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THE REACTION OF 8,8-DISUBSTITUTED HEPTAFULVENES WITH AMINES IN THE PRESENCE OF COPPER(II) ACETATE

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The reaction of 8,8-dicyanoheptafulvene (1a) with ammonia and several kinds of amines in the presence of copper(II) acetate afforded 1,2-dihydro-2-iminocyclohepta[b]pyrrole derivatives (2) and/or 3-aminoisoquinoline derivatives (3). The reaction of 8-cyano-8-methoxycarbonylheptafulvene (1b) and amines has also been described.

In the course of the investigations on the oxidative amination of seven-membered aromatics,[1] it was found that the reaction of 8,8-dicyanoheptafulvene (1a) and 8-cyano-8-methoxycarbonylheptafulvene (1b) with amines in the presence of copper(II) acetate gave cyclohepta[b]pyrrole derivatives (2) and/or 3-aminoisoquinoline derivatives (3). Present communication describes these novel oxidative cyclization and rearrangement reactions.

The treatment of 1a (1.54 g) and copper(II) acetate (4.00 g) in methanol (30 ml) with concd. ammonia (8 ml) at room temperature for 70 h gave 1,2-dihydro-2-iminocyclohepta[b]pyrrole-3-carbonitrile (2a)[2] and 3-aminoisoquinoline-4-carbonitrile (3a) [mp 168-169°C; UV (EtOH), λ_{Max}, nm (log ε): 241 (4.76), 276 (3.77), 286 (3.70), 384 (3.67); NMR (DMSO-d_6), δ, ppm: 7.1~8.2 (C_5-H~C_8-H, and NH_2, m), 9.12 (C_1-H, s)] in about 44% and 26% yields, respectively. The acid hydrolysis and decarboxylation of 3a gave 3-aminoisoquinoline. The similar treatment of 1a with methylamine, ethylamine, and benzylamine (room temperature, 0.5~1 h) gave corresponding 1,2-dihydro-1-methyl[2]-(ethyl, and benzyl)-2-iminocyclohepta[b]pyrrole-3-carbonitriles (2b, 2c, and 2d), respectively. Their melting points, yields, and the spectral data are shown in Table 1.

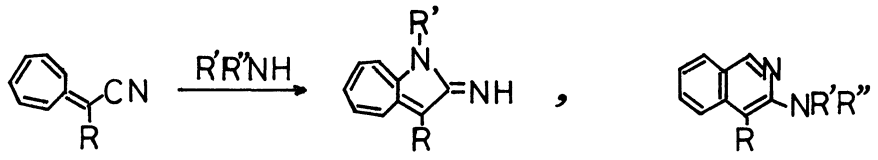
Table 1. The melting points, yields, and the spectral data of 1,2-dihydro-2-iminocyclohepta[b]pyrrole derivatives (2)

Compounds	Mp (°C)	Yields (%)	UV (EtOH) λ_{Max}, nm (log ε)			NMR ($CDCl_3$, ppm) =NH
2b	181-183	30	228 (4.11)	283 (4.38)	435[a] (4.05)	----
2c	147-148	30	230 (4.14)	283 (4.43)	434 (4.10)	6.32
2d	158-159	26	230 (4.13)	284 (4.38)	437 (4.12)	6.17
2e	130-131	10	245 (4.25)	286 (4.41)	420 (4.08)	6.5~7.5[b]

a) Lit.,[2] mp 185°C. UV (EtOH), λ_{Max}, nm (log ε): 228 (4.16), 281 (4.45), and 433 (4.17).
b) Overlapped with aromatic protons.

On the other hand, the reaction of 1a with pyrrolidine in the presence of copper(II) acetate at room temperature for 1 h gave 3-pyrrolidinoisoquinoline--4-carbonitrile (3b) as yellow needles, mp 152-153.5°C, yield, 68%. UV (EtOH), λ_{Max}, nm (log ε): 255 (4.65), 295 (4.17), 405 (3.68). NMR ($CDCl_3$), δ, ppm: 7.2~8.1 (C_5-H~C_8-H, m), 8.97 (C_1-H, s). Permanganate oxidation of 3b gave phthalic acid. Acid hydrolysis and decarboxylation of 3b gave 3-pyrrolidino-isoquinoline (4), mp 84-85.5°C. UV (EtOH), λ_{Max}, nm (log ε): 246 (4.60), 294 (4.19), 303 (4.28), 393 (3.41). Similarly, the treatment of 1a with dimethylamine, piperidine, and morpholine gave 3-dimethylamino-(piperidino, and morpholino)-isoquinoline-4-carbonitriles (3c, 3d, and 3e), respectively. Their melting points, yields, and the spectral data are shown in Table 2.

The reaction of 8-cyano-8-methoxycarbonylheptafulvene (1b), which was prepared under a similar manner for the preparation of 8-cyano-8-ethoxycarbonylheptafulvene,[3] with benzylamine in the presence of copper(II) acetate



(1a, 1b) (2a~2e) (3a~3j)

Table 2. The melting points, yields, and the spectral data of 3-amino-isoquinoline derivatives (3)

Compounds	Mp (°C)	Yields (%)	UV (EtOH) λ_{Max}, nm (log ε)				NMR ($CDCl_3$, ppm) C_1-H
3c	103-104	37	253 (4.61)	293 (4.09)	398 (3.65)		9.00 (s)
3d	88-89	52	257 (4.56)	298 (4.17)	402 (3.61)		9.05 (s)
3e	116-117	22	254 (4.51)	295 (4.10)	390 (3.57)		9.04 (s)
3f	101-102	46	249 (4.71)	401 (3.77)			8.88 (s)
3g	98-99	28	225 (4.34)	266 (4.51)	312 (4.37)	406 (3.77)	8.95 (s)
3h	109-110	29	225 (4.34)	266 (4.51)	312 (4.36)	411 (3.77)	8.95 (s)
3i	114-115	19	228 (4.33)	266 (4.50)	310 (4.32)	413 (3.76)	8.92 (s)
3j	153-154	18	228 (4.37)	270 (4.52)	317 (4.50)	405 (3.84)	8.97 (s)

gave orange red needles (2e), mp 130-131°C, and pale yellow needles (3f), mp 101-102°C. Elemental analysis and spectral data of 2e (Table 1) an 3f (Table 2) indicate that the former is methyl 1,2-dihydro-1-benzyl-2-iminocyclohepta[b]-pyrrole-3-carboxylate, and the latter is methyl 3-benzylaminoisoquinoline-4-carboxylate.

The reaction of 1a with aromatic amines did not afford clear results. However, the reaction of 1b with aniline, p-toluidine, p-anisidine, and p-bromoaniline under a similar condition (room temperature, 1~1.5 h), gave methyl 3-anilino-(3-p-toluidino, 3-p-anisidino, and 3-p-bromoanilino)-isoquinoline-4-carboxylates (3g, 3h, 3i, and 3j), respectively. Their structures were established by the elemental analyses and the spectral data, especially by the characteristic C_1-H signal (singlet at about 9 ppm) in the NMR spectra as shown in Table 2.

The rearrangement reaction of 2-amino-3-bromotropone derivatives with active methylene compounds to give quinoline derivatives has been reported.[4)]

However, the rearrangement of 8,8-disubstituted heptafulvenes into 3-amino-isoquinoline derivatives under an oxidative process is, in our knowledge, the first example in the seven-membered aromatic compounds.

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