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[1 + 4]Cycloaddition of Isocyanides with 2-Acetyl-1,4-benzoquinone; a Convenient Synthesis of Isobenzofuran-4,7-quinones†

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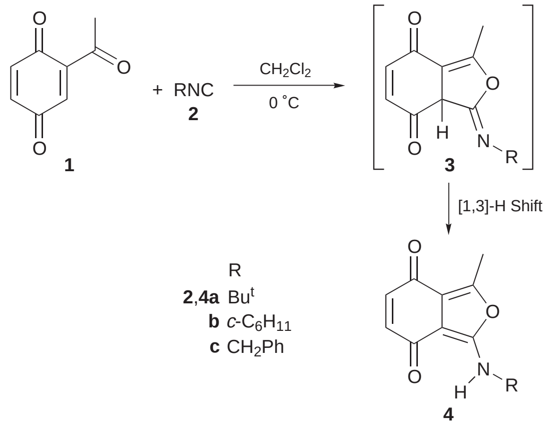
Isocyanides undergo formal [1 + 4]cycloaddition with 2-acetyl-1,4-benzoquinone to afford isobenzofuran-4,7-quinone derivatives.

The [1 + 4]cycloaddition reactions of isocyanides with electrophilic heterodienes are of interest for the synthesis of heterocyclic compounds. Cycloaddition of isocyanides with *N*-acylimines,[1] azadienes,[2] diazadienes,[3] α, β-unsaturated esters,[4] α, β-unsaturated ketones,[5] particularly with diethylaluminium chloride as a catalyst,[6] nitroalkanes,[7] vinyl isocyanates,[8] 1,1,1,5,5,5-hexafluoropentane-2,4-dione[9] and 3-(1-hydroxyethylidene)pentane-2,4-dione,[10] have been described. The work reported here was undertaken in order to synthesise substituted isobenzofuran-4,7-quinones[11–17] by the [1 + 4]cycloaddition of alkyl isocyanides, such as *tert*-butyl isocyanide, cyclohexyl isocyanide and benzyl isocyanide with 2-acetyl-1,4-benzoquinone **1**, as an electron-deficient hetero-1,3-diene. The [1 + 4]cycloaddition of isocyanides **2** with heterodiene **1** would afford compounds **3**, which isomerize to produce the stable *N*-substituted 1-alkylamino-3-methylisobenzofuran-4,7-quinones in high yields (Scheme 1).



Scheme 1

Structure **4** was assigned to isolated cycloadducts on the basis of their elemental analyses as well as their IR, ^{1}H, ^{13}C NMR and mass spectral data. IR spectroscopy was applied to distinguish structure **4** from the initial cycloadducts **3**, which apparently isomerize to produce *N*-substituted isobenzofurane derivatives under the present reaction conditions. Thus, the IR spectra of the isolated products showed strong NH stretching bands at *ca.* 3280 cm^{-1}. Further evidence was obtained from ^{1}H NMR spectra which showed the absence of a methine hydrogen resonance. Structure **4** was further confirmed by ^{1}H NMR spectra that revealed, in each case, a fairly broad singlet in the region of δ 3.7–4.8 which readily disappeared upon addition of D_2O. The mass spectra of the cycloadducts **4** are similar, as expected, and confirm their molecular weights. The ^{1}H NMR spectrum of **4a** exhibited three singlet signals arising from *tert*-butyl (δ 1.49), methyl (δ 2.58) and N–H [δ 3.71 (br)] along with two doublets [δ 6.62, (J = 10.3 Hz) and δ 6.77, (J = 10.3 Hz)], for the two vicinal CH groups. The proton decoupled ^{13}C NMR spectrum of **4a** displayed eleven singlet signals. The ^{1}H and ^{13}C NMR spectra of **4b** and **4c** are similar to that of **4a**. The structure assignments made on the basis of the NMR spectra of compounds **4a**–**c** were supported by their IR spectra; of special interest being N–H absorptions at 3285, 3270 and 3275 cm^{-1} for **4a**, **4b** and **4c**, respectively.

In summary, the reaction of alkyl isocyanides with an electron deficient heterodiene, 2-acetyl-1,4-benzoquinone, provides a simple one-pot entry into the synthesis of stable *N*-substituted 1-alkylamino-3-methylisobenzofuran-4,7-quinones under mild reaction conditions using a simple experimental procedure.

Experimental

All melting points are uncorrected. Elemental analyses were performed using a Heraeus CHN-O rapid analyzer. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were measured on a Shimadzu IR-470 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-500 Avance spectrometer at 500 and 125.77 MHz, respectively. The synthesis of 2-acetyl-1,4-benzoquinone **1** was carried out as described in the literature.[18]

General Procedure for the Preparation of N-*Substituted 1-Alkylamino-3-methylisobenzofuran-4,7-quinones* **4**.—To a magnetically stirred solution of **1** (150 mg, 1 mmol) in dichloromethane (10 ml) was added dropwise a mixture of *tert*-butyl isocyanide (0.113 μl, 1 mmol) in dichloromethane (10 ml) at −20 °C over 10 min. The reaction mixture was allowed to warm to 0 °C, stirred for 24 h and the solvent removed under reduced pressure to afford the red product. For further purification, the product was recrystallized from 5% ethyl acetate–petroleum ether.

1-(N-tert-*Butylamino*)-3-*methylisobenzofuran*-4,7-*quinone* **4a**: yield 85%; mp 87–90 °C (decomp.). ν_{max}(KBr)/cm^{-1} 3285 (N–H), 1650 (C=O), 1622 (C=C). δ_H($CDCl_3$, Me_4Si) 1.49 (9H, s, Bu^t), 2.58 (3H, s, Me), 3.71 (1H, br s, NH), 6.62 (1H, d, J = 10.3 Hz), 6.77 (1H, d, J = 10.3 Hz). δ_C($CDCl_3$, Me_4Si) 13.42 (CH_3), 29.79 (CMe_3), 53.75 (CMe_3), 96.07 (C=C–N), 116.29 (C=C–O), 139.61 and 142.66 (2CH), 150.45 (C=C–N), 158.88 (C=C–O), 177.19 and 182.41 (2C=O). MS m/z(%) 233(M^+, 21), 177(100), 162(55), 57(67) (Found: C, 66.81; H, 6.63; N, 5.90. $C_{13}H_{15}O_3N$ requires: C, 66.93; H, 6.80; N, 6.00%).

1-(N-*Cyclohexylamino*)-3-*methylisobenzofuran*-4,7-*quinone* **4b**: yield 90%; mp 106–108 °C (decomp.). ν_{max}(KBr)/cm^{-1} 3270 (N–H), 1671 (C=O), 1635 (C=C). δ_H($CDCl_3$, Me_4Si) 1.26–2.05 (11H, m, C_6H_{11}, 2.61 (3H, s, CH_3) 3.71 (1H, br s, NH), 6.62 (1H, d, J = 10.3 Hz), 6.77 (1H, d, J = 10.3 Hz). δ_C($CDCl_3$, Me_4Si) 13.37 (CH_3), 24.66, 25.18 and 33.51 ($3CH_2$), 52.16 (CH), 95.16 (C=C–N), 116.71 (C=C–O), 139.53 (CH), 142.74 (CH), 150.22 (C=C–N),

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158.38, (C=C–O), 177.11 and 182.46 (2C=O). MS *m/z*(%) 259(M^+, 44), 178(100), 97(2) (Found: C, 69.30; H, 6.51; N, 5.46. $C_{15}H_{17}O_3N$ requires: C, 69.48; H, 6.60; N, 5.40%).

1-(N-*Benzylamino*)-3-*methylisobenzofuran*-4,7-*quinone* **4c**: yield 80%; mp 88–90 °C (decomp.). ν_{max}(KBr)/cm^{-1} 3275 (N–H), 1660 (C=O), 1638 (C=C). δ_H($CDCl_3$, Me_4Si) 2.57 (3H, s, CH_3), 4.66 (2H, s, CH_2), 4.86 (1H, br s, NH), 6.61 (1H, d, $J = 10.4$ Hz), 6.71 (1H, d, $J = 10.4$ Hz), 7.28–7.49 (5H, m, C_6H_5). δ_C($CDCl_3$, Me_4Si) 13.35 (CH_3), 46.51 (CH_2), 95.49 (C=C–N), 116.73 (C=C–O), 127.95, 128.21, 128.99 and 136.49 (C_6H_5), 139.86 (CH), 142.45 (CH), 150.33 (C=C–N), 158.51 (C=C–O), 117.62 and 182.36 (2C=O). MS *m/z*(%) 267(M^+, 21), 91(100), 65(17) (Found: C, 71.01; H, 4.84; N, 5.10. $C_{16}H_{13}O_3N$ requires: C, 71.9; H, 4.90; N, 5.23%).

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References

1 J. A. Deyrup and K. K. Killion, *J. Heterocycl. Chem.*, 1972, **9**, 1045.

2 G. Morel, E. Marchand, A. Foucaud and L. Toupet, *J. Org. Chem.*, 1989, **54**, 1185; G. Morel, E. Marchand and A. Foucaud, *J. Org. Chem.*, 1985, **50**, 771; W. Ott and V. Formacek, *Angew. Chem., Int. Ed. Engl.*, 1981, **20**, 982.

3 G. Morel, E. Marchand, A. Foucaud and L. Toupet, *J. Org. Chem.*, 1990, **55**, 1721, P. Imming, R. Mohr, E. Muller, W. Overhen and G. Seitz, *Angew. Chem., Int. Ed. Engl.*, 1982, **21**, 284.

4 E. A. Avetisyan and N. P. Gambaryan, *Izv. Akad. Nauk SSSR, Ser. Khim,*, 1973, 2559 (*Chem. Abstr.*, 1974, **80**, 59809).

5 I. Yavari, A. Shaabani and M. T. Maghsoodlou, *Monatsh. Chem.*, 1997, **128**, 697; G. Kollenz, W. Ott, E. Ziegler, E. M. Peters, K. Peters, H. G. vonSchnerir, V. Formacek and H. Quast, *Liebigs Ann. Chem.*, 1984, 1137.

6 Y. Ito, H. Kato and T. Saegusa, *J. Org. Chem.*, 1982, **47**, 741.

7 A. Foucaud, C. Razorilalana-Rabearivony, E. Loukakou and H. Person, *J. Org. Chem.*, 1983, **48**, 363.

8 J. H. Rigby and M. Qabar, *J. Am. Chem. Soc.*, 1991, **113**, 8975.

9 I. Yavari, A. Shaabani, S. Asghari, M. M. Olmstead and N. Safari, *J. Fluorine Chem.*, 1997, **86**, 77.

10 A. Shaabani and F. Farrokhzad, *J. Chem. Res.*, 1997, *(S)* 344.

11 M. Chakraborty, D. B. McConville, G. F. Koser, C. A. Tessier, T. Saito, P. L. Rinaldi and W. J. Youngs, *J. Org. Chem.*, 1997, **62**, 8193.

12 D. W. Cameron, I. T. Crosby, G. I. Feutrill and G. A. Pietersz, *Aust. J. Chem.*, 1992, **45**, 2003.

13 G. M. L. Cragg, R. G. F. Giles and G. H. P. Roos, *J. Chem. Soc., Perkin Trans. 1,* 1975, 1339.

14 R. G. F. Giles and G. H. P. Roos, *J. Chem. Soc., Chem. Commun.*, 1975, 260.

15 J. Hanbrecht, H. Straub and E. Muller, *Tetrahedron Lett.*, 1976, 1789.

16 A. A. Hofmann, I. Wyrsch-Walraf, P. X. Iten and C. H. Eugster, *Helv. Chim. Acta*, 1979, **62**, 2211.

17 D. Passerieux, M. Casteignau and L. Lepage, *Bull. Soc. Chim. Fr.*, 1989, 441.

18 N. N. Vorozhtsov and V. P. Mamaev, *Sborniok Statei Obshchei Khim., Akad. Nauk SSSR,* 1953, **1**, 533 (*Chem. Abstr.*, 1955, **49**, 925f).