines in hydrochloric acid solution at 0-5°C, followed by azidation of the resulting diazonium chlorides with sodium azide in buffered (NaOAc) solution as described previously.[26] [CAUTION - all operations using sodium azide must be carried out in an efficient fume-cupboard. All azides are potentially explosive and should not be heated as the neat solid or liquid. All azide decompositions described in this paper were carried out in solution.] Aryl azides: methyl p-azido-benzoate (5a) (84%), m.p. 38°C (lit.[27] 39°C); ethyl p-azidobenzoate (5b) (88%), oil (lit.[28] b.p. 135°C/8 mmHg)]; p-cyanophenylazide (5c) (100%), m.p. 67°C (lit.[27] m.p. 70°C); p-trifluoromethylphenylazide (5d) (80%) oil , (lit.[29] b.p. 67°C/15 mm); 4-azido-p-toluenesulphonamide (5e) (98%), m.p. 114°C (lit.[28] 115°C); p-azidoacetophenone (5h), (90%), m.p. 39°C (lit.[30] 43°C); p-nitrophenyl azide (5j) (92%), m.p. 69°C (lit.[31], m.p. 73°C); p-azidobenzoic acid (5g) (96%), m.p. 181°C (lit.[32], 181°C); o-azidobenzoic acid (80%) m.p. 144°C (lit.[32] 144°C); 5-azidoisophthalic acid (11), m.p. 228°C (lit.[33] 230°C decomp.); 3-azido-2-naphthoic acid (80%) m.p. 180°C (lit.[7] 183°C). p-Azido-benzaldehyde (5i) was prepared by the method used for the synthesis of o-azidobenzaldehyde,[34] i.e. by reduction of p-aminobenzoic acid to p-aminobenzyl alcohol, m.p. 40°C (61%) with lithium aluminium hydride in diethyl ether; followed by diazotisation and azidation of the amino alcohol to

give p-azidobenzyl alcohol, yellow oil, (71%) ν_{max} (nujol) 3400 (OH), 2100 cm^{-1}. (N_3), which on oxidation furnished p-azidobenzaldehyde, oil, (63%), (lit.[35] oil) which was purified by flash chromatography (light petrol, b.p. 40-60°C)-EtOAc (9:1; v/v) as eluant. ν_{max} (liquid film) 2100 (N_3), 1695 (CHO) cm^{-1}.

Preparation of methyl 2-azido benzoates. - Dimethyl 2-azidoterephthalate (9) (75%; m.p. 76°C); methyl 5-chloro- (7e) (88%; m.p. 73°C) and methyl 5-methoxy- (7d) (66%; m.p. 39°C) benzoate were prepared as described previously.[10]

Methyl 5-methyl- (7c), and methyl N-acetyl-5-amino- (7a) 2-azidobenzoate were prepared from their respective amines[36,37] by the general method outlined for the aryl azides.

Methyl N-acetyl-5-amino-2-azidobenzoate (7a) (66%), m.p. 134°C; ν_{max} 3250, 3275 (NH), 2100 (N_3), 1700 (ester CO), 1680 (amide CO), cm^{-1}.

Methyl 5-methyl-2-azidobenzoate (7c), (69%), low melting solid; ν_{max} 2100 (N_3), 1710 (CO) cm^{-1}.

Methyl 5-(N-morpholinyl)-2-azidobenzoate (7b). - To a solution of methyl 5-chloro-2-nitrobenzoate (6 g; 27 mmol) in dimethyl formamide (40 ml) was added morpholine (3 g; 6.4 ml; 35 mmol) and the solution then heated at 100°C for 3.5 hours. Removal of the solvent under reduced pressure gave a yellow sticky residue, which on crystallisation from ethanol yielded methyl 5-(N-morpholinyl)-2-nitrobenzoate (6.9 g; 94%), m.p. 123-4°C as yellow needles; ν_{max} 1718 cm^{-1} ; δ ($CDCl_3$: 90 MHz), 8.05 (1H, d, 3-H), 6.9 (2H, m, 4-H, 6-H), 3.94 (3H, s, CH_3CO), 3.87 (4H, t, CH_2OCH_2), 3.38 (4H, t, CH_2NCH_2).

Reduction of the nitro-compound (4 g; 16 mmole) in methanol with H_2 and 10% Pd-C in a standard atmospheric hydrogenation apparatus gave the amine as a dark oil which on extraction with hot light petrol gave, on cooling, methyl 2-amino-5-(N-morpholinyl)benzoate (2 g; 58%) as pale yellow crystals, m.p. 95-98°C; ν_{max} 3450, 3350 (NH_2), 1695 (CO) cm^{-1}, which was used without purification.

Diazotisation of the amine (1.5 g) and azidation by the general method described for aryl azides gave methyl 2-azido-5-(N-morpholinyl)benzoate (7b) (1 g; 60%), m.p. 65°C as a pale brown solid: ν_{max} 2250 (N_3), 1720 (CO) cm^{-1}, which was used without further purification.

Diphenylmethyl 4-azidobenzoate (5f). - To a solution of 4-azidobenzoic acid (0.9 g; 5 mmol) in dry THF was added diphenyl diazomethane[38] (1.1 g; 5 mmole), and the mixture stirred overnight at room temperature. The solvent was removed under vacuum and the residue purified by column chromatography on alumina with light petrol - ethyl acetate (3:2) as eluant. Diphenylmethyl 4-azidobenzoate (1.5 g; 85%) was obtained as a pale-yellow solid m.p. 69.5-71.5°C ν_{max} (nujol) 2200 cm^{-1} (N_3), 1715 cm^{-1} (C=O).

Photolysis of Aryl azides (5a-i) and azido-esters (7a-e) in aqueous-THF - General method.

A solution of the azide (2 g) in water (115 ml) and THF (115 ml) was irradiated under nitrogen using a 400 watt medium pressure u.v. lamp (pyrex filter). The irradiation was continued until the azide had disappeared as indicated by examination of the photolysate by t.l.c. (Irradiation times are indicated in Table 1). When the reaction was complete, the solvent was removed under vacuum and the dark residue separated and purified by column chromatography either on alumina, or more commonly on silica (flash chromatography). Elution with

light petrol-ethyl acetate in some cases gave initially unchanged azide, accompanied by amino-compound. In other cases amino- and azo-compound were also obtained (see Table 1). 3H-Azepin-2-ones were obtained subsequently as solid products which were crystallised from a mixture of ethyl acetate and light petrol.

Physical and spectroscopic data for the 3H-azepin-2-ones are given in Tables 1 and 2.

Table 1 3H-Azepin-2-ones and methyl 3H-Azepin-2-one-3-carboxylates

azide	Azepinone (R)	Irradiation Time (h)	m.p. (°C)	Yield (%)	Found (%) C	H	N	Mol. formula	Required (%) C	H	N
(5a)	6a	20	112[a]	45	--	--	--	--	--	--	--
(5b)	6b	24	82	42	59.5	6.1	7.7	$C_9H_{11}NO_3$	59.65	6.1	7.7
(5c)	6c	24	115	60	62.6	4.5	20.9	$C_7H_6N_2O$	62.7	4.5	20.9
(5d)	6d	24	50	60	47.5	3.3	7.8	$C_7H_6F_3NO$	47.5	3.4	7.9
(5e)	6e	8	171[b]	32		--	--	--	--	--	--
(5f)	6f	26	154	25	74.9	5.5	4.4	$C_{20}H_{17}NO_3$	75.2	5.4	4.4
(5g)	6g	19	180	36	[c] ---	--	--	--	--	--	
(5h)	-- [d]										
(5i)	-- [e]										
(5j)	-- [f]										
(7e)	8	9	153	45	48.1	3.9	7.0	$C_8H_8ClNO_3$	47.7	4.0	6.9
(9)	10	10	138	84	53.0	4.8	6.2	$C_{10}H_{11}NO_5$	53.3	4.9	6.2

[a]Lit.[7] m.p. 113°C - also cited in ref. 40 but no data given.

[b]Lit.[39] m.p. 178°C.

[c]Analysed as diphenylmethyl ester.

[d]Azide (27%) and amine (14%) isolated.

[e]Only azide and amine recovered.

[f]4-Nitroaniline (19%) and 4,4'-dinitroazobenzene (30%) only products isolated.

Table 2 Spectral data for 3H-azepin-2-ones and methyl 3H-azepin-2-one-3-carboxylates (6a-f), (8) and (10).

Compound No.	NH	3-CH_2	4-H	6-H	7-H	Others
(6b)	8.7 s	2.95 (2H, d)	6.62 (t)	6.3 (d)	6.3 (d)	4.15 (2H, q, OCH_2) 1.25 (3H, t, CH_3)
(6c)	8.6 s	3.03 (2H, d)	6.23 (t)	5.87 (d)	6.35 (q)	---
(6d)	8.05 s	2.95 (2H, d)	6.09 (t)	5.88 (d)	6.35 (q)	---
(6e)[a]	10.08 d	2.89 (2H, d)	6.26 (t)	6.0 (d)	6.46 (q)	7.2 (2H, s, SO_2NH_2)
(6f)	7.6 d	3.03 (2H, d)	6.8 (t)	6.35 (d)	6.27 (q)	7.3 (m, Ar) 6.97 (s, C<u>H</u>Ph_3)
(6g)[a]	9.8 d	2.8 (2H, d)	6.45 (t)	6.11 (d)	6.27 (q)	
(8)	8.37 s	---	5.83 (d)	6.02 (q)	6.24 (q)	3.8 (3H, s, Me) 3.55 (1H, d, 3-CH)
(10)[a]	10.89 d		5.83 (dd)	---	7.24 (dd)	6.64 (1H, dd, 5-H) 3.33 (1H, s, 2 x Me) 3.67 (1H, d, 3-CH)

[a] in d^6-DMSO

<u>Diphenylmethyl 3H-azepin-2-one-3-carboxylate</u> (6f). - A solution of 3H-azepin-2-one-3-carboxylic acid (60 mg; 0.39 mmol) and diphenyldiazomethane (76 mg; 0.392 mmol) in dry THF (20 ml) was stirred overnight at room temperature. Removal of the solvent under vacuum gave a dark residue which was purified by column chromatography on alumina with light-petrol - ethyl acetate (2:8; v:v) as eluant, to yield ester (6f) (88%) as pale yellow needles, m.p. 154°C, which was identical (t.l.c.; i.r.; ^1H n.m.r.) with the azepinone ester obtained by photolysis of azido-ester (5f) in aqueous-THF.

<u>3H-Azepin-2-one-4,6-dicarboxylic acid</u> (12) - A solution of 5-azidoisophthalic acid (2 g; 96 mmol) in THF (115 ml) and water (115 ml) was irradiated, as described in the general method, for 15 hours. Removal of the solvent furnished a dark-brown residue which was purified by flash chromatography on silica (light petrol-EtOAc - 2:8; v/v) as eluant. <u>3H-Azepin-2-one-4,6-dicarboxylic acid</u> (0.6 g; 32%) was obtained as a pale-yellow solid, which crystallised from ethanol-light petrol, m.p. 225°C (decomp.). (Found: C, 48.8; H, 3.85; N, 6.9 $C_8H_7NO_5$ requires C, 48.9; H, 3.6; N, 7.1%); ν_{max} 3502, 3425, 3198, 3136 (NH and OH), 1668b (CO) cm^{-1}; δ_H 10.08 (1H, d, 1-H), 7.35 (1H, s, 5-H), 7.14 (1H, d, 7-H), 2.79 (2H, s, 3-CH_2).

<u>Photolysis of 2-azidobenzoic acid in Aqueous-THF</u>: - A solution of 2-azidobenzoic acid (1.5 g; 9.2 mmol) in THF (115 ml) and water (115 ml) was irradiated, as described in the general method, for 15 hours. Removal of the solvent, as previously, and flash chromatography of the dark residue on SiO_2, using light petrol-ethyl acetate (3:5; v/v) as eluant gave initially 6H-azepino[2,1-b]quinazolin-12-one (14), as a pale yellow solid (0.01 g) which recrystallised from light petrol - EtOAc m.p. 140.5°C (lit.[23], 139.5°C); ν_{max} 1663 cm^{-1} (C=O); δ_H 8.24 (1H, dd, 1-H); 7.66 (1H, m, 2-H); 7.61 (1H, d, 10-H); 7.58 (1H, d, 4-H), 7.42 (1H, m, 3-H); 6.28 (1H, dd, 9-H); 6.18 (1H, dd, 8-H); 6.0 (1H, dt, 7-H); 3.4 (2H, d, 6-CH_2); m/z 210 (M^+).

Further elution gave a trace of anthranilic acid, followed by 3H-azepin-2-one (0.05 g; 5%) as a pale yellow solid, m.p. 47°C (lit.[20] m.p. 47°C); ν_{max} 3225 (NH), 1670 cm^{-1} (C=O); δ_H 8.22 (1H, bs, NH); 6.16 (2H, dd, 6-H; 7-H); 5.79 (1H, dd, 5-H); 5.57 (1H, dt, 4-H); 2.87 (2H, d, 3-CH_2).

Finally, further elution gave 3H-azepin-2-one-3-carboxylic acid (0.5 g, 36%) as an orange solid, which was purified further by flash chromatography on silica using CH_2Cl_2-AcOH (95:5) as eluant; yellow crystals m.p. 144-5°C; ν_{max} 3200 (NH); 1710 (CO_2H); 1660 cm^{-1} (amide CO); δ_H (300 MHz; d^6-DMSO) 12.79 (1H, bs, OH); 10.06 (1H, d, NH); 6.23, (2H, m, 5-H, 6-H); 5.82 (1H, dd, 7-H); 5.72 (1H, dd, 4-H); 3.28 (1H, d, 3-H). Found: C, 55.3; H, 4.7; N, 8.9. $C_7H_7NO_3$ requires C, 54.9; H, 4.6; N, 9.1%: m/z 153 (M^+).

Photolysis of 2-azidobenzoic acid in aqueous-THF in the presence of anthranilic acid. - A solution of 2-azidobenzoic acid (2 g; 12 mmol) and anthranilic acid (1.64 g; 12 mmol) in water (115 ml) and THF (115 ml) was photolysed (15 h) and the photolysate worked up as directed in the general method for the photolysis of aryl azides. 6H-Azepino[2,1-b]quinazolin-12-one (1.25 g; 50%) was obtained unaccompanied by 3H-azepin-2-one or the 3-carboxylic acid derivative.

Varying the amount of added anthranilic acid (0, 0.25, 0.5 and 1 mole equivalents) brought about an increase of yield of (14) (1, 10, 22 and 50%).

Photolysis of a solution of 2-azidobenzoic acid and anthranilic acid in THF resulted in a dark photolysate which on work-up by the general procedure gave azepino[2,1-b]quinazolin-12-one (50%) accompanied by unidentified tarry products.

Photolysis of 2-azidobenzoic acids in aqueous-THF in the presence of other o-amino-acids. These photolyses were carried out under the same conditions described for the irradiation of 2-azidobenzoic acid in the presence of anthranilic acid.

a) In the presence of 3-amino-2-naphthoic acid (irradiation time - 15 h) 5H-azepino[2,1-b]benzo[g]-quinazolin-13-one (17) was obtained (1.25 g; 40%) as an orange-solid, which crystallised from light petrol-EtOAc, m.p. 181°C (lit.[23] 179°C). δ_H 8.88 (1H, s, 12-H), 8.04 (1H, s, 7-H), 8.01 (1H, d, 11-H), 7.9 (1H, d, 8-H), 7.64 (1H, d, 1-H), 7.0 (2H, m, 9-H and 10-H), 6.26 (1H, dd, 2-H), 6.18 (1H, dd, 3-H), 6.07 (1H, m, 4-H), 3.46 (2H, d, 5-CH_2); m/z 278 (M^+).

b) In the presence of 5-methyl-2-aminobenzoic acid (irradiation time - 15 h) 2-methyl-6H-azepino-[2,1-b]quinazolin-12-one (16a) was obtained (49%) as a yellow solid which crystallised from light petrol-EtOAc as pale yellow needles, m.p. 133°C. Found: C, 74.8; H, 5.2; N, 12.2. $C_{14}H_{12}N_2O$ requires C, 75.0; H, 5.4; N, 12.5%.

c) In the presence of dimethyl 2-aminoterephthalate (irradiation time - 15 h) methyl 6H-azepino[2,1-b]-quinazolin-12-one-3-carboxylate (18c) was obtained (52%), which crystallised from light petrol-EtOAc as white needles, m.p. 170°C. Found: C, 67.2; H, 4.6; N, 10.6: $C_{15}H_{12}N_2O_3$ requires C, 67.5; H, 4.5; N, 10.4%.

d) In the presence of 4-nitro-2-aminobenzoic acid (irradiation time 15 h.) 4-nitro-6H-azepino[2,1-b]-quinazolin-12-one (18a) was obtained (10%), which crystallised from light petrol - EtOAc as yellow needles, m.p. 127-33°C. Satisfactory elemental analysis was not obtained for this compound.

e) In the presence of 4-chloro-2-aminobenzoic acid (irradiation time - 13 h.) two products were obtained. Chromatographic separation of the crude residue, after removal of solvent, on alumina (light petrol-EtOAc - 1:1; v/v) gave an impure yellow solid which was re-chromatographed (flash) on silica using light petrol-EtOAc (3:7; v/v) as eluant. 3-Chloro-6H-azepino[2,1-b]quinazolin-12-one (16b) (15%) separated first which

crystallised from light petrol-EtOAc, m.p. 154°C. (Found: C, 63.9; H, 3.55; N, 11.4 $C_{13}H_9ClN_2O$ requires C, 63.8; H, 3.7; N, 11.45%).

Further elution gave 6H-azepino[2,1-b]quinazolin-12-one (10%), m.p. 140.5°C.

f) In the presence of 5-chloro-2-aminobenzoic acid (irradiation time - 13 h.) two products were again obtained which on repeated chromatographic separation as in (e) gave 2-chloro-6H-azepino[2,1-b]quinazolin-12-one (18b) (0.5%), which crystallised from light petrol-EtOAc as pale-yellow needles, m.p. 149.5°C. (Found: C, 63.7; H, 3.7; N, 11.3. $C_{13}H_9ClN_2O$ requires C, 63.8; H, 3.7; N, 11.45%). Further elution gave 6H-azepino-[2,1-b]quinazolin-12-one (14), m.p. 140.5°C, as the major product (25%).

g) Photolysis of 5-chloro-2-azidobenzoic acid in the presence of 2-aminobenzoic acid (irradiation time - 13 h.) gave a mixture of products which were separated by column chromatography as in (e) and (f). 8-Chloro-6H-azepino[2,1-b]quinazolin-12-one (19b) was obtained (4%) which crystallised from light petrol-EtOAc as pale yellow needles, m.p. 170°C (Found: C, 63.7; H, 3.75; N, 10.75. $C_{13}H_9ClN_2O$ requires C, 63.8; H, 3.7; N, 11.45%).

The major product (25%) was 6H-azepino[2,1-b]quinazolin-12-one (14).

h) Photolysis of 5-chloro-2-azidobenzoic acid in the presence of 5-methyl-2-aminobenzoic acid (irradiation time - 13 h.) also gave a mixture of products which were separated by column chromatography as in (e) and (f). 8-Chloro-2-methyl-6H-azepino[2,1-b]quinazolin-12-one (19c) was obtained in (8%) which crystallised from light petrol-EtOAc as white needles, m.p. 160°C (Found: C, 64.9; H, 4.20; N, 10.3 $C_{14}H_{11}ClN_2O$ requires C, 65.0; H, 4.3; N, 10.8%).

The major product (28%) was again the azepinoquinazolinone (14).

i) Photolysis of 4-cyanophenyl azide in the presence of 2-aminobenzoic acid (irradiation time - 24 h. with a 125 watt u.v. lamp) gave 8-cyano-6H-azepino[2,1-b]quinazolin-12-one (19a) (15%) which crystallised from light petrol-EtOAc as white needles, m.p. 177°C (Found: C, 71.6; H, 3.9; N, 18.1 $C_{14}H_9N_3O$ requires C, 71.5; H, 3.85; N, 17.9%).

j) Photolysis of dimethyl 2-azidoterephthalate in the presence of 2-aminobenzoic acid gave dimethyl 6H-azepino[2,1-b]quinazolin-12-one-6,9-dicarboxylate (20) (4%) which crystallised from light petrol-EtOAc, as white crystals, m.p. 160°C (Found: C, 62.9; H, 4.4; N, 8.8 $C_{17}H_{14}N_2O_5$ requires C, 62.6; H, 4.3; N, 8.6%).

Spectral data for the azepinoquinazolinones are given in Table 3.

Photolysis, under the general conditions already described of 2-azidobenzoic acid in the presence of 5-nitro-2-aminobenzoic acid gave only tarry products; likewise with 4-azidobenzoic acid in the presence of 2-aminobenzoic acid, and with 2-azidobenzoic acid in the presence of methyl β-aminocrotonate, 2-aminobenzene-sulphonic acid, and 2-aminopyridine-3-carboxylic acid. In each of the last three cases anthranilic acid was isolated along with tarry products.

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Table 3 Spectral data (I.r., ^{1}H n.m.r., mass) for azepino[2,1-b]quinazolin-12(6H)-ones

Compound	^{1}H n.m.r.										I.r.	m/z
	1-H	2-H	3-H	4-H	6-CH_2	7-H	8-H	9-H	10-H	Other	ν_{max} cm^{-1}	(EI)
(16a)	8.04 d	--	7.51 dd	7.61 d	3.38 d	6.0 m	6.17 dd	6.26 dd	7.46 d	2.13 (3H, s, Me)	1680 (CO)	M^+ 224
(18c)	8.29 d	8.01 dd	--	8.25 d	3.41 d	6.03 m	6.19 dd	6.31 dd	7.4 d	3.93 (3H, s, OMe)	1726 (CO_2R) 1686 (CON)	M^+ 268
(18a)	8.41 d	8.17 dd	--	8.42 d	3.43 d	6.04 m	6.23 dd	6.37 dd	7.61 d	--	1688 (CO)	M^+ 255
(18b)	8.15 d	7.36 dd	--	7.56 d	3.38 d	6.01 m	6.20 dd	6.31 dd	7.59 d	–	1680 (CO)	M^+ 244, 246
(16b)	8.19 d	--	7.61 dd	7.51 d	3.38 d	6.01 m	6.19 dd	6.31 dd	7.58 d	–	1680 (CO)	M^+ 244, 246
(19b)	8.27 dd	7.72 m	7.4 m	7.58 dd	3.40 d	6.08 t	--	6.21 d	7.66 d	–	1680 (CO)	M^+ 244, 246
(19c)	8.04 d	--	7.51 dd	7.51 d	3.40 d	6.0 t	--	6.20 d	7.65 d	2.46 (3H, s, Me)	1680 (CO)	M^+ 258, 260
(19a)	8.25 dd	7.78 m	7.47 m	7.71 dd	3.56 d	6.78 t	--	6.24 d	7.57 d	–	2225 (CN), 1690 (CO)	M^+ 235
(20)	8.27 dd	7.74 m	7.47 m	6.7 dd	--	6.45 dd	7.60 d	--	8.71 s	3.87 (3H, s,OMe) 3.85 (3H, s, OMe) 4.13 (1H, d, 6-H)	1751, 1724 (CO_2R); 1698 (CON)	M^+ 326

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