SHORT PAPER

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Novel dispiro iminodioxolane derivatives: synthesis by reaction of isocyanides with ninhydrin†

Ahmad Shaabani,[a]* Mohammad Bagher Teimouri[a] and Hamid Reza Bijanzadeh[b]

[a]*Department of Chemistry, Shahid Beheshti University, Zip Code 1983963113, Tehran, Iran*

[b]*Department of Chemistry, Tarbiat Modarres University, PO Box 14155–4838, Tehran, Iran*

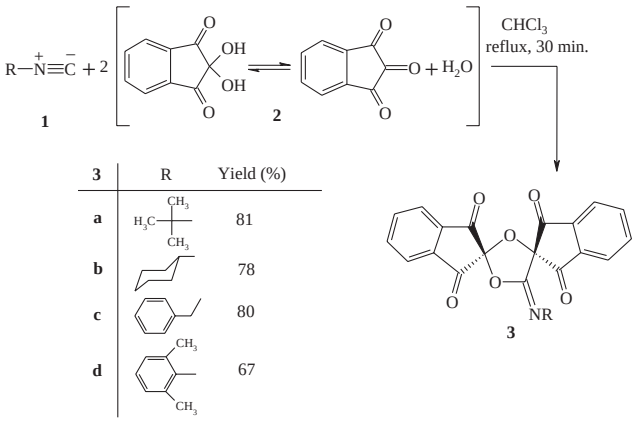
The reaction of isocyanides **1** with two equivalent of ninhydrin **2** gives C_s symmetry dispiro iminodioxolanes **3** at refluxing conditions in chloroform in fairly high yields.

Keywords: ioscyanide, ninhydrin, dispiro, iminodioxolane

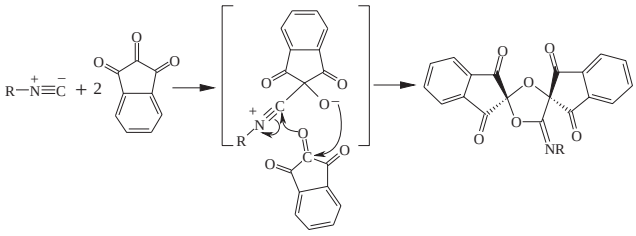
Isocyanides by virtue their carbenic character, react readily with most common multiple bonds to give acyclic or cycloadducts derived by formal 1:1, 1:2 and 2:1 substrate-isocyanide interactions.[1-3] Cycloaddition of this type is unique to isocyanides. The reaction of isocyanides with carbon-centered double bonds occurs in stepwise manner and is initiated by a zwitterionic intermediate whose ultimate fate appears to be dictated by the nature of the original double bond in the substrate.[4,5] Isocyanides insert preferentially into the carbon–oxygen double bond of electron-deficient ketones, such as hexafluoroacetone, to afford imino-1,3-dioxolanes in high yield.[6,7]

Ninhydrin is a unique tricarbonyl compound which is widely used in biochemical and medical settings for the analysis of amino acids.[8] Although the reactivity of the central carbonyl of ninhydrin has long been recognised, this highly electron-deficient moiety has not been utilised in synthesis. In view of our general interest in chemistry of isocyanides,[9-17] we have examined the reaction of ninhydrin as a compound which has an electron-deficient carbonyl group similar to hexafluoroacetone[6] with isocyanides and our results have been reported here.

The reaction of isocyanides **1** with ninhydrin **2** was carried out in refluxing chloroform for 30 min. and a 2:1 adduct of the ninhydrin and isocyanide was formed. This adduct, which is a C_s symmetry dispiro iminodioxolane **3**, is the only product formed regardless of the molar ratio of the reactant or order of addition.



Scheme 1



Scheme 2

The structure of these adducts were established as **3** by their elemental analysis and their IR, ^{1}H NMR and ^{13}C NMR spectra. The nature of these compounds as 1:2 adduct was also apparent from the elemental analysis as well as from the mass spectra, which for **3a** and **3b** displayed M+1 peaks instead of molecular ion peaks at *m/z* 404 and 430, respectively. For **3c** and **3d** molecular ion peak was seen at *m/z* 437 and 451, respectively.

The ^{1}H NMR spectrum of **3a** exhibited a single sharp line readily recognised as arising from *tert*-butyl (δ_H 1.12) and along with four multiplets (δ_H 7.91–8.15) for four kinds of aromatic protons. The ^{1}H decoupled ^{13}C NMR spectrum of **3a** showed 13 distinct resonances which is in agreement with C_s symmetry of structure and the characteristic signals due to two spiro carbons were discernible at δ_C 82.50 and 96.93.

The ^{1}H decoupled ^{13}C NMR spectra of **3b–d** are similar to those of **3a** except for the alkyl or arylimino group, which exhibit characteristic signals with appropriate chemical shifts.

We have not established a mechanism for the formation of 4-alkyl(aryl)imino-2,5-bis(2',2'-spiro-1',3'-dioxoindanyl)-1,3-dioxolane **3**. However, a possible explanation is shown in Scheme 2.

In conclusion, we have found that the one-pot reaction of isocyanides with two equivalents of ninhydrin leads to a facile synthesis of dispiro iminodioxolane derivatives under neutral conditions and without using any catalyst after several minutes.

Experimental

Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at an ionisation potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-500 Avance spectrometer at 500.13 and 125.77 MHz, respectively. NMR spectra were obtained on solutions in $CDCl_3$ using TMS as internal standard. The ninhydrin and *tert*-butyl, cyclohexyl and 2,6-dimethylphenyl isocyanides used in this work were purchased from Fluka (Buchs, Switzerland) chemical company and the benzyl isocyanide were obtained from Aldrich chemical company.

* To receive any correspondence. E-mail: a-shaabani@cc.sbu.ac.ir

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Typical procedure for preparation of 4-tert-Butylimino-2,5-bis(2', 2'-spiro-1',3'-dioxoindanyl)-1,3-dioxolane **(3a):** To a magnetically stirred solution of ninhydrin (0.356 g, 2 mmol) in dry chloroform (20 ml) was added *tert*-butyl isocyanide (0.084 g, 1 mmol) via a syringe and refluxing was continued for 30 min. The solvent was removed under vacuum and the residue was washed with diethyl ether. It was recrystallised from ethanol to give a cream powder. (0.327 g, 81 %). M.p. 253–254 °C. IR (KBr) (ν_{max}, cm^{-1}): 1754 and 1721 (C=O), 1586 (N=C). ^{1}H NMR ($CDCl_3$, Me_4Si): δ_H 1.12 (9 H, s, $C(CH_3)_3$), 7.91–8.15 (8 H, m, arom.). ^{13}C NMR ($CDCl_3$, Me_4Si): δ_C 29.47 (3 CH_3), 55.44 (*C*$(CH_3)_3$), 82.50 and 96.93 (2 spiro carbons), 124.47, 124.73, 136.47, 137.47, 140.15 and 141.75 (arom.), 145.90 (N=*C*), 190.45, 191.06 (4 C=O). MS (*m/z*, %) 404 (MH^+, 22), 348 (17), 149 (51), 104 (44), 76 (47), 57 (100), 41 (30). Anal. Calcd. for $C_{23}H_{17}NO_6$ (403.43): C, 68.47; H, 4.24; N, 3.47%. Found: C, 68.4; H, 4.3; N, 3.4%.

4-Cyclohexylimino-2,5-bis(2',2'-spiro-1',3'-dioxoindanyl)-1,3-dioxolane **(3b):** Cream powder. (0.335 g, 78 %). M.p. 252–253 °C. IR (KBr) (ν_{max}, cm^{-1}): 1739 and 1714 (C=O), 1578 (N=C). ^{1}H NMR ($CDCl_3$, Me_4Si): δ_H 1.12–1.64 (10 H, m, 5 CH_2), 3.50 (1 H, m, N-CH) 7.92–8.16 (8H, m, arom). ^{13}C NMR ($CDCl_3$, Me_4Si): δ_C 24.29, 25.53 and 32.97 (5 CH_2), 57.11 (N-*C*H), 82.03 and 96.70 (2 spiro carbons), 124.60, 124.74, 136.65, 137.53, 140.14 and 141.70 (arom.), 148.49 (N=*C*), 190.40, 190.77 (4 C=O). MS (*m/z*, %) 430 (MH^+, 34), 172 (63), 149 (98), 132 (22), 104 (85), 83 (70), 76 (80), 55 (100), 41 (73). Anal. Calcd. for $C_{25}H_{19}NO_6$ (429.46): C, 69.91; H, 4.46; N, 3.26%. Found: C, 69.8; H, 4.5; N, 3.2%.

4-Benzylimino-2,5-bis(2',2'-spiro-1',3'-dioxoindanyl)-1,3-dioxolane **(3c):** Light brown powder. (0.350 g, 80 %). M.p. 199–200 °C. IR (KBr) (ν_{max}, cm^{-1}): 1724 and 1718 (C=O), 1577 (N=C). ^{1}H NMR ($CDCl_3$, Me_4Si): δ_H 4.53 (2 H, s, CH_2), 7.09-7.23 (5 H, m, C_6H_5), 7.92–8.17 (8 H, m, 2 C_6H_4). ^{13}C NMR ($CDCl_3$, Me_4Si): δ_C 51.90 (CH_2), 82.59 and 97.17 (2 spiro carbons), 124.72, 124.83, 126.76, 127.16, 128.28, 136.84, 137.66, 138.19, 140.10 and 141.62 (arom.), 151.27 (N=*C*), 189.95, 190.30 (4 C=O). MS (*m/z*, %) 437 (M^+, 4), 264 (10), 223 (5), 132 (7), 104 (39), 91 (100), 76 (46). Anal. Calcd. for $C_{26}H_{15}NO_6$ (437.44): C, 71.38; H, 3.45; N, 3.20%. Found: C, 71.3; H, 3.5; N, 3.2%.

4-(2,6-Dimethylphenylimino)-2,5-bis(2',2'-spiro-1',3'-dioxoindanyl)-1,3-dioxolane **(3d):** Cream powder. (0.303 g, 67 %). M.p. 286–287 °C. IR (KBr) (ν_{max}, cm^{-1}): 1754 and 1731 (C=O), 1586 (N=C). ^{1}H NMR ($CDCl_3$, Me_4Si): δ_H 2.08 (6 H, s, 2 CH_3), 6.84–8.18 (11 H, m, arom.). ^{13}C NMR ($CDCl_3$, Me_4Si): δ_C 17.70 (2 CH_3), 82.82 and 97.42 (2 spiro carbons), 124.25, 124.71, 124.78, 127.55, 127.96, 137.04, 137.61, 140.07, 141.66 and 142.42 (arom.), 150.37 (N=*C*), 189.39, 189.92 (4 C=O). MS (*m/z*, %) 451 (M^+, 32), 275 (97), 246 (30), 218 (16), 132 (34), 104 (100), 76 (98), 50 (40). Anal. Calcd. for $C_{27}H_{17}NO_6$ (451.47): C, 71.83; H, 3.79; N, 3.10%. Found: C, 71.7; H, 3.9; N, 3.1%.

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