

Synthesis and transformations of picrylactaldehyde

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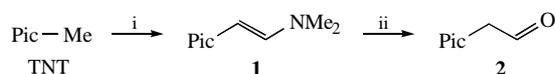
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A method for the synthesis of picrylactaldehyde was developed, and its reactivity was examined.

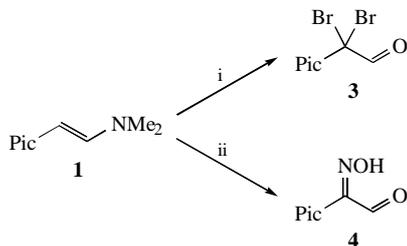
In the context of chemical utilisation of 2,4,6-trinitrotoluene (TNT),¹ we developed a procedure for preparing picrylactaldehyde starting from TNT. This previously unknown aldehyde is of interest as a new building block because of the presence of a highly reactive formyl group, an active methylene unit, nitro groups, and an aromatic ring of the picryl moiety (nucleophilic substitution for nitro groups, vicarious and oxidative nucleophilic substitution for hydrogen, *etc.*).

Picrylactaldehyde **2** was prepared by acidic hydrolysis of β -dimethylamino-2,4,6-trinitrostyrene **1**, which in turn was readily formed by TNT condensation with dimethylformamide dimethyl acetal.



Reagents and conditions: i, 1 equiv. $\text{H}_2\text{NCH}(\text{OMe})_2$, toluene, 20 °C, 24 h, 70% yield; ii, 2 M HCl in $\text{H}_2\text{O}/\text{CHCl}_3$, 61 °C, 5 h, 78% yield.

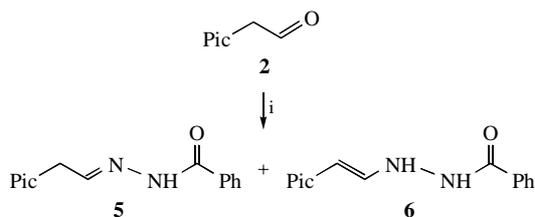
Enamine **1** can be used as a masked form of picrylactaldehyde because it easily undergoes hydrolysis in acidic media. For example, bromination and nitrosation of **1** results in picrylactaldehyde modified at the methylene group



Reagents and conditions: i, 1 equiv. Br_2 , CHCl_3 , 20 °C, 5 h, 52% yield; ii, 2 equiv. NaNO_2 , HCl (conc.), 20 °C, 3 h, 66% yield.

The same products (**3** and **4**) were also obtained using picrylactaldehyde as the starting compound.

A tendency to deformylation under the action of even weak bases such as pyridine with the regeneration of TNT is a characteristic property of picrylactaldehyde. In particular, for this reason picrylactaldehyde does not form arylhydrazones and oximes with arylhydrazines and hydroxylamine. Hydrazone **5** was formed only by the interaction of picrylactaldehyde with an extremely weak base, benzoic acid hydrazide. We also detected a trace impurity of tautomer **6**.

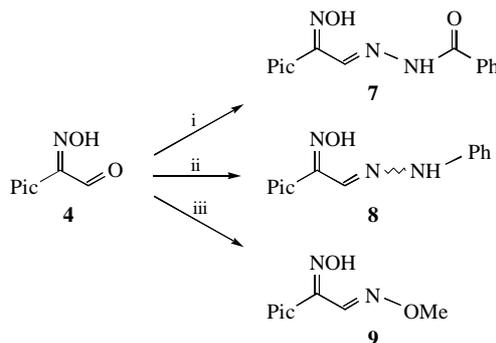


Reagents and conditions: i, 1 equiv. PhCONHNH_2 , EtOH, 78 °C, 1 h, 80% yield of **5**.

At the same time, under neutral and acidic conditions, picrylactaldehyde behaves as a typical aliphatic aldehyde. Picrylgllyoxal

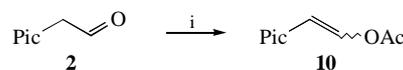
monooxime **4**, which is a picrylactaldehyde derivative without an α -methylene group, exhibit similar properties.

Oxime **4** gives with nitrogen nucleophiles usual derivatives at the formyl group. Apart from benzoic acid hydrazide, phenylhydrazine and *O*-methylhydroxylamine also react with oxime **4**.



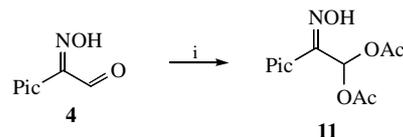
Reagents and conditions: i, 1 equiv. PhCONHNH_2 , EtOH, 78 °C, 3 h, 61% yield; ii, 1 equiv. $\text{PhNHNH}_2 \cdot \text{HCl}$, EtOH, 78 °C, 3 h, 91% yield; iii, 1 equiv. MeONH_2 , EtOH, 78 °C, 3 h, 76% yield.

The acylation of picrylactaldehyde with acetic anhydride afforded enol acetate **10**



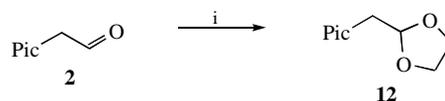
Reagents and conditions: i, Ac_2O , 80–90 °C, 78% yield, *E/Z* \approx 1:2.

The acylation of picrylactaldehyde derivative **4** having no methylene group resulted in acylal **11**.



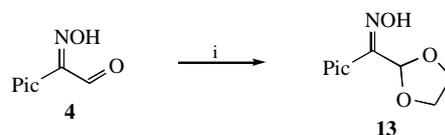
Reagents and conditions: i, Ac_2O , 80–90 °C, 5 h, 89% yield.

Picrylactaldehyde with ethylene glycol forms cyclic acetal **12**.



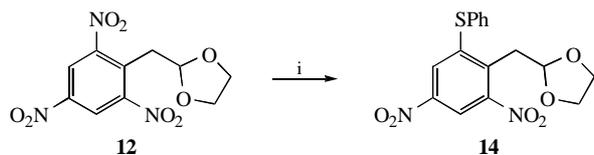
Reagents and conditions: i, 2 equiv. $\text{HO}(\text{CH}_2)_2\text{OH}$, 0.1 equiv. TsOH, benzene, 81 °C, 2 h, 95% yield.

Oxime **4** also forms analogous acetal **13** under more severe conditions.



Reagents and conditions: i, 2 equiv. $\text{HO}(\text{CH}_2)_2\text{OH}$, 0.1 equiv. TsOH, toluene, 110 °C, 5 h, 87% yield.

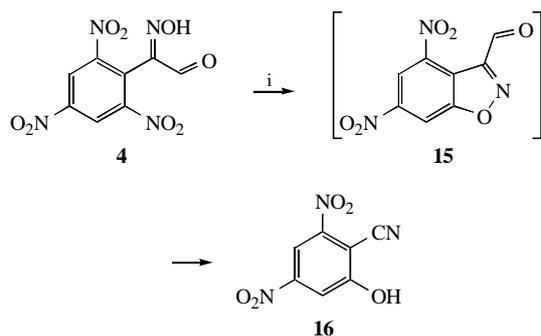
As a protected aldehyde, dioxolane **12** is stable to alkaline media. Using the reaction with thiophenol in *N*-methylpyrrolidone in the presence of K_2CO_3 as an example, we found the nucleophilic substitution for a nitro group in **12**.



Reagents and conditions: i, 1 equiv. PhSH, 1 equiv. K_2CO_3 , *N*-methylpyrrolidone, 20 °C, 24 h, 32% yield.

The reaction is regioselective: only the *ortho*-nitro group was replaced, and sulfide **14** was formed.

In contrast to picrylacetaldehyde, under the action of bases, oxime **4** forms 2-cyano-3,5-dinitrophenol **16**. 3-Carbonyl-4,6-dinitro-1,2-benzisoxazole **15** is a probable intermediate.



Reagents and conditions: i, 1 equiv. K_2CO_3 , EtOH, 20 °C, 24 h, 75% yield.

Such benzisoxazoles are unstable in alkaline media and are transformed into salicylic acid nitriles.²

All of the compounds prepared were characterised by physico-chemical methods.[†]

[†] ¹H NMR spectra were measured on a Bruker AM 300 spectrometer in [²H₆]DMSO with TMS as a standard.

- 1: mp 155–157 °C (toluene) (lit.,³ 155–157 °C).
- 2: mp 90–91 °C ($CHCl_3$). ¹H NMR, δ : 4.5 (s, 2H, CH_2), 9.0 (s, 2H, H_{arom}), 9.8 (s, 1H, O=CH).
- 3: mp 149–151 °C ($CHCl_3$). ¹H NMR, δ : 8.9 (s, 2H, H_{arom}), 9.2 (s, 1H, O=CH).
- 4: mp 108–110 °C ($CHCl_3$). ¹H NMR, δ : 9.1 (br. s, 1H, OH), 9.2 (s, 2H, H_{arom}), 9.8 (s, 1H, O=CH).
- 5: mp 198–200 °C (decomp.) (EtOH). ¹H NMR, δ : 4.1 (s, 2H, CH_2), 7.2–7.6 (m, 4H, Ph, HC=N), 7.8 (m, 2H, Ph), 9.0 (2H, Pic), 11.4 (1H, NH).
- 7: mp 142–145 °C (EtOH). ¹H NMR, δ : 7.4–7.6 (m, 3H, Ph), 7.7–7.9 (m, 2H, Ph), 8.5 (s, 1H, N=CH), 9.1 (s, 2H, Pic), 11.9 (s, 1H, NH), 12.7 (s, 1H, OH).
- 8: mp 126–127 °C ($CHCl_3$). ¹H NMR (major stereoisomer) δ : 6.7–6.8 (m, 3H, Ph), 7.0–7.2 (m, 2H, Ph), 7.8 (s, 1H, N=CH), 9.1 (s, 2H, Pic), 10.6 (s, 1H, NH), 12.0 (s, 1H, OH).

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9: mp 154–156 °C ($CHCl_3$). ¹H NMR, δ : 3.8 (s, 3H, OMe), 8.0 (s, 1H, N=CH), 9.1 (s, 2H, H_{arom}), 12.8 (s, 1H, OH).

10: mp 71–75 °C (*E/Z* mixture). ¹H NMR δ : (*Z*)-isomer, 2.0 (s, 3H, Me), 6.3 (d, 1H, α -H, ³*J* 6.9 Hz), 7.5 (d, 1H, β -H, ³*J* 6.9 Hz), 9.0 (s, 2H, Pic); (*E*)-isomer, 2.0 (s, 3H, Me), 6.7 (d, 1H, α -H, ³*J* 12.7 Hz), 7.4 (d, 1H, β -H, ³*J* 12.7 Hz), 9.1 (s, 2H, Pic).

11: mp 178–180 °C (EtOH). ¹H NMR, δ : 2.0 (s, 6H, 2Me), 2.05 (s, 3H, Me), 7.7 [s, 1H, CH(OAc)₂], 9.3 (s, 2H, Pic).

12: mp 102–104 °C (EtOH). ¹H NMR, δ : 3.6 (d, 2H, CH_2 , ³*J* 4.2 Hz), 3.6–3.8 [dm, 4H, O(CH_2)₂O], 5.15 (t, 1H, OCHO, ³*J* 4.2 Hz), 8.95 (s, 2H, Pic).

13: mp 85–87 °C (EtOH). ¹H NMR, δ : 3.6–3.9 [dm, 4H, O(CH_2)₂O], 5.6 (s, 1H, OCHO), 9.1 (s, 2H, Pic), 12.2 (s, 1H, OH).

14: mp 103–106 °C (EtOH). ¹H NMR, δ : 3.6 (d, 2H, CH_2 , ³*J* 5.3 Hz), 3.7 [m, 4H, O(CH_2)₂O], 5.2 (t, 1H, OCHO, ³*J* 5.3 Hz), 7.5–7.6 (m, 5H, Ph), 7.9 (s, 1H, arom.), 8.5 (s, 1H, arom.).

16: mp 187–188 °C ($CHCl_3$). ¹H NMR, δ : 8.0 (d, 1H, arom., ⁴*J* 2.0 Hz), 8.3 (d, 1H, arom., ⁴*J* 2.0 Hz); this compound was described in ref. 4; however, the melting point was not given.