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Synthesis of γ-dispiro-iminolactones using bromo substituted α-dicarbonyl phenanthraquinone

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ABSTRACT

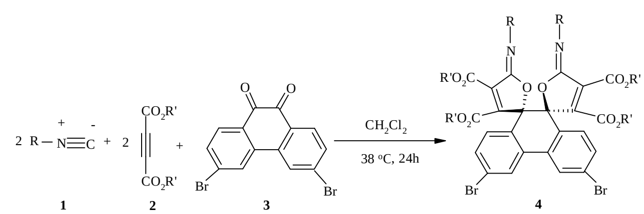
γ-Dispiro-iminolactones have been synthesized by the three component reaction between 3,6- dibromophenanthraquinone, dialkyl acetylenedicarboxylates and isocyanides *via* a one-pot mode in high yields. The method offers advantages such as ease of the work-up, high yields of products, mild reaction condition and short reaction times.

KEYWORDS

γ-Dispiro-iminolactones;
Three component reaction;
Dialkyl acetylenedicarboxylates;
Isocyanides.

INTRODUCTION

Multicomponent reactions (MCRs) have been one of the most important developing fields in organic chemistry. Due to some advantages such as high yields of products, they have been one of the best strategies to produce important organic compounds such as heterocycles. The heterocyclic compounds are used in the design of biologically active compounds[1]. Also their pharmacological properties and easy synthetic conditions has made heterocycles as one of the best target molecules in organic synthesis[2-5]. Saegusa et al. reported Et_2AlCl-Mediated reaction of α,β-unsaturated carbonyls with methyl isocyanide leading to heterocyclic iminolactones. Also chactani et al. reported the synthesis of iminolactone derivatives in the presence of catalytic amount of $GaCl_3$[6-19]. In the present work we report a three component reaction between a dibromo substituted dicarbonyl compound, dialkyl acetylenic diesters and isocyanides in which dibromo γ-dispiro-iminolactones can be synthesized *via* a cyclization reaction (Scheme 1).



4	R	R′	Yield%
a	t-Bu	Me	85
b	t-Bu	Et	77
c	Cyclohexyl	Me	88
d	Cyclohexyl	Et	78
e	2,6-dimethyl phenyl isocyanide	Me	80

Scheme 1

EXPERIMENTAL

General remarks

NMR spectra were recorded with BRUCKER

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DRX-400 AVANCE spectrometer (at 400.1 MHz for ^{1}H and 100.6 MHz for ^{13}C NMR) with $CDCl_3$ as solvent. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded on a FT-IR, Brucker, VECTOR22 spectrometer. TLC was carried out on Fluka silica gel TLC cards. All other reagents and solvents were used as received from commercial suppliers. All of the coupling constants are given in Hertz.

General preparative procedure (exemplified by 4a)

The solution of *tert*-butyl isocyanide (0.15 ml, 1.2 mmol) in CH_2Cl_2 (1 ml) was slowly added dropwise to the mixture of 3,6- dibromophenanthraquinone (0.183 g, 0.5 mmol) and DMAD (0.15 ml, 1.2 mmol) in dry CH_2Cl_2 (5 ml) for 5 min at room temperature. The solution was heated to 38 °C for 24h. Then, the reaction mixture was solidified into a solid product, the solvent was removed by filtration and the crystals of the products were washed with cold diethyl ether.

Spectroscopic data

Tetramethyl(5Z)-3′,6′-dibromo-5,5″ -bis(tert-butylimino)-5H,5″H-dispiro]furan-2,9′-phenanthrene-10′ ,2″-furan[-3,3″,4,4″-tetracarboxylate (4a)

White powder, yield: 85 %. m.p. 227-230 °C. IR (KBr) (υ_{max}/cm^{-1}): 1749 and 1699 (4 C=O), 1650 (2 C=N). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.37 (s, 18H, $2CMe_3$), 3.28 and 3.79 (2s, 12H, $4OCH_3$), 7.16 (d, 2H, $^{3}J_{HH}$= 8.4 Hz, 2CH), 7.51 and 7.53 (dd, 2H, $^{3}J_{HH}$= 8.4 Hz, $^{4}J_{HH}$= 1.6Hz, 2CH), 7.91 (d, 2H, $^{4}J_{HH}$= 1.6 Hz, 2CH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 29.5 ($2CMe_3$),52.4 and 52.8 ($4OCH_3$), 55.15 ($2NCMe_3$), 91.32 ($2C_{spiro}$), 124.6, 126.6, 127.1, 130.5, 131.9, 132.3, 134,2, and 148.2 (C aromatic and iminolactones), 150.05 ($2N=C_{iminolactone}$), 160.7 and 161.4 (4 C=O esters). MS: *m/z* (%): 818 (M^+ + 4, 2), 816 (M^+ + 2, 4), 814 (M^+, 2), 762 (30), 760 (60), 758 (30), 706 (15), 704 (30), 702 (15), 196 (100), 194 (100), 57 (99), Anal. Calcd. for $C_{36}H_{36}O_{10}N_2Br_2$ (816.49); C, 52.95; H, 4.44; N, 3.43 %. Found: C, 52.36; H, 4.41; N, 3.39 %.

Tetraethyl(5Z)-3′,6′-dibromo-5,5″-bis(tert-butylimino)-5H,5″H-dispiro]furan-2,9′-phenanthrene-10′,2″-furan[-3,3″,4,4″-tetracarboxylate (4b)

White powder, yield: 77 %. m.p. 217-220 °C. IR (KBr) (υ_{max}/cm^{-1}): 1737 and 1705 (4C=O), 1687 (2C=N). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 0.94 (t, 6H, $^{3}J_{HH}$= 7.2 Hz, $2OCH_2CH_3$), 1.32 (s, 18H, $2CMe_3$), 1.39 (t, 6H, $^{3}J_{HH}$= 7.2 Hz, $2OCH_2CH_3$), 3.94 (m, 4H, $2OCH_2CH_3$), 4.42 (q, 4H, $^{3}J_{HH}$= 7.2 Hz, $2OCH_2CH_3$), 7.21 (d, 2H, $^{3}J_{HH}$= 8.4 Hz, 2CH), 7.63 and 7.65 (dd, 2H, $^{3}J_{HH}$= 8.4 Hz, $^{4}J_{HH}$= 1.6 Hz, 2CH), 8.12 (d, 2H, $^{4}J_{HH}$= 1.6 Hz, 2CH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.8 and 13.9 ($4OCH_2CH_3$), 28.3 ($2CMe_3$), 58.9 ($2NCMe_3$), 62.2 and 63.2 ($4OCH_2CH_3$), 86.5 (C_{spiro}) 121.9, 126.2, 126.3, 127.3, 127.7, 131.0, 131.1 and 142.0 (C aromatic and iminolactones) 151.1 ($2C=N_{iminolactone}$), 161.1 and 166.5 ($4C=O_{ester}$). MS: m/z (%): 874 (M^+ +4, 1), 872 (M^+ + 2), 870 (M^+, 1), 621 (20), 619 (40), 617 (20), 518 (50), 516 (100), 514 (50), 179 (50), 57 (32), Anal. Calcd. for $C_{40}H_{44}O_{10}N_2Br_2$ (872.59); C, 55.05; H, 5.08; N, 3.21 %. Found: C, 55.01; H, 5.02; N, 3.18 %.

Tetramethyl(5Z)-3′,6′-dibromo-5,5″-bis(cyclohexylimino)-5H,5″H-dispiro]furan-2,9′-phenanthrene-10′,2″-furan[-3,3″, 4,4″-tetracarboxylate (4c)

Yellow powder, yield: 88%. m.p. 210-213 °C. IR (KBr) (υ_{max}/cm^{-1}): 1749 and 1685 (4C=O), 1645 (2C=N). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.17-1.83 (m, 20H, $10CH_2$), 3.31 (s, 6H, $2OCH_3$), 3.6 (m, 2H, 2N-CH), 3.83 (s, 6H, $2OCH_3$), 7.15 (d, 2H, $^{3}J_{HH}$= 8.4 Hz, 2CH), 7.52 and 7.54 (dd, 2H, $^{3}J_{HH}$= 8.4 Hz, $^{4}J_{HH}$= 1.6 Hz, 2CH), 7.92 (d, 2H, $^{4}J_{HH}$== 1.6 Hz, 2CH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 24.8, 24.9, 25.6, 33.0 and 33.2 ($10CH_2$), 52.5 and 52.9 (4OMe), 57.5 (2N-CH), 90.8 ($2C_{spiro}$), 124.6, 126.6, 127.2, 130.0, 131.8, 132.3, 134.4 and 147.9 (C aromatic and iminolactones), 152.6 ($2C=N_{iminolactone}$), 160.8 and 161.0 ($4C=O_{ester}$). MS: m/z (%): 870 (M^+ + 4, 3), 868 (M^+ + 2, 6), 866 (M^+, 3), 786 (50), 784 (100), 782 (50), 196 (70), 83 (50), Anal. Calcd. for $C_{40}H_{40}O_{10}N_2Br_2$ (868.56); C, 55.31; H, 4.64; N, 3.22 %. Found: C, 55.28; H, 4.59; N, 3.14 %.

Tetraethyl(5Z)-3′,6′-dibromo-5,5″-bis(cyclohexylimino)-5H,5″H-dispiro]furan-2,9′-phenanthrene-10′,2″-furan[-3,3″,4,4″-tetracarboxylate (4d)

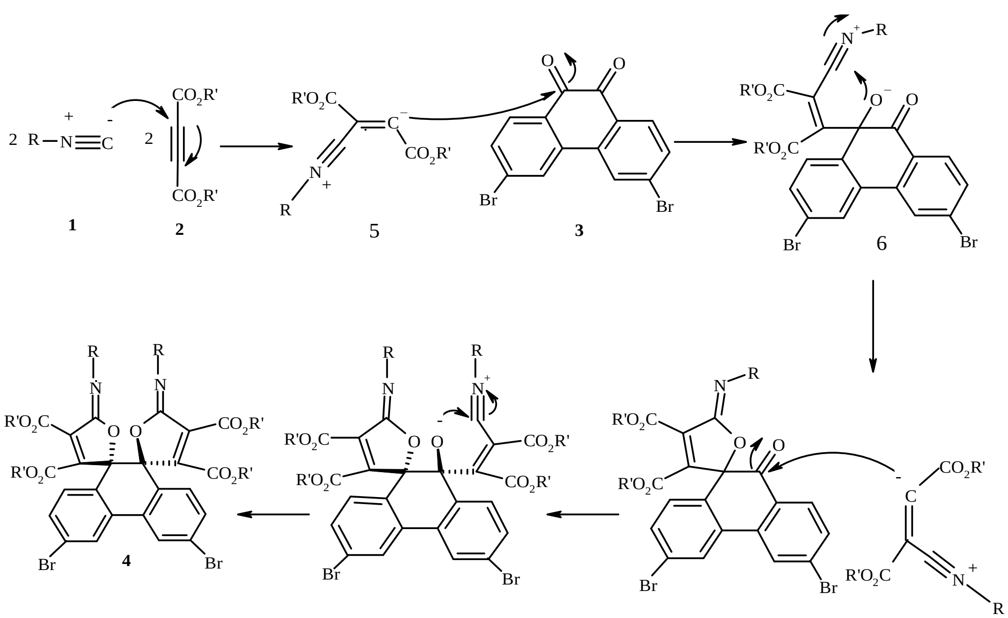
White powder, yield: 78%. m.p. 171-174 °C. IR (KBr) ($\upsilon_{max/}$cm^{-1}): 1745 and 1690 (4C=O), 1650 (2C=N). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 0.9 (t, 6H, $^3J_{HH}$= 7.2 Hz, $2OCH_2CH_3$), 1.21-1.84 (m, 20H, $10CH_2$), 1.27 (t, 6H, $^3J_{HH}$= 7.2 Hz, $2OCH_2CH_3$), 3.6 (m, 4H, $2OCH_2CH_3$), 3.8 (m, 2H, 2N-CH), 4.3 (m, 4H, $2OCH_2CH_3$), 7.15 (m, 2H, d, $^3J_{HH}$= 8.4 Hz, 2CH), 7.51 and 7.53 (dd, 2H, $^3J_{HH}$= 8.4 Hz, $^4J_{HH}$= 1.6 Hz, 2CH), 7.92 (d, 2H, $^4J_{HH}$= 1.6 Hz, 2CH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.5 and 13.9, ($4OCH_2CH_3$), 24.8, 25.7, 32.9 and 33.1 (10 CH_2), 57.4 (2N-CH), 61.9 and 61.92 ($4OCH_2CH_3$), 90.7 (C_{spiro}), 124.6, 126.5, 127.3, 130.3, 131.0, 132.2, 134.2 and 148.0 (C aromatic and iminolactones), 152.8 (2C=$N_{iminolactone}$), 160.2 and 160.7 (4C=O_{ester}). MS: *m/z* (%): 926 (M^+ + 4, 1), 924 (M^+ + 2, 2), 922 (M^+, 1), 797 (25), 795 (50), 793 (25), 618 (100), 616 (100), 83 (45), Anal. Calcd. for $C_{44}H_{48}O_{10}N_2Br_2$ (924.67); C, 57.15; H, 5.23; N, 3.02 %. Found: C, 57.11; H, 5.16; N, 3.01 %.

Tetramethyl(5Z)-3′,6′-dibromo-5,5″-bis(2,6-dimethylphenylimino)-5H,5″H-dispiro]furan-2,9′-phenanthrene-10′,2″-furan[-3,3″,4,4″-tetracarboxylate (4e)

Brown powder, yield: 80%. m.p. 153-156 °C. IR (KBr) ($\upsilon_{max/}$cm^{-1}): 1741 and 1693 (4C=O), 1655 (2C=N). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.24 (s, 12H, $4CH_3$), 3.13 and 3.95 (s, 12H, $4OCH_3$), 6.89-7.04 (m, 6H, 6CH), 7.01 (d, 2H, $^3J_{HH}$= 8 Hz, $^4J_{HH}$= 1.6 Hz, 2CH), 7.48 and 7.50(dd, 2H, $^3J_{HH}$= 8 Hz, $^4J_{HH}$= 1.6 Hz, 2CH), 7.97 (d, 2H, $^4J_{HH}$= 1.6 Hz, 2CH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.5 ($4CH_3$), 52.6 and 53.1 ($4OCH_3$), 91.7 (C_{spiro}), 123.8, 124.7, 126.4, 127.2 127.3, 127.4, 129.8, 131.5, 132.1, 133.2, 143.1 and 148.3 (C aromatic and iminolactones), 153.4 (2C=$N_{iminolactone}$), 159.6 and 160.7 (4C=O_{ester}). MS: m/z (%): 914 (M^+ + 4, 20), 912 (M^+ + 2, 4), 910 (M^+, 2), 794 (25), 792 (50), 790 (25), 105 (100), 59 (25), Anal. Calcd. for $C_{44}H_{36}O_{10}N_2Br_2$ (912.58); C, 57.91; H, 3.97; N, 3.06 %. Found: C, 57.89; H, 3.92; N, 3.02 %.

RESULTS AND DISCUSSION

The reaction mechanism is depicted in Scheme 2. In this process we can assume that in the first step nucleophilic isocyanide **(1)** attacks to the acetylenic diester **(2)**. Then, the direct attack of zwitterion **(5)** to the carbonyl group of compound **(3)** leads to the formation of intermediate **(6)** which undergoes a cyclization reaction to afford the heterocyclic γ-dispiro-iminolactone **(4)** in high yield.



Scheme 2

The structures of the products **(4a-e)** were confirmed with their ^{1}H, ^{13}C NMR, IR, Mass and elemeatal analysis. All of the products of these reactions were stable solids. The IR spectrum of compound **(4a)** exhibited strong absorption bands at 1749 and 1699 cm^{-1} due to the esteric groups and also 1647 cm^{-1} due to C=N. The ^{1}H NMR spectrum of **(4a)** showed one singlet for *tert*-butyl group (δ = 1.37ppm) and two singlets for the methoxy groups (δ = 3.28 and 3.70 ppm). The ^{13}C NMR spectrum of **(4a)** showed 16 distinct rosonances which confirmed the proposed structure of **(4a)**. The structure of **(4a)** was confirmed from the mass spectrum by displaying molecular ion peaks at m/z 816. The details of the structural analysis of all of the products can be found in the experimental section. The structure of **(4b-e)** showed the consistent peaks similar to **(4a)** except for the alkoxy and isocyanide groups that could be found in appropriate chemical shifts.

CONCLUSION

This study presents a one-pot three component reaction to synthesize halogenated iminolactones that can be a new strategy for the synthesis of halogenated heterocycles in high yields. The method offers advantages such as ease of the work-up, high yields of products, mild reaction condition and short reaction time.

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