1,3-Dipolar Cycloadditions, 101[1]

# Isoquinolinium *N*-Arylimides and Some Cycloadditions to Heterocumulenes☆

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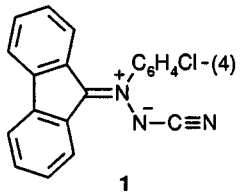
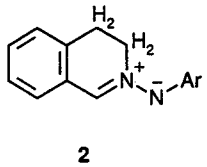
The red isoquinolinium *N*-arylimides **19**–**23** are azomethine imines of which the C=N bond is part of an aromatic ring. The *N*-(4-nitrophenyl)imide **22** and the *N*-(2-pyridyl)imide **23** were obtained crystalline; in solution the latter equilibrates with the hexahydrotetrazine **24** as its dimer. The *N*-phenylimide **19** is not stable; an isolated solid appears to be a tetramer. Generated by deprotonation of **11**–**13**, the *N*-arylimides **19**–**21** undergo *in situ* cycloadditions to carbon disulfide, phenyl isocyanate, phenyl isothiocyanate, and diphenylketene. The storable $CS_2$ adduct **29** offers a neutral source of the *N*-phenylimide **19**, since a cycloreversion equilibrium is established in solution.

## Introduction

When the general concept of 1,3-dipolar cycloaddition reactions was conceived in 1960, azomethine imines belonged to the first touchstones for testing the synthetic utility[2]. In the crystalline azomethine imine **1**, the 1,3-dipolar system is stabilized by substituents, but is not part of an aromatic system[3]; it easily combines with olefinic and acetylenic dipolarophiles furnishing pyrazolidines and 3-pyrazolines, respectively[4]. The deeply colored, but not isolable 3,4-dihydroisoquinolinium *N*-arylimides (**2**) display an unusual 1,3-dipolar activity[5][6].



**1**



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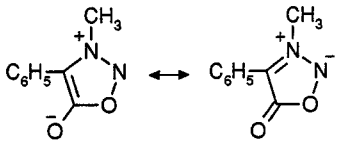

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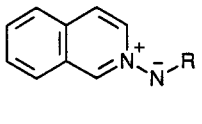


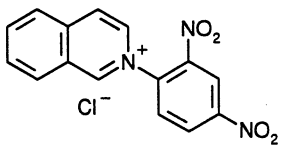
**4**

In sydnones (*e.g.*, **3**) the azomethine imine system is *in toto* embedded in the mesoionic aromatic ring; nevertheless, it combines with CC double and triple bonds to bicyclic intermediates which eliminate $CO_2$ and afford 2-pyrazolines and pyrazoles, respectively, in high yields[7][8]. In the isoquinolinium *N*-imides **4** the C=N double bond of the azomethine imine is involved in the aromatic heteroring. The – at least transitory – loss of aromaticity in the course of the cycloadditions of **4**, R = H, leads to a decrease of 1,3-dipolar activity[9], compared with nonaromatic types. Whereas the zwitterions **4**, R = H[9] and R = $CH_3$[10] occur in small equilibrium concentrations alongside of dimers, the *N*-acylimides **4**, R = CO–R′ are stable in the monomeric state[9][11][12].

The investigation of cycloadditions of **4**, R = Ar, began in 1960 and was interrupted for longer periods[13]. Since its discovery, the chemistry of azomethine imines has been repeatedly reviewed[14], sometimes with emphasis on heteroaromatic *N*-imides[15][16].

## Preparation of 2-(Arylamino)isoquinolinium Salts

The classic *Zincke cleavage* of the pyridine ring affording derivatives of glutaconaldehyde was applied to isoquinoline by Zincke and Weisspfenning[17]. In the treatment of *N*-(2,4-dinitrophenyl)isoquinolinium chloride (**5**) with phenylhydrazine, addition of 1 equiv. of triethylamine for the binding of HCl saves a second equiv. of phenylhydrazine[18]. We obtained the black crystalline enaminohydrazone **6** in 73%



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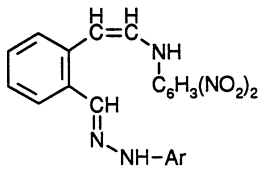

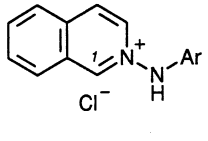

| | | |
|---|---|---|
| **6** | Ar = $C_6H_5$ | **11** |
| **7** | $C_6H_4CH_3$-(4) | **12** |
| **8** | $C_6H_4Cl$-(4) | **13** |
| **9** | $C_6H_4NO_2$-(4) | **14** |
| **10** | $C_5H_4N$-(2) | **15** |

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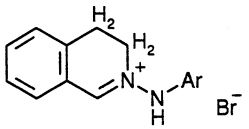
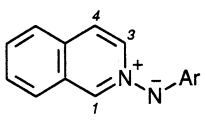
yield on the 100-g scale. The cyclization of **6** by HCl in aqueous ethanol furnished 85−91% of 2-(anilino)isoquinolinium chloride (**11**) besides 2,4-dinitroaniline. The same procedure provided the chlorides **12**−**15** via **7**−**10**. In the $^1$H NMR spectra of **11**−**15** ($CH_3OD$) the 1-H was observed at lowest field (δ = 10.13−10.24).

We opened a further pathway to the 2-(arylamino)isoquinolinium salts by dehydrogenation of the dihydro compounds **16**−**18** which were prepared by the procedure of Schmitz from 2-β-bromoethylbenzaldehyde and arylhydrazines[19][6]. The reaction of **16**−**18** with 2 equiv. of nitrosobenzene in DMF at room temp. is exothermic and produced **11**, **13**, and **14**, $Br^-$ instead of $Cl^-$, in yields of 74−80%.

### Properties of Isoquinolinium *N*-Arylimides

Formula **19** (in 1913 with pentacovalent nitrogen) was ascribed to a "deep-red amorphous solid" which Zincke and Weisspfenning obtained from **11** and aqueous alkali; **11** was regenerated with hydrochloric acid[17].

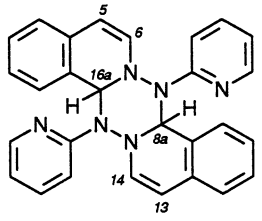




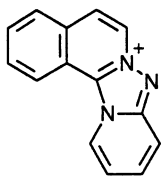
**16** Ar = $C_6H_5$
**17** $C_6H_4Cl$-(4)
**18** $C_6H_4NO_2$-(4)

**19** Ar = $C_6H_5$
**20** $C_6H_4CH_3$-(4)
**21** $C_6H_4Cl$-(4)
**22** $C_6H_4NO_2$-(4)
**23** $C_5H_4N$-(2)

We found the *N*-(4-nitrophenyl)imide **22** being capable of short-time existence as carmine crystals which were characterized by spectra and elemental analyses. The $^1$H NMR signals are high-field shifted, compared with **14**, *e.g.*, δ = 9.22 *vs.* 10.24 for 1-H. The lifetime of **22** was smaller in dichloromethane than in DMSO; after 30 min the $^1$H NMR signals of the zwitterion **22** were replaced by broad bands, but the solution still showed 1,3-dipolar reactivity.



**24**



**25**

The *N*-(2-pyridyl)imide **23** was casually mentioned by Beyer and Thieme[18]. We obtained it in red-orange needles (91%) which showed in $CDCl_3$ the doublet of 1-H at $\delta_H$ = 10.58 and the dd of 3-H at 8.24, both allyl-coupled with $J_{1,3}$ = 1.8 Hz. We interpret a new AX spectrum at δ = 5.43 and 6.22 as the vinylic protons of the hexahydrotetrazine **24**; within several hours a dimerization equilibrium of **23** is attained. It is this kind of dimerization which was previously established for **4**, R = H, $CH_3$[9][10]. The dimer **24** is conceivable in a *cis* ($C_2$) or a *trans* structure ($C_i$) with respect to 8a-H and 16a-H. The occurrence of only *one* AX spectrum for 5-H/6-H (13-H/14-H) argues for the presence of *one* form.

Qualitatively, the mobility of the dimerization equilibrium was demonstrated by the cycloaddition of the monomer to dimethyl fumarate; after several days, **23** and **24** have disappeared, and adduct formation is complete. The $^1$H NMR spectrum established the quantitative aspects. Specific signals allowed to monitor the equilibration at 25°C in $CDCl_3$:

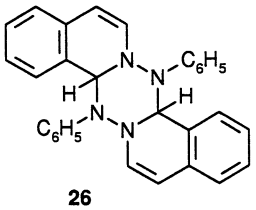
| time | 0 | 400 min | 25 h | 32 h | 97 h |
|---|---|---|---|---|---|
| **23** | 0.906 M | 0.576 M | 0.402 M | 0.394 M | 0.391 M |

The last value provided $K_{ass}$ = 1.7 $M^{-1}$, *i.e.*, in 1 M **23** 58% will be dimeric. The approach to the equilibrium is controlled by the integrated rate eq. 2 (see Experimental Section). A provisional value, $k_2 = 3 \cdot 10^{-5}$ $M^{-1}s^{-1}$, comes from the concentration after 400 min. The addition of triethylenediamine did not influence the rate in $CDCl_3$, but a trace of 4-toluenesulfonic acid strongly accelerated.

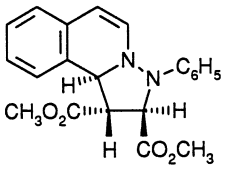
The dimer **24** was isolated in red-brown prisms with about 6% of the monomer **23** still admixed. Our hope of determining the thermodynamic parameters of the equilibrium from the temp. dependence of the Vis spectrum was thwarted by the lack of constancy of the extinction.

The MS of the dimer **24** shows a peak for $M^+ - 2$ H (*m*/*z* = 440, 8%); a strong signal at *m*/*z* = 220 (84%, $\mathbf{23}^{+\bullet} - H$) is tentatively assigned to the aromatic cation **25**, the result of an electrocyclization of $\mathbf{23}^{+\bullet}$ and loss of a H-atom. Base peak is isoquinoline$^{+\bullet}$. In the MS of pyridinium *N*-acylimides, Ikeda et al. likewise found $[M - H]^+$, usually as the base peak[20].

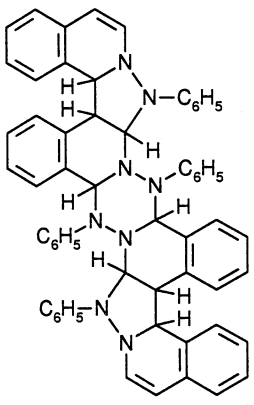
In the case of isoquinolinium *N*-imide (**4**, R = H), the dimer of the hexahydrotetrazine type dominated to such an extent in the equilibrium, that the monomer no longer appeared in the spectra[9][21]. The *N*-phenyl in **19**, the *N*-(2-pyridyl) in **23** and the *N*-acyl in **4**, R = R′CO, increasingly stabilize the zwitterion. A gradual decrease of the oligomerization and dimerization tendency is expected.



**26**



**27**



**28**

When sodium carbonate was added to the aqueous solution of **11**, the red amorphous isoquinolinium *N*-phenylimide (**19**) precipitated and was isolated *via* its solution in $CCl_4$. On triturating the deep-red evaporation residue with petroleum ether, it was slowly converted into a light-red-brown microcristalline powder with the C,H analyses of **19**. The molecular mass, determined by vapor phase osmometry in benzene, suggested a *tetramer* of **19**. The $^1$H NMR spectrum ($CDCl_3$, 60 MHz) of the fresh solution was not fully resolved, but the characteristic AX type of 1,2-dihydroisoquinolines at $\delta$ = 5.26 and 6.13 with $J$ = 7.8 Hz (ene-hydrazine bond) was clearly discernible. The high signal density could well originate from a mixture of diastereoisomers, possibly with participation of further oligomers. The IR absorption at 1618 $cm^{-1}$ is consistent with the C=C of the ene-hydrazine group.

We assume that **19** dimerizes to a pentacyclic hexahydrotetrazine **26**; the ene-hydrazine double bonds act as dipolarophiles and accept two further molecules of **19**, forming the undecacyclic tetramer **28**. There is little doubt about the regiochemistry of these 1,3-cycloadditions; it is the exclusive addition direction of **19** to various types of enamines[22].

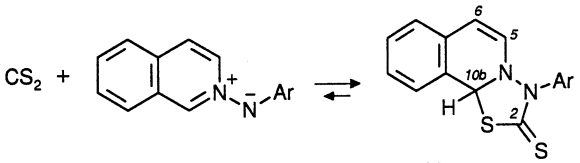
The whole tetramerization is reversible. The deep-red color of the solution of **28** in warm dichloromethane suggests dissociation. According to the $^1$H NMR spectrum, **28** combined slowly, but completely, with dimethyl fumarate furnishing adduct **27**.

A storable azomethine imine is not a prerequisite to the successful application in cycloadditions. The stable isoquinolinium salts **11**–**14** served as precursors. The 1,3-dipoles **19**–**22**, precipitated with base in aqueous medium, were transferred to dichloromethane; the washed and dried solutions were reacted with dipolarophiles. In the case of slow cycloadditions, it was advantageous to suppress the oligomerization of **19**–**22** by a low stationary concentration of the 1,3-dipoles. The dipolarophile was added to the stirred suspension of the salts **11**–**14** in dichloromethane; the dropwise introduction of 1.1 equiv. of triethylamine was so regulated that the red color of the active species did not become intense. Subsequently, the triethylammonium chloride and the excess of triethylamine was extracted by water, and the cycloadduct was isolated from the organic phase.

Acid-catalyzed rearrangements of the 1,3-cycloadducts will be discussed in the following papers. Some were even induced by the salts **11**–**14** and triethylammonium chloride. The reversibly formed carbon disulfide adducts offered a neutral source of isoquinolinium *N*-arylimides.

### Carbon Disulfide Adducts

When the *N*-phenylimide **19**, precipitated in water by alkali, was extracted into carbon disulfide, the yellow $CS_2$ adduct **29** crystallized from the organic phase at −10°C in 86% yield. The solution of **29** in $CS_2$ is at room temp. yellow-brown and becomes red at the boiling point. The red color occurs *at room temp.* in all other solvents, revealing a partial cycloreversion. The deep-red solution in chloroform (0.35 M **29**) showed broad absorptions at 470 and 405 nm which indicate some *N*-phenylimide **19**. The $^1$H NMR spectrum is essentially that of **29**. The mobility of the equilibrium is extraordinary and offers another demonstration for the *superdipolarophilic* character of the C=S double bond[23].




**19** Ar = $C_6H_5$ **29**
**20** $C_6H_4CH_3$-(4) **30**

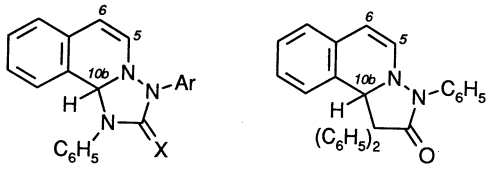
The regiochemistry assumed for **29** is based on the analogy with the $CS_2$ adduct of 3,4-dihydroisoquinolinium *N*-phenylimide (**2**, Ar = $C_6H_5$) where the reduction with lithium aluminium hydride established the structure[6]. The singlet of 10b-H occurrs at $\delta_H$ = 6.93; C-10b is found at $\delta_C$ = 71.5 and C-2 (thiocarbonyl) at 192.2 ppm. According to NMR and IR spectra, the C=C double bond of the ene-hydrazine type is intact.

The *N*-(*p*-tolylimide) **20** was converted to the light-yellow needles of the thiadiazole-2-thione **30**, but the *N*-(4-nitrophenyl)imide **22** and the *N*-(2-pyridyl)imide **23** failed to give $CS_2$ adducts; the stabilization of the negative charge by the substituents shifts the equilibria to the side of the reactants.

The crystalline $CS_2$ adducts **29**, **30** can be stored; they are suitable for the preparation of sensitive cycloadducts in inert solvents. As in the triethylamine procedure described above, the stationary concentration of the active species is small, here with the advantage of an acid-free medium. Cycloadditions to very active dipolarophiles can be carried out as titrations using the change of color from red to pale-yellow as an indicator.

### Further Heterocumulenes as Dipolarophiles

The addition of the *N*-phenylimide **19** to phenyl isocyanate in moist ether was completed in 2 min and afforded 87% of the colorless triazolidone **31a**. Catalytic hydrogenation furnished *N*,*N*′-diphenylurea and isoquinoline; the hydrogenolysis of the N−N bond was followed by β-elimination.




**31** Ar = $C_6H_5$ **33**
**32** $C_6H_4Cl$-(4)

**a** X = O, **b** X = S

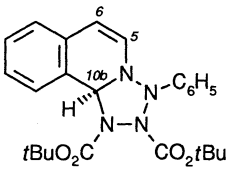
On warming the benzene solution of **31a**, the red color indicated a regeneration of **19**. Reaction of **31a** with aniline in hot benzene as well as refluxing with 90% dioxane/water produced *N*,*N*′-diphenylurea; the phenyl isocyanate set free by cycloreversion reacted with aniline or water. The anal-

ogous adduct **32a** was isolated in 99% yield. The $^1$H NMR data of 5-H/6-H signaled the untouched ene-hydrazine system.

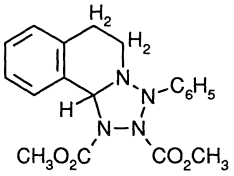
According to the color change, the cycloaddition of **19** and **21** to phenyl isothiocyanate was slower. The structure of **31b** and **32b** was based on the analogy with the cycloadducts of **2**, where the regiochemistry was established[6].

The red solution of the $CS_2$-adduct **29** in dichloromethane was immediately decolorized on addition of diphenylketene, and 84% of the pale-yellow pyrazolidone **33** was obtained. The lactam carbonyl and the 5,6 double bond are responsible for IR absorptions at 1710 and 1636 $cm^{-1}$.

Both termini of 1,3-dipoles are ambivalent[24], a phenomenon, which does not exclude a strong predominance of *one* charge distribution pattern. The aromaticity of the isoquinolinium ion in **19**−**23** predestinates the imide nitrogen to be the nucleophilic center of these 1,3-dipoles.




**34**




**35**

### Azodicarboxylic Ester

Tetrazoles and pentazoles demonstrate the readiness of NN bonds to participate in *aromatic* ring systems. Tetrazolidines, however, are rare. The red solution of **19** was decolorized within seconds by di-*tert*-butyl azodicarboxylate. The crystalline **34** was sufficiently stable for procuring elemental analyses and spectroscopic data. The 10b-H occurs at $\delta_H = 6.07$ and the enamine type NMR pattern confirms the structure. The pink solutions of **34** in chloroform or benzene reversibly turned red on warming. The cycloaddition/cycloreversion equilibrium renders the tetrazolidine structure of **34** highly probable, unlike the cycloadduct of benzonitrile oxide to azodicarboxylic ester which enters into a cascade of subsequent rearrangements[25]. Adduct **35**, obtained from **2**, Ar = $C_6H_5$, and dimethyl azodicarboxylate, was probably the first representative of a tetrazolidine[6].

We express our gratitude to the *Fonds der Chemischen Industrie*, Frankfurt, for support. Our thanks are going to *Helmut Huber* for his help in the spectroscopic measurements, and to *Helmut Schulz* and *Magdalena Schwarz* for the elemental analyses.

## Experimental Section

*General*. IR: Perkin-Elmer 125. − UV-Vis: Zeiss RPQ 20C. − NMR: Varian A60 for $^1$H (60 MHz) and Varian XL 100 for $^{13}$C (25.2 MHz). TMS as internal standard; $CDCl_3$ stored over dry $K_2CO_3$. Evaluation by first order, if not otherwise stated (*e.g.*, AB). − MS: AEI, Manchester, MS 902. − Mol.mass: Mechrolab vapor phase osmometer. − Melting points are uncorrected.

### 2-Arylaminoisoquinolinium Salts

*2-Anilinoisoquinolinium Chloride* (**11**)[17]. − *Modified Procedures:* (a) *N*-(2,4-Dinitrophenyl)isoquinolinium chloride (**5**, 116.1 g, 350 mmol)[17] was dissolved in 2 l of hot ethanol. A mixture of 37.9 g (350 mmol) of freshly distilled phenylhydrazine, 36.4 g (360 mmol) of triethylamine, and 100 ml of ethanol was slowly introduced into the stirred solution of **5** at room temp.; the precipitation of crystals from the dark-red solution started after a few s. With continued stirring, the reaction mixture was heated for about 10 min on the steam-bath, until the sticky precipitate was converted to fine crystals. After warm filtration, the hydrazone **6** was successively washed with highly dilute HCl (pH 5), ethanol, and ether. We obtained 103.1 g (73%) of black glistening needles, m.p. 179−181°C (pure, m.p. 183−184°C[17]). Without further purification, **6** was dissolved in 900 ml of ethanol and 250 ml of aqueous conc. HCl by warming on the steam-bath for 20 min. The cooled solution was poured into 3 l of water; the thick yellow precipitate of 2,4-dinitroaniline was filtered after storing overnight, and washed with 30%-ethanol. The yellow-brown filtrate was concentrated (10 Torr) to 500 ml; after filtering of additional 2,4-dinitroaniline and evaporation to dryness, the yellow residue was dissolved in little ethanol. After cooling, chloride **11** was slowly precipitated by addition of ether. The crystalline yellow powder was dried over KOH: 55.7 g (85%) of **11** with m.p. 203−204°C (dec.; 198−200°C[17]). − $^1$H NMR ($CH_3OD$): δ = 6.82−7.48 (m, $C_6H_5$), 7.92−8.63 (m, 3-H − 8-H), 10.16 (s, broadened by allyl coupling, 1-H).

(b) A modification avoids the evaporation of large volumes of water. Hydrazone **6** (110 g, 0.27 mol) was added in portions while stirring and warming the mixture of 1 l of methanol and 100 ml of conc. HCl until solution was complete. After cooling, the solvent was evaporated, the residue triturated with 500 ml of acetone, and stored for 1 d. Filtering, washing with acetone and drying on air afforded 63.4 g (91%) of **11**.

*2-(p-Toluidino)isoquinolinium Chloride* (**12**): **5** was treated with 4-tolylhydrazinium chloride and 2 equiv. of triethylamine. Hydrazone **7** (83%), recrystallized from acetone, had m.p. 184−185°C (185−186°C[17]). Chloride **12** (76%) came from ethanol/ether; m.p. 179−181°C (dec., red). − $^1$H NMR ($CH_3OD$): δ = 2.26 (s, $CH_3$), 6.88−7.13 (AA′BB′, $C_6H_4$), 7.92−8.48 (m, 4-H−8-H), 8.57 (dd, $J_{3,4}$ = 6.5 Hz, 3-H), 10.13 (d, $J_{1,3} \approx 1$ Hz, 1-H). − $C_{16}H_{15}ClN_2$ (270.8): calcd. C 70.97, H 5.58, N 10.35; found C 70.98, H 5.74, N 10.28.

*2-(4-Chloroanilino)isoquinolinium Chloride* (**13**)[26]: Hydrazone **8**, 81%, m.p. 180−182°C. Recyclization gave 96% of **13**, m.p. (dec.) 183−185°C (ethanol/ether).

*2-(4-Nitroanilino)isoquinolinium Chloride* (**14**): 73% of hydrazone **9**, m.p. 217−218°C (acetone). Chloride **14**, m.p. 241−242°C (dec.), 71% (ethanol/ether). $^1$H NMR ($CH_3OD$): δ = 6.96, 8.19 (2 mc, AA′BB′, $C_6H_4$), 7.7−8.5 (m, 4-H − 8-H), 8.65 (dd, 3-H), 10.24 (s, broadened, 1-H).

*2-(2-Pyridinioamino)isoquinolinium Dichloride* (**15** + HCl): Hydrazone **10**, 75%, showed m.p. 162−163°C after recrystallization from acetone (77%, 164°C[18]). The dichloride (**15** + HCl, 73%) was obtained from ethanol/ether and dried over conc. $H_2SO_4$, m.p. 205−208°C; (66%, m.p. 205−206°C, designated by Beyer and Thieme[18] as monohydrate of monochloride **15**, solely on the basis of the N-analysis). − $^1$H NMR ($CH_3OD$ + 10% of $D_2O$): δ = 7.0−7.32 (m, 2 H, 3′-H, 5′-H of pyridinio), 7.90−8.25 (m, 10 H, 3-H − 8-H, 4′-H, 6′-H), 10.17 (d, *J* 1 Hz, 1-H). − $C_{14}H_{13}Cl_2N_3$ (294.2): calcd. C 57.16, H 4.45, N 14.29; found C 57.22, H 4.68, N 14.30.

*Dehydrogenation of N-Anilino-3,4-dihydroisoquinolinium Bromide:* Nitrosobenzene (47.1 g, 440 mmol) was added to the solution of 60.6 g (200 mmol) of **16**[6] in 800 ml of DMF. The temp. rose from 20°C to 40°C within 20 min and sank during 3 h; the dark-green color turned to blackbrown. After 24 h the solvent was removed in vac.; the dark residue crystallized from ethanol: 39.2 g, of yellow **11**, Br instead of Cl, m.p. 191−192°C (dec.). The mother liquor was treated with benzene/water, and additional bromide (8.8 g, in total 80%) was obtained from the aqueous phase. Recrystallized from acetonitrile, the lightgreen-yellow salt showed m.p. 193−194°C (dec.). − $C_{15}H_{13}BrN_2$ (301.2): calcd. C 59.81, H 4.35, N 9.30; found C 59.51, H 4.38, N 9.13. − Attempts of effecting the dehydrogenation of **16** with nitrobenzene, chloranil, iodine or $Hg(OAc)_2$ in DMF or with aqueous sodium nitrate or sodium chlorate were as unsuccessful as the shaking of the aqueous solution with $O_2$ and palladium on carbon.

*2-(4-Chloroanilino)isoquinolinium Bromide* (**13**, Br instead of Cl): The same procedure with 33.8 g (100 mmol) of **17**[6] and 23.0 g (215 mmol) of nitrosobenzene in 400 ml of DMF provided the yellow title bromide (24.8 g, 74%) which was recrystallized from ethanol and acetonitrile, m.p. 197−198°C (dec.). − $C_{15}H_{12}BrClN_2$ (335.6): calcd. C 53.67, H 3.60; found C 53.89, H 3.90.

*2-(4-Nitroanilino)isoquinolinium Bromide* (**14**, Br instead of Cl): By the same procedure, nitrosobenzene (4.4 mmol) and **18** (2.2 mmol)[6] in 40 ml of DMF gave 530 mg (77%) of the light yellow-brown bromide, m.p. 233°C (dec.). The red color of the aqueous solution stems from the equilibrium with **22**.

**Properties and Reactions of Isoquinolinium *N*-Arylimides**

*Isoquinolinium N-(4-Nitrophenyl)imide* (**22**): 1.04 g (3.00 mmol) of **14**, Br instead of Cl, was dissolved in 250 ml of warm water and a few drops of acetic acid. After cooling, 50 ml of 2 N $Na_2CO_3$ gave rise to a red precipitate which was taken up in 100 ml of $CH_2Cl_2$. After quick drying and filtering, 200 ml of ether was added: 566 mg carmine **22** crystallized within some min; further 175 mg (together 93%) came from the mother liquor, m.p. 201−202°C (dec.). − IR (KBr): $\tilde{\nu}$ = 741 $cm^{-1}$, 780 (arom. CH out-of-plane def.), 1083, 1108, 1177; 1262 sst ($NO_2$ sy); 1477, 1549; 1584 st ($NO_2$ as). − $^1H$ NMR ([$D_6$] DMSO): δ = 6.15, 7.80 (2 mc, AA′XX′, $J$ = 9.6 Hz, $C_6H_4$), 7.32−8.16 (m, 3-H − 8-H), 9.73 (s, 1-H). ($CD_2Cl_2$): the signal at δ = 9.22 (s, 1-H) had disappeared after 30 min, but the solution was still red. − $C_{15}H_{11}N_3O_2$ (265.3): calcd. C 67.91, H 4.18, N 15.84; found C 68.20, H 4.27, N 16.05.

*Isoquinolinium N-(2-Pyridyl)imide* (**23**): Salt **15** + HCl (11.0 g, 37.4 mmol) was dissolved in 100 ml of water and treated with 4.0 g $Na_2CO_3$ in water. The intensely orange-red solution was extracted with 4 × 70 ml of $CS_2$; the dried organic phase was concentrated in vac., until crystals separated. After 48 h at −18°C, **23** (7.55 g, 91%) was isolated in fine red-orange crystals, m.p. 126−130°C. We have doubts, whether the crystals of m.p. 116°C obtained by Beyer and Thieme[18] after "longer storing of the aqueous alkaline solution" were **23**; only the N-analysis was offered as proof. In $CS_2$, the monomer **23** is less soluble than the dimer **24**. − IR (KBr): $\tilde{\nu}$ = 753 $cm^{-1}$, 768, 863 (arom. CH out-of-plane def.), 1336, 1414, 1473; 1536, 1594 st, 1634 m. − UV-Vis ($CHCl_3$, fresh solution): $\lambda_{max}$ (log ε) = 460 nm (4.20), 280 (sh, 3.00), 257 (4.25). − $^1H$ NMR ($CDCl_3$): δ = 6.35−6.86, 7.49−7.82 (2 m, 8 arom. H), 8.02 (mc, probably 6′-H of py), 8.24 (dd, $J_{3,4}$ = 7.5 Hz, $J_{1,3}$ = 1.8 Hz, 3-H), 10.58 (d, $J_{1,3}$ 1.8 Hz, 1-H). − $^{13}C$ NMR ($CDCl_3$): δ = 112.3, 114.5, 122.4, 126.0, 126.2, 129.0, 129.5, 129.9, 135.4, 136.1, 136.3, 145.6, 162.7; disturbed by signals of **24**. − $C_{14}H_{11}N_3$ (221.3): calcd. C 75.99, H 5.01, N 18.99; found C 76.12, H 4.92, N 18.94.

*8,8a,16,16a-Tetrahydro-8,16-di(2-pyridyl)-s-tetrazino[6,1-a;3,4-a′]diisoquinoline* (**24**): The deep-red solution of 4.43 g (20.0 mmol) of **23** in 50 ml of $CH_2Cl_2$ was kept at room temp. for 7 d. The solvent was removed in vac., and trituration of the residue with $CHCl_3$/ether furnished 1.84 g (42%) of **24** in red-brown crystals, m.p. 135−140°C (dec.). The coarse prisms obtained by recrystallization from $CS_2$ still contain some **23**. Solutions of **24** slowly assume the red color of **23**. − IR (KBr): $\tilde{\nu}$ = 684 $cm^{-1}$, 766, 1290, 1478, 1633. − UV-Vis ($CHCl_3$, fresh solution): $\lambda_{max}$ (log ε) = 460 nm (2.98), 308 (4.39); the long-wave absorption suggests 6% of monomer **23** in the specimen of **24**. − $^1H$ NMR ($CDCl_3$): δ = 5.43, 6.22 (AM, $J$ = 7.8 Hz, 5-H/13-H and 6-H/14-H), 5.5−8.4 (m, 18 H). − $^{13}C$ NMR ($CDCl_3$): δ = 71.5 (d, C-8a/C-16a), 98.8 (d, C-5/C-13); 109.0, 115.6, 123.8, 125.4, 128.3, 128.4 (6 d), 130.7 (s), 137.0, 137.5, 147.1 (3 d), 156.9 (s); the subtraction of the signals of **23** is not always unambiguous. − MS (70 eV, 195°C); *m/z* (%): 440 (8) [$M^+$ − 2 H], 360 (5) [440 − pyridyl, $C_{23}H_{14}N_4^+$], 347 (9) [440 − $C_5H_5N_2$], 310 (10) [M − H − isoquinoline, $C_{19}H_{12}N_5^+$], 220 (84) [440/2, **25**], 129 (100) [isoquinoline$^+$], 102 (20) [$C_8H_6^+$]. In the MS at 120°C, *m/z* = 220 is the highest value and the base peak. − $C_{28}H_{22}N_6$ (442.5): calcd. C 75.99, H 5.01, N 18.99; found C 76.27, H 5.07, N 18.82.

*Rate and Equilibrium of Dimerization of* **23** *at 25°C:* 400 mg of **23** was dissolved in $CDCl_3$ in a 2-ml volumetric flask (0.906 M). $^1H$ NMR signals for analysis: δ = 10.58 (1-H) for **23**, 5.43 for **24** (5-H + 13-H). For each concentration measurement, 7 machine integrals were recorded; the sum of the arithmetic means was set equal to 100, and the part of **23** was expressed in% of that sum. The equilibrium (association) constant of m(onomer) and d(imer) was calculated by

$$K_{ass} = d_e/m_e^2 = (m_o - m_e)/2\ m_e^2 \quad (1)$$

We are dealing with a reversible system of a second-order reaction (equal starting concentrations) and one of first-order. $m_o$, $m_t$, and $m_e$ are the concentrations of **23** at time 0, t, and at equilibrium. The data were evaluated by the integrated rate equation[27]:

$$k_2 t = \frac{m_o - m_e}{2m_o m_e - m_e^2} \ln \frac{(m_o - m_e)(m_o m_e + m_t m_o - m_t m_e)}{m_o^2 (m_t m_e)} \quad (2)$$

Starting with $m_o$ = 0.906 M, $m_t$ = 0.576 M after 400 min corresponded to 64% approach to $m_e$ (0.391 M); $k_2$ = 3.1 $10^{-5}$ $M^{-1}s^{-1}$ was calculated. In the presence of a trace of 4-toluenesulfonic acid, nearly half of **23** was dimerized after 70 min.

*Tetramer* **28** *of Isoquinolinium N-Phenylimide* (**19**): The solution of 2.0 g (7.8 mmol) of **11** in 25 ml of water was treated with aqueous $Na_2CO_3$; the dark-red amorphous precipitate was extracted with 100 ml of $CCl_4$. Trituration of the dark oil (after removal of the solvent) with 50 ml of petroleum ether (bp. 30−50°C) inititiated a slow conversion to a microcrystalline state; a light reddish-brown powder (1.05 g, 62%), m.p. 137−141°C (dec.), was obtained. Since recrystallization did not succeed, a specimen washed with petroleum ether and dried was analyzed. The supposed tetramer was little soluble in cold $CH_2Cl_2$; on warming, it slowly dissolved with deep-red color. The color must be due to **19**, since it quickly disappeared with some drops of ethyl acrylate. − IR (KBr): $\tilde{\nu}$ = 695 $cm^{-1}$, 712, 747, 766 (arom. CH out-of-plane def.), 1495, 1600 st (ring vibr.), 1618 st (C=C); the somewhat broadened bands suggest inhomogeneity. − $^1H$ NMR (fresh solution in $CDCl_3$): The multiplets at δ = 4.4−6.4 are not well resolved except for δ = 5.26, 6.13 (2 d, $J$ = 7.8 Hz, enhydrazine groups); 6.4−7.8 (structured m, arom. H). − $(C_{15}H_{12}N_2)_4$ (884.5): calcd. C 81.47, H 5.47; found C

81.79, H 5.95. − Mol. mass. 860, 933 (vapor-phase osmometry, benzene, 37°C). − *Reaction with dimethyl fumarate*: It proceeded in $CDCl_3$ in the NMR tube at room temp.; after several h, the $^1H$ NMR spectrum showed only small extra signals beyond those of adduct **27**[28] and the excess of the dipolarophile.

**Cycloadditions to Heterocumulenes**

*3-Phenyl-10bH-1,3,4-thiadiazolo[2,3-a]-isoquinoline-2(3H)-thione* (**29**): Salt **11** (25.6 g, 99.4 mmol) in 60 ml of water was basified with 11.7 g (110 mmol) of sodium carbonate in 40 ml of water. The deep red-brown suspension was extracted with 5 × 100 ml of $CS_2$. The dried organic phase was concentrated up to beginning crystallization; after 2 d at −10°C, 25.6 g (86%) of coarse yellow-brown rhombes of **29** were filtered. Due to the cycloreversion, only $CS_2$ is suitable for recrystallization, m.p. 101−105°C (dec., red). The crystalline **29** can be stored at room temp. − IR (KBr): $\tilde{\nu}$ = 690 $cm^{-1}$, 744, 776 (arom. CH out-of-plane def.), 1059 st (C=S ?), 1282; 1495, 1595 st (arom. ring vibr.), 1636 m (C=C). − UV-Vis (0.35 mM in $CHCl_3$): $\lambda_{max}$ (log ε) = 470 nm (3.76), 405 (3.83), 290 sh (3.93), 260 sh (4.08); the long-wave absorption is that of **19**. − $^1H$ NMR ($CS_2$): δ = 5.86, 6.02 (AB, $J_{5,6}$ = 8.0 Hz, 6-H and 5-H), 6.93 (s, 10b-H), 7.0−8.0 (m, 9 arom. H). − $^{13}C$ NMR ($CDCl_3$): δ = 71.5 (s, 10b-H), 108.1 (d, C-6), 192.1, 192.2 (2 s, C-2, $CS_2$); the other signals of **19** and **29** cannot be distinguished. − $C_{16}H_{12}N_2S_2$ (296.4): calcd. C 64.83, H 4.08, N 9.45, S 21.64; found C 64.76, H 4.10, N 9.47, S 21.28.

*3-(p-Tolyl)-10bH-1,3,4-thiadiazolo[2,3-a]isoquinoline-2(3H)-thione* (**30**): Analogously, salt **12** was converted to 82% of pale yellow, long needles, m.p. 109−111°C (dec., red above 80°C). − IR (KBr): $\tilde{\nu}$ = 770 $cm^{-1}$, 775, 830, 838 (arom. CH out-of-plane def.), 1057 st (C=S ?); 1493, 1505 (ring vibr.), 1634 (C=C). − $^1H$ NMR ($CS_2$): δ = 2.37 (s, $CH_3$), 5.82, 6.00 (AB, $J_{5,6}$ = 8.0 Hz, 6-H, 5-H), 6.90 (s, 10b-H), 6.98−7.30, 7.53−7.83 (2 m, 8 arom. H). − $^{13}C$ NMR ($CDCl_3$): δ = 21.2 (q, $CH_3$), 71.4 (d, C-10b), 108.0 (d, C-6), 192.7 (s, C-2, $CS_2$). For most $C_{ar}$ signals the distinction between **20** and **30** was unsuccessful; 20.9 (s, $CH_3$) belongs to **20**. − $C_{17}H_{14}N_2S_2$ (310.4): calcd. C 65.77, H 4.55, N 9.02, S 20.66; found C 65.45, H 4.51, N 9.11, S 20.75.

*1,10b-Dihydro-1,3-diphenyl-1,2,4-triazolo[5,1-a]isoquinoline-2(3H)-one* (**31a**): Salt **11**, Br instead of Cl (1.51 g, 5.00 mmol), was dissolved in 75 ml of water and some drops of acetic acid; the 1,3-dipole **19**, set free with $Na_2CO_3$, was extracted with ether (125 ml). The organic phase was briefly clarified with dry $Na_2SO_4$, but still contained water dissolved. After addition of 655 mg (5.5 mmol) of *phenyl isocyanate*, the red color faded to pale-yellow in about 2 min; thus, the cycloaddition is faster than the hydrolysis of the phenyl isocyanate. Colorless crystals (1.47 g, 87%) came from a small vol. of ether, m.p. 133°C (dec., red) after recrystallization from ethanol. − IR (KBr): $\tilde{\nu}$ = 688 $cm^{-1}$, 737, 750, 779 (arom. CH out-of-plane def.), 1594 st (arom. ring vibr.), 1631 m (C=C), 1704 st (C=O). − UV ($CHCl_3$): $\lambda_{max}$ (log ε) = 308 nm sh (3.56), 261 (4.35). − $C_{22}H_{17}N_3O$ (339.4): calcd. C 77.85, H 5.05, N 12.38; found C 77.57, H 5.10, N 12.47. − *Hydrogenolysis*: **31a** (679 mg, 2.00 mmol) in 25 ml of methanol and 10 ml of ethyl acetate was shaken with Raney nickel and hydrogen; 2.5 mmol of $H_2$ were consumed in 45 min, and *N,N′*-diphenylurea (297 mg, 70%), m.p. 238°C (mixed m.p.) was obtained. The residue of the mother liquor was distilled at 120°C (bath)/10 Torr and afforded 139 mg (54%) of isoquinoline (picrate m.p. and mixed m.p. 226°C). − *Reaction with aniline:* **31a** (2.00 mmol) in 20 ml of benzene and 1.0 ml of aniline was refluxed for 15 h; on cooling, 83% of diphenylurea (m.p. 236°C) crystallized. − *Thermolysis*: 1.00 mmol of **31a** was refluxed in 10 ml of 90% aqueous dioxane for 15 h; 81 mg (76%) of *N,N′*-diphenylurea came from benzene, m.p. 237−238°C.

*3-(4-Chlorophenyl)-1,10b-dihydro-1-phenyl-1,2,4-triazolo[5,1-a]-isoquinoline-2(3H)-one* (**32a**): With salt **13**, the above procedure furnished 99% of colorless crystals from ether, m.p. 176°C (dec.). − $^1H$ NMR ($CDCl_3$): δ = 6.07 (s, 10b-H, coincides with low-field branch of AB), 6.00, 6.25 (AB, $J_{5,6}$ = 7.6 Hz, 6-H and 5-H), 6.5−7.6 (m, 9 arom. H), 7.38, 7.83 (2 mc, AA′MM′ of $C_6H_4Cl$). − $C_{22}H_{16}ClN_3O$ (373.8): calcd. 70.68, H 4.31, N 11.24; found C 70.89, H 4.48, N 11.06.

*1,10b-Dihydro-1,3-diphenyl-1,2,4-triazolo[5,1-a]isoquinoline-2(3H)-thione* (**31b**): The ethereal solution of **19**, prepared from 1.51 g (5.00 mmol) of **11**, Br instead of Cl, was treated with 810 mg (6.0 mmol) of *phenyl isothiocyanate* at room temp.; within 15 h the deep red color turned orange. On recrystallization from acetonitrile, 1.36 g (77%) of crude **31b** gave colorless needles, m.p. 130−131°C (dec., red). The red color of hot solutions signals some cycloreversion. − $^1H$ NMR ($CDCl_3$): δ = 6.11 (s, 10b-H), 5.93, 6.17 (AB, $J_{5,6}$ = 7.8 Hz, 6-H, 5-H), 6.40−8.23 (m, 14 arom. CH). − $C_{22}H_{17}N_3S$ (355.5): calcd. C 74.34, H 4.82, N 11.82; found C 74.73, H 4.80, N 11.66.

*3-(4-Chlorophenyl)-1,10b-dihydro-1-phenyl-1,2,4-triazolo[5,1-a]-isoquinoline-2(3H)-thione* (**32b**) was analogously prepared from **13**, Br instead of Cl, in 84% yield; colorless **32b**, m.p. 137−139°C (dec.), was obtained from acetonitrile. − $C_{22}H_{16}ClN_3S$ (389.9): calcd. C 67.77, H 4.14, N 10.78; found C 67.77, H 4.05, N 10.60.

*1,10b-Dihydro-1,1,3-triphenylpyrazolo[5,1-a]isoquinoline-2(3H)-one* (**33**): Addition of 1.16 g (5.98 mmol) of *diphenylketene* in 5 ml of $CH_2Cl_2$ to 1.78 g (6.00 mmol) of **29** in 20 ml of $CH_2Cl_2$ led to immediate decolorization. 2.09 g (84%) of pale-yellow cubes, m.p. 104−105°C, came from petrol ether. − IR (KBr): $\tilde{\nu}$ = 699 $cm^{-1}$, 753, 775 st (arom. CH out-of-plane def.); 1497, 1599 st (ring vibr.); 1636 m (C=C), 1710 vst (C=O). − $^1H$ NMR ($CDCl_3$): δ = 4.98, 6.16 (AX, $J_{5,6}$ = 8.0 Hz, 6-H, 5-H), 6.16 (s, 10b-H), 6.57−8.07 (m, 19 arom. CH). − $C_{29}H_{22}N_2O$ (414.5): calcd. C 84.03, H 5.35, N 6.76; found C 84.02, H 5.45, N 6.54.

*Di-tert-butyl 1,2,3,10b-Tetrahydro-3-phenyltetrazolo[5,1-a]isoquinoline-1,2-dicarboxylate* (**34**): 1.48 g (5.00 mmol) of **29** in 10 ml of $CH_2Cl_2$ reacted with 1.15 g (5.00 mmol) of *di-tert-butyl azodicarboxylate*[29]; the red color disappeared immediately. Pale yellow cubes, m.p. 98−100°C, crystallized from ether/petroleum ether. The pink solutions of **34** in benzene or $CHCl_3$ reversibly assume the red color of **19** on heating. − IR (KBr): $\tilde{\nu}$ = 703 $cm^{-1}$, 770, 781, 806 (arom. CH out-of-plane def.); 1161, 1292, 1327 st (C−O); 1497, 1576, 1598 (arom. ring vibr.), 1647 m (C=C); 1710, 1751 st (C=O). − $^1H$ NMR ($CDCl_3$): δ = 1.28 (s, 2 *t*Bu), 6.07 (s, 10b-H), 5.56, 6.53 (AX, $J_{5,6}$ = 7.9 Hz, 6-H, 5-H), 6.7−7.6 (m, 8 arom. H), 8.04 (mc, 1 arom. H). − $C_{25}H_{30}N_4O_4$ (450.5): calcd. C 66.65, H 6.71, N 12.44; found C 66.94, H 6.72, N 12.56.

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☆ This paper is dedicated to *George A. Olah*, University of Southern California, on the occasion of his 70th birthday.


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