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2-TERT-BUTYL-2H-BENZO[F]ISOINDOLE [1)]

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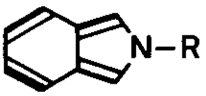
Abstract: The tricyclic 14π-system can be prepared via a convenient route developed for 2H-isoindoles. The investigated cycloaddition and substitution reactions reveal relations between structure and property and confirm theoretical predictions.

During the last decade 2H-isoindoles (1) attracted synthetic and theoretical attention [3)]. In the meantime, chemical efforts have been extended to annelated hetarenes (2) and (3) with an o-quinonoid structure. Attention is directed towards the effect of the annelation type and the influence of heteroatoms upon the thermal stability and the chemical reactivity of the cyclic conjugated π-system.



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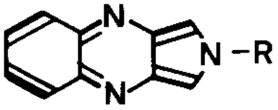

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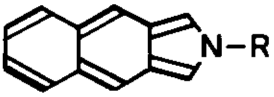

(3)

As a rule, 2H-isoindoles (1) and related N-heterocycles are extremely sensitive and considerably reactive towards protonic acids and electrophiles. In our experience o-quinonoid π-hetarenes (1) and (2) - substituted at the heteroatom with a tertiary butyl group [4,5)] - are resistant to these reagents.

In order to obtain additional evidence for the stabilizing effect of the tertiary butyl group, the hitherto unknown 2-*tert*-butyl-2H-benzo[f]isoindole (3) has been synthesized via a general and practicable route. The conveniently accessible 2-*tert*-butyl-2H-benzo[f]isoindoline (yield 91 %, mp 181 °C) was treated with a 30 % hydrogen peroxide solution in methanol. Acetolysis [6)] of the resulting 2-*tert*-butyl-2H-benzo[f]isoindoline-N-oxide (yield 93 %, mp 132-133 °C) with acetic anhydride in the presence of triethylamine proceeds under very mild conditions and only leads to the formation of 2-*tert*-butyl-2H-benzo[f]isoindole (3). After sublimation the tricyclic hetarene can be stored under nitrogen at room temperature without decomposing.

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The 2-methyl-2H-benzo[f]isoindole has been prepared by different routes 7,8); the existence of the parent compound (3, R_t = H) was established by Remy and Bissett 9). Concerning the stability, both representatives cannot be compared with the tricyclic hetarene (3, R_t = *tert*-butyl), substituted with a tertiary butyl group at the heteroatom. So far systematic investigations of the chemical reactivity of benzo[f]isoindoles (3) have not been carried out.

In our experience dienophiles possessing an activated CC-double or triple bond - e.g. maleic acid N-methylimide or dimethyl acetylenedicarboxylate - predominantly undergo cycloaddition at 1,3-position of the o-quinonoid hetarene (3), leading to the formation of 1:1-adducts (4) and (5). In spite of steric protection - caused by the bulky tertiary butyl group - cycloaddition does not occur at the peri-position of the central six membered ring system; in the case of the isoelectronic anthracene 10,11) this reaction has been observed only.

In the same manner dienophiles with an activated NN-double bond prefer the attack of the tricyclic hetarene (3) at 1,3-position. In the case of dimethyl azodicarboxylate the formation of disubstituted benzo[f]isoindoles (7) can be deduced from analytical and spectroscopic data. This transformation may be classified as a modified "ene-reaction" and provides an elegant route for the preparation of hetarenes associated with donor substituents adjacent to the heteroatom 2). In contrast to this observation anthracene reacts with azodienophiles via cycloaddition at 9,10-position giving rise to the formation of thermally instable Diels-Alder-adducts; subsequent isomerization takes place under the influence of protonic acids and yields the 9-hydrazino-derivative 12).

The o-quinonoid hetarene (3, R_t = *tert*-butyl) can be converted into a remarkably stable 1H-benzo[f]isoindolium salt (6) by treatment with concentrated perchloric acid; in agreement with the ^{1}H-NMR spectrum protonation takes place at the nucleophilic α-position adjacent to the heteroatom, and apparently profits by the formation of the conjugated naphthalene system. The steric influence of the tertiary butyl group seems to be an essential factor for the kinetic stability and may be attributed to the protection of the heterocyclic imonium group. In methanolic solution an equilibrium is observable between the cationic salt (6) and the neutral hetarene (3), which can be detected in the UV-spectra.

In practical operation the reaction of the tricyclic hetarene (3, R_t = *tert*-butyl) with arene-diazonium tetrafluoroborates has been achieved in absolute acetone at 0 °C. The regiospecific attack of the α-position of the tricyclic hetarene results in the formation of stable and isolable 1-arylhydrazono-1H-benzo[f]isoindolium salts (8). Deprotonation can be realized by treatment with aqueous sodium hydroxide. The resulting azo compounds (9) are intensively coloured and characterized by a long wave absorption band between 480 and 530 nm in the UV-spectra.

The tricyclic hetarene (3, R_t = *tert*-butyl) displays the same behaviour as 2-*tert*-butyl-2H-isoindole (1). Both the tertiary butyl group at the heteroatom and the annelated six membered π-system do not change the reaction type, but exert an essential influence upon chemical reactivity; dienophiles and electrophiles prefer the attack of the 1,3-position adjacent to the heteroatom, while there is no experimental evidence for an attack of the central 9,10-position.

In this regard remarkable differences exist in comparison with the chemical behaviour of the isoelectronic 2-*tert*-butyl-2H-pyrrolo[3,4-b]quinoxaline (2); in this compound the attack of electrophiles predominantly takes place at the central heteroatoms [5].

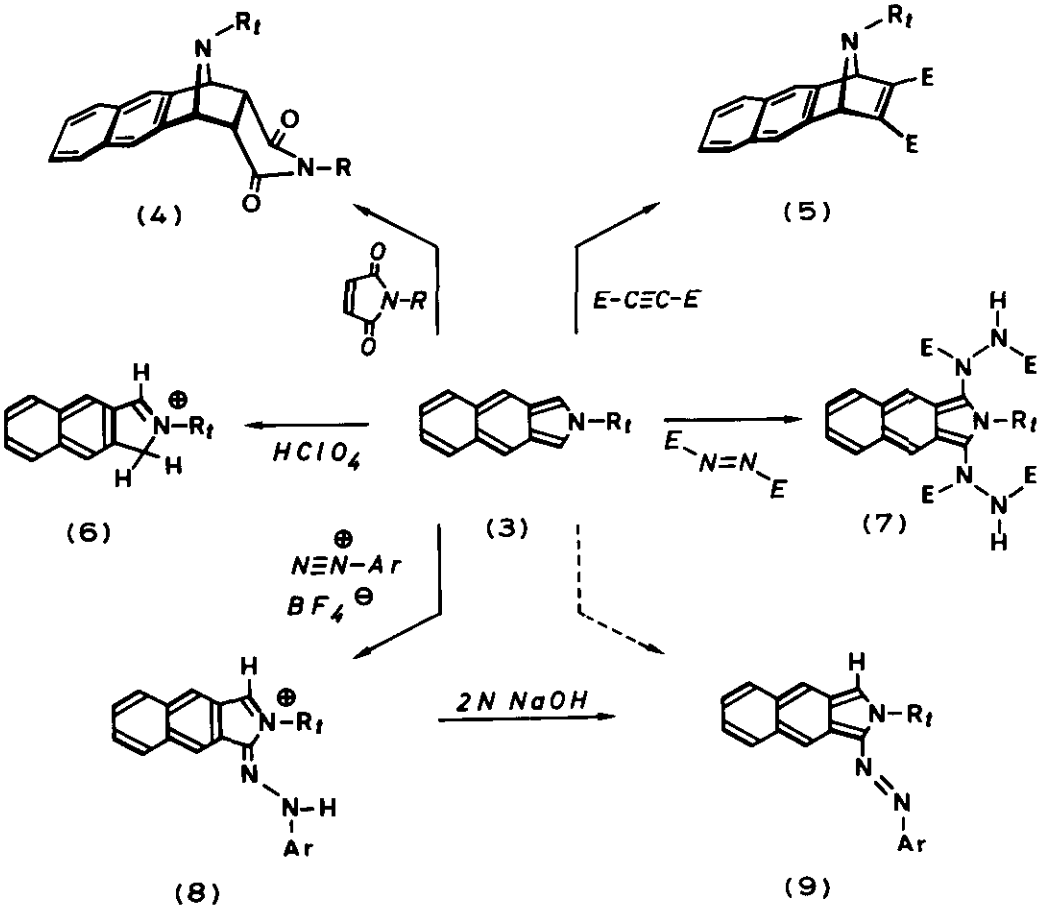

Table: 2-*tert*-Butyl-2H-benzo[f]isoindole (3) and reaction products with dienophiles and electrophiles

2-*tert*-Butyl-2H-benzo[f]isoindole (3): yield 90 %, mp 140-141 °C (under N_2); subl. by 0.05 Torr/ 100-105 °C.- ^{1}H-NMR(CDCl$_3$): τ = 2.13 (s, 2H, H-4/9), 2.33-2.60 (m, 2H, H-5/8), 2.71 (s, 2H, H-1/3; D_2O-exchangeable), 2.99-3.27 (m, 2H, H-6/7), 8.43 (s, 9H, C(CH$_3$)$_3$).- UV(CH$_3$OH): λ_{max} = 226 nm (log ε = 4.30), 253 (4.97), 313 (3.41), 328 (3.09), 336 (2.61 sh), 344 (2.34 sh), 362 (2.49 sh), 390 (3.06 sh), 413 (3.41 sh), 433 (3.61), 456 (3.60).

endo-1,4-*tert*-Butylimino-1,2,3,4-tetrahydroanthracene-2,3-dicarboxylic acid N-methylimide (4): yield 96 %, mp 235-240 °C (dec.).- ^{1}H-NMR(CDCl$_3$): τ = 2.28-2.52 (m, 2H, aromatic-H), 2.57 (s, 2H, *H*-5/10), 2.62-2.86 (m, 2*H*, aromatic-*H*), 5.08-5.18 (m, 2*H*, *H*-1/4), 6.36-6.45 (m, 2*H*, *H*-2/3), 7.98 (s, 3H, CH$_3$), 9.16 (s, 9H, C(CH$_3$)$_3$).

1,4-*tert*-Butylimino-1,4-dihydroanthracene-2,3-dicarboxylic acid dimethyl ester (5): yield 66 %, mp 95-97 °C.- ^{1}H-NMR($CDCl_3$): τ = 2.39-2.59 (m, 4H, aromatic-H; 2H-singlet at τ = 2.50, H-5/10), 2.66-2.87 (m, 2H, aromatic-H), 4.78 (s, 2H, H-1/4), 6.33 (s, 6H, OCH_3), 8.93 (s, 9H, $C(CH_3)_3$).-
2-*tert*-Butyl-1H-benzo[f]isoindoliumperchlorate (6): yield 93 %, mp 258-260 °C (dec.).- ^{1}H-NMR (CF_3COOH): τ = 0.70 (dt, J = 1.9 Hz and 0.7 Hz; 1H, H-3), 1.47 (s, 1H, H-4), 1.98 (s, 1H, H-9), 2.03-2.28 (m, 2H, H-5/8), 2.35-2.62 (m, 2H, H-6/7), 4.67 (dd, J = 1.9 Hz and 1.4 Hz; 2H, CH_2), 8.19 (s, 9H, $C(CH_3)_3$).
2-*tert*-Butyl-1,3-bis[N,N'-bis(methoxycarbonyl)]hydrazino-2H-benzo[f]isoindole (7): yield 56 %, (preparation in chloroform), 78-96 % (preparation in ether), mp 130 °C (dec.).- UV(CH_3OH): λ_{max} = 227 nm (log ε = 4.23), 255 (4.97), 298 (3.59 sh), 314 (3.39), 330 (3.11), 347 (2.63), 388 (3.26 sh), 410 (3.63 sh), 428 (3.87), 452 (3.89).
2-*tert*-Butyl-1-arylhydrazono-1H-benzo[f]isoindolium tetrafluoroborate (8): Aryl = 4-ethoxycarbonylphenyl, yield 93 %, mp 226 °C (dec.).- Aryl = 4-nitrophenyl, yield 87 %, mp 227 °C (dec.).-
2-*tert*-Butyl-1-arylazo-2H-benzo[f]isoindole (9): Aryl = 4-ethoxycarbonylphenyl, yield 94 %, mp 90-95 °C (dec.); UV(CH_2Cl_2): λ_{max} = 256 nm (log ε = 4.59), 279 (4.27), 346 (4.04), 353 (4.03 sh), 374 (3.70 sh), 443 (3.95 sh), 468 (4.03), 545 (4.45 sh), 562 (4.49), 594 (4.27).- Aryl = 4-nitrophenyl, yield 87 %, mp 209-210 °C (dec.); UV(CH_2Cl_2): λ_{max} = 251 nm (log ε = 4.51), 287 (4.14), 353 (3.93), 364 (3.91 sh), 383 (3.79 sh), 456 (3.88), 477 (3.97), 558 (4.64).

The experimental results demonstrate the pronounced thermal stability and distinguished chemical reactivity of 2H-benzo[f]isoindole (3) with a tertiary butyl group at the heteroatom. Theoretical predictions of Dewar et al. 13) on the basis of HMO-calculations are impressively confirmed.

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